酢酸ビニルのラット及びマウスを用いた 経口投与によるがん原性試験(混水試験)報告書

# APPENDIX

(L1~R2) がん原性:ラット/0162;マウス/0163 APPENDIXES (CONTINUED)

- APPENDIX L 1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (TWO-YEAR STUDY:SUMMARY) RAT:MALE:DEAD AND MORIBUND ANIMALS
- APPENDIX L 2 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (TWO-YEAR STUDY:SUMMARY) RAT:FEMALE:DEAD AND MORIBUND ANIMALS
- APPENDIX L 3 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (TWO-YEAR STUDY:SUMMARY) RAT:MALE:SACRIFICED ANIMALS
- APPENDIX L 4 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (TWO-YEAR STUDY:SUMMARY) RAT:FEMALE:SACRIFICED ANIMALS
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- APPENDIX L 6 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (TWC-YEAR STUDY:SUMMARY) MOUSE:FEMALE:DEAD AND MRIBUND ANIMALS
- APPENDIX L 7 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (TWO-YEAR STUDY:SUMMARY) MOUSE:MALE:SACRIFICED ANIMALS
- APPENDIX L 8 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (TWO-YEAR STUDY:SUMMARY) MOUSE:FEMALE:SACRIFICED ANIMALS
- APPENDIX M 1 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED RAT:MALE
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- APPENDIX M 3 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED MOUSE:MALE

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- APPENDIX M 4 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED MOUSE:FEMALE
- APPENDIX N 1 NEOPLASTIC LESIONS INCIDENCE AND TIME OF TUMOR OCCURRENCE RAT:MALE
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APPENDIXES (CONTINUED)

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- APPENDIX 0 2 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS RAT:FEMALE
- APPENDIX 0 3 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS MOSE:MALE
- APPENDIX 0 4 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS MOUSE:FEMALE
- APPENDIX P 1 HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TWO-YEAR STUDY:SUMMARY) RAT:MALE:DEAD AND MORIBUND ANIMALS
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- APPENDIX P 3 HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TWO-YEAR STUDY:SUMMARY) RAT:MALE:SACRIFICED ANIMALS
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## APPENDIX L 1

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

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

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| 0rgan         | No                                       | oup Name<br>. of Animals on Study<br>ade <u>1</u><br>(%) | Contro<br>6<br>2 3<br>(%) (%) | <u>4</u> (%) (%) | 400<br>10<br><u>2</u> 3<br>) (%) (% | 8 4            | <u>1</u> (%) | 20<br>14<br>2<br>(%) | 00 ppm<br><u>3 4</u><br>(%) (%) | <u>    1</u><br>(%) |                   | ppm<br>3 <u>4</u><br>%) (%) |
|---------------|------------------------------------------|----------------------------------------------------------|-------------------------------|------------------|-------------------------------------|----------------|--------------|----------------------|---------------------------------|---------------------|-------------------|-----------------------------|
| [Integumentar | y system/appandage]                      |                                                          |                               |                  |                                     |                |              |                      |                                 |                     |                   |                             |
| skin/app      | scar:dermis                              | 0<br>( 0) (                                              | < 6><br>0 0<br>0) ( 0)        | 0 (10)           | <10><br>0 (<br>) ( 0) ( 0           | ) 0<br>))(0)   | 0<br>( 0) (  | <14<br>0<br>( 0) (   |                                 | 0<br>( 0) (         | <11><br>0<br>0) ( | 0 0<br>0) ( 0)              |
| [Respiratory  | system]                                  |                                                          |                               |                  |                                     |                |              |                      |                                 |                     |                   |                             |
| nasal cavit   | eosinophilic change:olfactory epithelium |                                                          | < 6><br>0 0<br>0) ( 0)        | 0 (<br>( 0) ( 60 | <10><br>0 (<br>) ( 0) ( (           |                | 4<br>(29)    | <14<br>1<br>( 7) (   |                                 | 0<br>( 0) (         | <11><br>0<br>0) ( | 0 0<br>0) ( 0)              |
|               | eosinophilic change:respiratory epitheli | um 0<br>(0)(                                             | 0 0<br>0) ( 0)                | 0 (10)           | 0 (<br>) ( 0) ( (                   | ) 0<br>)) ( 0) | 0<br>( 0) (  | 0<br>( 0) (          | 0 0<br>( 0) ( 0)                | 0<br>( 0) (         | 0<br>0) (         | 0 0<br>0) ( 0)              |
|               | inflammation:foreign body                | 0<br>( 0) (                                              | 2 0<br>33) ( 0)               | 0 (0)            | ) ( 0) ( (                          | ) 0<br>)) ( 0) | 2<br>(14)    | 0<br>( 0) (          | 0 0<br>( 0) ( 0)                | 0<br>( 0) (         | 0<br>0) (         | 1 0<br>9) ( 0)              |
|               | respiratory metaplasia:olfactory epithel | ium 0<br>(0)(                                            | 0 0<br>0) ( 0)                | 0<br>(0) (1      | ) (_0) ( (                          | ) 0<br>)) ( 0) | 1<br>(7)     | 0<br>(0) (           | 0 0<br>(0)(0)                   | 0<br>( 0) (         | 0<br>0) (         | 0 0<br>0) ( 0)              |
|               | respiratory metaplasia:gland             | 1<br>(17) (                                              | 1 0<br>17) ( 0)               | 0 (<br>( 0) ( 5  | i 0 (<br>) ( 0) ( (                 | ) 0<br>))(0)   | 8<br>(57)    | 1<br>(7)(            | 0 0<br>(0)(0)                   | 3<br>(27) (         | 1<br>9) (         | 0 0<br>0) ( 0)              |
| lung          | congestion                               | 0<br>( 0) (                                              | < 6><br>1 0<br>17) ( 0)       |                  | <10><br>1 (<br>) (10) ( (           | ) 0<br>))(0)   | 1<br>(7)     | <14<br>0<br>( 0) (   | 1><br>0 0<br>( 0) ( 0)          | 0<br>( 0) (         | <11><br>1<br>9) ( | 0 0<br>0) ( 0)              |

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

- 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)

| SEX          | : MALE                       |                                                                                                                                                                                              |                                                                                                                       |                                                                                                                               | PAGE :                                                |
|--------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| Organ        | Findings                     | Group Name         Control           No. of Animals on Study         6           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 14 \\ \underline{1 \ 2 \ 3 \ 4} \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| [llematopoie | tic system]                  |                                                                                                                                                                                              |                                                                                                                       |                                                                                                                               |                                                       |
| spleen       | atrophy                      | < 6><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                | <14><br>0 2 0 0<br>( 0) ( 14) ( 0) ( 0)                                                                                       | <11><br>0 2 1 0<br>( 0) ( 18) ( 9) ( 0)               |
|              | deposit of hemosiderin       | 0 2 0 0<br>( 0) ( 33) ( 0) ( 0)                                                                                                                                                              | 2 0 0 0<br>(20) ( 0) ( 0) ( 0)                                                                                        | 0 1 0 0<br>( 0) ( 7) ( 0) ( 0)                                                                                                | 1 0 0 0<br>(9)(0)(0)(0)(0)                            |
|              | extramedullary hematopoiesis | 0 0 1 0<br>( 0) ( 0) ( 17) ( 0)                                                                                                                                                              | 0 1 1 0<br>( 0) ( 10) ( 10) ( 0)                                                                                      | 0 2 1 0<br>( 0) ( 14) ( 7) ( 0)                                                                                               | 0 0 2 0<br>( 0) ( 0) ( 18) ( 0)                       |
| [Circulator: | y system]                    |                                                                                                                                                                                              |                                                                                                                       |                                                                                                                               |                                                       |
| heart        | thrombus                     | <pre>&lt; 6&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>                                                                                                                                            | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                        | <11><br>0 0 1 0<br>( 0) ( 0) ( 9) ( 0)                |
|              | mineralization               | 0 0 1 0<br>( 0) ( 0) ( 17) ( 0)                                                                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                        | 0 1 0 0<br>( 0) ( 7) ( 0) ( 0)                                                                                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|              | hypertrophy                  | 0 1 0 0<br>( 0) ( 17) ( 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)                        |
|              | myocardial fibrosis          | 3 0 1 0<br>(50) (0) (17) (0)                                                                                                                                                                 | 5 0 0 0<br>(50)(0)(0)(0)                                                                                              | 10 0 0 0<br>(71) (0) (0) (0)                                                                                                  | 6 0 0 0<br>(55) (0) (0) (0)                           |

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

(c)

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

(IIPT150)

BAIS2

3 \_\_\_\_

| SEX          | : MALE              |                                                                                                                                                                                              |                                                                                                                  |                                                                                             | PAGE :                                                                                                                    |
|--------------|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| Organ        | Findings            | Group Name         Control           No. of Animals on Study         6           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 14 \\ \frac{1}{(\%)}  (\%)  (\%)  (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|              |                     |                                                                                                                                                                                              |                                                                                                                  |                                                                                             |                                                                                                                           |
| [Circulatory | system]             |                                                                                                                                                                                              |                                                                                                                  |                                                                                             |                                                                                                                           |
| artery/aort  | mineralization      | $\begin{array}{cccc} & < 6 \\ 1 & 0 & 0 \\ (17) & (0) & (0) & (0) \end{array}$                                                                                                               | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    |
| [Digestive s | ystem]              |                                                                                                                                                                                              |                                                                                                                  |                                                                                             |                                                                                                                           |
| tooth        | inflammation        | <pre>&lt; 6&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>                                                                                                                                            | $\begin{array}{cccc} <10> & & \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 10) & ( & 0) & ( & 0) \end{array}$                | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | <11><br>0 1 0 0<br>( 0) ( 9) ( 0) ( 0)                                                                                    |
| tangue       | mineralization      | $\begin{pmatrix} < 6 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 17 ) & ( & 0 ) & ( & 0 ) \\ \end{pmatrix}$                                                                                             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | <10><br>0 0 0 0 (<br>( 0) ( 0) ( 0) ( 0)                                                                                  |
|              | arteritis           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                               | 2 0 0 0<br>(20)(0)(0)(0)                                                                                         | 1 0 0 0<br>(7)(0)(0)(0)                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                            |
| stomach      | mineralization      | $\begin{pmatrix} < 6 \\ 0 & 0 & 1 & 0 \\ ( & 0) & ( & 0) & ( & 17 ) & ( & 0) \end{pmatrix}$                                                                                                  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <14><br>0 1 0 0<br>( 0) ( 7) ( 0) ( 0)                                                      | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    |
|              | erosion:forestomach | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                               | 1 0 0 0<br>(10)(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

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

b

c:b/a\*100 (c)

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

(IIPT150)

BAIS2

## HISTOLOGICAL RINDINGS .NON-NEOPLASTIC LECTONS (CHAMARY)

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### STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

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

PAGE: 5

| Organ        | Findings                  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | Control<br>6<br>2 3 4<br>(%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 14 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|--------------|---------------------------|-------------------------------------------------------------|--------------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| [Digestive s | ystem]                    |                                                             |                                      |                                                                                                                  |                                                                                                                        |                                                                                                                           |
| stomach      | ulcer:forestomach         | 0<br>( 0) (                                                 | < 6><br>0 0 0<br>0) ( 0) ( 0)        | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <14><br>1 0 0 0<br>( 7) ( 0) ( 0) ( 0)                                                                                 | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    |
|              | hyperplasia:forestomach   | 0<br>( 0) (                                                 | 0 0 0<br>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)                                                                                            |
|              | erosion:glandular stomach | 0<br>( 0) (                                                 | 0 0 0<br>0) ( 0) ( 0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 1 0 0 0<br>(7)(0)(0)(0)                                                                                                | 1 0 0 0<br>(9)(0)(0)(0)                                                                                                   |
|              | ulcer:glandular stomach   | 0<br>( 0) (                                                 | 0 0 0<br>0) ( 0) ( 0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 1 0 0 0<br>(7)(0)(0)(0)                                                                                                | 1 0 0 0<br>(9)(0)(0)(0)                                                                                                   |
| liuer        | necrasis:central          | 0<br>( 0) (                                                 | < 6><br>0 0 0<br>0) ( 0) ( 0)        | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                          | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                 | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    |
|              | fatty change              | 1<br>(17) (                                                 | 0 0 0<br>0)(0)(0)                    | 0 1 0 0<br>( 0) (10) ( 0) ( 0)                                                                                   | 1 3 0 0<br>(7)(21)(0)(0)                                                                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                            |
|              | inflammatory infiltration | 0 ( 0) (                                                    | 0 0 0<br>0) ( 0) ( 0)                | 1 0 0 0<br>(10) (0) (0) (0)                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                            |
|              | granulation               | 0<br>( 0) (                                                 | 0 0 0<br>0)(0)(0)                    | 1 0 0 0<br>(10) (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

< 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

| SEX          | : MALE                 |                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                       | PAGE :                                                                                                             |
|--------------|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Organ        | Findings               | Group Name         Control           No. of Animals on Study         6           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 10 \\ \hline (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ (\%) \\ ($ | $ \begin{array}{c} 2000 \text{ ppm} \\ 14 \\ \underline{14} \\ (\%) (\%) (\%) (\%) (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| [Digestive : | system]                |                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                       |                                                                                                                    |
| liver        | vacualated cell focus  | <pre></pre>                                                                                                                                                                      | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                | <11><br>0 2 0 0<br>( 0) ( 18) ( 0) ( 0)                                                                            |
|              | spongiosis hepatis     | 2 0 0 0<br>(33)(0)(0)(0)                                                                                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 2 0 0 0<br>(14) ( 0) ( 0) ( 0)                                                                        | 1 0 0 0<br>(9)(0)(0)(0)(0)                                                                                         |
|              | bile duct hyperplasia  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                             | 0 6 3 0<br>(0)(60)(30)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 3 8 1 0<br>(21)(57)(7)(0)                                                                             | 1 4 4 0<br>(9) (36) (36) (0)                                                                                       |
| pancreas     | atrophy                | <pre></pre>                                                                                                                                                                      | <10><br>4 0 0 0<br>( 40) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <14><br>2 4 0 0<br>(14) (29) (0) (0)                                                                  | <11><br>1 0 1 0<br>( 9) ( 0) ( 9) ( 0)                                                                             |
| [Urinary sys | stem]                  |                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                       |                                                                                                                    |
| kidney       | hyaline droplet        | <pre></pre>                                                                                                                                                                      | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <14><br>0 2 0 0<br>( 0) ( 14) ( 0) ( 0)                                                               | $\begin{array}{c} <11>\\ 0 & 0 & 0 & 0\\ ( & 0) & ( & 0) & ( & 0) & ( & 0)\end{array}$                             |
|              | deposit of hemosiderin | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0 2 0 0<br>( 0) ( 14) ( 0) ( 0)                                                                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     |

STUDY NO. : 0162

| 1L9C6 | 1:       | Slight    | Z :     | Moderate    | 3 : Marked | 4 : Sever |
|-------|----------|-----------|---------|-------------|------------|-----------|
| ( a ) | <u>.</u> | Number of | opimata | overined at | the eite   |           |

<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

(IIPT150)

BAIS2

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

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| ANIMAL : RAT F344<br>REPORT TYPE : A1<br>SEX : MALE |                     | HISTOLOGICAL FINDINGS :NON-N<br>DEAD AND MORIBUND ANIMALS (0-                              | PAGE: 7                                                                                                          |                                                                                                                        |                                                                                                                           |
|-----------------------------------------------------|---------------------|--------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| Organ                                               | Findings            | Group Name Control<br>No. of Animals on Study 6<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 14 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| [Urinary sys                                        | tem]                |                                                                                            |                                                                                                                  |                                                                                                                        |                                                                                                                           |
| kidney                                              | chronic nephropathy | $\langle 6 \rangle$<br>0 1 1 2<br>( 0) (17) (17) (33)                                      | <10><br>1 3 3 0<br>(10) (30) (30) (0)                                                                            | <14><br>2 2 1 3<br>(14) (14) (7) (21)                                                                                  | <11><br>2 0 2 0<br>( 18) ( 0) ( 18) ( 0)                                                                                  |
|                                                     | hydranephrasis      | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                       | 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)                                                                                          |
|                                                     | tubular necrosis    | 0 0 1 0<br>( 0) ( 0) ( 17) ( 0)                                                            | 0 0 1 0<br>( 0) ( 0) ( 10) ( 0)                                                                                  | 0 0 2 0<br>( 0) ( 0) ( 14) ( 0)                                                                                        | 1 2 4 0<br>(9)(18)(36)(0)                                                                                                 |
| [Endocrine s)                                       | ystem]              |                                                                                            |                                                                                                                  |                                                                                                                        |                                                                                                                           |
| pituitary                                           | angiectasis         | <pre></pre>                                                                                | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                 | <11><br>1 0 0 0<br>(9) (0) (0) (0)                                                                                        |
|                                                     | cyst                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             | 2 0 0 0<br>(20)(0)(0)(0)                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                            |
|                                                     | hyperplasia         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             | 2 0 0 0<br>(20) ( 0) ( 0) ( 0)                                                                                   | 3 0 0 0<br>(21)(0)(0)(0)                                                                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                            |
| thyraid                                             | C-cell hyperplasia  | <pre></pre>                                                                                | < 9><br>1. 0 0 0<br>(11) (0) (0) (0)                                                                             | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                 | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                                   |

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

<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

STUDY NO. : 0162

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

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|               | 0162<br>RAT F344<br>A1    | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0-105W) |                                      |   |  |   |
|---------------|---------------------------|---|--------------------------------------|---|--|---|
|               | MALE                      |   |                                      |   |  | PAGE :  |
| 0rgan         | Findings                  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%)                                   | Control<br>6<br>2 3 4<br>(%) (%) (%) | $ \begin{array}{c} 400 \text{ ppm} \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 2000 \text{ ppm} \\ 14 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| [Endocrine sy | stem]                     |   |                                      |   |  |   |
| parathyroid   | hyperplasia               | 1<br>(17) (   | < 6><br>0 0 0<br>0) ( 0) ( 0)        | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| adrenal       | hyperplasia:medulla       | 4<br>(67) (   | < 6><br>0 0 0<br>0) ( 0) ( 0)        | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)   | <14><br>1 1 0 0 *<br>(7) (7) (0) (0)   | <11><br>0 0 0 0 *<br>( 0) ( 0) ( 0) ( 0)  |
|               | focal fatty change:cortex | 1<br>(17) (   | 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)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| [Reproductive | system]                   |   |                                      |   |  |   |
| testis        | atrophy                   | 0<br>( 0) (   | < 6><br>1 0 0<br>17) ( 0) ( 0)       | <10><br>1 2 0 0<br>( 10) ( 20) ( 0) ( 0)  | $\begin{array}{c} <14 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 7) & ( & 0) & ( & 0) \end{array}$                                 | <11><br>0 2 3 0<br>( 0) ( 18) ( 27) ( 0)  |

0 0 0 0

0 1 0 0

( 0) ( 17) ( 0) ( 0)

1 0 0 0

(10) (0) (0) (0)

0 0 0 0

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

0 0 0 0

0 1 0 0

(0)(7)(0)(0)

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

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

b b : Number of animals with lesion

mineralization

arteritis

(c) c:b/a\*100

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

(HPT150)

BAIS2

0 0 0 0

0 0 0 0

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

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### STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1

## SEX : MALE

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

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PAGE : 9

| Organ         | Findings                      | Group Name<br>No. of Animals on Study<br>Grade <u>1 2</u><br>(%) (% | Control<br>6<br>3 <u>4</u><br>) (%) (%) | 400 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | <u>1</u> (%) | 2000 ppm<br>14<br>2 3 4<br>(%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|---------------|-------------------------------|---|---|--|--------------|--|---|
| [Reproductive | system]                       |   |   |  |              |  |   |
| testis        | interstitial cell hyperplasia | 1 (   | < 6><br>0 0<br>0) ( 0) ( 0) (           | <10><br>3 0 0 0<br>30) ( 0) ( 0) ( 0)              | 1<br>(7)(    | <14><br>0 0 0<br>0) ( 0) ( 0)          | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| epididymis    | degeneration                  | 0 0   | < 6><br>0 0<br>0) ( 0) ( 0) (           | <10><br>2 0 0 0<br>20) ( 0) ( 0) ( 0)              | 3<br>(21) (  | <14><br>0 0 0<br>0) ( 0) ( 0)          | <11><br>3 0 0 0<br>( 27) ( 0) ( 0) ( 0)               |
| prostate      | inflammation                  | 1 (   | < 6><br>0 0 0<br>1) ( 0) ( 0) (         | <10><br>1 0 0 0<br>10) ( 0) ( 0) ( 0)              | 1<br>( 7) (  | <14><br>0 0 0<br>0) ( 0) ( 0)          | <11><br>1 1 0 0<br>( 9) ( 9) ( 0) ( 0)                |
| ammary gl     | galactocale                   | 1 (   | < 6>                                    | <10><br>1 0 0 0<br>10) ( 0) ( 0) ( 0)              | 1<br>(7)(    | <14><br>0 0 0<br>0) ( 0) ( 0)          | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Nervous syste | əm]                           |   |   |  |              |  |   |
| rain          | hemorrhage                    | 1 (   | < 6><br>) 0 0<br>)) ( 0) ( 0) (         | <10><br>1 0 0 0<br>10) ( 0) ( 0) ( 0)              | 0<br>( 0) (  | <14><br>1 0 0<br>7) ( 0) ( 0)          | <11><br>0 1 0 0<br>( 0) ( 9) ( 0) ( 0)                |
| spinal cord   | hemorrhage                    | 0   | < 6><br>0 0<br>7) ( 0) ( 0) (           | <10><br>0 1 0 0<br>0) ( 10) ( 0) ( 0)              |              | <14><br>1 0 0<br>7) ( 0) ( 0)          | <11><br>0 1 0 0<br>( 0) ( 9) ( 0) ( 0)                |

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

### ANIMAL : RAT F344 REPORT TYPE : A1 SEX ; MALE PAGE : 10 Group Name Control 400 ppm 2000 ppm 10000 ppm No. of Animals on Study 6 10 14 11 Grade 2 3 2 3 2 3 2 3 4 0rgan Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Special sense organs/appandage] өуө < 6> <10> <14> $\langle 11 \rangle$ cataract 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 (17) (0) (0) (0) (10) (0) (0) (0)(0)(0)(0)(0) (0)(0)(0)(0)retinal atrophy 0 0 0 0 0 1 1 0 1 1 1 0 0 0 1 0 (0)(0)(0)(0)( 0) ( 10) ( 10) ( 0) (7) (7) (7) (0) (0)(0)(9)(0). keratitis 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(17)(0)(0)(0)(0)(0)(0)degeneration:cornea 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(7)(0)(0) (0) (0) (0) (0)llarder gl < 6> <10> <14> <11> degeneration 1 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (17) (0) (0) (0)(0)(0)(0)(0)(7) (0) (0) (0) (0)(0)(0)(0)inflammation 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0)(0)(10)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0)inflammatory infiltration 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0)(0)(7)(0)(0) (0) (0) (0) (0)nasolacr d < 6> <10> <14> <11>

0 0 0 0

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

0 1 0 0

( 0) ( 10) ( 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

inflammation

(c) c:b/a\*100

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

STUDY NO. : 0162

0 0 0 0

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

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

| STUDY NO.<br>ANIMAL<br>REPORT TYPE<br>SEX | : 0162<br>: RAT F344<br>: A1<br>: MALE   | HISTOLOGICAL FINDINGS :NON-<br>DEAD AND MORIBUND ANIMALS (                                 | NEOPLASTIC LESIONS (SUMMARY)<br>0-105W)  |   | PAGE : 11  |
|---|--|--|--|---|--|
| Organ                                     | Findings   | Group Name Control<br>No. of Animals on Study 6<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{c} 400 \text{ ppm} \\ 10 \\ \frac{1}{(\%)} (\%) (\%) (\%) (\%) \end{array} $ | $ \begin{array}{c} 2000 \text{ ppm} \\ 14 \\ \frac{1}{(\%)} (\%) (\%) (\%) (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 11 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array} $ |
| [Musculoske                               | oletal system]   |  |  |   |  |
| bane                                      | ostitis fibrosa  | $\langle 6 \rangle$<br>0 1 0 0<br>( 0) ( 17) ( 0) ( 0)                                     | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | $\begin{array}{cccc} <14 \\ 1 & 0 & 0 & 0 \\ ( 7) & ( 0) & ( 0) & ( 0) \end{array}$           | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| Grade<br>< a ><br>b<br>(c)<br>Significant | 1 : Slight2 : Moderatea : Number of animals examined ab : Number of animals with lesidc : b / a $* 100$ c difference ; $* : P \leq 0.05$ |  |  | · · · · · · · · · · · · · · · · · · ·   |  |

BAIS2

(HPT150)

## APPENDIX L 2

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

Organ\_\_\_\_ Findings\_\_\_

[Respiratory system]

nasal cavit

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

|                                       | Group Name<br>No. of Animals on Study | Control<br>9                    | 400 ppm<br>10  | 2000 ppm<br>9  | 10000 ppm<br>13  |
|---------------------------------------|---------------------------------------|---------------------------------|--|--|--|
| Findings                              | Grade <u>1</u> (%)                    | 2 3 4<br>(%) (%) (%)            | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $(\%)$ $(\%)$ |
| system]                               |                                       |                                 |  |  |  |
| inflammation                          | 0<br>( 0)                             | < 9><br>0 0 0<br>( 0) ( 0) ( 0) | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <pre></pre>  | <13><br>0 0 0<br>( 0) ( 0) ( 0) (                                |
| easinaphilic change:alfactory epithel |                                       | 1 0 0<br>(11) (0) (0)           | 3 1 0 0<br>(30)(10)(0)(0)  | 5 2 0 0<br>(56)(22)(0)(0)  | 1 5 0<br>(8)(38)(0)(   |
| inflammation:foreign body             | 1<br>(11)                             | 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)                                   | 0 1 0<br>( 0) ( 8) ( 0) (  |

|         |                              | (11) (0) (0) (0)                       | ( 0) ( 0) ( 0) ( 0)                     | ( 0) ( 0) ( 0) ( 0)                    | ( 0) ( 8) ( 0) ( 0)                    |
|---------|------------------------------|--|---|--|--|
|         | respiratory metaplasia:gland | 3 0 0 0<br>(33)(0)(0)(0)               | 6 0 0 0<br>(60)(0)(0)(0)                | 6 0 0 0<br>(67)(0)(0)(0)               | 5 0 0 0<br>(38) (0) (0) (0)            |
| trachea | inflammation                 | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre></pre>                            | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| lung    | cangestian                   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <10><br>0 1 0 0<br>( 0) ( 10) ( 0) ( 0) | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
|         | inflammatory infiltration    | 1 0 0 0<br>(11) (0) (0) (0)            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | 1 0 0 0<br>(11) (0) (0) (0)            | 3 0 0 0<br>(23)(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)

PAGE: 12

4

(%)

0 0)

0 \* 0)

0

## STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

PAGE : 13

| Organ          | Findings                     | Group Name         Control           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $ \begin{array}{c}     400 \text{ ppm} \\     10 \\     1 2 3 4 \\     (\%) (\%) (\%) (\%) (\%) \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|----------------|------------------------------|--|---|--|---|
| [Nematopoietic | c system]                    |  |   |  |   |
| bone marrow    | angiectasis                  | <pre></pre>  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <13><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)  |
|                | 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>(8)(0)(0)(0)(0)  |
|                | increased hematopoiesis      | 2 0 0 0<br>(22) (0) (0) (0)  | 1 0 0 0<br>(10) (0) (0) (0)   | 3 0 0 0<br>(33) (0) (0) (0)  | 1 0 0 0<br>(8)(0)(0)(0)(0)  |
| spleen         | atrophy                      | < 9><br>1 0 0 0<br>(11) (0) (0) (0)  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|                | deposit of hemosiderin       |  | 1 1 1 0<br>(10) (10) (10) (0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 3 0 0 0<br>(23) (0) (0) (0)   |
|                | 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)   | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)  |
|                | extramedullary hematopoiesis | 2 0 2 0<br>(22) (0) (22) (0)   | 1 I 0 0<br>(10)(10)(0)(0)   | 0 0 5 0<br>( 0) ( 0) ( 56) ( 0)  | 0 0 2 0<br>( 0) ( 0) ( 15) ( 0)   |
| [Circulatory s | system]                      |  |   |  |   |
| hear-t         | thrombus                     | <pre> &lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) </pre>   | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre></pre>  | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |

b b:Number of anim (c) c:b/a\*100

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

| )rgan        | Findings                  | Group Name Control<br>No. of Animals on Study 9<br>Grade <u>1 2 3</u><br>(%) (%) (%) ( | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 4 \\ \% \end{array} \qquad \begin{array}{c} 1 & 2 & 3 & 4 \\ \hline \% & (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 8 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|--------------|---------------------------|--|---|--|--|
| Circulatory  | system]                   |  |   |  |  |
| neart        | mineralization            | <pre> &lt; 9&gt;     1 0 0     ( 11) ( 0) ( 0) (</pre>                                 | <10><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|              | myocardial fibrosis       | 3 0 0<br>(33)(0)(0)(   | 0 3 0 0 0<br>0) (30) (0) (0) (0)  | 3 1 0 0<br>(33)(11)(0)(0)  | 4 0 0 0<br>(31)(0)(0)(0)   |
| )igestive sy | stem]                     |  |   |  |  |
| al cavity    | inflammation              | <pre></pre>  | <pre> &lt;10&gt;<br/>0 0 0 0 0<br/>0) ( 0) ( 0) ( 0) ( 0)</pre>   | <pre></pre>  | $\begin{array}{c} <13>\\ 0 & 1 & 0 & 0\\ ( & 0) & ( & 8) & ( & 0) & ( & 0) \end{array}$                            |
|              | fibrosis                  | 0 0 0<br>( 0) ( 0) ( 0) (  | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 1 0<br>( 0) ( 0) ( 8) ( 0)   |
| ophagus      | squamous cell hyperplasia | <pre></pre>  | <pre> &lt;10&gt;<br/>0 0 0 0 0<br/>0) ( 0) ( 0) ( 0) ( 0)</pre>   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | $\begin{array}{c} <13>\\ 0 & 1 & 0 & 0\\ ( & 0) & ( & 8) & ( & 0) & ( & 0) \end{array}$                            |
| omach        | mineralization            | <pre> &lt; 9&gt;<br/>0 0 1<br/>( 0) ( 0) ( 11) (</pre>                                 | <10><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)   | < 9><br>1 0 0 0<br>(11) (0) (0) (0)  | <13><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)

STUDY NO. : 0162

BA1S2

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

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| STUDY NO. : 0162<br>ANIMAL : RAT F344<br>REPORT TYPE : A1<br>SEX : FEMALE |                           | HISTOLOGICAL FINDINGS :NON-N<br>DEAD AND MORIBUND ANIMALS (0-                              |  |   | PAGE: 15  |
|---|---------------------------|--|--|---|---|
| Organ   | Findings                  | Group Name Control<br>No. of Animals on Study 9<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 10 \\ \hline \frac{1}{(\%)}  (\%)  (\%)  (\%) \end{array}$ | $\begin{array}{c} 2000 \\ 9 \\ \hline 1 \\ \hline 2 \\ \hline 3 \\ \hline 4 \\ \hline \% \\ \hline \hline \hline \% \\ \hline \hline \% \\ \hline \hline \% \\ \hline \hline \hline \hline$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| [Digestive s  | system]                   |  |  |   |   |
| stomach   | ulcer:forestomach         | <pre></pre>  | <10><br>1 1 0 0<br>(10) (10) (0) (0)   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|   | erosion:glandular stomach | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10) (0) (0) (0)  | 1 0 0 0<br>(11) (0) (0) (0)   | 1 0 0 0<br>( 8) ( 0) ( 0) ( 0)  |
|   | ulcer: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>(11)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| liver   | herniation                | <pre>&lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) </pre>  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | < 9><br>1 0 0 0<br>(11) ( 0) ( 0) ( 0)  | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|   | necrosis:central          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 1 0 0<br>( 8) ( 8) ( 0) ( 0)  |
|   | necrosis:focal            | 1 0 0 0<br>(11)(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)  |
|   | fatty change              | 0 2 0 0<br>( 0) ( 22) ( 0) ( 0)  | 2 0 0 0<br>(20)(0)(0)(0)   | 0 1 0 0<br>( 0) ( 11) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|   | granulation               | 0 1 0 0<br>( 0) ( 11) ( 0) ( 0)  | 0 0 1 0<br>( 0) ( 0) ( 10) ( 0)  | 1 0 0 0<br>(11) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(15)(0)(0)(0)  |

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

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

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

| )rgan       | Findings                            | Group Name         Control           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 1 & 2 & 3 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|-------------|-------------------------------------|--|--|--|---|
| Digestive : | system]                             |  |  |  |   |
| iver        | basophilic cell focus               | $\begin{array}{c} \langle 9 \rangle \\ 2 & 1 & 0 & 0 \\ (22) & (11) & (0) & (0) \end{array}$   | <10><br>1 1 0 0<br>(10) (10) (0) (0)   | < 9><br>1 0 0 0<br>( 11) ( 0) ( 0) ( 0)  | <13><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0                 |
|             | vacuolated cell focus               | 1 0 0 0<br>(11) (0) (0) (0)  | 0 1 0 0<br>( 0) ( 10) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(8)(0)(0)(0)                               |
|             | spongiosis hepatis                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(11)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                         |
|             | bile duct hyperplasia               | $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 3 1 0 0<br>(30)(10)(0)(0)  | 0 1 0 0<br>( 0) ( 11) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                         |
| ncreas      | atrophy                             | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <10><br>1 0 0 0<br>(10) ( 0) ( 0) ( 0)   | < 9><br>1 0 0 0<br>(11) (0) (0) (0)  | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Drinary sys | stem]                               |  |  |  |   |
| dney        | hyperplasia:tubular epithelial cell | <pre>&lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0)</pre>   | <10><br>1 0 0 0<br>(10) (0) (0) (0)  | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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(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)

STUDY NO. : 0162

### STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

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| Organ  | N  | roup Name Control<br>o. of Animals on Study 9<br>rade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{c} 400 \text{ ppm} \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | 2000 ppm<br>9<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|--|--|---|---|--|--|
| [Urinary sy  | vstem]   |   |   |  |  |
| <idney< td=""><td>infarct</td><td><pre> &lt; 9&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre></td><td>&lt;10&gt;<br/>1 0 0 0<br/>( 10) ( 0) ( 0) ( 0)</td><td>&lt; 9&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</td><td>&lt;13&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</td></idney<> | infarct  | <pre> &lt; 9&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>                              | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|  | hyaline druplet  | 0 0 1 0<br>( 0) ( 0) ( 11) ( 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)   |
|  | deposit of hemosiderin   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 1 1 0<br>( 0) ( 11) ( 11) ( 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>(11)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|  | chronic nephropathy  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 2 2 1 0<br>(20)(20)(10)(0)  | 2 0 1 0<br>(22) (0) (11) (0)                       | 3 1 0 1<br>(23)(8)(0)(8)   |
|  | hydronephros i s   | 0 1 0 0<br>( 0) ( 11) ( 0) ( 0)   | 0 0 0 0<br>(0)(0)(0)(0)(0)  | 0 1 0 0<br>( 0) ( 11) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|  | tubular necrosis   | $\begin{pmatrix} 0 & 1 & 2 & 0 \\ ( & 0) & ( & 11) & ( & 22) & ( & 0) \end{pmatrix}$    | 1 1 1 0<br>(10) (10) (10) (0)   | 0 0 3 0<br>( 0) ( 0) ( 33) ( 0)                    | 0 2 3 0<br>( 0) (15) (23) ( 0)   |
|  | mineralization:cortico-medullary juncti  | on 0 0 0 0<br>(0)(0)(0)(0)  | 1 0 0 0<br>(10) (0) (0) (0)   | 1 0 0 0<br>(11)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| Grade<br>< a ><br>b<br>(c)   | 1: Slight 2: Moderate 3:<br>a: Number of animals examined at the sit<br>b: Number of animals with lesion<br>c: b / a * 100 | Marked 4 : Severe<br>e  |   |  |  |

(c) c: b/a \* 100 Significant difference ; \*: P  $\leq 0.05$  \*\* : P  $\leq 0.01$  Test of Chi Square

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STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

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| 0rgan                                     | Group<br>No. of<br>Grade<br>Findings  | Name Control<br>Animals on Study 9<br>                      | $ \begin{array}{c} 400 \text{ ppm} \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline \% & (\%) & (\%) & (\%) \\ \hline \end{pmatrix}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|---|---|---|---|--|---|
| [Urinary sys                              | stem]   |   |   |  |   |
| kidney                                    | mineralization:papilla  | < 9><br>1 0 0 0<br>(11) (0) (0) (0)                         | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <13><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)  |
|   | mineralization:pelvis   | 1 0 0 0<br>(11) (0) (0) (0)                                 | 1 0 0 0<br>(10)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| (Endocrine s                              | system]   |   |   |  |   |
| pituitary                                 | angiectasis   | <pre> &lt; 9&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>  | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)   | < 9><br>2 0 0 0<br>(22) (0) (0) (0)  | <13><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)  |
|   | 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)   | 2 0 0 0<br>(15) (0) (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) ( 11) ( 0) ( 0)  | 1 0 0 0<br>(8)(0)(0)(0)   |
| thyroid                                   | ultimibranchial body remanet  | <pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0)</pre> | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre> &lt; B&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>   | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| Grade<br>< a ><br>b<br>(c)<br>Significant | 1 : Slight2 : Moderate3 : Marka : Number of animals examined at the siteb : Number of animals with lesionc : b / a * 100difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ |   |   |  |   |

(HPT150)

BAIS2

### STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

PAGE: 19

| Organ       | Findings                       | Group Name         Control           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $ \begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 10 \\ \hline (\%) (\%) (\%) (\%) (\%) (\%) \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|-------------|--------------------------------|--|---|--|--|
| Endocrine s | vstem]                         |  |   |  |  |
| thyroid     | C-cell hyperplasia             | <pre> &lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) </pre>   | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0).   | <pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0) </pre>   | <13><br>2 0 0 0<br>( 15) ( 0) ( 0) ( 0)  |
| adrenal     | hemorrhage                     | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | $\langle 13 \rangle$<br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)   |
|             | peliasis-like lesion           | $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 1 0 0 0<br>(10) (0) (0) (0)   | 1 0 0 0<br>(11)(0)(0)(0)   | 1 0 0 0<br>( 8) ( 0) ( 0) ( 0)   |
|             | neorasis                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>(0)(0){0)(0)   | 1 0 0 0<br>(11)(0)(0)(0)   | 1 0 0 0<br>(8)(0)(0)(0)(0)   |
|             | hyperplasia:cortical cell      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(11)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|             | hyperplasia:medulla            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(11)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|             | focal fatty change:cortex      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10)(0)(0)(0)(0)   | 1 0 0 0<br>(11)(0)(0)(0)   | 1 0 0 0<br>(8)(0)(0)(0)  |
| Reproductiv | ve system]                     |  |   |  |  |
| rterus      | cystic endometrial hyperplasia | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | <10><br>1 0 0 0<br>(10) ( 0) ( 0) ( 0)  | <pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0)</pre>  | <13><br>1 0 0 0<br>( 8) ( 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

|              |                      | Group Name Control  | 400 ppm  | 2000 ppm  | 10000 mag                              |
|--------------|----------------------|---|--|---|--|
| )rgan        | Findings             | No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\frac{100 \text{ ppm}}{10}$ $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ |  |
| Reproductive | ) system]            |   |  |   |  |
| aammary gl   | hyperplasia          | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <10><br>2 0 0 0<br>( 20) ( 0) ( 0) ( 0)  | <pre></pre>   | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
|              | galactocele          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(10)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                | 1 0 0 0<br>(8)(0)(0)(0)                |
| Vervous syst | tem]                 |   |  |   |  |
| ain          | hemorrhage           | <pre>&lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>   | <10><br>1 1 0 0<br>( 10) ( 10) ( 0) ( 0)   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| pinal cord   | hemorr hage          | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | $\langle 10 \rangle$<br>1 $1$ $0$ $0(10)$ $(10)$ $(0)$ $(0)$                               | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| Special sens | se organs/appandage] |   |  |   |  |
| УÐ           | hemorrhage           | <pre></pre>   | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <pre> &lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) </pre>                | <13><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0) |

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

(HPT150)

BAIS2

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

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PAGE : 21

| 0rgan   | Findings  | Group Name         Control           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $ \begin{array}{c} 400 \text{ ppm} \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \underline{1 \ 2 \ 3 \ 4} \\ \underline{(\%) \ (\%) \ (\%) \ (\%)} \end{array} $ |
|---|---|--|---|--|--|
| [Special sens                                 | e organs/appandage]   |  |   |  |  |
| өуө   | retinal atrophy   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <10><br>1 0 1 0<br>( 10) ( 0) ( 10) ( 0)  | <pre></pre>  | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|   | keratitis   | $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 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)   |
|   | iritis  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 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)   |
| larder gl                                     | degeneration  | <pre></pre>  | <10><br>1 0 0 0<br>(10) (0) (0) (0)   | < 9><br>1 0 0 0<br>(11) (0) (0) (0)  | <13><br>1 1 0 0<br>( 8) ( 8) ( 0) ( 0)   |
| nasolaer d                                    | inflammation  | <pre>&lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) </pre>  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre></pre>  | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| Musculoskele                                  | otal system]  |  |   |  |  |
| xane  | osteosclerosis  | $\begin{pmatrix} & 9 \\ 1 & 0 & 0 \\ (11) & (0) & (0) & (0) \end{pmatrix}$   | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)   | <pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0)     ( 0)</pre>   | <13><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)   |
| Grade<br>< a ><br>b<br>( c )<br>Significant d | 1 : Slight2 : Moderatea : Number of animals examined at thb : Number of animals with lesionc : b / a * 100lifference ; * : $P \leq 0.05$ ** : 1 | 3 : Marked 4 : Severe<br>e site<br>P ≦ 0.01 Test of Chi Square   |   |  |  |

(HPT150)

| ANIMAL<br>REPORT TYPE                     |   |  | HCAL FINDINGS :NON-ND<br>MORIBUND ANIMALS (O | EOPLASTIC LESIONS (SUMMARY)<br>-105W)  |   |  |
|---|---|--|--|--|---|--|
| SEX                                       | : FEMALE  |  |  |  |   | PAGE : 22  |
| 0rgan                                     | Findings  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>9<br><u>2 3 4</u><br>(%) (%) (%)  | $\begin{array}{c} 400 \text{ ppm} \\ 10 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 9 \\ \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)} \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 13 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| [Body caviti                              | es]   |  |  |  |   |  |
| retroperit                                | inflammation  | 0<br>( 0)  | < 9><br>0 0 0<br>( 0) ( 0) ( 0)              | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | < 9><br>0 0 0 1<br>( 0) ( 0) ( 0) ( 11)   | <13><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| Grade<br>< a ><br>b<br>(c)<br>Significant | 1 : Slight 2 : Modera<br>a : Number of animals examin<br>b : Number of animals with L<br>c : b / a * 100<br>difference ; * : P ≤ 0.05 | ed at the site<br>esion  |  |  |   |  |

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(HPT150)

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## APPENDIX L 3

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

| )rgan        |   | up Name<br>of Animals on Study<br>de <u>1</u> (%) | Cantrol<br>44<br>2 <u>3.4</u><br>(%)(%)(%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 36 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | 10000 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|---|---|--|--|--|--|
| Integumentar | v system/appandage]                       |   |  |  |  |  |
| skin/app     | hyperplasia:epithelium                    | 0<br>( 0)   | <44><br>0 0 0<br>( 0) ( 0) ( 0)            | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)   | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|              | hyperplasia:epidermis                     | 0<br>( 0)   | 0 0 0<br>( 0) ( 0) ( 0)                    | 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)                       |
|              | duct ectasia:sebaceous gland              | 0<br>( 0)   | 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)   | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                       |
| Respiratory  | system]                                   |   |  |  |  |  |
| asal cavit   | eosinophilic change:olfactory epithelium  | 24<br>(55)  | <44><br>2 1 0<br>(5) (2) (0)               | <40><br>22 3 1 0<br>(55) (8) (3) (0)   | <36><br>20 3 0 0<br>(56)(8)(0)(0)  | <39><br>17 0 0 0<br>(44) (0) (0) (0)                 |
|              | eosinophilic change:respiratory epitheliu |   | 0 0 0<br>( 0) ( 0) ( 0)                    | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)   | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 2 0 0 0<br>(5)(0)(0)(0)                              |
|              | inflammation:foreign body                 | 5<br>(11)   | 2 0 0<br>(5)(0)(0)                         | 6 0 0 0<br>(15) (0) (0) (0)  | 5 1 0 0<br>(14) (3) (0) (0)  | 1 1 0 0<br>(3)(3)(0)(0)                              |
|              | respiratory metaplasia:olfactory epitheli |   | 0 0 0<br>( 0) ( 0) ( 0)                    | 5 0 0 0<br>(13) (0) (0) (0)  | 1 0 0 0<br>(3)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |

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

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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STUDY NO. : 0162 ANIMAL : RAT E344

|                | G                                     | iroup Name Control  | 400 ppm  | 2000 ppm  | 10000 ppm   |
|----------------|---------------------------------------|---|--|---|---|
| Organ          |                                       | 0. of Animals on Study 44<br>Frade <u>1 2 3 4</u><br>(%) (%) (%) (%)        | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| [Respiratory : | system]                               |   |  |   |   |
| nasal cavit    | respiratory metaplasia:gland          | <44><br>21 7 0 0<br>(48) (16) (0) (0)                                       | <40><br>24 3 0 0<br>(60) (8) (0) (0)                 | <36><br>22 0 0 0 *<br>(61) (0) (0) (0)                | <39><br>23 5 0 0<br>(59) (13) (0) (0)                 |
| Lung           | accumulation of foamy cells           | <44><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                                      | <40><br>2 0 0 0<br>(5) (0) (0) (0)                   | <36><br>1 1 0 0<br>( 3) ( 3) ( 0) ( 0)                | <39><br>2 0 0 0<br>(5) (0) (0) (0)                    |
|                | bronchiolar-alveolar cell hyperplasia | 4 2 0 0<br>(9)(5)(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)                        |
| Nematopoieti   | c system]                             |   |  |   |   |
| one marrow     | granulation                           | $\begin{array}{c} <44>\\ 1 & 0 & 0 & 0\\ (2) & (0) & (0) & (0) \end{array}$ | <40><br>3 1 0 0<br>( 8) ( 3) ( 0) ( 0)               | (36)<br>1 1 0 0<br>(3) (3) (0) (0)                    | <39><br>3 3 0 0<br>( 8) ( 8) ( 0) ( 0)                |
|                | fibrosis                              | 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)                        |
|                | increased hematopoiesis               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 2 0 0 0<br>(6)(0)(0)(0)                               | 1 0 0 0<br>(3)(0)(0)(0)                               |

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

(IIPT150)

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|               |                              | Group Name Control  | 400 ppm  | 2000 ppm  | PAGE  |
|---------------|------------------------------|---|--|---|---|
| Organ         | Findings                     | Grade         1         2         3         4           Grade         (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $     \begin{array}{c}       10000 \text{ ppm} \\       39 \\       \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}     \end{array} $ |
| llematopoieti | c system]                    |   |  |   |   |
| lymph node    | ectasia of sinus             | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <39><br>2 0 0 0<br>(5) (0) (0) (0)  |
| spleen        | deposit of hemosiderin       | <44><br>3 0 0 0<br>( 7) ( 0) ( 0) ( 0)  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <35><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                | <39><br>2 0 0 0<br>(5) (0) (0) (0)  |
|               | fibrosis                     | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 1 0 1 0<br>(3)(0)(3)(0)  | 0 3 0 0<br>(0)(9)(0)(0)                               | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  |
|               | extramedullary hematopoiesis | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 1 0 0 0<br>(3)(0)(0)(0)  | 1 1 0 0<br>(3)(3)(0)(0)                               | 2 0 0 0<br>(5)(0)(0)(0)   |
|               | lymphoid 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) ( 3) ( 0) ( 0)  |
| [Circulatory  | system]                      |   |  |   |   |
| neart         | myocardial fibrosis          | $\begin{array}{cccc} <44 \rangle \\ 21 & 2 & 0 & 0 \\ (48) & (5) & (0) & (0) \end{array}$                                 | <40><br>19 4 0 0<br>( 48) ( 10) ( 0) ( 0)  | <36><br>23 0 0 0<br>(64) (0) (0) (0)                  | <39><br>17 1 0 0<br>(44) (3) (0) (0)  |

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(c) c:b/a\*100

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

(HPT150)

BAIS2

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1

## SEX : MALE

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

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| PAGE | ; | 4 |
|------|---|---|
|------|---|---|

| Drgan          | Group Name<br>No. of Animals on St<br>Grade | $\begin{array}{c} & \text{Control} \\ \text{Jdy} & 44 \\ \hline \frac{1}{(\%)} & (\%) & (\%) & (\%) \\ \hline \end{array}$ | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 36 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|----------------|---|--|--|--|---|
| [Circulatory s | system]                                     |  |  | · · · · · · · · · · · · · · · · · · ·  |   |
| artery/aort    | arteritis                                   | <44><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)   | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>2 0 0 0<br>( 6) ( 0) ( 0) ( 0)   | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| [Digesti∪e sys | stem]                                       |  |  |  |   |
| oral cavity    | inflammation                                | <41>><br>4 2 0 0<br>(9) (5) (0) (0)  | <40><br>2 3 0 0<br>( 5) ( 8) ( 0) ( 0)   | <36><br>0 4 0 0<br>( 0) ( 11) ( 0) ( 0)  | <39><br>5 3 0 0<br>(13) (8) (0) (0)                   |
|                | basal cell activation                       | 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)   | 2 0 0 0<br>(5)(0)(0)(0)                               |
| tooth          | inflammation                                | <44><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)   | <40><br>1 2 0 0<br>( 3) ( 5) ( 0) ( 0)   | <36><br>1 1 0 0<br>( 3) ( 3) ( 0) ( 0)   | <39><br>3 0 0 0<br>( 8) ( 0) ( 0) ( 0)                |
| tongue         | inflammation                                | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <39><br>2 0 0 0<br>(5) (0) (0) (0)                    |
|                | arteritis                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(3)(0)(0)(0)  | 4 0 0 0<br>(11) (0) (0) (0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |

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

(HPT150)

| STUDY NO. : 0162<br>ANIMAL : RAT F344<br>REPORT TYPE : A1<br>SEX : MALE |                           | HISTOLOGICAL FINDINGS :NON-NE<br>SACRIFICED ANIMALS (105W)  | PAGE : 5   |   |  |
|---|---------------------------|---|--|---|--|
| Organ   | Findings                  | Group Name         Control           No. of Animals on Study         44           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 36 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 39 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ |
| [Digestive sy   | /stem]                    |   |  |   |  |
| salivary gl   | inflammation              | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| esophagus   | squamous cell hyperplasia | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <39><br>1 0 0 0<br>(3) (0) (0) (0)   |
| stomach   | basal cell activation     | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <39><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)   |
|   | erosion:forestomach       | 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)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|   | ulcer:forestomach         | 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>(3)(0)(0)(0)  |
|   | hyperplasia:forestomach   | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 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)   |
|   | erosion:glandular stomach | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(3)(0)(0)(0)  | 3 0 0 0<br>(8)(0)(0)(0)   | 1 0 0 0<br>(3)(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)

BAIS2

### ANIMAL : RAT F344 SACRIFICED ANIMALS (105W) REPORT TYPE : A1 SEX : MALE PAGE : 6 Group Name 400 ppm Control 2000 ppm 10000 ppm No. of Animals on Study 44 40 36 39 Grade 2 3 3 4 2 4 2 3 2 3 4 4 0rgan Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Digestive system] stomach <44> <40> <36> <39> ulcer:glandular stomach 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 1 (3) (0) (0) (0) lymph node with epithelial hyperplasia 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (0)(0)(0)(0)(3)(0)(0)(0) Liver <44> <40> <36> <39> herniation 3 0 0 0 0 0 0 0 0 0 0 1 0 0 0 3 (7) (0) (0) (0) (0) (0) (0) (0)(8) (0) (0) (0) (3) (0) (0) (0)fatty change 2 0 0 0 1 0 0 1 0 0 0 0 0 0 0 0 (5) (0) (0) (0)(3)(0)(0)(0) (3) (0) (0) (0) (0)(0)(0)(0)lymphocytic infiltration 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) granulation 92 2 0 10 1 1 0 3 5 2 0 12 4 6 0 (20) (5) (5) (0) (25) (3) (3) (0) (8) (14) (6) (0) (31) (10) (15) (0)hyperplasia 0 0 1 0 1 0 1 0 0 0 0 0 0 0 0 0 (0)(0)(2)(0) (3) (0) (3) (0) (0)(0)(0)(0)

6 1 0 0

(14) (2) (0) (0)

9

1

(23) (3) (0) (0)

0

0

7 1

0

(19) (3) (0) (0)

0

3

2 0 0

(8) (5) (0) (0)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

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

clear cell focus

(c) c:b/a\*100

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

STUDY NO. : 0162

|            |                        | Group Name<br>No. of Animals on Study | Control 44   | 400 ppm<br>40                               | 2000 ppm<br>36  |                 |
|------------|------------------------|---------------------------------------|--|---|---|-----------------|
| 0rgan      | Findings               | Grade <u>1</u><br>(%)                 | $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$ | $\frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}$ | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ | <u>1</u><br>(%) |
| [Digestive | system]                |                                       |  |   |   |                 |
| liver      | acidophilic cell focus | ( <sup>1</sup><br>( <sup>2</sup> )    | <44><br>1 0 0<br>( 2) ( 0) ( 0)                    | (40><br>1 0 0 0<br>(3) (0) (0) (0)          | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                        | 3<br>(8)(       |
|            | basophilic cell focus  | 4<br>( 9)                             | 0 0 0<br>( 0) ( 0) ( 0)                            | 3 0 0 0<br>(8)(0)(0)(0)                     | 7 1 0 0<br>(19) (3) (0) (0)                                   | 4<br>(10) (     |
|            | vacuolated cell focus  | 2<br>( 5)                             | 0 0 0<br>( 0) ( 0) ( 0)                            | 6 0 0 0<br>(15) (0) (0) (0)                 | 3 0 0 0<br>(8)(0)(0)(0)                                       | 2<br>(5)(       |
|            | spongiosis hepatis     | 9<br>(20)                             | 2 0 0<br>(5)(0)(0)                                 | 9 1 0 0<br>(23) (3) (0) (0)                 | 4 2 0 0<br>(11) (6) (0) (0)                                   | 11<br>(28) (    |
|            | bile duct hyperplasia  | 3<br>( 7)                             | 27 14 0<br>(61)(32)(0)                             | 0 28 12 0<br>( 0) ( 70) ( 30) ( 0)          | 2 28 6 0<br>(6)(78)(17)(0)                                    | 0<br>( 0) (     |
|            | biliary cyst           | 1<br>( 2)                             | 0 0 0<br>( 0) ( 0) ( 0)                            | 0 0 0 0<br>(0)(0)(0)(0)(0)                  | 0 0 0 0<br>(0)(0)(0)(0)(0)                                    | 0<br>( 0) (     |
| pancreas   |                        |                                       | <44>   | <40>  | <36>  |                 |

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

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE SEX

PAGE: 7

10000 ppm 39  $\frac{2}{(\%)}$   $\frac{3}{(\%)}$   $\frac{4}{(\%)}$ 

| (Digestive s                 | system]  |  |                                       |  |  |
|------------------------------|--|--|---------------------------------------|--|--|
| liver                        | acidophilic cell focus   | $\begin{array}{c} <44 \\ 1 & 1 & 0 & 0 \\ (2) & (2) & (0) & (0) \end{array}$ | (3) (0) (0) (0)                       | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0) | <pre> &lt;39&gt;<br/>3 0 0 0<br/>( 8) ( 0) ( 0) ( 0)</pre> |
|                              | basophilic cell focus  | 4 0 0 0<br>( 9) ( 0) ( 0) ( 0)   | 3 0 0 0<br>(8)(0)(0)(0)               | 7 1 0 0<br>(19) (3) (0) (0)            | 4 2 0 0<br>(10)(5)(0)(0)                                   |
|                              | vacuolated cell focus  | 2 0 0 0<br>(5)(0)(0)(0)  | 6 0 0 0<br>(15)(0)(0)(0)              | 3 0 0 0<br>(8)(0)(0)(0)                | 2 0 0 0<br>(5)(0)(0)(0)                                    |
|                              | spongiosis hepatis   | 9 2 0 0<br>(20)(5)(0)(0)   | 9 1 0 0<br>(23) (3) (0) (0)           | 4 2 0 0<br>(11) (6) (0) (0)            | 11 0 0 0<br>(28) (0) (0) (0)                               |
|                              | bile duct hyperplasia  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                         | 0 28 12 0<br>( 0) ( 70) ( 30) ( 0)    | 2 28 6 0<br>(6)(78)(17)(0)             | 0 33 7 0<br>( 0) ( 85) ( 18) ( 0)                          |
|                              | biliary cyst   | 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)                             |
| Pancreas                     | atrophy  | <44><br>14 5 0 0<br>(32) (11) (0) (0)  | <40><br>11 5 1 1<br>(28) (13) (3) (3) | <36><br>14 9 2 0 *<br>(39)(25)(6)(0)   | <39><br>9 4 1 0<br>(23) (10) (3) (0)                       |
|                              | arteritis  | 0 0 1 0<br>( 0) ( 0) ( 2) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           |
| 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 | 4 : Severe   |                                       |  |  |

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

| Organ        | Findings                  | Group Name Control<br>No. of Animals on Study 44<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (9 | $ \begin{array}{c}                                     $ | 2000 ppm<br>36<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|--------------|---------------------------|--|--|---|---|
| [Digestive s | ystem]                    |  | · · · · · · · · · · · · · · · · · · ·                    |   |   |
| Dancreas     | hyperplasia:acinar cəll   | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |  | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| [Urinary sys | tem]                      |  |  |   |   |
| idney        | infarct                   | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |  | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <39><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                |
|              | inflammatory infiltration | 0  |  | 0 0 0 1<br>( 0) ( 0) ( 0) ( 3)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|              | chronic nephropathy       | 2 7 19 18<br>(5)(16)(43)(34  | 5 0 7 10 23<br>1) ( 0) ( 18) ( 25) ( 58)                 | 1 11 12 10<br>(3)(31)(33)(28)                       | 10 9 14 6 *<br>(26) (23) (36) (15)                    |
|              | mineralization:pelvis     | 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)                        |
| Endocrine s  | ystem]                    |  |  |   |   |
| pituitary    | angiectasis               | <44><br>1 0 0 (<br>( 2) ( 0) ( 0) ( 0)   |  | <36><br>3 0 0 0<br>( 8) ( 0) ( 0) ( 0)              | <39><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                |

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

### STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : MALE

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

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PAGE: 9

| Organ         | Findings                     | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>44<br><u>2 3 4</u><br>(%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline 1 & 2 & 3 & 4 \\ \hline \% & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 36 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | $ \begin{array}{c} 10000 \\ 39 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ |
|---------------|------------------------------|--|--|--|---|--|
| [Endocrine sy | stem]                        |  |  |  |   |  |
| pituitary     | cyst                         | 3<br>( 7)  | <44><br>0 0 0<br>( 0) ( 0) ( 0)              | <40><br>2 0 0 0<br>(5) (0) (0) (0)   | <36><br>2 0 0 0<br>( 6) ( 0) ( 0) ( 0)  | <39><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   |
|               | hyperplasia                  | 11<br>( 25)  | 0 0 0<br>( 0) ( 0) ( 0)                      | 7 3 0 0<br>(18) (8) (0) (0)  | 6       2       0       0         (17)       (6)       (0)       (0)  | 5 1 0 0<br>(13) (3) (0) (0)  |
|               | Rathke pouch                 | 0<br>( 0)  | 0 0 0<br>( 0) ( 0) ( 0)                      | 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)   |
| thyroid       | cyst                         | 1<br>( 2)  | <44><br>0 0 0<br>( 0) ( 0) ( 0)              | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <39><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)   |
|               | ultimibranchial body remanet | 0<br>( 0)  | 0 0 0<br>( 0) ( 0) ( 0)                      | 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)   |
|               | C-cell hyperplasia           | 8<br>(18)  | 0 0 0<br>( 0) ( 0) ( 0)                      | 2 1 0 0<br>(5)(3)(0)(0)  | 4 0 0 0<br>(11)(0)(0)(0)  | 5 0 0 0<br>(13)(0)(0)(0)   |
| panc islet    | islet cell hyperplasia       | 0<br>( 0)  | <44><br>0 0 0<br>( 0) ( 0) ( 0)              | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |

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

(IIPT150)

| EPORT TYPE  | · AI<br>· MALE            |   |  |   | PAGE   |
|-------------|---------------------------|---|--|---|--|
| rgan        | Findings                  | Group Name Control<br>No. of Animals on Study 44<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \\ 40 \\ \hline 1 \\ \hline 2 \\ \hline 3 \\ \hline 4 \\ \hline 6 \\ $ | $\begin{array}{c} 2000 \text{ ppm} \\ 36 \\ \hline 1 & 2 & 3 & 4 \\ \hline \% & (\%) & (\%) & (\%) \end{array}$ | 10000 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| indocrine s | vstem]                    |   |  |   |  |
| Irenal      | thrombus                  | $\begin{array}{c} <44 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 2) & ( & 0) & ( & 0) \end{array}$    | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|             | hyperplasia:cortical cell | $\begin{pmatrix} 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{pmatrix} $               | 2 0 0 0<br>(5)(0)(0)(0)  | 2 0 0 0<br>(6)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|             | hyperplasia:medulla       | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 10 2 0 0<br>(25) (5) (0) (0)   | 6 1 0 0<br>(17) (3) (0) (0)   | 4 1 0 0<br>(10) (3) (0) (0)                          |
|             | focal fatty change:cortex | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(5)(0)(0)(0)  | 1 0 0 0<br>(3)(0)(0)(0)   | 3 0 0 0<br>(8)(0)(0)(0)                              |
| eproductive | ə system]                 |   |  |   |  |
| stis        | atrophy                   | $ \begin{array}{cccccc}                                $                                    | <40><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)   | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <39><br>0 1 1 0<br>( 0) ( 3) ( 3) ( 0)               |
|             | mineralization            | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 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)                       |
|             | arteritis                 | 1 4 0 0<br>(2)(9)(0)(0)   | 1 3 0 0<br>(3)(8)(0)(0)  | 0 2 0 0<br>( 0) ( 6) ( 0) ( 0)  | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                       |

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#### (c) c:b/a\*100

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

### BAISZ

| STUDY NO. : 0162<br>ANIMAL : RAT F344<br>REPORT TYPE : A1<br>SEX : MALE |                               | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>SACRIFICED ANIMALS (105W)        |   |   |   |
|---|-------------------------------|---|---|---|---|
| 0rgan   | Findings                      | Group Name Control<br>No. of Animals on Study 44<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \underline{1} & \underline{2} & \underline{3} & \underline{4} \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | مرم 2000<br>36<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | PAGE : 11<br>10000 ppm<br>39<br>$\frac{1 \ 2 \ 3 \ 4}{(\%) \ (\%) \ (\%) \ (\%)}$ |
| [Reproductive   | e system]                     |   |   |   |   |
| testis  | interstitial cell hyperplasia | $\begin{array}{c} <44>\\ 2 & 1 & 0 & 0\\ (5) & (2) & (0) & (0) \end{array}$                 | <40><br>8 0 0 0<br>(20) (0) (0) (0)   | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)              | <39><br>4 0 0 0<br>(10) (0) (0) (0)   |
| epididymis  | degeneration                  | <44><br>6 0 0 0<br>(14) (0) (0) (0)   | <40><br>7 0 0 0<br>(18) (0) (0) (0)   | <36><br>12 0 0 0<br>(33) (0) (0) (0)                | <39><br>8 0 0 0<br>(21) (0) (0) (0)   |
| prostate  | inflammation                  | <44><br>4 0 0 0<br>(9) (0) (0) (0)  | <40><br>5 0 0 0<br>(13) (0) (0) (0)   | <35><br>3 0 0 0<br>( 9) ( 0) ( 0) ( 0)              | <39><br>2 0 0 0<br>(5) (0) (0) (0)  |
|   | hyperplasia                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 1 0 0<br>(3)(3)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| mammary gl  | inflammation                  | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|   | galactocele                   | 0 2 0 0<br>( 0) ( 5) ( 0) ( 0)  | 1 1 0 0<br>(3)(3)(0)(0)   | 1 0 0 0<br>(3)(0)(0)(0)                             | 1 0 0 0<br>(3)(0)(0)(0)   |
| (Nervous syst   | rem]                          |   |   |   |   |
| brain   | mineralization                | $\begin{array}{cccc} & <44 \\ 2 & 0 & 0 & 0 \\ ( & 5) & ( & 0) & ( & 0) \end{array}$        | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <39><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: Number of animals with lesion c: b / a \* 100 b

(c)

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

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

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| STUDY NO. : 0162<br>ANIMAL : RAT F344<br>REPORT TYPE : A1<br>SEX : MALE |                          | HISTOLOGICAL FINDINGS :NON-NE<br>SACRIFICED ANIMALS (105W)                                  | BOPLASTIC LESIONS (SUMMARY)   |  | PAGE : 12  |  |
|---|--------------------------|---|---|--|--|--|
| 0rgan   | Findings                 | Group Name Control<br>No. of Animals on Study 44<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%)  (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 36 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \end{array}$ | 10000 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |  |
| [Special sens   | e organs/appandage]      |   |   |  |  |  |
| өуө   | hemorrhage               | <44><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |  |
|   | cataract                 | 2 0 0 0<br>(5)(0)(0)(0)   | 7 0 0 0<br>(18) (0) (0) (0)   | 4 0 0 0<br>(11)(0)(0)(0)   | 2 0 0 0<br>(5)(0)(0)(0)                              |  |
|   | retinal atrophy          | 5 4 1 0<br>(11) (9) (2) (0)   | 5 10 7 0 **<br>(13) (25) (18) (0)   | 4 7 3 0<br>(11)(19)(8)(0)  | 9 5 2 0<br>(23)(13)(5)(0)                            |  |
|   | degeneration:cornea      | 2 0 0 0<br>(5)(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)                       |  |
| Ilarder gl  | degeneration             | $\begin{array}{c} <44>\\ 0 & 1 & 0 & 0\\ ( & 0) & ( & 2) & ( & 0) & ( & 0) \end{array}$     | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <36><br>4 0 0 0<br>(11) (0) (0) (0)  | <39><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)               |  |
|   | lymphocytic infiltration | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(3)(0)(0)(0)                              |  |
|   | hyperplasia              | 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)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |  |

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

b : Number of animals with lesion b

(c) c:b/a\*100

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

(HPT150)

BAIS2

# APPENDIX L 4

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

RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

| STUDY NO. :<br>ANIMAL :<br>REPORT TYPE : | RAT F344                                    | NISTOLOGICAL FINDINGS :NON-NI<br>SACRIFICED ANIMALS (105\) | EOPLASTIC LESIONS (SUMMARY)  |  |  |
|--|---|--|--|--|--|
| SEX :                                    | FEMALE                                      |  |  |  | PAGE :   |
| Organ                                    | Group Name<br>No. of Anim<br>Grade          | Control<br>als on Study 41<br>(%) (%) (%) (%)              | $ \begin{array}{c} 400 \text{ ppm} \\ 40 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | $ \begin{array}{c} 2000 \text{ ppn} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $     \begin{array}{c}             10000 \text{ ppm} \\             37 \\             \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}             (\%)         $ |
|  |   |  |  |  |  |
| [Integumentar                            | y system/appandage]                         |  |  |  |  |
| skin/app                                 | inflammation                                | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <37><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   |
|  | duct ectasia:sebaceous gland                | 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)  |
| [Respiratory                             | system]                                     |  |  |  |  |
| nasal cavit                              | inflammation                                | <41><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                     | <00> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <37><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|  | eosinophilic change:olfactory epithelium    | 14 12 3 0<br>(34) (29) (7) (0)                             | 12 7 2 0<br>(30)(18)(5)(0)   | 15 13 3 0<br>(37)(32)(7)(0)  | 15 11 5 0<br>(41)(30)(14)(0)   |
|  | eosinophilic change:respiratory epithelium  | 3 0 0 0<br>(7) (0) (0) (0)                                 | 1 0 0 0<br>(3)(0)(0)(0)  | 1 0 0 0<br>(2)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|  | inflammation:foreign body                   | 1 0 0 0<br>(2)(0)(0)(0)(0)                                 | 1 1 0 0<br>(3)(3)(0)(0)  | 2 1 0 0<br>(5)(2)(0)(0)  | 1 0 0 0<br>(3)(0)(0)(0)  |
|  | respiratory metaplasia:olfactory epithelium | 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)   |
| Grade                                    | 1: Slight 2: Moderate 3: Marked             | 4 : Severe   |  |  |  |

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

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

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

### BAIS2

13

| SEX :           | FEMALE                       |   |                            |   |  | PAGE  |
|-----------------|------------------------------|---|----------------------------|---|--|---|
| Organ           | Findings                     | Group Name<br>No. of Animals on Study<br>Grade <u>1 2</u><br>(%) (% |                            | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                        | $ \begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|                 |                              |   |                            |   |  |   |
| [Respiratory s  | system]                      |   |                            |   |  |   |
| nasal cauit     | respiratory metaplasia:gland | 30 1  | <41><br>0 0<br>) ( 0) ( 0) | <40><br>29 1 0 0<br>(73) (3) (0) (0)  | <11><br>28 1 0 0<br>(68) (2) (0) (0)   | <37><br>25 2 0 0<br>(68) (5) (0) (0)  |
| lung            | hemorrhage                   | 0 0   | <41><br>0 0<br>) ( 0) ( 0) | <40><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <37><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|                 | inflammatory infiltration    |   | 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>(3)(0)(0)(0)   |
|                 | accumulation of foamy cells  |   | 0 0<br>) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(5)(0)(0)(0)  | 1 0 0 0<br>( 3) ( 0) ( 0) ( 0)  |
| (llematopoietic | c system]                    |   |                            |   |  |   |
| oone marrow     | granulation                  | 7 2   | <41><br>0 0<br>) ( 0) ( 0) | <40><br>5 0 0 0<br>(13) (0) (0) (0)   | $\begin{array}{c} <41>\\ 5 & 1 & 1 & 0\\ (12) & (2) & (2) & (0) \end{array}$ | <pre> &lt;37&gt;     7 3 0 0     (19) ( 8) ( 0) ( 0)</pre>  |
|                 | increased hematopoiesis      | 2 0<br>(5)(0  | 0 0<br>) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                         | 3 0 0 0<br>(8)(0)(0)(0)   |

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(HPT150)

#### STUDY NO. : 0162 ANIMAL : RAT F344

### REPORT TYPE : A1

SEX : FEMALE

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

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PAGE: 15

|                     |   | oup Name Control<br>. of Animals on Study 41                   | 400 ppm<br>40   | 2000 ppm<br>41  | 10000 maa<br>37  |
|---------------------|---|--|---|---|--|
| -gan                |   | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{41}{(\%)}$ | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)} \frac{4}{(\%)} \frac{4}{(\%)}$ | $\frac{\begin{array}{ccccccccccccccccccccccccccccccccccc$ | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ |
| llematopoietic      | c system]   |  |   |   |  |
| one marrow          | reticulosis   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         | <40><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | <37><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       |
| pleen               | atrophy   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)  | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | <37><br>2 0 0 0<br>(5) (0) (0) (0)   |
|                     | deposit of hemosiderin  | 8 0 0 0<br>(20) (0) (0) (0)                                    | 9 0 0 0<br>(23)(0)(0)(0)  | 2 0 0 0<br>(5)(0)(0)(0)                                   | 2 0 0 0<br>(5)(0)(0)(0)  |
|                     | 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)                            | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)   |
|                     | extramedullary hematopoiesis  | 4 3 0 0<br>(10) (7) (0) (0)                                    | 4 4 0 0<br>(10)(10)(0)(0)   | 3 0 1 0<br>(7)(0)(2)(0)                                   | 2 2 1 0<br>(5)(5)(3)(0)  |
| Circulatory :       | system]   |  |   |   |  |
| eart                | fibrosis  | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | <37><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                       |
| < a ><br>b<br>( c ) | 1: Slight2: Moderate3:a: Number of animals examined at the siteb: Number of animals with lesionc: b / a * 100ifference;*: $P \leq 0.05$ **: $P \leq 0.05$ |  |   |   |  |
| (IIPT150)           |   |  |   |   |  |

| SEX :        | FEMALE                       |  |  |   |  | PAGE :  |
|--------------|------------------------------|--|--|---|--|---|
| Organ        | Findings                     | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>41<br><u>2 3 4</u><br>(%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c} 2000 \\ 41 \\ \underline{1 & 2 & 3 & 4} \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| Circulatory  | system]                      |  |  |   | <u></u>  |   |
| eart         | myocardial fibrosis          | 8<br>(20)  | <41><br>0 0 0<br>( 0) ( 0) ( 0)              | <40><br>10 1 0 0<br>( 25) ( 3) ( 0) ( 0)              | <41><br>13 0 0 0<br>(32) (0) (0) (0)   | <37><br>9 1 0 0<br>( 24) ( 3) ( 0) ( 0)               |
|              | endothelial cell hyperplasia | 1<br>( 2)  | 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)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
| -tery/aort   | arteritis                    | 0<br>( 0)  | <41><br>0 0 0<br>( 0) ( 0) ( 0)              | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <37><br>0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| Digestive sy | stem]                        |  |  |   |  |   |
| al cavity    | inflammation                 | 3<br>( 7)  | <41><br>7 0 0<br>(17) (0) (0)                | <40><br>3 6 0 0<br>( 8) (15) ( 0) ( 0)                | <41><br>4 6 0 0<br>(10) (15) (0) (0)   | <37><br>3 3 0 0<br>( 8) ( 8) ( 0) ( 0)                |
|              | basal coll activation        | 0<br>( 0)  | 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>(3)(0)(0)(0)                               |
|              | epithelial dysplasia         | 0<br>( 0)  | 0 0 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)                               |

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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:b/a\*100 (c)

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

(IIPT150)

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

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PAGE : 17

| Drgan        | Findings                 | Group Name         Control           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline \\ \frac{1}{(\%)} (\%) (\%) (\%) (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 41 \\ \hline (\%) (\%) (\%) (\%) (\%) (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|--------------|--------------------------|---|--|---|---|
| Digestive sy | rstem]                   |   |  |   |   |
| tooth        | inflammation .           | $\begin{array}{c} <41 > \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$  | <40><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)   | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)  | <37><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  |
| tongue       | lymphocytic infiltration | $\begin{array}{cccc} <41 > \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$   | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | arteritis                | 2 0 0 0<br>(5)(0)(0)(0)   | 2 0 0 0<br>(5)(0)(0)(0)  | 3 0 0 0<br>(7)(0)(0)(0)   | 1 0 0 0<br>(3)(0)(0)(0)(0)  |
| esophagus    | basal cell activation    | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>4 0 0 0<br>(11) (0) (0) (0)   |
| stomach      | basal cell activation    | <pre> &lt;41&gt;     0 0 0 0     ( 0) ( 0) ( 0) ( 0)</pre>  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>5 0 0 0 *<br>(14) (0) (0) (0)   |
| iver         | herniation               | <41><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)  | <40><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>2 0 0 0<br>(5) (0) (0) (0)  |
|              | peliasis-like lesian     | $\begin{pmatrix} 1 & 0 & 0 & 0 \\ ( & 2) & ( & 0) & ( & 0) \\ \end{pmatrix} $   | 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

| ANIMAL<br>REPORT TYPE<br>SEX |           |
|------------------------------|-----------|
|                              | Group Nar |

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

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| PAGE | : | 18 |
|------|---|----|
|------|---|----|

| Organ        | Findings                  | Group Name Control<br>No. of Animals on Study 41<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \\ \end{array} $ |
|--------------|---------------------------|---|--|--|---|
| [Digestive s | vstem]                    |   |  |  |   |
| liver        | necrosis:focal            | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <37><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)  |
|              | fatty change              | · 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)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | inflammatory infiltration | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 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)  |
|              | lymphocytic infiltration  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(3)(0)(0)(0)   |
|              | granulation               | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 11 4 4 0<br>(28) (10) (10) (0)   | 15 5 4 0<br>(37) (12) (10) (0)   | 14 4 3 0<br>(38) (11) (8) (0)   |
|              | clear cell focus          | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 0 0 0 0 *<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(2)(0)(0)(0)  | 4 1 0 0<br>(11) (3) (0) (0)   |
|              | basophilic cell focus     | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 18 2 0 0<br>(45)(5)(0)(0)  | 19 2 0 0<br>(46)(5)(0)(0)  | 14 1 0 0<br>(38) (3) (0) (0)  |
|              | vacuolated cell focus     | 2 0 0 0<br>(5)(0)(0)(0)   | 3 0 0 0<br>(8)(0)(0)(0)  | 3 0 0 0<br>(7)(0)(0)(0)  | 1 0 0 0<br>(3)(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) c:b/a\*100

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

| STUDY NO.   | : | 0162     |
|-------------|---|----------|
| ANIMAL      | : | RAT F344 |
| REPORT TYPE | : | A1       |
| SEX         | : | FEMALE   |

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

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| 0rgan                     |  | Group Name         Control           No. of Animals on Study         41           Grade         1         2         3           (%)         (%)         (%) | 40<br>4 1 2                                  | $\frac{3  4}{(\%)  (\%)}  \frac{1}{(\%)}$ | 2000 ppm<br>41<br>2 3 4<br>(%) (%) (%) | $\begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|---------------------------|--|---|--|---|--|--|
| [Digestive sy             | /stem]                                 |   |  |   |  |  |
| liver                     | bile duct hyperplasia                  | <pre>&lt;41&gt; 2 4 0 ( 5) ( 10) ( 0)</pre>   | <0<br>0<br>5<br>0<br>(0)<br>(13)<br>(0)<br>( | 0 0 5                                     | <41><br>1 0 0<br>( 2) ( 0) ( 0)        | <37><br>6 0 0 0 *<br>(16) (0) (0) (0)  |
| pancreas                  | atrophy                                | <pre> &lt;41&gt;     3 2 0     ( 7) ( 5) ( 0)</pre>   | <40><br>0 8 1<br>( 0) ( 20) ( 3) (           | 0 0 2                                     | <41><br>4 2 0<br>(10) (5) (0)          | <37><br>5 4 0 0<br>(14) (11) (0) (0)   |
| [Urinary sys <sup>.</sup> | tem]                                   |   |  |   |  |  |
| kidney                    | infarct                                | <11><br>0 0 0<br>( 0) ( 0) ( 0)   | <40><br>0 0 0<br>( 0) ( 0) ( 0) (            | 0 0 0                                     | <41><br>0 0 0<br>( 0) ( 0) ( 0)        | <37><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   |
|                           | chronic nephropathy                    | 16 7 4<br>(39) (17) (10)  | 3 15 8<br>( 7) ( 38) ( 20) (                 | 8 1 19<br>20) (3) (46)                    | 10 4 4<br>(24) (10) (10)               | 12 9 4 2<br>(32) (24) (11) (5)   |
|                           | mineralization:cortico-medullary junct | tion 5 0 0<br>(12) ( 0) ( 0)  | 0 3 0<br>( 0) ( 8) ( 0) (                    | 0 0 3<br>0)(0)(7)                         | 0 0 0<br>( 0) ( 0) ( 0)                | 1 0 0 0<br>(3)(0)(0)(0)  |
|                           | mineralization:papilla                 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | 0 0 0<br>( 0) ( 0) ( 0) (                    | 0 0 0<br>0) ( 0) ( 0)                     | 0 0 0<br>( 0) ( 0) ( 0)                | 1 0 0 0<br>(3)(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

(IIPT150)

PAGE: 19

| REPORT TYPE<br>SEX | : A1<br>: FEMALE             |   |  |  | PAGE :   |
|--------------------|------------------------------|---|--|--|--|
| 0rgan              | Findings                     | Group Name Control<br>No. of Animals on Study 41<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array} $ |
| [Urinary sys       | tem]                         |   |  |  |  |
| kidney             | mineralization:pelvis        | (41) $(2) (2) (2) (3) (3) (3)$  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <37><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| [Endocrine s       | vstem]                       |   |  |  |  |
| pituitary          | angiectasis                  | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                       | <40><br>5 1 0 0<br>(13) (3) (0) (0)  | <41><br>5 1 0 0<br>(12) (2) (0) (0)  | <37><br>1 1 0 0<br>( 3) ( 3) ( 0) ( 0)   |
|                    | cyst                         | 8 0 0 0<br>(20) (0) (0) (0)   | 3 1 0 0<br>(8)(3)(0)(0)  | 2 0 0 0<br>(5)(0)(0)(0)  | 6 0 0 0<br>(16)(0)(0)(0)   |
|                    | hyperplasia                  | 5 1 0 0<br>(12) (2) (0) (0)   | 10 2 0 0<br>(25)(5)(0)(0)  | 6 5 0 0<br>(15)(12)(0)(0)  | 2 1 0 0<br>(5)(3)(0)(0)  |
|                    | Rathke pouch                 | 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)   | 1 0 0 0<br>(3)(0)(0)(0)  |
| thyroid            | ultimibranchial body remanet | $\begin{array}{cccc} <41>\\ 3 & 0 & 0 & 0\\ ( 7) & ( 0) & ( 0) & ( 0)\end{array}$           | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | $\langle 37 \rangle$<br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   |

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

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

b: Number of animals with lesion b

c:b/a\*100 (c)

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

(HPT150)

BAIS2

| Organ       | Findings                  | Group Name         Control           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 400<br>40<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 2000 \text{ ppm} \\ 41 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|-------------|---------------------------|---|--|---|---|
| Endocrine   | system]                   |   |  |   |   |
| thyroid     | follicular hyperplasia    | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>1 0 0 0<br>(3)(0)(0)(0)   |
|             | C-cell hyperplasia        | $\begin{array}{cccccc} 7 & 0 & 0 & 0 \\ (17) & (0) & (0) & (0) \end{array}$   | 5 1 0 0<br>(13) (3) (0) (0)                    | 7 0 0 0<br>(17) (0) (0) (0)   | 6 1 0 0<br>(16)(3)(0)(0)  |
| adrenal     | peliosis-like lesion      | <41><br>7 1 0 0<br>(17) (2) (0) (0)   | <40><br>11 2 0 0<br>(28) (5) (0) (0)           | <41><br>7 0 0 0<br>(17) (0) (0) (0)   | <37><br>8 0 0 0<br>(22) ( 0) ( 0) ( 0)  |
|             | hyperplasia:cortical cell | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 3 0 0 0<br>(8)(0)(0)(0)                        | 2 0 0 0<br>(5)(0)(0)(0)   | 2 0 0 0<br>(5)(0)(0)(0)   |
|             | hyperplasia:medulla       | 3 0 0 0<br>(7)(0)(0)(0)   | 2 0 0 0<br>(5)(0)(0)(0)                        | 3 0 0 0<br>(7)(0)(0)(0)   | 3 0 0 0<br>(8)(0)(0)(0)   |
|             | focal fatty change:cortex | $\begin{pmatrix} 1 & 0 & 0 & 0 \\ (2) & (0) & (0) & (0) \end{pmatrix}$  | 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)   |
| (Repraducti | ve system]                |   |  |   |   |
| JUary       | cyst                      | $\begin{array}{cccc} <41>\\ 2 & 0 & 0 & 0\\ (5) & (0) & (0) & (0)\end{array}$   | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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 Grade
 1: Stight
 2: moderate
 3: Narked
 4: Severe

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

 b
 b: Number of animals with lesion

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

STUDY NO. : 0162

<sup>(</sup>c) c:b/a \* 100

#### STUDY NO. : 0162 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ANIMAL : RAT F344 SACRIFICED ANIMALS (105W) REPORT TYPE : A1 SEX : FEMALE Group Name Control No. of Animals on Study 41

40 41 37 Grade 2 3 2 3 2 3 4 4 2 3 4 4 Findings\_ (%) (%) (%) 0rgan\_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Reproductive system] uterus <41> <40> <41> <37> hyperplasia:gland 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0)mucous plug 0 1 0 0 0 1 0 0 0 1 0 0 0 0 0 0 (0)(2)(0)(0) (0)(3)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0)cystic endometrial hyperplasia 6 1 0 0 7 0 0 32 2 5 0 0 0 0 0 (15) (2) (0) (0) (18) (0) (0) (0)(7) (5) (0) (0) (5) (14) (0) (0) mammary gl <41> <40> <41> <37> inflammation 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0)(0)(0)(0)(0)(0)(0)(0)(0)(0) (3) (0) (0) hyperplasia 2 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 (5)(0)(0)(0) (3) (0) (0) (0) atypical hyperplasia 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0)(3)(0)(0)(0) (0)(0)(0)(0) galactocele 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 (0) (0) (0) (0)[Nervous system] brain **<**41> <40> **<41>** <37> mineralization 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0)(0)(0)(0)(0)

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

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

b b: Number of animals with lesion

(c) c:b/a\*100

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

#### PAGE : 22

10000 ppm

2000 ppm

400 ppm

#### STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

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PAGE : 23

| 0rgan         | Findings                 | Group Name         Control           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 40 \\ \hline 1 & 2 & 3 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 41 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|---------------|--------------------------|---|--|---|---|
| [Special sens | se organs/appandage]     |   |  |   |   |
| өуө           | hemorrhage               | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|               | cataract                 | 4 0 0 0<br>(10) (0) (0) (0)   | 5 0 0 0<br>(13) (0) (0) (0)  | 6 0 0 0<br>(15) (0) (0) (0)   | 4 0 0 0<br>(11) (0) (0) (0)   |
|               | retinal atrophy          | 4 6 5 0<br>(10) (15) (12) (0)   | 7 3 7 0<br>(18) (8) (18) (0)   | 10 6 9 0<br>(24)(15)(22)(0)   | 4 1 7 0<br>(11) (3) (19) (0)  |
|               | keratitis                | 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)  |
| llarder gl    | degeneration             | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <37><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|               | inflammation             | 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)  | 0 0 0 0<br>( 0) ( 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)  |
|               | 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)  |

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

| STUDY NO. : 0162<br>ANIMAL : RAT F344<br>REPORT TYPE : A1<br>SEX : FEMALE   | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>SACRIFICED ANIMALS (105W)<br>PAGE : 24 |  |   |   |  |  |  |
|---|---|--|---|---|--|--|--|
| Organ Findings  | Group Name Control<br>No. of Animals on Study 41<br>Grade <u>1 2 3 4</u><br>(%) (%) (%)           |  | $\begin{array}{c} 2000 \text{ ppm} \\ 41 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 37 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |  |  |  |
| [Special sense organs/appandage]  |   |  |   |   |  |  |  |
| nasolacr d<br>inflammation  | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0) | $\begin{array}{cccc} & <41> \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$    | <37><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)  |  |  |  |
| [Musculoskeletal system]  |   |  |   |   |  |  |  |
| bane<br>asteosclerasis  | <41><br>7 2 4 0<br>(17) (5) (10) (0)  |  | <41><br>12 3 1 0<br>(29) (7) (2) (0)  | <37><br>8 4 2 0<br>(22) (11) (5) (0)  |  |  |  |
| Grade1 : Slight2 : Mode $\langle a \rangle$ a : Number of animals exarbb : Number of animals with(c)c : b / a * 100Significant difference ;* : P $\leq 0.0$ | nined at the site<br>n lesion   |  |   |   |  |  |  |

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(IIPT150)

BAIS2

# APPENDIX L 5

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

MOSUE : MALE : DEAD AND MORIBUND ANIMALS

MOSUE (2-YEAR STUDY)

STUDY NO, : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

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

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PAGE: 1

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| )rgan          | N                                       | roup Name Control<br>o. of Animals on Study 15<br>rade <u>1 2 3 (</u> (%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 8 \\ 4 \\ \frac{1}{3} \\ \frac{1}{3}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 12 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $\begin{array}{c} 10000 \text{ ppm} \\ 17 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|----------------|-----------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| [Integumentary | v system/appandage]                     |                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                   |                                                                                                                    |
| skin/app       | ulcer                                   | <15><br>0 1 0<br>( 0) ( 7) ( 0) (                                                     | <pre></pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                             |
|                | inflammation                            | 0 1 0<br>( 0) ( 7) ( 0) (                                                             | 0 0 1 0 0<br>0) ( 0) ( 13) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     |
| [Respiratory : | system]                                 |                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                   |                                                                                                                    |
| nasal cavit    | inflammation -                          | <15><br>0 0 0<br>( 0) ( 0) ( 0) (                                                     | <pre></pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <12><br>0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          | <17><br>0 2 0 0<br>( 0) ( 12) ( 0) ( 0)                                                                            |
|                | eosinophilic change:olfactory epitheliu | m 2 1 0<br>(13)(7)(0)(                                                                | 0 4 0 0 0<br>0) (50)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    | 7 0 0 0<br>(41)(0)(0)(0)                                                                                           |
|                | eosinophilic change:respiratory epithel | ium 2 3 1<br>(13)(20)(7)(                                                             | 0 1 0 0 0<br>0) (13)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 2 1 0 0<br>(17) (8) (0) (0)                                                                                       | 3 0 0 0<br>(18) (0) (0) (0)                                                                                        |
|                | inflammation:foreign body               | 0 0 0 ( 0) ( 0) ( 0) (                                                                | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                                                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     |
|                | respiratory metaplasia:olfactory epithe | lium 1 0 0<br>(7)(0)(0)(                                                              | 0 2 0 0 0<br>0) (25)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    | 1 0 0 0<br>(6)(0)(0)(0)                                                                                            |

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

(c)

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

#### STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

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

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PAGE : 2

| )rgan                      | Findings                                                                                                                   | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>15<br><u>2 3 4</u><br>(%) (%) (%) | $ \begin{array}{c} 400 \text{ ppm} \\ 8 \\ \frac{1}{(\%)} & (\%) \\ (\%) & (\%) \\ \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 12 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|----------------------------|----------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|----------------------------------------------|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| Respiratory :              | system]                                                                                                                    |                                                                | , <u>``</u>                                  |                                                                                                  |                                                                                                                   |                                                       |
| nasal cavit                | respiratory metaplasia:gland                                                                                               | 2<br>(13)                                                      | <15><br>3 0 0<br>(20) (0) (0)                | < 8><br>1 1 0 0<br>(13) (13) (0) (0)                                                             | <12><br>3 2 0 0<br>( 25) ( 17) ( 0) ( 0)                                                                          | <17><br>3 1· 0 0<br>(18) (6) (0) (0)                  |
| .ar yn x                   | basal cell activation                                                                                                      | 0<br>( 0)                                                      | <15><br>0 0 0<br>( 0) ( 0) ( 0)              | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                           | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)                |
|                            | epithelial dysplasia                                                                                                       | 0<br>( 0)                                                      | 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>(6)(0)(0)(0)                               |
| lung                       | congestion                                                                                                                 | 0<br>( 0)                                                      | <15><br>1 0 0<br>( 7) ( 0) ( 0)              | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                           | <12><br>1 1 0 0<br>( 8) ( 8) ( 0) ( 0)                                                                            | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0                 |
|                            | inflammatory infiltration                                                                                                  | 2<br>(13)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                      | 1 1 0 0<br>(13)(13)(0)(0)                                                                        | 2 0 0 0<br>(17)(0)(0)(0)                                                                                          | 3 0 0 0<br>(18)(0)(0)(0)                              |
|                            | bronchiolar-alveolar cell hyperplasi                                                                                       |                                                                | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                   | 1 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
| [llematopoieti             | c system]                                                                                                                  |                                                                |                                              |                                                                                                  |                                                                                                                   |                                                       |
| oone marrow                | granulation                                                                                                                | 0<br>( 0)                                                      | <15><br>0 0 0<br>( 0) ( 0) ( 0)              | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                           | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0                 |
| Grade<br>< a ><br>b<br>(c) | <pre>1 : Slight 2 : Moderate a : Number of animals examined at the b : Number of animals with lesion c : b / a * 100</pre> | 3: Marked 4: Sever<br>site                                     | Э                                            |                                                                                                  |                                                                                                                   | · · · · · · · · · · · · · · · · · · ·                 |

| Organ          | Findings                     | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | Control<br>15<br><u>2 3 4</u><br>(%) (%) (%) | 400 ppm<br>8<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 2000 \\ 12 \\ \underline{12} \\ 1$ | .10000 ppm<br>17<br><u>1 2 3 4</u><br>(%) (%) (%) (% |
|----------------|------------------------------|-------------------------------------------------------------|----------------------------------------------|---------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
| [llematopoieti |                              |                                                             |                                              |                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                      |
| spleen         | atrophy                      | 0<br>( 0) (                                                 | <15><br>0 0 0<br>0) ( 0) ( 0)                | <pre></pre>                                       | <12><br>0 0 1 0<br>( 0) ( 0) ( 8) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                |
|                | deposit of melanin           | 0<br>( 0) (                                                 | 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>(6)(0)(0)(0)                              |
|                | extramedullary hematopoiesis | 3<br>(20) (                                                 | 1 0 0<br>7)(0)(0)                            | 2 1 0 0<br>(25)(13)(0)(0)                         | 1 2 0 0<br>(8) (17) (0) (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1 3 1 0<br>(6)(18)(6)(0                              |
| [Circulatory   | system]                      |                                                             |                                              |                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                      |
| heart          | mineralization               | 0<br>( 0) (                                                 | <15><br>0 0 0<br>0) ( 0) ( 0)                | <pre></pre>                                       | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                |
|                | myocardial fibrosis          | 1                                                           | 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 1 0 0<br>(6)(6)(0)(0                               |
| [Digestive sy  | vstem]                       |                                                             |                                              |                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                      |
| oral cavity    | squamous cell hyperplasia    | 0<br>( 0) (                                                 | <15><br>0 0 0<br>0) ( 0) ( 0)                | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <12><br>0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0                |

STUDY NO. : 0163

| oral cavity               | <15>                | < 8>                | <12>                | <17>                |
|---------------------------|---------------------|---------------------|---------------------|---------------------|
| squamous cell hyperplasia | 0 0 0 0             | 0 0 0 0             | 0 0 0 0             | 1 0 0 0             |
|                           | ( 0) ( 0) ( 0) ( 0) | ( 0) ( 0) ( 0) ( 0) | ( 0) ( 0) ( 0) ( 0) | ( 6) ( 0) ( 0) ( 0) |

### b:Number of animals with lesion c:b / a \* 100 b

(c)

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

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

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| STUDY NO.   | : | 0163       |
|-------------|---|------------|
| ANIMAL      | : | MOUSE BDF1 |
| REPORT TYPE | : | A1         |
| SEX         | : | MALE       |

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PAGE: 4

| Organ         | Findings                  | Group Name         Control           No. of Animals on Study         15           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 8 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 2000 \\ 12 \\ 12 \\ \hline (\%) (\%) (\%) (\%) (\%) \end{array}$ | $\begin{array}{c} 10000 \text{ ppm} \\ 17 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|---------------|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| [Digestive sy | /stem]                    |                                                                                                                                                                                   |                                                                                                                      |                                                                                    |                                                                                                                    |
| oral cavity   | basal cell activation     | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                             | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                                                             |
|               | epithelial dysplasia      | 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>(18)(0)(0)(0)                                                                                           |
| tooth         | inflammation              | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                             | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                             |
|               | dysplasia                 | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                              | 1 0 0 0<br>(13) (0) (0) (0)                                                                                          | 2 0 1 0<br>(17) (0) (8) (0)                                                        | 4 0 1 0<br>(24) (0) (.6) (0)                                                                                       |
| saliuary gl   | atrophy                   | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                             | <17><br>0 4 0 0<br>( 0) ( 24) ( 0) ( 0)                                                                            |
| esophagus     | squamous cell hyperplasia | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                             | <17><br>2 0 0 0<br>(12) (0) (0) (0)                                                                                |
|               | basal cell activation     | 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>(6)(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

(IIPT150)

| STUDY NO.   | ; | 0163  |      |
|-------------|---|-------|------|
| ANIMAL      | : | MOUSE | BDF1 |
| REPORT TYPE | : | Λ1    |      |
| SEX         | : | MALE  |      |

0rgan\_\_\_\_

esophagus

stomach

liver

[Digestive system]

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

| Findings                      | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>15<br><u>2 3 4</u><br>(%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 8 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 12 \\ \hline 1 & 3 \\ \hline (\%) & (\%) & (\%) \\ \hline (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|-------------------------------|----------------------------------------------------------------|----------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| vstem]                        |                                                                |                                              |                                                                                                                 |                                                                                                                                 |                                                       |
| epithelial dysplasia          | 0<br>( 0)                                                      | <15><br>0 0 0<br>( 0) ( 0) ( 0)              | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | <17><br>0 1 0 0<br>( 0) ( 6) ( 0) ( 0)                |
| erosion:forestomach           | 0<br>( 0)                                                      | <15><br>0 0 0<br>( 0) ( 0) ( 0)              | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)                |
| erosion:glandular stomach     | 0<br>( 0)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                      | 1 0 0 0<br>(13) (0) (0) (0)                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                  | 1 1 0 0<br>(6)(6)(0)(0)                               |
| hyperplasia:glandular stomach | 1<br>( 7)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                  | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                                                                                                  | 1 0 0 0<br>(6)(0)(0)(0)                               |
| necrosis:focal                | 0                                                              | <15><br>1 0 0                                | < 8><br>0 1 0 0                                                                                                 | <12><br>2 2 0 0                                                                                                                 | <17><br>2 0 0 0                                       |

( 0) ( 13) ( 0) ( 0)

0 0 0 0

0 0 0

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

0

(17) (17) (0) (0)

0 1 0 0

0 0

(0)(8)(0)(0)

0 0

(0)(7)(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

fatty change:central

fatty change

(c) c:b/a\*100

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

(HPT150)

BAIS2

(12) (0) (0) (0)

0 0 0 0

1 0 0 0

(6)(0)(0)(0)

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

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| STUDY NO.   | : | 0163  |      |
|-------------|---|-------|------|
| ANIMAL      | : | MOUSE | BDF1 |
| REPORT TYPE | : | Δ1    |      |
| SEX         | : | MALE  |      |

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| 0rgan                                       | Findings                                                                                                                                      | Group Name Control<br>No. of Animals on Study 15<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c} 2000 \text{ ppm} \\ 12 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 17 \\ \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)} \end{array} $ |
|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| (Digestive sy                               | vstem]                                                                                                                                        |                                                                                             |                                                       |                                                                                                                   |                                                                                                       |
| liver                                       | granulation                                                                                                                                   | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            | <17><br>2 0 0 0<br>(12) (0) (0) (0)                                                                   |
|                                             | basophilic cell focus                                                                                                                         | $\begin{pmatrix} 1 & 2 & 0 & 0 \\ ( & 7) & ( & 13) & ( & 0) & ( & 0) \end{pmatrix}$         | 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)                                                                        |
| gall bladd                                  | granulation                                                                                                                                   | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <12><br>0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                                                                            | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                |
| [Urinary syst                               | rem]                                                                                                                                          |                                                                                             |                                                       |                                                                                                                   |                                                                                                       |
| kidney                                      | hyaline droplet                                                                                                                               | $\begin{array}{cccc} <15> & & \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{array}$  | < 8><br>2 0 0 0<br>( 25) ( 0) ( 0) ( 0)               | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            | <17><br>2 0 0 0<br>( 12) ( 0) ( 0) ( 0)                                                               |
|                                             | basophilic change                                                                                                                             | 3 0 0 0<br>(20)(0)(0)(0)                                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(8)(0)(0)(0)                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                        |
|                                             | deposit of hemosiderin                                                                                                                        | 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)                                                                        |
| Grade<br>< a ><br>b<br>(c)<br>Significant d | 1 : Slight2 : Moderatea : Number of animals examined at thb : Number of animals with lesionc : b / a * 100lifference ; * : $P \leq 0.05$ ** : | 3 : Marked 4 : Severe<br>ne site<br>P ≦ 0.01 Test of Chi Square                             |                                                       |                                                                                                                   |                                                                                                       |

(IIPT150)

BAIS2

| STUDY NO.   | : | 0163  |      |
|-------------|---|-------|------|
| ANIMAL      | : | MOUSE | BDF1 |
| REPORT TYPE | ; | Λ1    |      |
| SEX         | : | MALE  |      |

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| 0rgan        | Findings                              | Group Name Control<br>No. of Animals on Study 15<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 12 \\ \hline \frac{1}{(\%)} (\%) (\%) (\%) (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 17 \\ \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)} \end{array} $ |
|--------------|---------------------------------------|---|---|--|---|
| [Urinary sys | stem]                                 |   |   |  |   |
| k i dney     | lymphocytic infiltration              | $\begin{array}{c} <15 \\ 1 & 0 & 0 \\ (7) & (0) & (0) & (0) \end{array}$                    | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | inflammatory polyp                    | 0 2 0 0<br>( 0) ( 13) ( 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)  |
|              | vacuolization of proximal tubule      | 4 0 0 0<br>(27) (0) (0) (0)   | 2 0 0 0<br>(25)(0)(0)(0)                              | 5 0 0 0<br>(42)(0)(0)(0)   | 6 0 0 0<br>(35)(0)(0)(0)  |
|              | hydronephrosis                        | 0 0 2 0<br>( 0) ( 0) ( 13) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 1<br>( 0) ( 0) ( 0) ( 6)  |
|              | tubular necrosis                      | 0 1 0 0<br>( 0) ( 7) ( 0) ( 0)  | 0 1 0 0<br>( 0) ( 13) ( 0) ( 0)                       | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | mineralization:cortico-medullary junc | tion 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(13) (0) (0) (0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(6)(0)(0)(0)   |
|              | mineralization:pelvis                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(25)(0)(0)(0)                              | 1 0 0 0<br>(8)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | mineralization:cortex                 | 7 0 0 0<br>(47)(0)(0)(0)  | 4 0 0 0<br>(50)(0)(0)(0))                             | 9 0 0 0<br>(75)(0)(0)(0)   | 12 0 0 0<br>(71) (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

| STUDY NO.   | :   | 0163  |      |
|-------------|-----|-------|------|
| ANIMAL      | :   | MOUSE | BDF1 |
| REPORT TYPE | :   | Å1    |      |
| SEX         | : 1 | MALE  |      |

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| PAGE | : | 8 |
|------|---|---|
| <br> |   |   |

| pouch              | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)    | < 8>   | 7100   |  |
|--------------------|---|--|--|--|
| pouch              | 0 0 0 0                                   | < 8>   | (19)   |  |
|                    |   | 1 0 0 0<br>(13) (0) (0) (0)  | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| asia:cortical cell | <15>                                      | < 8>   | <12>   | <17>   |
|                    | 0 0 0 0                                   | 0 0 0 0  | 1 0 0 0  | 0 0 0 0  |
|                    | ( 0) ( 0) ( 0) ( 0)                       | ( 0) ( 0) ( 0) ( 0)  | ( 8) ( 0) ( 0) ( 0)                                  | ( 0) ( 0) ( 0) ( 0)  |
|                    |   |  |  |  |
|                    | (15)                                      | < 8>   | <12>   | <17>   |
|                    | 1 	 0 	 0 	 0                             | 0 0 0 0  | 0 0 0 0  | 0 0 0 0  |
|                    | (7) 	 0) 	 0) 	 0) 	 0)                   | ( 0) ( 0) ( 0) ( 0)  | ( 0) ( 0) ( 0) ( 0)                                  | ( 0) ( 0) ( 0) ( 0)  |
| zation             | 0 2 0 0                                   | 1 0 0 0  | 1 0 0 0  | 2 1 0 0  |
|                    | ( 0) ( 13) ( 0) ( 0)                      | (13)(0)(0)(0)  | ( 8) ( 0) ( 0) ( 0)                                  | (12) (6) (0) (0)   |
| ogenic granuloma   | (15)                                      | < 8>   | <12>   | <17>   |
|                    | 1 	 0 	 0 	 0                             | 0 0 0 0  | 0 0 0 0  | 1 0 0 0  |
|                    | (	 7) 	 (	 0) 	 (	 0) 	 (	 0)             | ( 0) ( 0) ( 0) ( 0)  | ( 0) ( 0) ( 0) ( 0)                                  | ( 6) ( 0) ( 0) ( 0)  |
| ation              | <15>                                      | < 8>   | <12>   | <17>   |
|                    | 1 1 0 0                                   | 0 0 0 0  | 0 0 0 0  | 0 0 0 0  |
|                    | ( 7) ( 7) ( 0) ( 0)                       | ( 0) ( 0) ( 0) ( 0)  | ( 0) ( 0) ( 0) ( 0)                                  | ( 0) ( 0) ( 0) ( 0)  |
|                    | genic granuloma<br>tion<br>2 : Moderate 3 | 1       0       0       0         (7)       0)       (0)       0)       0         genic granuloma       0       2       0       0         (10)       (13)       (0)       (0)       0         (15)       1       0       0       0         (15)       1       0       0       0         (15)       1       1       0       0         (15)       1       1       0       0         (15)       1       1       0       0         (15)       1       1       0       0         (15)       1       1       0       0         (15)       1       1       0       0         (7)       (7)       (0)       (0)       0         (11)       1       0       0       0         (12)       2       Moderate       3       Marked       4         (11)       1       0       0       0       0         (12)       2       Moderate       3       Marked       4       Severe | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c} 1 & 0 & 0 & 0 \\ (7) & (0) & (0) & (0) \\ 2ation \\ genic granuloma \\ tion \\ 2 & Noderate \\ 0 & 1 \\ 2 & Noderate \\ 0 & 1 \\ 3 & 1 \\ 0 \\ 1 \\ 1 \\ 0 \\ 1 \\ 1 \\ 0 \\ 1 \\ 1 \\$ |

(c) c:b/a \* 100 Significant difference; \*:P≦0.05 \*\*:P≦0.01 Test of Chi Square

(IIPT150)

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

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

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| Organ                                     | N   | roup Name Control<br>o. of Animals on Study 15<br>rade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 400 ppm<br>8<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 2000 \text{ ppm} \\ 12 \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|---|---|--|---|--|---|
| [Reproductive                             | ə system]   | · · · · · · · · · · · · · · · · · · ·  |   |  |   |
| prep/cli gl                               | duct ectasia  | <pre> &lt;15&gt;<br/>0 1 0 0<br/>( 0) ( 7) ( 0) ( 0)</pre>                               | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <12><br>0 1 0 0<br>( 0) ( 8) ( 0) ( 0)   | <17><br>0 3 0 0<br>( 0) ( 18) ( 0) ( 0)               |
| [Nervous syst                             | tem]  |  |   |  |   |
| brain                                     | mineralization  | <15><br>3 0 0 0<br>( 20) ( 0) ( 0) ( 0)  | < 8><br>2 0 0 0<br>(25) (0) (0) (0)               | <12><br>3 0 0 0<br>( 25) ( 0) ( 0) ( 0)  | <17><br>5 0 0 0<br>(29) (0) (0) (0)                   |
| [Special sens                             | se organs/appandage]  |  |   |  |   |
| llarder gl                                | degeneration  | <15><br>0 1 0 0<br>( 0) ( 7) ( 0) ( 0)   | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| nasolacr d                                | inflammation  | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)                |
| [Musculoskele                             | otal system]  |  |   |  |   |
| muscle                                    | degeneration  | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <12><br>0 1 0 0<br>( 0) ( 8) ( 0) ( 0)   | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Grade<br>(a)<br>b<br>(c)<br>Significant d | 1: Slight2: Moderate3:a: Number of animals examined at the siteb: Number of animals with lesionc: b / a * 100lifference; $*: P \leq 0.05$ |  |   |  |   |

# APPENDIX L 6

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

MOSUE : FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO.:0163ANIMAL:MOUSE BDF1REPORT TYPE:A1SEX:FEMALE

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

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| 0rgan          | Findings                             | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 24<br>2          | Control<br>4<br>3<br>(%) | -<br>     | <u>1</u> (%) | 2<br>(%)  | 400 ppn<br>23<br><u>3</u><br>(%) | n<br>(%)  | <u>1</u><br>(%) | 25<br>2             | 00 ppm<br><u>3 4</u><br>(%) (%) | 1(%)      | 26<br>2             | 00 ppm<br><u>3 4</u><br>(%) (%) | 5 |
|----------------|--------------------------------------|--|------------------|--------------------------|-----------|--------------|-----------|----------------------------------|-----------|-----------------|---------------------|---------------------------------|-----------|---------------------|---------------------------------|---|
| [Respiratory s | ystem]                               |  |                  |                          |           | • .          |           |                                  |           |                 |                     |                                 |           |                     |                                 |   |
| nasal cavit    | inflammation                         | 2<br>( 8)  | <2-<br>0<br>( 0) | 0                        | 0<br>( 0) | 0<br>( 0)    | 0         | 23><br>0<br>( 0) (               | 0<br>( 0) | 1<br>( 4)       | <25><br>0<br>( 0) ( | 00<br>0)(0)                     | 2<br>( 8) | <26><br>0<br>( 0) ( | ><br>0 0<br>0) ( 0)             | ) |
|                | squamous cell metaplasia             | 0<br>( 0)  | 0<br>( 0)        | 0<br>( 0)                | 0<br>(0)  | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) (                      | 0<br>( 0) | 0<br>( 0)       | 1<br>( 4) (         | 0 0<br>0) ( 0)                  | 0<br>( 0) | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | ) |
|                | epidermal cyst                       | 0<br>( 0)  | 0<br>( 0)        | 0                        | 0<br>( 0) | 0<br>( 0)    | 1<br>( 4) | 0<br>( 0) (                      | 0         | 0<br>( 0)       | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | 0<br>( 0) | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | ) |
|                | eosinophilic change:olfactory epithe | lium 1<br>(4)  | 2<br>( 8)        | 0(0)                     | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0)                        | 0<br>( 0) | 3<br>(12)       | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | 3<br>(12) | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | ) |
|                | eosinophilic change:respiratory epit |  | 3<br>(13)        | 0<br>( 0)                | 0<br>( 0) | 6<br>(26)    | 3<br>(13) | 0                                | 0<br>( 0) | 9<br>(36)       | 5<br>(20) (         | 1 0<br>4) ( 0)                  | 7<br>(27) | 3<br>(12) (         | 0 1<br>0) ( 4)                  | ) |
|                | respiratory metaplasia:olfactory epi |  | 0<br>( 0)        | 0<br>( 0)                | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0                                | 0         | 1<br>(4)        | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | 1<br>( 4) | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | ) |
|                | respiratory metaplasia:gland         | 1<br>( 4)  | 0<br>) ( 0)      | 0<br>( 0)                | 0<br>( 0) | 2<br>(9)     | 0<br>( 0) | 0<br>( 0)                        | 0<br>( 0) | 2<br>( 8)       | 1<br>(4) (          | 0 0<br>0) ( 0)                  | 2<br>( 8) | 0<br>( 0) (         | 0 0<br>0) ( 0)                  |   |
|                | arteritis                            | 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>( 4)       | 0<br>( 0) (         | 0 0<br>0) ( 0)                  | 0<br>( 0) | 0<br>( 0) (         | 0 <sup>°</sup> 0)<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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

| ANIMAL<br>REPORT TYPE |                                       | HISTOLOGICAL FINDINGS :NON-N<br>DEAD AND MORIBUND ANIMALS (0-   |  |   |  |  |  |
|-----------------------|---------------------------------------|---|--|---|--|--|--|
| SEX                   | : FEMALE                              |   |  |   | PAGE :   |  |  |
| Organ                 |                                       | Group Name         Control           No. of Animals on Study         24           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $ \begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array} $ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 26 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array} $ |  |  |
| (Respiratory          | ′system]                              |   |  |   |  |  |  |
| larynx                | basal cell activation                 | <pre> &lt;24&gt;     0     0     0     ( 0) ( 0) ( 0)     ( 0)     ( 0) ( 0)</pre>  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   |  |  |
| ung                   | congestion                            | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)  | <26><br>3 0 0 0<br>(12) (0) (0) (0)  |  |  |
|                       | hemarrhage                            | 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)(4)(0)(0)  |  |  |
|                       | edema                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 1 0 0<br>( 0) ( 4) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |  |  |
|                       | inflammatory infiltration             | 2 0 0 0<br>(8)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(4)(0)(0)(0)   | 4 2 0 0<br>(15)(8)(0)(0)   |  |  |
|                       | lymphocytic infiltration              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 1 0 0<br>( 0) ( 4) ( 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)  | 1 0 0 0<br>(4)(0)(0)(0)  |  |  |
|                       | infiltration:alveolar macrophage      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 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)   |  |  |
|                       |                                       |   |  |   |  |  |  |

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

# STUDY NO.:0163ANIMAL:MOUSE BDF1REPORT TYPE:A1SEX:FEMALE

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

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PAGE: 12

| Organ   | No  | Dup Name Control<br>of Animals on Study 24<br>ade <u>1 2 3 4</u><br>(%) (%) (%) (%)      | $ \begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|---|---|--|--|---|---|
| [Nematopoieti                                 | ic system]  |  |  |   |   |
| bone marrow                                   | granulation   | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)                |
| lymph node                                    | lymphadenitis   | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <225><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)   | <26><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)                |
| spleen  | deposit of melanin  | <24><br>1 1 0 0<br>( 4) ( 4) ( 0) ( 0)   | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                |
|   | extramedullary hematopoiesis  | 4 9 0 0<br>(17)(38)(0)(0)  | 1 8 0 0<br>( 4) ( 35) ( 0) ( 0)  | 3 4 0 0<br>(12)(16)(0)(0)   | 1 5 0 0<br>(4)(19)(0)(0)                              |
| [Circulatory                                  | system]   |  |  |   |   |
| heart   | thrombus  | $\begin{array}{c} <24 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 4) & ( & 0) & ( & 0) \end{array}$ | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>2 0 0 0<br>( 8) ( 0) ( 0) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
|   | mineralization  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
| Grade<br>< a ><br>b<br>( c )<br>Significant ( | 1: Slight2: Moderate3:a: Number of animals examined at the siteb: Number of animals with lesionc: b / a * 100difference; $*: P \leq 0.05$ |  |  |   |   |

(HPT150)

BAIS2

| Organ        | Findings                  | Group Name<br>No. of Animals on Stu<br>Grade | Control<br>dy 24<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|--------------|---------------------------|--|---|--|---|---|
| Circulatory  | system]                   |  |   |  |   |   |
| eart         | myocardial fibrosis       | (  | <24><br>0 0 0 0<br>0) ( 0) ( 0) ( 0)                  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)                | <26><br>2 0 0 0<br>( 8) ( 0) ( 0) ( 0)                |
|              | arteritis                 | (  | 0 0 0 0<br>0) ( 0) ( 0) ( 0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 1 0<br>( 0) ( 0) ( 4) ( 0)                        |
| rtery/aort   | arteritis                 | (  | <24><br>0 0 0 0<br>0) ( 0) ( 0) ( 0)                  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <26><br>0 0 1 0<br>( 0) ( 0) ( 4) ( 0)                |
| Digestive sy | stem]                     |  |   |  |   |   |
| ral cavity   | squamous cell hyperplasia | (  | <24><br>0 0 0 0<br>0) ( 0) ( 0) ( 0)                  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <pre> &lt;26&gt; 0 1 0 0 ( 0) ( 4) ( 0) ( 0)</pre>    |
|              | basal cell activation     | (  | 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 1 0 0<br>(12) (4) (0) (0)                           |
|              | epithelial dysplasia      | (  | 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)                        | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  |

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(c) c:b/a\*100

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

(HPT150)

BAIS2

| STUDY NO. : 0163<br>ANIMAL : MOUSE BDF1<br>REPORT TYPE : A1<br>SEX : FEMALE |                           | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0-105W) |  |   |   | PAGE : 14   |  |
|---|---------------------------|---|--|---|---|---|--|
| Organ   | Findings                  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%)                                   | Control<br>24<br><u>2 3 4</u><br>(%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 26 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |  |
| [Digestive sys  | stem]                     |   |  |   |   |   |  |
| tooth   | inflammation              | 0<br>( 0)   | <24><br>0 0 0<br>( 0) ( 0) ( 0)              | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>2 0 0 0<br>( 8) ( 0) ( 0) ( 0)  |  |
|   | dysplasia                 | 1<br>( 4)   | 0 0 0<br>( 0) ( 0) ( 0)                      | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(8)(0)(0)(0)   | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |  |
| tongue  | erasion                   | 0<br>( 0)   | <24><br>0 0 0<br>( 0) ( 0) ( 0)              | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |  |
|   | inflammation              | 0<br>( 0)   | 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>( 4) ( 0) ( 0) ( 0)  |  |
|   | arteritis                 | 0(0)  | 1 0 0<br>( 4) ( 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)  |  |
| salivary gl   | atrophy                   | 0<br>( 0)   | <24><br>0 0 0<br>( 0) ( 0) ( 0)              | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)  |  |
| esophagus   | squamous cell hyperplasia | 0<br>( 0)   | <24><br>0 0 0<br>( 0) ( 0) ( 0)              | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | ( 25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <26><br>2 0 0 0<br>( 8) ( 0) ( 0) ( 0)  |  |

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

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

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

(IIPT150)

| SEX         | : FEMALE                      |   |  |  | PAGE :  |
|-------------|-------------------------------|---|--|--|---|
| 0rgan       | Findings                      | Group Name         Control           No. of Animals on Study         24           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 26 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| Digestive s | ystem]                        |   |  |  |   |
| esophagus   | basal cell activation         | $\begin{array}{cccc} & <24 \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{array}$   | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <26><br>5 1 0 0 *<br>( 19) ( 4) ( 0) ( 0)   |
|             | epithelial dysplasia          | 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>( 4) ( 0) ( 0) ( 0)  |
| stomach     | erosion:forestomach           | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |
|             | hyperplasia:forestomach       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 2 0 0 0<br>( 8) ( 0) ( 0) ( 0)  |
|             | hyperplasia:glandular stomach | 3 0 0 0<br>(13)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 3 0 0 0<br>(12) (0) (0) (0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| liver       | angiectasis                   | $\begin{array}{c} <24 \\ 1 & 0 & 0 \\ ( 4 ) & ( 0 ) & ( 0 ) & ( 0 ) \end{array}$  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <225><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|             | necrosis:focal                | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(9)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |

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

b

(c)

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

(HPT150)

| Organ        | Findings                  | Group Name<br>No. of Animals on Study<br>Grade <u>1 2</u><br>(%) (%) | Contral<br>24<br><u>3 4</u><br>(%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ \underline{(\%) \ (\%) \ (\%) \ (\%)} \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | 10000 ppm<br>26<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|---------------------------|--|--|--|---|--|
| [Digestive s | :vstem]                   |  |  |  |   |  |
| liver        | fatty change:central      | 0 1  | 24><br>0 0<br>( 0) ( 0)                | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|              | degeneration:central      | 0 1<br>( 0) ( 4)   | 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)                       |
|              | inflammatory infiltration | 0 1<br>( 0) ( 4)   | 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) ( 4) ( 0) ( 0)                       |
|              | granulation               | 0 0<br>( 0) ( 0)   | 0 0<br>( 0) ( 0)                       | 0 0 1 0<br>( 0) ( 0) ( 4) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|              | basophilic cell focus     | 0 0<br>( 0) ( 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>(4)(0)(0)(0)                              |
| pancreas     | atrophy                   | 0 0  | 24><br>0 0<br>( 0) ( 0)                | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)               |
| [Urinary sys | stem]                     |  |  |  |   |  |
| kidney       | infarct                   | 1 0  | 24><br>0 0<br>( 0) ( 0)                | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <226><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |

STUDY NO. : 0163

REPORT TYPE : A1

ANIMAL : MOUSE BDF1

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

b : Number of animals with lesion b

(c) c:b/a\*100

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

(HPT150)

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

GE : 16

| REPORT TYPE : A1<br>SEX : FEMALE |                                       | DEAD AND NORIBUND ANIMALS (0-105W)  |   |  |  |
|----------------------------------|---------------------------------------|---|---|--|--|
| 0rgan                            |                                       | Group Name         Control           No. of Animals on Study         24           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1 \ 2} \ 3 \ 4 \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | PAGE : 17<br>10000 ppm<br>26<br>$\frac{1}{(\%)}$ $(\%)$ $(\%)$ $(\%)$ $(\%)$ |
| [Urinary sys                     | tem]                                  |   |   |  |  |
| kidney                           | hvaline droplet                       | <24><br>2 4 0 0<br>( 8) ( 17) ( 0) ( 0)   | <23><br>2 6 1 0<br>( 9) ( 26) ( 4) ( 0)   | <25><br>1 6 0 0<br>( 4) ( 24) ( 0) ( 0)  | <26><br>1 4 0 0<br>( 4) ( 15) ( 0) ( 0)                                      |
|                                  | basophilic change                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 1 0 0<br>( 0) ( 4) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|                                  | deposit of hemosiderin                | 2 1 0 0<br>( 8) ( 4) ( 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 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 2 0 0<br>( 0) ( 8) ( 0) ( 0)   |
|                                  | hydronephros i s                      | 0 1 0 1<br>( 0) ( 4) ( 0) ( 4)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 2 0<br>( 0) ( 0) ( 8) ( 0)   | 0 1 3 0<br>( 0) ( 4) ( 12) ( 0)  |
|                                  | tubular necrosis                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 2 0 0<br>( 0) ( 9) ( 0) ( 0)  | 0 2 0 0<br>( 0) ( 8) ( 0) ( 0)   | 0 2 1 0<br>( 0) ( 8) ( 4) ( 0)   |
|                                  | mineralization:cortico-medullary junc | tion 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>( 4) ( 0) ( 0) ( 0)   |
|                                  | mineralization:papilla                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

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

STUDY NO. : 0163

: MOUSE BDF1

ANIMAL

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

| REPORT TYPE  | : MOUSE BDF1                   | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0-105W)<br>PAGE : 18 |   |  |  |  |
|--------------|--------------------------------|--|---|--|--|--|
| 0rgan        | Findings                       | Group Name Control<br>No. of Animals on Study 24<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)                | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $\frac{10000 \text{ ppm}}{26}$ $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ |  |
| [Endocrine s | vstem]                         |  |   |  |  |  |
| pituitary    | angiectasis                    | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <22><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)  | <25><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |  |
|              | ovst                           | 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)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |  |
|              | hyperplasia                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 2 0 0 0<br>(9)(0)(0)(0)   | 2 0 0 0<br>( 8) ( 0) ( 0) ( 0)   | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   |  |
| [Reproductiv | e system]                      |  |   |  |  |  |
| DVary        | hemorrhage                     | $\begin{array}{c} <24 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 4) & ( & 0) & ( & 0) \end{array}$                   | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |  |
|              | thrombus                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 1 0 0<br>( 0) ( 4) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   |  |
|              | 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)   |  |
| uterus       | cystic endometrial hyperplasia | $\begin{array}{c} <24 \\ 2 & 2 & 0 & 0 \\ ( & 8) & ( & 8) & ( & 0) & ( & 0) \end{array}$                   | <23><br>3 2 0 0<br>(13) (9) (0) (0)   | <25><br>3 5 0 0<br>(12) (20) (0) (0)   | <25><br>4 5 0 0<br>(16) (20) (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 ; \*:  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

| 0rgan        | Findings            | No. of Animals on Study 24<br>Grade 1 2 | ntrol<br><u>3 4</u><br>%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ 1 & 2 & 3 \\ (\%) & (\%) & (\%) & (\%) \\ (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array} $ | 10000 ppm<br>26<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|---------------------|---|-------------------------------|--|---|--|
| Reproductive | ə system]           |   |                               |  |   |  |
| ammary gl    | hyperplasia         | <24><br>0 0<br>( 0) ( 0) (              |                               | <23><br>1 0 0 0<br>4) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)               |
|              | galactocele         | 0 0<br>( 0) ( 0) (                      |                               | 1 0 0 0<br>4) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(4)(0)(0)(0)   | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                       |
| rep/cligl    | duct ectasia        | <24><br>0 0<br>( 0) ( 0) (              | 0 0<br>0)(0)(                 | <23><br>0 0 0 0<br>0) ( 0) ( 0) ( 0)   | <25><br>0 0 1 0<br>( 0) ( 0) ( 4) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                |
| lervous syst | rem]                |   |                               |  |   |  |
| ain          | hemorrhage          | <24><br>1 0<br>( 4) ( 0) (              | 0 0<br>0)(0)(                 | <23><br>0 0 0 0<br>0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|              | mineralization      | 8 0<br>(33)(0)(                         | 0 0<br>0)(0)(;                | 5 0 0 0<br>22) ( 0) ( 0) ( 0)  | 6 0 0 0<br>(24)(0)(0)(0)  | 7 0 0 0<br>(27)(0)(0)(0)                             |
| Special sens | e organs/appandage] |   |                               |  |   |  |
| V⊖           | retinal atrophy     | <24><br>1 0<br>( 4) ( 0) (              | 0 0<br>0)(0)(                 | <23><br>0 0 0 0<br>0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

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

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

STUDY NO. : 0163

ANIMAL : MOUSE BDF1

## STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

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

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| 0rgan          | Findings                  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | Control<br>24<br><u>2 3 4</u><br>(%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 23 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array} $ | $\begin{array}{c} 10000 \text{ ppm} \\ 26 \\ \hline (\%) & (\%) & (\%) & (\%) \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|----------------|---------------------------|---|--|--|---|--|
| [Special sense | e organs/appandage]       |   |  |  |   |  |
| llarder gl     | inflammatory infiltration | 0<br>( 0)   | <24><br>0 0 0<br>( 0) ( 0) ( 0)              | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   |
|                | hyperplasia               | 0<br>( 0)   | 0 0 0<br>( 0) ( 0) ( 0)                      | 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)   |
| [Musculoskelet | tal system]               |   |  |  |   |  |
| muscle         | mineralization            | 1 ( 4)  | <24><br>0 0 0<br>( 0) ( 0) ( 0)              | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |

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

(IIPT150)

BAIS2

## PAGE : 20

## APPENDIX L 7

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

| STUDY NO.   | : 0163 | 3       |
|-------------|--------|---------|
| ANIMAL.     | : MOUS | SE BDF1 |
| REPORT TYPE | : A1   |         |
| SEX         | : MALI | 3       |

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

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PAGE : 1

| 0rgan         |  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | Contro<br>35<br>2 3<br>(%) (%) | 4<br>(%)    | 1 2<br>(%) (%)    | 400 ppm<br>42<br>3 4<br>(%) (%) | <u>1</u><br>(%) | 2000 p<br>38<br>2 3<br>(%) (%) | pm<br>4<br>(%) | <u>1</u><br>(%) ( | 10000 ppm<br>33<br>2 3 4<br>%) (%) (%) |
|---------------|--|---|--------------------------------|-------------|-------------------|---------------------------------|-----------------|--------------------------------|----------------|-------------------|--|
| [Integumentar | y system/appandage]                    |   |                                |             |                   |                                 |                 |                                |                |                   |  |
| skin/app      | ulcer                                  | 0<br>( 0) (   | <35><br>0 0<br>( 0) ( 0)       | 0<br>( 0) ( | 0 3               | (42><br>0 0<br>( 0) ( 0)        | 0               | <38><br>1 0<br>3) ( 0)         | 0<br>( 0)      |                   | <33><br>0 0 0<br>0) ( 0) ( 0)          |
|               | inflammation                           | 0<br>( 0) (   | 0 0<br>( 0) ( 0)               | 0<br>( 0) ( | 0 1<br>0) ( 2)    | 0 0<br>( 0) ( 0)                | 0<br>( 0) (     | 0 0<br>0) ( 0)                 | 0<br>( 0)      | 0<br>( 0) (       | 0 0 0<br>0) ( 0) ( 0)                  |
|               | epidermal cyst                         | 0<br>( 0) (   | 0 0<br>(0)(0)                  | 0<br>( 0) ( | 0 1<br>0) ( 2)    | 0 0<br>( 0) ( 0)                | 1<br>( 3) (     | 0 0<br>0) ( 0)                 | 0<br>( 0)      | 0<br>( 0) (       | 0 0 0<br>0)(0)(0)                      |
| [Respiratory  | system]                                |   |                                |             |                   |                                 |                 |                                |                |                   |  |
| nasal cavit   | eosinophilic change:olfactory epitheli | um 11<br>(31)   | <35><br>0 0<br>( 0) ( 0)       | 0<br>( 0) ( | 22 0              | <42><br>0 0<br>0 ( 0) ( 0)      | 12<br>(32) (    | <38><br>0 0<br>0) ( 0)         | 0<br>( 0)      |                   | <33><br>0 0 0<br>0) ( 0) ( 0)          |
|               | eosinophilic change:respiratory epithe |   | 6 1<br>(17) (3)                | 0<br>( 0) ( | 11 2<br>26) ( 5)  | 0 0<br>( 0) ( 0)                | 14<br>(37) (    | 4 0<br>11) ( 0)                | 0<br>( 0)      | 7<br>(21) (       | 1 1 0<br>3) ( 3) ( 0)                  |
|               | respiratory metaplasia:olfactory epith |   | 0 0<br>( 0) ( 0)               |             | 11 0<br>26) ( 0)  | 0 0<br>( 0) ( 0)                | 4<br>(11) (     | 0 0<br>0) ( 0)                 | 0<br>( 0)      |                   | 0 0 0<br>0)(0)(0)                      |
|               | respiratory metaplasia:gland           | 10<br>( 29)   | 14 2<br>(40) (6)               |             | 13 14<br>31) (33) | 1 0<br>(2)(0)                   | 15<br>(39) (    | 10 1<br>26) ( 3)               | 0<br>( 0)      |                   | 3 0 0*<br>9)(0)(0)                     |

(c) c:b/a \* 100

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

#### STUDY NO. : 0163 ANIMAL : NOUSE BDF1 REPORT TYPE : A1 SEX : MALE

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

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PAGE: 2

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| Organ         |                                       | Group Name         Control           No. of Animals on Study         35           Grade         1         2         3           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 33 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|---------------|---------------------------------------|---|--|---|---|
| Respiratory   | system]                               |   |  |   |   |
| larynx        | squamous cell hyperplasia             | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <33><br>1 0 0 0<br>(3)(0)(0)(0)   |
|               | basal cell activation                 | 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)  | 2 0 0 0<br>(6)(0)(0)(0)   |
|               | epithelial dysplasia                  | 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)   |
| ung           | inflammation                          | $\begin{array}{cccc} <35 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 3) & ( & 0) & ( & 0) \end{array}$   | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <33><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<br>( 0) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(6)(0)(0)(0)   |
|               | bronchiolar-alveolar cell hyperplasia | 3 0 0 0<br>(9)(0)(0)(0)   | 1 0 0 0<br>(2)(0)(0)(0)  | 1 0 0 0<br>(3)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|               | infiltration:alveolar macrophage      | 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)  |
| [llematopoiet | ic system]                            |   |  |   |   |
| lymph node    | lymphadenitis                         | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <42><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)   | $\begin{array}{c} <38 \\ 1 & 0 & 0 & 0 \\ ( 3) & ( 0) & ( 0) & ( 0) \end{array}$                                  | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |

b b : Number of animals with lesion

(c) c: b / a \* 100 Significant difference ; \*:  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

| ANIMAL :<br>REPORT TYPE : | : 0163<br>: MOUSE BDF1<br>: A1<br>: MALE |   | J FINDINGS :NON-NI<br>NNIMALS (105W)        | EOPLASTIC LESIONS (SUMMARY)  |   | PAGE :   |
|---------------------------|--|---|---|--|---|--|
| Organ                     | Findings                                 | Group Name<br>No. of Animals on Study<br>Grade <u>1 2</u><br>(%) (% | Control<br>35<br>2 <u>3 4</u><br>%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%)  (\%) \end{array}$ | 10000 ppm<br>33<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| [llematopoieti            | ic system]                               |   |   |  |   |  |
| spleen                    | deposit of melanin                       | 0 (<br>( 0) ( 0   | <35><br>0 0 0<br>0) ( 0) ( 0)               | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <38><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <33><br>1 1 0 0<br>( 3) ( 3) ( 0) ( 0)               |
|                           | extramedullary hematopoiesis             |   | 0 0 0<br>0)(0)(0)                           | 2 4 0 0 <sup>-</sup><br>(5)(10)(0)(0)  | 2 1 0 0<br>(5)(3)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|                           | follicular hyperplasia                   |   | ) 0 0<br>))(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 2 0 0 0<br>(5)(0)(0)(0)   | 3 0 0 0<br>(9)(0)(0)(0)                              |
| Circulatory               | system]                                  |   |   |  |   |  |
| eart                      | mineralization                           |   | <35><br>) 0 0<br>)) ( 0) ( 0)               | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|                           | myocardial fibrosis                      |   | ) 0 0<br>))(0)(0)                           | 2 1 0 0<br>(5)(2)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| rtery/aort                | mineralization                           |   | <35><br>) 0 0<br>)) ( 0) ( 0)               | <42><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)   | <38><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |

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

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

b

(c)

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

(HPT150)

BAIS2

| STUDY NO.   | : 0163       |
|-------------|--------------|
| ANIMAL      | : MOUSE BDF1 |
| REPORT TYPE | ÷ A1         |
| SEX         | : MALE       |

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

 $\overline{\phantom{a}}$ 

| SEX :         | MALE                      |                                                                                             |                                                                                                                  |                                                                                                                          | PAGE : 4                                                                                                     |
|---------------|---------------------------|---------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| 0rgan         | Findings                  | Group Name Control<br>No. of Animals on Study 35<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 33 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ |
| [Circulatory  | system]                   |                                                                                             |                                                                                                                  |                                                                                                                          |                                                                                                              |
| artery/aort   | arteritis                 | $\begin{array}{ccc} & <35 \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{array}$      | <42><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                       |
| [Digestive sy | stem]                     |                                                                                             |                                                                                                                  |                                                                                                                          |                                                                                                              |
| oral cavity   | inflammation              | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | $\begin{array}{cccc} & <42> \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$                           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <33><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                       |
|               | squamous 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>(5)(0)(0)(0)                                                                                                  | 7 5 0 0 **<br>(21) (15) (0) (0)                                                                              |
|               | basal cell activation     | 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)                                                                                                  | 12 5 0 0 **<br>(36) (15) (0) (0)                                                                             |
|               | epithelial dysplasia      | 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)                                                                                           | 18 3 0 0 **<br>(55)(9)(0)(0)                                                                                 |
| tooth         | cyst                      | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                                   | <33><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: Number of animals with lesion c: b / a \* 100 b

(c)

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

(HPT150)

BAIS2

### STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1

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

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| REPORT | TYPE | : | Λ1   |
|--------|------|---|------|
| SEX    |      | : | MALE |

| Organ        | Findings              | Group Name Control<br>No. of Animals on Study 35<br>Grade <u>1 2 3</u><br>(%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \hline (\%) & \frac{1}{(\%)} & \frac{2}{(\%)} & \frac{3}{(\%)} & (\%) \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 33 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ |
|--------------|-----------------------|---------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| [Digestive s | vstem]                |                                                                                       |                                                                                                                                                                   |                                                                                                                          |                                                                                                              |
| tooth        | inflammation          | <35><br>5 0 0<br>(14) (0) (0) (                                                       | <pre>&lt;42&gt; 0 4 0 0 0 0) (10) (0) (0) (0)</pre>                                                                                                               | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                                   | <33><br>2 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                                                       |
|              | dysplasia             | $egin{array}{cccccccccccccccccccccccccccccccccccc$                                    | 0 7 2 1 0<br>0) (17) (5) (2) (0)                                                                                                                                  | 11 0 5 1<br>(29) (0) (13) (3)                                                                                            | 3 0 1 1<br>(9)(0)(3)(3)                                                                                      |
| tongue       | epithelial dysplasia  | <35><br>0 0 0<br>( 0) ( 0) ( 0) (                                                     | <42><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                       | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <33><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                       |
|              | arteritis             | 1 0 0<br>( 3) ( 0) ( 0) (                                                             | 0 0 1 0 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)                                                                               |
| salivary gl  | atrophy               | <35><br>0 0 0<br>( 0) ( 0) ( 0) (                                                     | 0         0         0         0         0           0)         (         0)         (         0)         (         0)                                             | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | $\begin{array}{c} <33>\\ 1 & 1 & 0 & 0\\ ( 3) & ( 3) & ( 0) & ( 0) \end{array}$                              |
|              | mineralization        | 0 0 0<br>( 0) ( 0) ( 0) (                                                             | 0 1 0 0 0<br>0) ( 2) ( 0) ( 0) ( 0)                                                                                                                               | 0 0 0 0<br>(0)(0)(0)(0)(0)                                                                                               | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                               |
| esophagus    | basal cell activation | <35><br>0 0 0<br>( 0) ( 0) ( 0) (                                                     | <pre> &lt;42&gt; 0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)</pre>                                                                                                           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <333><br>7 1 0 0 **<br>(21) (3) (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

PAGE : 5

| rgan         | Findings                      | Group Name         Control           No. of Animals on Study         35           Grade         1         2         3         4 | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \hline (\%) (\%) (\%) (\%) (\%) \\ (\%) (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 33 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|--------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| Digestive sy | rstem]                        |                                                                                                                                 |                                                                                                      |                                                                                                                  |                                                                                                                           |
| sophagus     | epithelial dysplasia          | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                               | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | $\begin{array}{c} \langle 33 \rangle \\ 1 & 0 & 0 & 0 \\ ( 3) & ( 0) & ( 0) & ( 0) \end{array}$                           |
| tomach       | basal cell activation         | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                               | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <33><br>1 0 0 0<br>(3) (0) (0) (0)                                                                                        |
|              | epithelial dysplasia          | 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:forestomach           | 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)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                            |
|              | 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)                                                                                   | 3 0 0 0<br>(9)(0)(0)(0)                                                                                                   |
|              | erosioniglandular stomach     | 1 0 0 0<br>(3)(0)(0)(0)                                                                                                         | 3 0 0 0<br>(7)(0)(0)(0)                                                                              | 1 0 0 0<br>(3)(0)(0)(0)                                                                                          | 1 0 0 0<br>(3)(0)(0)(0)                                                                                                   |
|              | hyperplasia:glandular stomach | 10 13 2 0<br>(29)(37)(6)(0)                                                                                                     | 19 11 1 0<br>(45)(26)(2)(0)                                                                          | 13 12 1 0<br>(34)(32)(3)(0)                                                                                      | 7 4 0 0 **<br>(21) (12) (0) (0)                                                                                           |
| arge intes   | inflammatory infiltration     | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                               | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <33><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                                    |

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BAIS2

| STUDY NO.   | : 0163       |
|-------------|--------------|
| ANIMAL      | : MOUSE BDF1 |
| REPORT TYPE | : A1         |
| SEX         | : MALE       |

| HISTOLOGICAL FINDIN | GS :NON-NEOPLASTIC | LESIONS | (SUMMARY) |
|---------------------|--------------------|---------|-----------|
| SACRIFICED ANIMALS  | (105W)             |         |           |

PAGE : 7

| 0rgan      | Findings                  | Group Name         Control           No. of Animals on Study         35           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 33 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|------------|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| [Digestive | system]                   |                                                                                                                                                                                   |                                                                                                                  |                                                                                                                  |                                                                                                                           |
| liver      | angiectasis               | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | <42><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                                                                           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <33><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                                    |
|            | necrosis:focal            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                    | 1 0 2 0<br>(2)(0)(5)(0)                                                                                          | 1 0 1 0<br>(3)(0)(3)(0)                                                                                          | 0 1 1 0<br>( 0) ( 3) ( 3) ( 0)                                                                                            |
|            | fatty change              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                    | 2 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)                                                                                            |
|            | inflammatory infiltration | 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)                                                                                            |
|            | granulation               | 3 0 0 0<br>(9)(0)(0)(0)                                                                                                                                                           | 1 2 0 0<br>(2)(5)(0)(0)                                                                                          | 4 3 0 0<br>(11) (8) (0) (0)                                                                                      | 2 1 0 0<br>(6)(3)(0)(0)                                                                                                   |
|            | 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)                                                                                            |
|            | clear cell focus          | 0 2 0 0<br>( 0) ( 6) ( 0) ( 0)                                                                                                                                                    | 1 0 0 0<br>(2)(0)(0)(0)                                                                                          | 4 0 0 0<br>(11) (0) (0) (0)                                                                                      | 2 0 0 0<br>(6)(0)(0)(0)                                                                                                   |
|            | basophilic cell focus     | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                              | 3 0 0 0<br>(7)(0)(0)(0)                                                                                          | 4 0 0 0<br>(11) (0) (0) (0)                                                                                      | 1 0 0 0<br>(3)(0)(0)(0)                                                                                                   |
| Grade      | 1:Slight 2:Moderate       | 3: Marked 4: Severe                                                                                                                                                               |                                                                                                                  |                                                                                                                  |                                                                                                                           |

Slight 2 : Moderate 3 : Marked 4 : Severe

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

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

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

| ANIMAL<br>REPORT TYPE | : 0163<br>: MOUSE BDF1<br>: A1<br>: MALE | HISTOLOGICAL FINDINGS :NON-<br>SACRIFICED ANIMALS (105W)                                                                                                                          | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>SACRIFICED ANIMALS (105W)<br>PAGE : 8                 |                                                     |                                                                                                                    |  |  |  |
|-----------------------|------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|--|--|--|
| Organ                 | Findings                                 | Group Name         Control           No. of Animals on Study         35           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 2000 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{c} 10000 \text{ ppm} \\ 33 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |  |  |  |
| (Digestive s          | system]                                  |                                                                                                                                                                                   |                                                                                                                  |                                                     |                                                                                                                    |  |  |  |
| liver                 | vacuolated cell focus                    | <35><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                                                                                            | <42><br>2 1 0 0<br>( 5) ( 2) ( 0) ( 0)                                                                           | <38><br>2 0 0 0<br>(5) (0) (0) (0)                  | <33><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                             |  |  |  |
|                       | mixed cell focus                         | 2 1 0 0<br>(6)(3)(0)(0)                                                                                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 2 0 0 0<br>(5)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     |  |  |  |
|                       | biliary cyst                             | 2 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)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     |  |  |  |
| [Urinary sys          | stem]                                    |                                                                                                                                                                                   |                                                                                                                  |                                                     |                                                                                                                    |  |  |  |
| kidney                | cyst                                     | <35><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                                                                                            | <42><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                             |  |  |  |
|                       | basophilic change                        | 17 0 0 0<br>(49)(0)(0)(0)(0)                                                                                                                                                      | 8 2 0 0 *<br>(19) (5) (0) (0)                                                                                    | 11 1 0 0<br>(29)(3)(0)(0)                           | 11 0 0 0<br>(33)(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<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     |  |  |  |
|                       | lymphocytic infiltration                 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                             | 2 0 0 0<br>(5)(0)(0)(0)                                                                                          | 2 0 0 0<br>(5)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     |  |  |  |

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

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

b

(c) c:b/a\*100

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

| STUDY NO.       : 0163         ANIMAL       : MOUSE BDF1         REPORT TYPE       : A1         SEX       : MALE |                                           | HISTOLOGICAL FINDINGS :NON-<br>SACRIFICED ANIMALS (105W) | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>SACRIFICED ANIMALS (105W)                             |                                                                                                                          |                                                                                                   |  |  |
|------------------------------------------------------------------------------------------------------------------|-------------------------------------------|----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|--|--|
| Organ                                                                                                            | Group                                     | f Animals on Study 35                                    | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | PAGE: 9<br>10000 ppm<br>33<br>$\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$ |  |  |
| [Urinary syst                                                                                                    | iem]                                      |                                                          |                                                                                                                  |                                                                                                                          |                                                                                                   |  |  |
| kidney                                                                                                           | osseous metaplasia                        | <35><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                   | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                            |  |  |
|                                                                                                                  | vacuolization of proximal tubule          | 23 0 0 0<br>(66)(0)(0)(0)                                | 30 0 0 0<br>(71) (0) (0) (0)                                                                                     | 36 0 0 0 **<br>(95)(0)(0)(0)                                                                                             | 22 0 0 0<br>(67)(0)(0)(0)                                                                         |  |  |
|                                                                                                                  | mineralization:cortico-medullary junction | 3 0 0 0<br>(9)(0)(0)(0)                                  | 1 0 0 0<br>(2)(0)(0)(0)                                                                                          | 2 0 0 0<br>(5)(0)(0)(0)                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                    |  |  |
|                                                                                                                  | mineralization:papilla                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | 1 0 0 0<br>(2)(0)(0)(0)                                                                                          | 3 0 0 0<br>(8)(0)(0)(0)                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                    |  |  |
|                                                                                                                  | mineralization:pelvis                     | 2 0 0 0<br>(6)(0)(0)(0)                                  | 3 0 0 0<br>(7)(0)(0)(0)                                                                                          | 2 0 0 0<br>(5)(0)(0)(0)                                                                                                  | 3 0 0 0<br>(9)(0)(0)(0)                                                                           |  |  |
|                                                                                                                  | mineralization:cortex                     | 26 0 0 0<br>(74) ( 0) ( 0) ( 0)                          | 37 0 0 0<br>(88) (0) (0) (0)                                                                                     | 29 0 0 0<br>(76) ( 0) ( 0) ( 0)                                                                                          | 30 0 0 0<br>(91)(0)(0)(0)                                                                         |  |  |
|                                                                                                                  | glomerulosclerosis                        | 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)                                                                                           | 0 0 1 0<br>( 0) ( 0) ( 3) ( 0)                                                                    |  |  |
| urin bladd                                                                                                       | inflammation                              | <35><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                   | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                            |  |  |

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Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a> a : Number of animals examined at the site b b : Number of animals with lesion (c) c:b/a\*100

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

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

Findings\_

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

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| Group Name       |         | (   | Control | l   |     |     | 100 ppr | n   |     | 20  | )00 ppr | n   |
|------------------|---------|-----|---------|-----|-----|-----|---------|-----|-----|-----|---------|-----|
| No. of Animals o | n Study | 3   | 5       |     |     | 4   | 2       |     |     | 30  | 3       |     |
| Grade            | 1       | 2   | 3       | 4   | 1   | 2   | 3       | 4   | 1   | 2   | 3       | 4   |
|                  | (%)     | (%) | (%)     | (%) | (%) | (%) | (%)     | (%) | (%) | (%) | (%)     | (%) |

[Endocrine system]

0rgan\_\_\_\_

| LANDON THE SY | Stem                      |  |  |  |  |
|---------------|---------------------------|--|--|--|--|
| pituitary     | angiectasis               | <34><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0) | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|               | cyst                      | 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)           |
| adrenal       | hyperplasia:cortical cell | <35><br>2 0 0 0<br>( 6) ( 0) ( 0) ( 0) | <42><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <38><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0) | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| [Reproductive | > system]                 |  |  |  |  |
| testis        | atrophy                   | <35><br>2 2 0 0<br>( 6) ( 6) ( 0) ( 0) | <42><br>5 5 0 0<br>(12) (12) (0) (0)   | <38><br>3 4 1 0<br>( 8) (11) ( 3) ( 0) | <333><br>0 6 0 0<br>( 0) ( 18) ( 0) ( 0) |
|               | mineralization            | 2 1 0 0<br>(6)(3)(0)(0)                | 9 6 0 0 *<br>(21) (14) (0) (0)         | 3 9 1 0 *<br>(8)(24)(3)(0)             | 6 1 0 0<br>(18) (3) (0) (0)              |
|               | xanthosranuloma           | 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)         | 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:b/a\*100 (c)

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

(HPT150)

BAIS2

PAGE : 10

10000 ppm

33  $\frac{2}{(\%)}$   $\frac{3}{(\%)}$   $\frac{4}{(\%)}$ 

(%)

#### STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

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

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| Organ         | Findings                  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>35<br>2 3 4<br>(%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 42 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 38 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 10000 \text{ ppm} \\ 33 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|---------------|---------------------------|--|---------------------------------------|--|---|--|
| [Reproductive | system]                   |  |                                       |  |   |  |
| epididymis    | lymphocytic infiltration  | 0<br>( 0)  | <35><br>1 0 0<br>( 3) ( 0) ( 0)       | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|               | spermatogenic granuloma   | 2<br>( 6)  | 0 0 0<br>( 0) ( 0) ( 0)               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 1 0<br>( 0) ( 0) ( 3) ( 0)  | 1 0 0 0<br>(3)(0)(0)(0)  |
| semin ves     | mineralization            | 0<br>( 0)  | <35><br>0 0 0<br>( 0) ( 0) ( 0)       | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <38><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|               | inflammatory infiltration | 0<br>( 0)  | 0 0 0<br>( 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)   |
| prep/cli gl   | duct ectasia              | 3<br>( 9)  | <35><br>12 0 0<br>( 34) ( 0) ( 0)     | <42><br>1 11 1 0<br>( 2) ( 26) ( 2) ( 0)   | $\langle 38 \rangle$<br>1 16 0 0<br>( 3) (42) ( 0) ( 0)   | <33><br>0 9 0 0<br>( 0) ( 27) ( 0) ( 0)  |

## [Nervous system]

| brain          | <35>             | <42>             | <38>             | <33>             |
|----------------|------------------|------------------|------------------|------------------|
| mineralization | 8 0 0 0          | 17 0 0 0         | 16 0 0 0         | 19 0 0 0 **      |
|                | (23) (0) (0) (0) | (40) (0) (0) (0) | (42) (0) (0) (0) | (58) (0) (0) (0) |

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

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

b : Number of animals with lesion b

(c) c:b/a\*100

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

(IIPT150)

BAIS2

PAGE: 11

STUDY NO.: 0163ANIMAL: MOUSE BDF1REPORT TYPE: Λ1SEX: MALE

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

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| _   | No. c<br>Grade   |  | 400 ppm<br>42<br>1 2 3 4   | متحرم 2000<br>38<br>1 2 3 4            | 10000 ppm<br>33<br>1 2 3 4             |
|---|--|--|--|--|--|
| 0rgan                                       | Findings   | (%) (%) (%) (%)                        | (%) (%) (%) (%)  | (%) (%) (%) (%)                        | (%) (%) (%) (%)                        |
| [Special ser                                | nse organs/appandage]  |  |  |  |  |
| llarder gl                                  | hyperplasia  | <35><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0) | <42><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)   | <38><br>2 0 0 0<br>(5) (0) (0) (0)     | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| (Musculoskel                                | etal system]   |  |  |  |  |
| bane  | osteosclerosis   | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | $\begin{array}{cccc} <42> & & \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$ | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| Grade<br>< a ><br>b<br>( c )<br>Significant | 1 : Slight2 : Moderate3 : Mara : Number of animals examined at the siteb : Number of animals with lesionc : b / a * 100difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ |  |  |  |  |

(HPT150)

BAIS2

PAGE: 12

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## APPENDIX L 8

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

|             |   |  |  | PAGE :                                |  |  |   |
|-------------|---|--|--|---------------------------------------|--|--|---|
| rgan        |   | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>26<br><u>2 3</u><br>(%) (%) ( | 27                                    | 0  ppm<br>$\frac{3}{(\%)} \frac{4}{(\%)} \frac{1}{(\%)}$ | 2000 ppm<br>25<br>2 3 4<br>(%) (%) (%) | $ \begin{array}{c} 10000 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| ntegumentar | y system/appandage]                     |  | · · · · · · · · · · · · · · · · · · ·    |                                       |  |  |   |
| kin/app     | squamous cell hyperplasia               | 0<br>( 0)  | <26><br>0 0<br>( 0) ( 0) (               | <27>) 0 0<br>)) ( 0) ( 0) (           | 0 0 0  | <25><br>0 0 0<br>0) ( 0) ( 0)          | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |
|             | xanthogranuloma                         | 0 ( 0)   | 0 0<br>( 0) ( 0) (                       | ) 0 0<br>)) (0)(0)(                   | 0 0 0<br>0) ( 0) ( 0)                                    | 0 0 0<br>( 0) ( 0) ( 0)                | 0 I 0 0<br>( 0) ( 4) ( 0) ( 0)  |
| Respiratory | system]                                 |  |  |                                       |  |  |   |
| asal cavit  | inflammation                            | 0<br>( 0)  | <26><br>0 0<br>( 0) ( 0) (               | <pre>&lt;27&gt; 1 0 ( 4) ( 0) (</pre> | 0 0 0  | <25><br>0 0 0<br>[ 0) ( 0) ( 0)        | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|             | eosinophilic change:olfactory epithelin |  | 1 0<br>( 4) ( 0) (                       | ) 0 0<br>)) ( 0) ( 0) (               | 0 0 5<br>0) ( 0) ( 20)                                   | 0 0 0 *<br>.0) ( 0) ( 0)               | 2 2 0 0<br>(9)(9)(0)(0)   |
|             | eosinophilic change:respiratory epithe  |  | 50<br>(19)(0)(                           | ) 16 2<br>)) (59)(7)(                 | 0 0 8<br>0)(0)(32)                                       | 900<br>(36)(0)(0)                      | 11 4 1 0<br>(48) (17) (4) (0)   |
|             | respiratory metaplasia:olfactory epith  |  | 0 0<br>( 0) ( 0) (                       | ) 0 0<br>)) (0)(0)(                   | 0 0 0<br>0) ( 0) ( 0)                                    | 1 0 0<br>(4)(0)(0)                     | 3 0 0 0<br>(13) (0) (0) (0)   |
|             | respiratory metaplasia:gland            | 5<br>(19)  | 1 0<br>(4)(0)(                           | ) 1 0<br>)) (4)(0)(                   | 0 0 9<br>0)(0)(36)                                       | 0 0 0<br>0)(0)(0)                      | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)  |

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- 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

| SEX         | FEMALE                                |   |   |   |   | PAGE :   |
|-------------|---------------------------------------|---|---|---|---|--|
| 0rgan       | Findings                              | Group Name<br>No. of Animals on Study<br>Grade <u>1 2</u><br>(%) (% | Control<br>26<br>2 <u>3 4</u><br>5) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 27 \\ \underline{1 \ 2 \ 3 \ 4} \\ \hline (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$      |
| Respiratory | system]                               |   |   |   |   |  |
| Larynx      | basal cell activation                 |   | <26><br>0 0 0<br>0) ( 0) ( 0)               | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>5 0 0 0 *<br>( 22) ( 0) ( 0) ( 0)                  |
|             | epithelial dysplasia                  |   | ) 0 0<br>))(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 2 1 0 0<br>(9) (4) (0) (0)                                 |
| ung         | lymphocytic infiltration              |   | <26><br>0 0 0<br>1) ( 0) ( 0)               | <27><br>1 2 0 0<br>( 4) ( 7) ( 0) ( 0)  | <25><br>2 0 0 0<br>( 8) ( 0) ( 0) ( 0)  | <pre> &lt;23&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> |
|             | bronchiolar-alveolar cell hyperplasia |   | 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>( 4) ( 0) ( 0) ( 0)                             |
| Nematopoiet | ic system]                            |   |   |   |   |  |
| ione marrow | myəlofibrosis                         | 1 0   | <25><br>0 0<br>) ( 0) ( 0)                  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| ymph nade   | lymphadenitis                         |   | <26><br>0 0<br>) ( 0) ( 0)                  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | <23><br>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

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(IIPT150)

BAIS2

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# ULCTOLOCICAL EINDINCE INON NEODLACTIC LECTONG (CUMMADW)

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| )rgan                  | Findings                     | No. of Animals on Study 26<br>Grade 1 2 |                              | $ \begin{array}{c} 400 \\ 7 \\ \hline 3 \\ \hline (\%) \\ \hline \%) \\ \hline (\%) \\ \hline 1 \\ \hline (\%) \\ \hline (\%) \\ \hline \% $ | 2000 ppm<br>25<br>2 3 4<br>) (%) (%) (%) | $ \begin{array}{c} 10000 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ \underline{(\%) \ (\%) \ (\%) \ (\%) \ (\%)} \end{array} $ |
|------------------------|------------------------------|---|------------------------------|--|--|---|
| •••                    |                              |   |                              |  |  |   |
| llematopoieti<br>pleen | atrophy                      | <26><br>0 0<br>( 0) ( 0) (              | 0 0 0 0                      | 27><br>0 0 0<br>( 0) ( 0) ( 0)   | <25><br>0 0 0<br>) ( 0) ( 0) ( 0)        | <23><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)  |
|                        | angiectasis                  | 2 0<br>( 8) ( 0) (                      | 0 0 0 0<br>0) ( 0) ( 0) ( 0) | 0 0 0<br>( 0) ( 0) ( 0)  | 0 0 0<br>) ( 0) ( 0) ( 0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|                        | deposit of melanin           | 0 0<br>( 0) ( 0) (                      | 0 0 0<br>0) ( 0) ( 0) ( 0)   | 0 0 0<br>( 0) ( 0) ( 0)  | 0 0 0<br>) ( 0) ( 0) ( 0)                | 2 1 0 0<br>( 9) ( 4) ( 0) ( 0)  |
|                        | extramedullary hematopoiesis | 0 0<br>( 0) ( 0) (                      | 0 0 1 0<br>0) ( 0) ( 4) ( 0) | 0 0 2<br>( 0) ( 0) ( 8)  | 0 0 0<br>) ( 0) ( 0) ( 0)                | 0 4 0 0<br>( 0) ( 17) ( 0) ( 0)   |
|                        | hyperplasia:vascular         | 0 0<br>( 0) ( 0) (                      | 0 0 0 0<br>0) ( 0) ( 0) ( 0) | 0 0 0<br>( 0) ( 0) ( 0)  | 0 0 0<br>) ( 0) ( 0) ( 0)                | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |
|                        | follicular hyperplasia       | 1 0<br>( 4) ( 0) (                      | 0 0 1 0<br>0) ( 0) ( 4) ( 0) | 0 0 2<br>( 0) ( 0) ( 8)  | 0 0 0<br>) ( 0) ( 0) ( 0)                | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)  |
| Digestive sy           | stem]                        |   |                              |  |  |   |
| al cauity              | squamous cell hyperplasia    | <26><br>0 0<br>( 0) ( 0) (              | 0 0 0 0                      |  | <25><br>0 0 0<br>) ( 0) ( 0) ( 0)        | <23><br>5 0 0 0<br>( 22) ( 0) ( 0) ( 0)   |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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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

b

STUDY NO. : 0163

| REPORT TYPE :  | NUSE BUT<br>A1<br>FEMALE           | SACRIFICED ANIMALS (105W)   |   |  | PAGE : 16  |
|----------------|------------------------------------|---|---|--|--|
| Organ          | Findings                           | Group Name Control<br>No. of Animals on Study 26<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 27 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  |
| (Digestive sys | stem]                              |   |   |  |  |
| oral cavity    | basal cell activation              | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   | <23><br>11 2 0 0 **<br>(48) (9) (0) (0)                |
|                | epithelial dysplasia               | 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)   | 14 0 0 0 **<br>(61)(0)(0)(0)                           |
|                | epithelial dysplasia:incisive duct | 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) ( 4) ( 0) ( 0)                         |
| tooth          | inflammation                       | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | <27><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | <25><br>6 0 0 0<br>(24) (0) (0) (0)  | <pre> &lt;23&gt;     2 0 0 0 ( 9) ( 0) ( 0) ( 0)</pre> |
|                | dysplasia                          | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)   | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                         |
| tonsue         | epithelial dysplasia               | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                 |
|                | arteritis                          | 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

a : Number of animals examined at the site ⟨a⟩

b : Number of animals with lesion b

(c) c:b/a\*100

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

(IIPT150)

STUDY NO. : 0163

ANIMAL : MOUSE BDF1

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

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## STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1

## SEX : FEMALE

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

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| PAGE | : | 17 |
|------|---|----|
|------|---|----|

| 0rgan                 | No  | DUP Name         Control           . of Animals on Study         26           ade         1         2         3         4 | $\begin{array}{c} 400 \text{ ppm} \\ 27 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|-----------------------|---|---|---|---|---|
| [Digestive sy         | stem]   |   |   |   |   |
| salivary gl           | atrophy   | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <23><br>0 3 0 0<br>( 0) ( 13) ( 0) ( 0)               |
|                       | lymphacytic infiltration  | 1 0 0 0<br>(4)(0)(0)(0)(0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 2 0 0 0<br>(9)(0)(0)(0)                               |
| esophagus             | basal cell activation   | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <23><br>7 2 0 0 **<br>( 30) ( 9) ( 0) ( 0)            |
|                       | epithelial dysplasia  | 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 1 2<br>(13)(0)(4)(9)                              |
| stomach               | lymphocytic infiltration  | <pre> &lt;26&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
|                       | basal cell activation   | 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>(4)(0)(0)(0)                               |
|                       | erosion: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>( 4) ( 0) ( 0) ( 0)                        |
| <a><br/>b<br/>(c)</a> | 1 : Slight2 : Moderate3 :a : Number of animals examined at the siteb : Number of animals with lesionc : b / a * 100lifference ; * : $P \leq 0.05$ ** : $P \leq 0$ | Marked 4 : Severe<br>.01 Test of Chi Square   |   |   |   |

(IIPT150)

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

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

PAGE : 18

| 0rgan         | Findings                      | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>26<br>               | $\begin{array}{c} 400 \text{ ppm} \\ 27 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | $ \begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \\ \end{array} $ | $ \begin{array}{c} 10000 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|---------------|-------------------------------|--|---------------------------------|--|--|---|
| [Digestive sy | vstem]                        |  |                                 |  |  |   |
| stomach       | hyperplasia:forestomach       | 0<br>( 0)  | <26><br>0 0 0<br>( 0) ( 0) ( 0) | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <23><br>2 0 0 0<br>(9) (0) (0) (0)  |
|               | erosion:glandular stomach     | 1<br>( 4)  | 0 0 0<br>( 0) ( 0) ( 0)         | 2 0 0 0<br>(7)(0)(0)(0)  | 1 0 0 0<br>(4)(0)(0)(0)  | 1 0 0 0<br>(4)(0)(0)(0)   |
|               | hyperplasia:glandular stomach | 6<br>( 23)   | 1 0 0<br>( 4) ( 0) ( 0)         | 8 4 0 0<br>(30)(15)(0)(0)  | 10 1 0 0<br>(40)(4)(0)(0)  | 4 0 0 0<br>(17) (0) (0) (0)   |
| liver         | angiectasis                   |  | <26><br>1 0 0<br>( 4) ( 0) ( 0) | <27><br>2 0 0 0<br>( 7) ( 0) ( 0) ( 0)   | <25><br>1 1 0 0<br>( 4) ( 4) ( 0) ( 0)   | <23><br>2 2 0 0<br>( 9) ( 9) ( 0) ( 0)  |
|               | necrosis:focal                | 0<br>( 0)  | 0 1 0<br>( 0) ( 4) ( 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)  |
|               | lymphocytic infiltration      | 1<br>( 4)  | 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) ( 4) ( 0) ( 0)  |
|               | granulation                   | 11<br>( 42)  | 4 0 0<br>(15)(0)(0)             | 8 5 0 0<br>(30)(19)(0)(0)  | 7 1 0 0<br>(28) (4) (0) (0)  | 5 1 0 0<br>(22) (4) (0) (0)   |
|               | clear cell focus              | 0<br>( 0)  | 0 0 0<br>( 0) ( 0) ( 0)         | 2 0 0 0<br>(7)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(4)(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

| SEX       | : FEMALE              |   |   |  | PAGE :   |
|-----------|-----------------------|---|---|--|--|
| )rgan     | Findings              | Group Name Control<br>No. of Animals on Study 26<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)       | $ \begin{array}{c} 400 \text{ ppm} \\ 27 \\ \frac{1}{(\%)} (\%) (\%) (\%) (\%) (\%) \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \end{array}$ | 10000 ppm<br>23<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| )igestive | system]               |   |   |  |  |
| iver      | basophilic cell focus | $\begin{array}{cccc} <26 > \\ 1 & 0 & 0 & 0 \\ ( \ 4 ) & ( \ 0 ) & ( \ 0 ) & ( \ 0 ) \end{array}$ | <27><br>1 1 0 0<br>( 4) ( 4) ( 0) ( 0)  | <225><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)               |
|           | vacuolated cell focus | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | 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)                       |
|           | mixed cell focus      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 2 0 0 0<br>(7)(0)(0)(0)   | 3 0 0 0<br>(12)(0)(0)(0)   | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                       |
|           | biliary cyst          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)  | 2 0 0 0<br>(8)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| rinary sy | rstem]                |   |   |  |  |
| dney      | cyst                  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <27><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|           | hvaline droplet       | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 2 1 0 0<br>(9)(4)(0)(0)                              |
|           | basophilic change     | 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)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |

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

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

(IIPT150)

BAIS2

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 : FEMALE SEX

Findings

polyp

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

Group Name 10000 ppm Control 400 ppm 2000 ppm No. of Animals on Study 26 27 25 23 3 3 2 3 2 3 Grade 2 4 4 4 2 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) <26> <27> <25> <23> lymphocytic infiltration 1 0 0 0 2 1 0 0 1 0 0 0 0 0 0 0 (4) (0) (0) (0) (7) (4) (0) (0) (4) (0) (0) (0) (0)(0)(0)(0) 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0)(0)(0)(0)(0)hydronephrosis 0 0 0 0 . 0 1 0 0 0 2 0 0 0 2 0 0 (0)(4)(0)(0) (0)(8)(0)(0) (0)(9)(0)(0) mineralization:cortico-medullary junction 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0) (0) (-0) (0)(4) (0) (0) (0)

0 0 0 0

0 0

0

0

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

0

0 0

0

1 0 0 0

2 0 0 0

0 0 0 0

(4) (0) (0) (0)

[Urinary system]

0rgan

kidney

[Endacrine system]

| pituitary   | <26> | <27>                    | <24>  | <23> |
|-------------|------|-------------------------|-------|------|
| angiectasis |      | 2 0 0 0<br>(7)(0)(0)(0) | • • • |      |

0 0 0 0

0 0 0 0

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

1 0 0 0

(4)(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

mineralization:papilla

mineralization:pelvis

mineralization:cortex

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

PAGE : 20

4

(%)

0 0 0 0

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

0 1 0 0

(0) (4) (0) (0)

1 0 0 0

(4) (0) (0) (0)

| STUDY NO.<br>ANIMAL<br>REPORT TYPE<br>SEX | :<br>: | MOUSE BDF1 |
|---|--------|------------|
| ····                                      |        | <u></u>    |

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

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| 0rgan          | Findings  | Group Name         Control           No. of Animals on Study         26           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 400 \text{ ppm} \\ 27 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 10000 ppm<br>23<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|----------------|---|---|--|---|--|
| [Endocrine sy  | vstem]  |   |  |   |  |
| pituitary      | cyst  | <26><br>2 0 0 0<br>( 8) ( 0) ( 0) ( 0)  | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <24><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|                | hyperplasia   | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 4 0 0 0<br>(15) (0) (0) (0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                       |
| thyroid        | ectopic thymic tissue   | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <27><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| [Reproductive  | ə system]   |   |  |   |  |
| ovary          | thrombus  | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | <27><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)   | <25><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)  | <23><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)               |
|                | cyst  | 3 0 0 0<br>(12) (0) (0) (0)   | 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)                       |
|                | 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>( 4) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| Grade<br>< a > | 1 : Slight 2 : Moderate<br>a : Number of animals examined at th | 3: Marked 4: Severe<br>e 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 als examined at the site

(IIPT150)

PAGE : 21

### STUDY NO. : 0163 ANIMAL : NOUSE BDF1 REPORT TYPE : A1

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

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REPORT TYPE : A1 SEX : FEMALE

| 0rgan   | Findings   | Group Name         Control           No. of Animals on Study         26           Grade         1         2         3         4 | $ \begin{array}{c} 400 \text{ ppm} \\ 27 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10000 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|---|--|---|--|---|---|
| [Reproductiv                                  | e system]  |   | •  |   |   |
| uterus  | thrombus   | <pre>&lt;26&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>   | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |
|   | cystic endometrial hyperplasia   | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | $\begin{array}{c} 2 & 2 \\ 2 & 14 & 0 & 0 \\ (7) & 52) & (0) & (0) \end{array}$                            | $\begin{array}{c} & & & \\ 5 & 12 & 0 & 0 \\ (20) & (48) & (0) & (0) \end{array}$                                 | び デ<br>9 9 0 0<br>(39)(39)(0)(0)  |
| nammary gl                                    | hyperplasia  | <pre>&lt;26&gt; 0 0 0 0. ( 0) ( 0) ( 0) ( 0)</pre>  | <pre></pre>  | $\begin{array}{cccc} <25>\\ 1 & 0 & 0 & 0\\ ( \ 4) & ( \ 0) & ( \ 0) & ( \ 0)\end{array}$                         | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|   | atypical hyperplasia   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|   | galactocele  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| Nervous sys                                   | tem]   |   |  |   |   |
| orain -                                       | mineralization   | <pre> &lt;26&gt;     10 0 0     ( 38) ( 0) ( 0) ( 0)</pre>  | <27><br>9 0 0 0<br>(33) (0) (0) (0)  | <25><br>5 0 0 0<br>(20) (0) (0) (0)   | <23><br>9 0 0 0<br>(39) (0) (0) (0)   |
| Grade<br>< a ><br>b<br>( c )<br>Significant ( | 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>difference ; * : P ≦ 0.05 *** : | 3 : Marked 4 : Se∪ere<br>me site<br>P ≦ 0.01 Test of Chi Square   |  |   |   |

## PAGE : 22

(IIPT150)

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

## HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (1050)

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| rgan          | Findings            | Group Name<br>No. of Animals on Study<br>Grade <u>1 2</u><br>(%) (%) | Contral<br>26<br><u>3 4</u><br>(%) (%) | $\begin{array}{c} 400 \text{ ppm} \\ 27 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 2000 \text{ ppm} \\ 25 \\ \underline{1 \ 2 \ 3 \ 4} \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{c} 10000 \text{ ppm} \\ 23 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|---------------|---------------------|--|--|---|---|--|
| Special sense | e organs/appandage] |  |  |   |   |  |
| arder gl      | hyperplasia         | 1 0  | 26><br>0 0<br>( 0) ( 0)                | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| Body cauities | 5]                  |  |  |   |   |  |
| ritoneum      | inflammation        | 0 0  | 26><br>0 0<br>( 0) ( 0)                | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre> &lt;25&gt; 0 1 0 0<br/>( 0) ( 4) ( 0) ( 0)</pre>  | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| ipose         | granulation         | 0 0  | 26><br>0 0<br>( 0) ( 0)                | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)   |

(HPT150)

BAIS2

## APPENDIX M 1

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

RAT : MALE

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

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PAGE: 1

| ime-related<br>Weeks | ltems                               | Group Name | Control | 400 mag | 2000 maga | 10000 mag |  |
|----------------------|-------------------------------------|------------|---------|---------|-----------|-----------|--|
| 0 - 52               | NO. OF EXAMINED ANIMALS             |            | 0       | 0       | 0         | 0         |  |
|                      | NO. OF ANIMALS WITH TUMORS          |            | 0       | 0       | 0         | 0         |  |
|                      | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0       | 0       | 0         | 0         |  |
|                      | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0       | 0       | 0         | 0         |  |
|                      | NO. OF BENIGN TUMORS                |            | 0       | 0       | 0         | 0         |  |
|                      | NO. OF MALIGNANT TUNORS             |            | 0       | 0       | 0         | 0         |  |
|                      | NO. OF TOTAL TUMORS                 |            | 0       | 0       | 0         | 0         |  |
| 53 - 78              | NO. OF EXAMINED ANIMALS             |            | 1       | 2       | 1         | 0         |  |
|                      | NO. OF ANIMALS WITH TUMORS          |            | 0       | 2       | 1         | 0         |  |
|                      | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0       | 1       | 0         | 0         |  |
|                      | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0       | 1       | 1         | 0         |  |
|                      | NO. OF BENIGN TUMORS                |            | 0       | 1       | 1         | 0         |  |
|                      | NO. OF MALIGNANT TUMORS             |            | 0       | 2       | 1         | 0         |  |
|                      | NO. OF TOTAL TUMORS                 |            | 0       | 3       | 2         | 0         |  |
| 79 - 104             | NO. OF EXAMINED ANIMALS             |            | 5       | 8       | 13        | 11        |  |
|                      | NO. OF ANIMALS WITH TUMORS          |            | 5       | 8       | 13        | 11        |  |
|                      | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 1       | . 4     | 2         | 2         |  |
|                      | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 4       | 4       | 11        | 9         |  |
|                      | NO. OF BENIGN TUMORS                |            | 9       | 11      | 19        | 16        |  |
|                      | NO. OF MALIGNANT TUMORS             |            | 2       | 5       | 13        | 8         |  |
|                      | NO. OF TOTAL TUMORS                 |            | 11      | 16      | 32        | 24        |  |
| 105 - 105            | NO. OF EXAMINED ANIMALS             |            | 44      | 40      | 36        | 39        |  |
|                      | NO. OF ANIMALS WITH TUMORS          |            | 43      | 40      | 36        | 39        |  |
|                      | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 14      | 10      | 9         | 14        |  |
|                      | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 29      | 30      | 27        | 25        |  |
|                      | NO. OF BENIGN TUMORS                |            | 90      | 75      | 80        | 73        |  |
|                      | NO. OF MALIGNANT TUMORS             |            | 5       | 7       | 7         | 11        |  |
|                      | NO. OF TOTAL TUMORS                 |            | 95      | 82      | 87        | 84        |  |

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

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

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PAGE : 2

| F EXAMINED ANIMALS              | 50  | 50  | 50      | 50             |                             |
|---------------------------------|-----|-----|---------|----------------|-----------------------------|
| F ANIMALS WITH TUMORS           | 48  | 50  | 50      | 50             |                             |
| OF ANIMALS WITH SINGLE TUMORS   | 15  | 15  | 11      | 16             |                             |
| OF ANIMALS WITH MULTIPLE TUMORS | 33  | 35  | 39      | 34             |                             |
| OF BENIGN TUMORS                | 99  | 87  | 100     | 89             |                             |
| OF MALIGNANT TUMORS             | 7   | 14  | 21      | 19             |                             |
| DF TOTAL TUMORS                 | 106 | 101 | 121     | 108            |                             |
|                                 |     |     | · · · · | , <b>** **</b> | MALIGNANT TUMORS 7 14 21 19 |

(IIPT070)

BAIS2

# APPENDIX M 2

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

RAT : FEMALE

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

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STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

PAGE : 3

| Time-related<br>Weeks | Items  | Group Name                            | Control        | 400 ppm        | 2000 ppm       | 10000 mqq      |  |
|-----------------------|--|---------------------------------------|----------------|----------------|----------------|----------------|--|
| 0 - 52                | NO. OF EXAMINED ANIMALS  |                                       | 1              | 0              | 0              | 0              |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |                                       | 1<br>1<br>0    | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0    |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |                                       | 0<br>1<br>1    | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0    |  |
| 53 - 78               | NO. OF EXAMINED ANIMALS  | · · · · · · · · · · · · · · · · · · · | 0              | 1              | 2              | 2              |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |                                       | 0<br>0<br>0    | 1<br>1<br>0    | 2<br>1<br>1    | 2<br>2<br>0    |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |                                       | 0<br>0<br>0    | 1<br>0<br>1    | 1<br>2<br>3    | 1<br>1<br>2    |  |
| 79 - 104              | NO. OF EXAMINED ANIMALS  |                                       | 8              | 9              | 7              | 11             |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |                                       | 8<br>7<br>1    | 9<br>3<br>6    | 7<br>2<br>5    | 10<br>7<br>3   |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |                                       | 3<br>6<br>9    | 12<br>6<br>18  | 10<br>4<br>14  | 10<br>8<br>18  |  |
| 105 - 105             | NO. OF EXAMINED ANIMALS  |                                       | 41             | 40             | 41             | 37             |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |                                       | 25<br>15<br>10 | 24<br>14<br>10 | 29<br>17<br>12 | 28<br>17<br>11 |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |                                       | 31<br>4<br>35  | 31<br>4<br>35  | 34<br>11<br>45 | 30<br>11<br>41 |  |

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STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

| ime-related<br>Weeks | [tems                               | Group Name | Control | 400 ppm | 2000 ppm | 10000 ppm |  |
|----------------------|-------------------------------------|------------|---------|---------|----------|-----------|--|
| 0 - 105              | NO. OF EXAMINED ANIMALS             |            | 50      | 50      | 50       | 50        |  |
|                      | NO. OF ANIMALS WITH TUMORS          |            | 34      | 34      | 38       | 40        |  |
|                      | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 23      | 18      | 20       | 26        |  |
|                      | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 11      | 16      | 18       | 14        |  |
|                      | NO. OF BENIGN TUMORS                |            | 34      | 44      | 45       | 41        |  |
|                      | NO. OF MALIGNANT TUMORS             |            | 11      | 10      | 17       | 20        |  |
|                      | NO. OF TOTAL TUMORS                 |            | 45      | 54      | 62       | 61        |  |

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## APPENDIX M 3

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

MOUSE : MALE

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

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

| Time-related | Items  | Group Name                             | Control        | 400 ppm        | 2000 ppm       | 10000 ppm      |
|--------------|--|--|----------------|----------------|----------------|----------------|
| 0 - 52       | NO. OF EXAMINED ANIMALS  |  | 2              | 0              | I              | 1              |
|              | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |  | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0    | 1<br>1<br>0    |
|              | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |  | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>1<br>1    |
| 53 - 78      | NO. OF EXAMINED ANIMALS  |  | 6              | 2              | 1              | 2              |
|              | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |  | 4<br>3<br>1    | 2<br>2<br>0    | 1<br>1<br>0    | 2<br>2<br>0    |
|              | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |  | 2<br>6<br>8    | 0<br>2<br>2    | 0<br>1<br>1    | 0<br>2<br>2    |
| 79 - 104     | NO. OF EXAMINED ANIMALS  |  | 7              | 6              | 10             | - 14           |
|              | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |  | 6<br>3<br>3    | 6<br>3<br>3    | 10<br>5<br>5   | 12<br>7<br>5   |
|              | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |  | 3<br>7<br>10   | 2<br>7<br>9    | 3<br>13<br>16  | 3<br>17<br>20  |
| 105 - 105    | NO. OF EXAMINED ANIMALS  | ······································ | 35             | 42             | 38             | 33             |
|              | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |  | 24<br>15<br>9  | 24<br>16<br>8  | 27<br>18<br>9  | 25<br>13<br>12 |
|              | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |  | 10<br>27<br>37 | 14<br>24<br>38 | 17<br>21<br>38 | 15<br>26<br>41 |

PAGE: 1

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

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STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

| SEX : MALE            |  |            |                |                |                | PAGE : 2       |  |
|-----------------------|--|------------|----------------|----------------|----------------|----------------|--|
| Time-related<br>Weeks | Items  | Group Name | Control        | 400 ppm        | 2000 ppm       | 10000 ppm      |  |
| 0 - 105               | NO. OF EXAMINED ANIMALS  |            | 50             | 50             | 50             | 50             |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 34<br>21<br>13 | 32<br>21<br>11 | 38<br>24<br>14 | 40<br>23<br>17 |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 15<br>40<br>55 | 16<br>33<br>49 | 20<br>35<br>55 | 18<br>46<br>64 |  |

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# APPENDIX M 4

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

MOUSE: FEMALE

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

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STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

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| Time-related<br>Weeks | Items  | Group Name | Control        | 400 ppm        | 2000 ppm       | 10000 ppm      |  |
|-----------------------|--|------------|----------------|----------------|----------------|----------------|--|
| 0 - 52                | NO. OF EXAMINED ANIMALS  |            | 0              | 2              | 0              | 2              |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0<br>0<br>0    | 1<br>1<br>0    | 0<br>0<br>0    | 1<br>1<br>0    |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 0<br>0<br>0    | 0<br>1<br>1    | 0<br>0<br>0    | 0<br>1<br>1    |  |
| 53 - 78               | NO. OF EXAMINED ANIMALS  |            | 7              | 7              | 4              | 6              |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 6<br>4<br>2    | 6<br>6<br>0    | 2<br>2<br>0    | 5<br>5<br>0    |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 1<br>7<br>8    | 1<br>5<br>6    | 0<br>2<br>2    | 0<br>5<br>5    |  |
| 79 - 104              | NO. OF EXAMINED ANIMALS  |            | 17             | 14             | 21             | 18             |  |
|                       | NO. OF ANIMALS WITH TUNORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 17<br>13<br>4  | 14<br>10<br>4  | 19<br>14<br>5  | 17<br>11<br>6  |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 6<br>16<br>22  | 3<br>20<br>23  | 3<br>22<br>25  | 1<br>23<br>24  |  |
| 105 - 105             | NO. OF EXAMINED ANIMALS  |            | 26             | 27             | 25             | 23             |  |
|                       | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 15<br>8<br>7   | 18<br>11<br>7  | 17<br>9<br>8   | 20<br>9<br>11  |  |
|                       | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 11<br>14<br>25 | 16<br>12<br>28 | 19<br>11<br>30 | 18<br>22<br>40 |  |

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

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STUDY NO.: 0163ANIMAL: MOUSE BDF1REPORT TYPE: A1SEX: FEMALE

#### Time-related Items\_ Group Name Control 400 ppm 2000 ppm 10000 ppm \_\_\_\_Weeks\_ 0 - 105 NO. OF EXAMINED ANIMALS 50 50 50 49 NO. OF ANIMALS WITH TUMORS 38 39 38 43 NO. OF ANIMALS WITH SINGLE TUMORS 25 28 25 26 NO. OF ANIMALS WITH MULTIPLE TUMORS 13 11 17 13 NO. OF BENIGN TUMORS 20 22 19 18 NO. OF MALIGNANT TUMORS 38 51 37 35 NO. OF TOTAL TUMORS 55 58 57 70

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# APPENDIX N 1

### NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

RAT : MALE :

(2-YEAR STUDY)

|               | : 0162<br>: RAT F344<br>: A1 | HISTOLOGICAL FINDINGS : NEOF<br>ALL ANIMALS (0-105W) | PLASTIC LESIONS (SU | IMMARY)  |                  |                 |
|---------------|------------------------------|--|---------------------|--|------------------|-----------------|
|               | : MALE                       | ·  |                     | 1. <u>1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1</u> |                  | PAGE            |
| 0rgan         | Findings                     | Group Name<br>No. of animals on Study                | Control<br>50       | 400 ppm<br>50                                      | 2000 ppm<br>50   | 10000 ppm<br>50 |
| [Integumentar | ry system/appandage]         |  |                     |  |                  |                 |
| skin/app      | squamous cell papilloma      |  | <50><br>0 ( 0%)     | <50><br>0 ( 0%)                                    | <50><br>1 ( 2%)  | <50><br>0 ( 0%) |
|               | trichoepithelioma            |  | 1 ( 2%)             | 0 ( 0%)  | 1 ( 2%)          | 1 ( 2%)         |
|               | keratoacanthoma              |  | 3 ( 6%)             | 2 ( 4%)  | 4 ( 8%)          | 1 ( 2%)         |
|               | calcifying epitheliama       |  | 0 ( 0%)             | 0 ( 0%)  | 0 ( 0%)          | 2 ( 4%)         |
|               | sebaceous adenoma            |  | 0 ( 0%)             | 1 ( 2%)  | 0 ( 0%)          | 1 ( 2%)         |
|               | schwannoma:malignant         |  | 0 ( 0%)             | 1 ( 2%)  | 0 ( 0%)          | 1 (2%)          |
| subcutis      | fibroma                      |  | <50><br>3 ( 6%)     | <50><br>4 ( 8%)                                    | <50><br>8 ( 16%) | <50><br>3 ( 6%) |
|               | lipoma                       |  | 1 ( 2%)             | 0 ( 0%)  | 3 ( 6%)          | 0 ( 0%)         |
|               | fibrosarcoma                 |  | 0 ( 0%)             | 1 ( 2%)  | 1 ( 2%)          | 2 ( 4%)         |
|               | schwannoma:malignant         |  | 0 (0%)              | 1 ( 2%)  | 0 ( 0%)          | 0 ( 0%)         |
|               | histiocytic sarcoma          |  | 0 ( 0%)             | 0 ( 0%)  | 2 ( 4%)          | 0 ( 0%)         |
|               | tumor:malignant:NOS          |  | 1 ( 2%)             | 0 ( 0%)  | 0 ( 0%)          | 0 ( 0%)         |
|               | sarcoma:NOS                  |  | 0 ( 0%)             | 0 ( 0%)  | 0 ( 0%)          | 1 ( 2%)         |
| [Respiratory  | system]                      |  |                     |  |                  |                 |
| larynx        | squamous cell carcinoma      |  | <50><br>0 ( 0%)     | <50><br>0 ( 0%)                                    | <50><br>0 ( 0%)  | <50><br>1 ( 2%) |

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

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

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| REPORT TYPE :<br>SEX : | AI<br>MALE                       |  |                  |                 | PAGE : 2        |
|------------------------|----------------------------------|--|------------------|-----------------|-----------------|
| 0rgan                  |                                  | o Name Control<br>of animals on Study 50 | 400 ppm<br>50    | 2000 ppm<br>50  | 10000 ppm<br>50 |
| [Respiratory s         | system]                          |  |                  |                 |                 |
| lung                   | bronchiolar-alveolar adenoma     | <50><br>3 (6%)                           | <50><br>1 ( 2%)  | <50><br>3 ( 6%) | <50><br>1 ( 2%) |
| [Hematopoietic         | c system]                        |  |                  |                 |                 |
| lymph nade             | malignant lymphoma               | <50><br>0 ( 0%)                          | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| spleen                 | mononuclear cell leukemia        | <50><br>3 ( 6%)                          | <50><br>5 ( 10%) | <49><br>7 (14%) | <50><br>4 (8%)  |
|                        | hemang i osarcoma                | 0 ( 0%)                                  | 0 ( 0%)          | 0 ( 0%)         | 1 (2%)          |
| [Digestive sys         | stem]                            |  |                  |                 |                 |
| oral cavity            | squamous cell papilloma          | <50><br>0 ( 0%)                          | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <50><br>2 ( 4%) |
|                        | squamous cell carcinoma          | 0 ( 0%)                                  | 0 ( 0%)          | 0 ( 0%)         | 5 (10%)         |
| tongue                 | osteosarcoma                     | <50><br>0 ( 0%)                          | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <49><br>1 ( 2%) |
| stomach                | squamous cell papilloma          | <50><br>1 ( 2%)                          | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                        | keratoacanthoma                  | 2 ( 4%)                                  | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         |
|                        | squamous cell carcinoma          | 0 ( 0%)                                  | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         |
| small intes            | adenocarcinoma                   | <50><br>0 ( 0%)                          | <50><br>0 ( 0%)  | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| large intes            | neuroendocrine cell tumor:benign | <50><br>0 ( 0%)                          | <50><br>0 ( 0%)  | <50><br>1 ( 2%) | <50><br>0 (0%)  |
| liver                  | histiacytic sarcoma              | <50><br>0 ( 0%)                          | <50><br>0 ( 0%)  | <50><br>2 (4%)  | <50><br>0 ( 0%) |

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

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ALL ANIMALS (0-105W)

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1

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

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

| STUDY NO. :<br>ANIMAL :<br>REPORT TYPE : | RAT F344                   | HISTOLOGICAL FINDINGS : NEOF<br>ALL ANIMALS (0-105W) | PLAST | TIC LESIONS (S | SUMMARY) |                |    |                 |    |                 |          |  |
|--|----------------------------|--|-------|----------------|----------|----------------|----|-----------------|----|-----------------|----------|--|
| SEX :                                    | MALE                       |  |       |                |          |                |    |                 |    |                 | PAGE : 3 |  |
| Organ                                    | Findings                   | Group Name<br>No. of animals on Study                |       | Control<br>50  |          | 400 ppm<br>50  |    | 2000 ppm<br>50  | 1  | 10000 ppm<br>50 |          |  |
| [Digestive sy                            | stem]                      |  |       |                |          |                |    |                 |    |                 |          |  |
| liver                                    | hepatocellular carcinoma   |  | 0     | <50><br>( 0%)  | 0        | <50><br>( 0%)  | 0  | <50><br>( 0%)   | 1  | <50><br>( 2%)   |          |  |
| [Endocrine sy                            | stem]                      |  |       |                |          |                |    |                 |    |                 |          |  |
| pituitary                                | adenoma                    |  | 19    | <50><br>( 38%) | 16       | <50><br>( 32%) | 14 | <50><br>(28%)   | 11 | <50><br>(22%)   |          |  |
|  | adenocarcinoma             |  | 0     | ( 0%)          | 0        | ( 0%)          | 1  | ( 2%)           | 0  | ( 0%)           |          |  |
| thyroid                                  | C-cell adenoma             |  | 7     | <50><br>( 14%) | 9        | <49><br>( 18%) | 3  | <49><br>( 6%)   | 7  | <49><br>( 14%)  |          |  |
|  | follicular adenoma         |  | 0     | ( 0%)          | 1        | ( 2%)          | 0  | ( 0%)           | 1  | ( 2%)           |          |  |
|  | C-cell carcinoma           |  | 1     | ( 2%)          | 2        | ( 4%)          | 2  | ( 4%)           | 0  | ( 0%)           |          |  |
|  | follicular adenocarcinoma  |  | 0     | ( 0%)          | 2        | ( 4%)          | 0  | ( 0%)           | 0  | ( 0%)           |          |  |
| panc islet                               | islet cell adenoma         |  | 6     | <50><br>( 12%) | 5        | <50><br>( 10%) | 4  | <50><br>( 8%)   | 3  | <50><br>( 6%)   |          |  |
| adrenal                                  | pheachromocytoma           |  | 8     | <50><br>( 16%) | 4        | <50><br>( 8%)  | ę  | <50><br>( 18%)  | 7  | <50><br>( 14%)  |          |  |
|  | cortical adenoma           |  | 0     | ( 0%)          | 0        | ( 0%)          | C  | ) ( 0%)         | 1  | ( 2%)           |          |  |
|  | pheochromocytoma:malignant |  | 1     | ( 2%)          | 0        | ( 0%)          | 1  | (2%)            | 0  | ( 0%)           |          |  |
| [Reproductive                            | e system]                  |  |       |                |          |                |    |                 |    |                 |          |  |
| testis                                   | interstitial cell tumor    |  | 42    | <50><br>( 84%) | 40       | <50><br>( 80%) | 44 | <50><br>4 (88%) | 47 | <50><br>(94%)   |          |  |
| mammary gl                               | adenoma                    |  | 1     | <50><br>(2%)   | 1        | <50><br>(2%)   | (  | <50><br>) ( 0%) | 0  | <50><br>( 0%)   |          |  |
|  |                            |  |       |                |          |                |    |                 |    |                 |          |  |

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

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

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| REPORT TYPE :  | RAT F344              | ALL ANIMALS (0-105W)                  |                 |                 |                 |                 |  |  |  |  |
|----------------|-----------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|--|--|--|--|
|                |                       |                                       |                 |                 |                 | PAGE: 4         |  |  |  |  |
| 0r-gan         | Findings              | Group Name<br>No. of animals on Study | Control<br>50   | 400 ppm<br>50   | 2000 ppm<br>50  | 10000 mqq<br>50 |  |  |  |  |
| [Reproductive  | system]               |                                       |                 |                 |                 |                 |  |  |  |  |
| mammary gl     | fibroadenoma          |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>2 ( 4%) | <50><br>0 ( 0%) |  |  |  |  |
| prep/cli gl    | adenoma               |                                       | <50><br>1 ( 2%) | <50><br>2 ( 4%) | <50><br>2 ( 4%) | <50><br>0 (0%)  |  |  |  |  |
| (Nervous syste | em]                   |                                       |                 |                 |                 |                 |  |  |  |  |
| brain          | meningioma:benign     |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |  |  |  |  |
|                | malignant reticulosis |                                       | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         |  |  |  |  |
|                | glioma                |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |  |  |  |  |
| [Special sense | e organs/appandage]   |                                       |                 |                 |                 |                 |  |  |  |  |
| Zymbal gl      | sebaceous adenoma     |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |  |  |  |  |
| [Musculoskelet | tal system]           |                                       |                 |                 |                 |                 |  |  |  |  |
| muscle         | sarcoma:NOS           |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |  |  |  |  |
| bane           | osteosarcoma          |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |  |  |  |  |
| vertebra       | sarcoma:NOS           |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 (2%)  | <50><br>0 ( 0%) |  |  |  |  |
| [Body cavities | s]                    |                                       |                 |                 |                 |                 |  |  |  |  |
| peritoneum     | mesothelioma          |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>1 (2%)  |  |  |  |  |

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

(HPT085)

# APPENDIX N 2

### NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

RAT : FEMALE :

(2-YEAR STUDY)

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

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STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

| )rgan         | Findings                     | Group Name<br>No. of animals on Study | Control<br>50   | 400 ppm<br>50   | 2000 ppm<br>50    | מסק 10000<br>50 |
|---------------|------------------------------|---------------------------------------|-----------------|-----------------|-------------------|-----------------|
| [Integumentar | y system/appandage]          |                                       |                 |                 |                   |                 |
| skin/app      | trichoepithelioma            |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%)   | <50><br>0 ( 0%) |
|               | keratoacanthoma              |                                       | 0 ( 0%)         | 0 (0%)          | 1 (2%)            | 0 ( 0%)         |
|               | schwannoma:malignant:        |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)           | 0 ( 0%)         |
| ubcutis       | fibroma                      |                                       | <50><br>1 ( 2%) | <50><br>2 ( 4%) | <50><br>0 ( 0%)   | <50><br>1 ( 2%) |
|               | fibrosarcoma                 |                                       | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)           | 0 ( 0%)         |
|               | histiocytic sarcoma          |                                       | 0 ( 0%)         | 1 (2%)          | 0 ( 0%)           | 0 ( 0%)         |
|               | sarcoma:NOS                  |                                       | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)           | 1 ( 2%)         |
| Respiratory   | system]                      |                                       |                 |                 |                   |                 |
| ung           | bronchiolar-alveolar adenoma |                                       | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50> .<br>1 ( 2%) | <50><br>1 ( 2%) |
|               | squamous cell carcinoma      |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)           | 0 ( 0%)         |
| llematopoieti | ic system]                   |                                       |                 |                 |                   |                 |
| one marrow    | malignant histiocytosis      |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%)   | <50><br>0 ( 0%) |
| pleen         | fibrosarcoma                 |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%)   | <50><br>0 ( 0%) |
|               | mononuclear cell leukemia    |                                       | 4 ( 8%)         | 5 (10%)         | 8 (16%)           | 7 (14%)         |
| Digestive sy  | /stem]                       |                                       |                 |                 |                   |                 |
| ral cavity    | squamous cell carcinoma      |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>1 ( 2%)   | <50><br>3 ( 6%) |

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

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

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

· ·

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

| rgan         | Findings                            | Group Name<br>No. of animals on Study | Control<br>50    | 400 ppm<br>50    | 2000 ppm<br>50   | 10000 maa<br>50   |
|--------------|-------------------------------------|---------------------------------------|------------------|------------------|------------------|-------------------|
| Digestive sy | stem]                               |                                       |                  |                  |                  |                   |
| sophagus     | squamous cell carcinoma             |                                       | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)   |
| tomach       | neuroendocrine cell tumor:malignant |                                       | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  | <50><br>0 ( 0%)   |
| ver          | histiocytic sarcoma                 |                                       | <50><br>0 ( 0%)  | <50><br>1 (2%)   | <50><br>0 ( 0%)  | <50><br>1 ( 2%)   |
| indocrine sy | stem]                               |                                       |                  |                  |                  |                   |
| ituitary     | adenoma                             |                                       | <50><br>8 ( 16%) | <50><br>11 (22%) | <50><br>9 (18%)  | <50><br>14 ( 28%) |
|              | adenocarcinoma                      |                                       | 0 ( 0%)          | 1 ( 2%)          | 0 ( 0%)          | 0 ( 0%)           |
| nyroid       | C-cell adenoma                      |                                       | <50><br>2 ( 4%)  | <50><br>7 (14%)  | <50><br>8 ( 16%) | <50><br>5 ( 10%)  |
|              | C-cell carcinoma                    |                                       | 0 ( 0%)          | 0 ( 0%)          | 1 ( 2%)          | 2 ( 4%)           |
| nc islet     | islet cell adenoma                  |                                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  | <50><br>3 ( 6%)  | <50><br>1 ( 2%)   |
| drenal       | pheochromacytama                    |                                       | <50><br>4 ( 8%)  | <50><br>1 ( 2%)  | <50><br>1 ( 2%)  | <50><br>2 ( 4%)   |
|              | cortical adenoma                    |                                       | 0 ( 0%)          | 0 ( 0%)          | 1 ( 2%)          | 0 ( 0%)           |
|              | cortical adenocarcinoma             |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)          | 1 ( 2%)           |
| Reproductive | system]                             |                                       |                  |                  |                  |                   |
| Jary         | granulosa-theca cell tumor          |                                       | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)   |
| terus        | hemang i cina                       |                                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)   |

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

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

PAGE: 6

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| 0rgan          | Findings                    | Group Name<br>No. of animals on Study | Control<br>50    | 400 ppm<br>50    | 2000 ppm<br>50    | 10000 ppm<br>50 |
|----------------|-----------------------------|---------------------------------------|------------------|------------------|-------------------|-----------------|
| [Reproductive  | system]                     |                                       |                  |                  |                   |                 |
| uterus         | endometrial stromal polyp   |                                       | <50><br>5 ( 10%) | <50><br>5 ( 10%) | <50><br>10 ( 20%) | <50><br>4 ( 8%) |
|                | adenocarcinoma              |                                       | 1 ( 2%)          | 0 ( 0%)          | 1 ( 2%)           | 0 ( 0%)         |
|                | leiomyosarcoma              |                                       | 1 ( 2%)          | 1 ( 2%)          | 0 ( 0%)           | 0 ( 0%)         |
|                | endometrial stromal sarcoma |                                       | 1 ( 2%)          | 0 ( 0%)          | 1 ( 2%)           | 0 ( 0%)         |
| Vagina         | squamous cell papilloma     |                                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  | <50><br>0 ( 0%)   | <50><br>0 ( 0%) |
| mammary gl     | adenoma                     |                                       | <50><br>1 ( 2%)  | <50><br>3 ( 6%)  | <50><br>0 ( 0%)   | <50><br>1 ( 2%) |
|                | fibroadenoma                |                                       | 9 (18%)          | 10 ( 20%)        | 8 (16%)           | 9 (18%)         |
|                | adenocarcinoma              |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)           | 3 (6%)          |
| prep/cli gl    | adenoma                     |                                       | <50><br>2 ( 4%)  | <50><br>0 ( 0%)  | <50><br>3 ( 6%)   | <50><br>1 ( 2%) |
| (Nervous syste | sm]                         |                                       |                  |                  |                   |                 |
| brain          | glioma                      |                                       | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)   | <50><br>0 ( 0%) |
| [Special sense | e organs/appandage]         |                                       |                  |                  |                   |                 |
| Zymbal gl      | squamous cell carcinoma     |                                       | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)   | <50><br>0 ( 0%) |
| [Body cauities | 5]                          |                                       |                  |                  |                   |                 |
| retroperit     | sarcoma:NOS                 |                                       | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)   | <50><br>1 ( 2%) |

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

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

STUDY NO. : 0162

REPORT TYPE : A1

: RAT F344

: FEMALE

ANIMAL

SEX

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

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# APPENDIX N 3

### NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

MOUSE: MALE

(2-YEAR STUDY)

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

STUDY NO. : 0163 : MOUSE BDF1 ANIMAL REPORT TYPE : A1 : MALE SEX

| -gan          | Findings                       | Group Name<br>No. of animals on Study | Control<br>50    | 400 ppm<br>50   | מפס 2000<br>50  | 10000 ppm<br>50 |
|---------------|--------------------------------|---------------------------------------|------------------|-----------------|-----------------|-----------------|
| Integumentary | y system/appandage]            |                                       |                  |                 |                 |                 |
| ubcutis       | xanthoma                       |                                       | <50><br>2 ( 4%)  | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
|               | mastcytoma:benign              |                                       | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
|               | hemang i oma                   |                                       | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |
|               | hemang i osar coma             |                                       | 0 ( 0%)          | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |
| Respiratory   | system]                        |                                       |                  |                 |                 |                 |
| агупх         | squamous cell carcinoma        |                                       | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>2 ( 4%) |
| ung           | bronchiolar-alveolar adenoma   |                                       | <50><br>3 ( 6%)  | <50><br>3 ( 6%) | <50><br>4 (8%)  | <50><br>3 ( 6%) |
|               | bronchiolar-alveolar carcinoma |                                       | 7 (14%)          | 3 ( 6%)         | 5 (10%)         | 2 ( 4%)         |
| Hematopoieti  | ic system]                     |                                       |                  |                 |                 |                 |
| xone marrow   | hemang i oma                   |                                       | <50><br>2 ( 4%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>0 ( 0%) |
| .ymph nade    | malignant lymphoma             |                                       | <50><br>5 ( 10%) | <50><br>6 (12%) | <50><br>6 (12%) | <50><br>3 ( 6%) |
|               | mastcytoma malignant           |                                       | 0 ( 0%)          | 1 ( 2%)         | 0 ( 0%)         | 1 (2%)          |
| spleen        | hemangiama                     |                                       | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
|               | malignant lymphoma             |                                       | 1 (2%)           | 1 ( 2%)         | 2 ( 4%)         | 0 ( 0%)         |
|               | hemangiosarcoma                |                                       | 2 ( 4%)          | 1 (2%)          | 4 ( 8%)         | 0 ( 0%)         |

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

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

PAGE: 1

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

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STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

PAGE: 2

| -gan          | Findings                 | Group Name<br>No. of animals on Study | Control<br>50   | 400 ppm<br>50   | 2000 ppm<br>50  | 10000 ppm<br>50 |
|---------------|--------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Circulatory s | system]                  |                                       |                 |                 |                 |                 |
| eart          | hemangioma               |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| Digestive sys | stem]                    |                                       |                 |                 |                 |                 |
| ral cauity    | squamous cell papilloma  |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>4 ( 8%) |
|               | squamous cell carcinoma  |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 13 (26%)        |
| sophagus      | squamous cell carcinoma  |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>7 (14%) |
| tomach        | squamous cell papilloma  |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>2 ( 4%) |
|               | adenoma                  |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |
|               | squamous cell carcinoma  |                                       | 1 (2%)          | 0 ( 0%)         | 0 ( 0%)         | 7 (14%)         |
|               | mastcytoma:malignant     |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
| iver          | hepatocellular adenoma   |                                       | <50><br>2 ( 4%) | <50><br>6 (12%) | <50><br>4 ( 8%) | <50><br>3 ( 6%) |
|               | angiomyolipoma           |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
|               | histiocytic sarcoma      |                                       | 0 ( 0%)         | 2 ( 4%)         | 0 ( 0%)         | 1 ( 2%)         |
|               | hemangiosarcoma          |                                       | 4 ( 8%)         | 5 ( 10%)        | 5 (10%)         | 4 ( 8%)         |
|               | hepatocellular carcinoma |                                       | 13 (26%)        | 10 ( 20%)       | 9 (18%)         | 4 ( 8%)         |
| [Urinary syst | tem]                     |                                       |                 |                 |                 |                 |
| urin bladd    | histiocytic sarcoma      |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 (2%)  | <50><br>0 ( 0%) |

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

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

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

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

| Drgan          | Findings             | Group Name<br>No. of animals on Study | Control<br>50   | 400 ppm<br>50   | מרוק 2000<br>50 | 10000 maa<br>50 |
|----------------|----------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| [Endocrine sys | stem]                |                                       |                 |                 |                 |                 |
| pituitary      | adenoma              |                                       | <49><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
|                | adenocarcinoma       |                                       | 1 ( 2%)         | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |
| thyroid        | follicular adenoma   |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 (2%)  | <50><br>0 ( 0%) |
| adrenal        | cortical adenoma     |                                       | <50><br>0 ( 0%) | <50><br>1 (2%)  | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| [Reproductive  | system]              |                                       |                 |                 |                 |                 |
| pididymis      | histiocytic sarcoma  |                                       | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| semin ves      | fibrosarcoma         |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| prostate       | adenoma              |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| (Nervous syst  | tem]                 |                                       |                 |                 |                 |                 |
| periph nerv    | histiocytic sarcoma  |                                       | <50><br>1 (2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| [Special sens  | se organs/appandage] |                                       |                 |                 |                 |                 |
| llarder gl     | adonoma              |                                       | <50><br>3 ( 6%) | <50><br>4 ( 8%) | <50><br>6 (12%) | <50><br>2 ( 4%) |
|                | adenocarcinoma       |                                       | 1 ( 2%)         | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |
| (Musculoskele  | ətal system]         |                                       |                 |                 |                 |                 |
| muscle         | hemang i usar coma   |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |

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

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

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| ANIMAL :<br>REPORT TYPE :                   | 0163<br>NOUSE BDF1<br>A1<br>MALE  | HISTOLOGICAL FINDINGS : NEOP<br>ALL ANIMALS (0-105W) | LASTIC LESIONS (S | JMMARY)         |                 | PAGE : 4        |
|---|---|--|-------------------|-----------------|-----------------|-----------------|
| 0rgan                                       | Findings  | Group Name<br>No. of animals on Study                | Control<br>50     | 400 ppm<br>50   | 2000 ppm<br>50  | 10000 ppm<br>50 |
| (Musculoskelet                              | tal system]   |  |                   |                 |                 |                 |
| bone  | osteoma   |  | <50><br>0 ( 0%)   | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>1 ( 2%) |
| [Body cavities                              | 5]  |  |                   |                 |                 |                 |
| mediastinum                                 | hemang i osarcoma   |  | <50><br>1 ( 2%)   | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| peritoneum                                  | hemangiosarcoma   |  | <50><br>1 ( 2%)   | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| retroperit                                  | hemangiosarcoma   |  | <50><br>1 ( 2%)   | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| <pre> &lt; a &gt;  b ( c )   (upress)</pre> | a : Number of animals examined at the site<br>b : Number of animals with neoplasm c : b | / a * 100  |                   |                 |                 | DATCO           |

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### APPENDIX N 4

### NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

MOUSE: FEMALE

(2-YEAR STUDY)

|                | 0163<br>MOUSE BDF1             | HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)<br>ALL ANIMALS (0-105W) |                 |                 |                 |                 |  |
|----------------|--------------------------------|--|-----------------|-----------------|-----------------|-----------------|--|
|                | FENALE                         |  |                 |                 |                 | PAGE : 5        |  |
| Organ          | Findings                       | Group Name<br>No. of animals on Study  | Cantral<br>50   | 400 ppm<br>50   | 2000 ppm<br>50  | 10000 pm<br>49  |  |
| [Integumentary | y system/appandage]            |  |                 |                 |                 |                 |  |
| skin/app       | squamous cell carcinoma        |  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>1 (2%)  |  |
| subcutis       | xanthoma                       |  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>1 ( 2%) |  |
|                | hemangiosarcoma                |  | 1 ( 2%)         | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |  |
| [Respiratory : | system]                        |  |                 |                 |                 |                 |  |
| nasal cavit    | histiocytic sarcoma            |  | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <49><br>0 ( 0%) |  |
| Larynx         | squamous cell carcinoma        |  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <49><br>1 (2%)  |  |
| lung           | bronchiolar-alueolar adenoma   |  | <50><br>1 ( 2%) | <50><br>3 ( 6%) | <50><br>1 ( 2%) | <49><br>2 (4%)  |  |
|                | bronchiolar-alveolar carcinoma |  | 2 ( 4%)         | 3 ( 6%)         | 1 ( 2%)         | 1 ( 2%)         |  |
| [llematopoieti | c system]                      |  |                 |                 |                 |                 |  |
| bone marrow    | hemang i oma                   |  | <49><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <49><br>0 ( 0%) |  |
|                | mastcytoma:malignant           |  | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |  |
|                | hemangiosarcoma                |  | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |  |
| lymph node     | mastcytoma:benign              |  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>1 ( 2%) |  |
|                | malignant lymphoma             |  | 11 (22%)        | 10 ( 20%)       | 17 ( 34%)       | 10 (20%)        |  |
|                | mastcytoma:malignant           |  | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         |  |

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

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

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| REPORT TYPE :  |                         | ALL ANIMALS (0-105W)                  | ·               |                  |                 |                 |
|----------------|-------------------------|---------------------------------------|-----------------|------------------|-----------------|-----------------|
| SEX :          | FEMALE                  |                                       |                 |                  |                 | PAGE : 6        |
| 0rgan          | Findings                | Group Name<br>No. of animals on Study | Control<br>50   | 400 ppm<br>50    | 2000 ppm<br>50  | 10000 ppm<br>49 |
| [Hematopoietic | ; system]               |                                       |                 |                  |                 |                 |
| thymus         | malignant lymphoma      |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <49><br>0 ( 0%) |
| spleen         | malignant lymphoma      |                                       | <50><br>0 ( 0%) | <50><br>5 ( 10%) | <50><br>1 ( 2%) | <49><br>1 ( 2%) |
|                | hemangiosarcoma         |                                       | 1 ( 2%)         | 1 ( 2%)          | 1 ( 2%)         | 0 ( 0%)         |
| [Digestive sys | stem]                   |                                       |                 |                  |                 |                 |
| oral cavity    | squamous cell papilloma |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <49><br>3 ( 6%) |
|                | squamous cell carcinoma |                                       | 0 ( 0%)         | 0 ( 0%)          | 0 ( 0%)         | 15 ( 31%)       |
| tongue         | squamous cell papilloma |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <49><br>1 ( 2%) |
|                | squamous cell carcinoma |                                       | 2 ( 4%)         | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         |
| sali∪ary gl    | adenocarcinoma          |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <49><br>0 ( 0%) |
| esophagus      | squamous cell papilloma |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>1 ( 2%) | <49><br>0 ( 0%) |
|                | squamous cell carcinoma |                                       | 0 ( 0%)         | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2.%)        |
| stomach        | squamous cell papilloma |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <49><br>1 ( 2%) |
|                | mastcytoma:benign       |                                       | 1 ( 2%)         | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)         |
|                | squamous cell carcinoma |                                       | 0 ( 0%)         | 0 ( 0%)          | 0 ( 0%)         | $3 (6^{v}_{h})$ |
| small intes    | hemangiosarcoma         |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <49><br>0 ( 0%) |

a : Number of animals examined at the site

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

ANIMAL : MOUSE BDF1

STUDY NO. : 0163

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

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STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

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

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|---------------|--------------------------|---------------------------------------|-------------------|-----------------|-----------------|-------------------|
| 0rgan         | Findings                 | Group Name<br>No. of animals on Study | Control<br>50     | 400 mag<br>50   | 2000 ppm<br>50  | 10000 ppm<br>49   |
| [Digestive sy | vstem]                   |                                       |                   |                 |                 |                   |
| liver         | hemangioma               |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%) | <50><br>0 ( 0%) | . <49><br>1 ( 2%) |
|               | hepatocellular adenoma   |                                       | 3 ( 6%)           | 1 ( 2%)         | 4 ( 8%)         | 0 ( 0%)           |
|               | histiocytic sarcoma      |                                       | 0 ( 0%)           | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)           |
|               | hemangiosarcoma          |                                       | 3 ( 6%)           | 3 ( 6%)         | 0 ( 0%)         | 1 ( 2%)           |
|               | hepatocellular carcinoma |                                       | 1 ( 2%)           | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)           |
| [Endocrine sy | /stem]                   |                                       |                   |                 |                 |                   |
| pituitary     | adenoma                  |                                       | <50><br>10 ( 20%) | <49><br>6 (12%) | <49><br>8 (16%) | <49><br>7 (14%)   |
|               | adenocarcinoma           |                                       | 0 ( 0%)           | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)           |
| adrenal       | pheochromocytoma         |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <49><br>0 ( 0%)   |
|               | cortical adenoma         |                                       | 0 ( 0%)           | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)           |
| [Reproductive | e system]                |                                       |                   |                 |                 |                   |
| в∪агу         | cystadenoma              |                                       | <50><br>2 ( 4%)   | <50><br>0 ( 0%) | <50><br>2 ( 4%) | <49><br>0 ( 0%)   |
|               | hemang i oma             |                                       | 1 ( 2%)           | 0 ( 0%)         | 1 ( 2%)         | 1 ( 2%)           |
|               | cystadenocarcinoma       |                                       | 0 ( 0%)           | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)           |
| uterus        | fibroma                  |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <48><br>0 ( 0%)   |

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

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

PAGE : 7

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

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STUDY NO.:0163ANIMAL:MOUSE BDF1REPORT TYPE:A1SEX:FEMALE

| )rgan          | Findings                  | Group Name<br>No. of animals on Study |      | ontrol<br>50  |    | 400 ppm<br>50 |   | 2000 ppm<br>50 | 1  | 0000 ppm<br>49 |
|----------------|---------------------------|---------------------------------------|------|---------------|----|---------------|---|----------------|----|----------------|
| Reproductive   | system]                   |                                       |      |               |    |               |   |                |    |                |
| iterus         | endometrial stromal polyp |                                       |      | (50><br>( 0%) | 1  | <50><br>( 2%) | 0 | <50><br>( 0%)  | 0  | <48><br>( 0%)  |
|                | Leiomyosarcoma            |                                       | 0 (  | ( 0%)         | 0  | ( 0%)         | 1 | ( 2%)          | 0  | ( 0%)          |
|                | histiocytic sarcoma       | 1                                     | 10 ( | ( 20%)        | 11 | (22%)         | 8 | ( 16%)         | 10 | ( 21%)         |
|                | hemangioendothelioma      |                                       | 1    | ( 2%)         | 0  | ( 0%)         | 0 | ( 0%)          | 1  | ( 2%)          |
| nammary gl     | adenoma                   |                                       |      | (50><br>( 0%) | 0  | <50><br>( 0%) | 1 | <50><br>( 2%)  | 0  | <49><br>( 0%)  |
|                | adenocarcinoma            |                                       | 2    | ( 4%)         | 1  | ( 2%)         | 2 | ( 4%)          | 0  | ( 0%)          |
| (Nervous syste | em]                       |                                       |      |               |    |               |   |                |    |                |
| periph nerv    | histiocytic sarcoma       |                                       |      | (50><br>( 0%) | 0  | <50><br>( 0%) | 0 | <50><br>( 0%)  | 1  | <49><br>( 2%)  |
| [Special sense | e organs/appandage]       |                                       |      |               |    |               |   |                |    |                |
| Harder gl      | adenoma                   |                                       |      | (50><br>(0%)  | 4  | <50><br>( 8%) | 3 | <50><br>( 6%)  | 0  | <49><br>( 0%)  |
|                | adenocarcinoma            |                                       | 0    | ( 0%)         | 0  | ( 0%)         | 0 | ( 0%)          | 1  | ( 2%)          |
| [Musculoskele  | tal system]               |                                       |      |               |    |               |   |                |    |                |
| muscle         | hemangiosarcoma           |                                       |      | <50><br>( 0%) | 0  | <50><br>( 0%) | 1 | <50><br>( 2%)  | 0  | <49><br>( 0%)  |
| ODIÐ           | osteoma                   |                                       |      | (49)<br>(0%)  | 1  | <50><br>( 2%) | 0 | <50><br>(0%)   | 1  | <49><br>( 2%)  |
|                | osteosarcoma              |                                       | 1    | ( 2%)         | 0  | ( 0%)         | 0 | ( 0%)          | 0  | ( 0%)          |

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

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

| ANIMAL<br>REPORT TYPE       | : 0163<br>: MOUSE BDF1<br>: A1<br>: FEMALE                                        | HISTOLOGICAL FINDINGS : NEOF<br>ALL ANIMALS (0-105W) | HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)<br>ALL ANIMALS (0-105W) |               |                |                 |  |  |  |
|-----------------------------|-----------------------------------------------------------------------------------|------------------------------------------------------|------------------------------------------------------------------------------|---------------|----------------|-----------------|--|--|--|
| Organ                       | Findings                                                                          | Group Name<br>No. of animals on Study                | Control<br>50                                                                | 400 ppm<br>50 | 2000 ppm<br>50 | 10000 ppm<br>49 |  |  |  |
| [Body cavitie<br>peritoneum | es]<br>hemangioma                                                                 |                                                      | <50>                                                                         | <50>          | <50>           | <49>            |  |  |  |
| <a>b (c)</a>                | a : Number of animals examined at the site<br>b : Number of animals with neoplasm | c:b/a*100                                            | 0 ( 0%)                                                                      | 1 (2%)        | 0 ( 0%)        | 0 ( 0%)         |  |  |  |
| (HPT085)                    |                                                                                   |                                                      |                                                                              |               |                |                 |  |  |  |

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### APPENDIX O 1

### NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : MALE

(2-YEAR STUDY)

STUDY No. : 0162 ANIMAL : RAT F344 SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                            | Control                                          | 400 ppm     | 2000 ppm    | 10000 ppm  |  |
|-------------------------------------------------------|--------------------------------------------------|-------------|-------------|------------|--|
|                                                       | SITE : skin/appendage<br>TUMOR : keratoacanthoma |             |             |            |  |
| umor rate                                             | ionor · Reratoacanthoma                          |             |             |            |  |
| Overall rates(a)                                      | 3/50( 6.0)                                       | 2/50( 4.0)  | 4/50( 8.0)  | 1/50( 2.0) |  |
| Idjusted rates(b)                                     | 6.82                                             | 5.00        | 10.53       | 2.56       |  |
| 'erminal rates(c)<br>:atistical analysis<br>'eto test | 3/44( 6.8)                                       | 2/40( 5.0)  | 3/36( 8.3)  | 1/39( 2.6) |  |
| Standard method(d)                                    | P =                                              |             |             |            |  |
| Prevalence method(d)                                  | P = 0.8230                                       |             |             |            |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)      | P =P = 0.3288                                    |             |             |            |  |
| Fisher Exact test(e)                                  | r - V.3200                                       | P = 0.4909  | P = 0.4895  | P = 0.3235 |  |
|                                                       |                                                  |             |             |            |  |
|                                                       | SITE : subcutis<br>TUMOR : fibroma               |             |             |            |  |
| umor rate<br>Verall rates(a)                          | 3/50( 6.0)                                       | 4/50( 8.0)  | 8/50( 16.0) | 3/50( 6.0) |  |
| Adjusted rates(b)                                     | 6.82                                             | 10.00       | 19.44       | 5,50( 5.13 |  |
| Ferminal rates(c)<br>tatistical analysis              | 3/44( 6.8)                                       | 4/40( 10.0) | 7/36(19.4)  | 2/39( 5.1) |  |
| Peto test<br>Standard method(d)                       | P = 0.1883                                       |             |             |            |  |
| Prevalence method(d)                                  | P = 0.7841                                       |             |             |            |  |
| Combined analysis(d)                                  | P = 0.6457                                       |             |             |            |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e)      | P = 0.6172                                       | P = 0.4895  | P = 0.1322  | P = 0.3392 |  |
|                                                       |                                                  | P = 0.4090  | F = 0.1322  | P = 0.3392 |  |
|                                                       | SITE : subcutis                                  |             |             |            |  |
| umor rate                                             | TUMOR : Lipoma                                   |             |             |            |  |
| Overall rates(a)                                      | 1/50( 2.0)                                       | 0/50( 0.0)  | 3/50( 6.0)  | 0/50( 0.0) |  |
| Adjusted rates(b)                                     | 2.27                                             | 0.0         | 8.33        | 0.0        |  |
| erminal rates(c)<br>atistical analysis                | 1/44( 2.3)                                       | 0/40( 0.0)  | 3/36( 8.3)  | 0/39( 0.0) |  |
| Peto test                                             |                                                  |             |             |            |  |
| Standard method(d)                                    | P =                                              |             |             |            |  |
| Prevalence method(d)<br>Combined analysis(d)          | P = 0.7438<br>P =                                |             |             |            |  |
| Cochran-Armitage test(e)                              | P = 0.4252                                       |             |             |            |  |
| isher Exact test(e)                                   |                                                  | P = 0.4950  | P = 0.3235  | P = 0.4950 |  |

STUDY No. : 0162 ANIMAL : RAT F344 Sex : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                   | Control                                            | 400 ppm                               | 2000 ppm           | 10000 maa          |  |
|----------------------------------------------|----------------------------------------------------|---------------------------------------|--------------------|--------------------|--|
|                                              | SITE : subcutis                                    |                                       |                    |                    |  |
| lumor rate                                   | TUMOR : fibroma,fibrosarcoma                       |                                       |                    |                    |  |
| Overall rates(a)                             | 3/50( 6.0)                                         | 5/50( 10.0)                           | 9/50(18.0)         | 5/50(10.0)         |  |
| Adjusted rates(b)                            | 6.82                                               | 10.00                                 | 22.22              | 10.26              |  |
| Terminal rates(c)                            | 3/44( 6.8)                                         | 4/40( 10.0)                           | 8/36(22.2)         | 4/39( 10.3)        |  |
| Statistical analysis<br>Peto test            |                                                    |                                       |                    |                    |  |
| Standard method(d)                           | P = 0.3122                                         |                                       |                    |                    |  |
| Prevalence method(d)                         | P = 0.4746                                         |                                       |                    |                    |  |
| Combined analysis(d)                         | P = 0.4113                                         |                                       |                    |                    |  |
| Cochran-Armitage test(e)                     | P = 0.9201                                         | <b>D</b>                              | D 0 0000           | D 0.0700           |  |
| Fisher Exact test(e)                         |                                                    | P = 0.3790                            | P = 0.0899         | P = 0.3790         |  |
|                                              | SITE : lung                                        |                                       |                    |                    |  |
|                                              | TUMOR : bronchiolar-alveolar adenor                | າລ                                    |                    |                    |  |
| Tumor rate                                   |                                                    | · · · · · · · · · · · · · · · · · · · |                    |                    |  |
| Overall rates(a)<br>Adjusted rates(b)        | 3/50( 6.0)<br>6.82                                 | 1/50( 2.0)<br>2.50                    | 3/50( 6.0)<br>6.82 | 1/50( 2.0)<br>2.56 |  |
| Terminal rates(c)                            | 3/44(6.8)                                          | 1/40( 2.5)                            | 2/36(5.6)          | 1/39( 2.6)         |  |
| Statistical analysis                         | 0,11( 0:0)                                         | 1/10( 2.0)                            | 2700( 010)         | 1,00( 1.0)         |  |
| Peto test                                    |                                                    |                                       |                    |                    |  |
| Standard method(d)                           | P =                                                |                                       |                    |                    |  |
| Prevalence method(d)<br>Combined analysis(d) | P = 0.7670<br>P =                                  |                                       |                    |                    |  |
| Cochran-Armitage test(e)                     | P = 0.4546                                         |                                       |                    |                    |  |
| Fisher Exact test(e)                         |                                                    | P = 0.3235                            | P = 0.3392         | P = 0.3235         |  |
|                                              |                                                    |                                       |                    |                    |  |
|                                              | SITE : spleen<br>TUMOR : mononuclear cell leukemia |                                       |                    |                    |  |
| Tumor rate                                   |                                                    |                                       |                    |                    |  |
| Overall rates(a)                             | 3/50( 6,0)                                         | 5/50( 10.0)                           | 7/49(14.3)         | 4/50( 8.0)         |  |
| Adjusted rates(b)                            | 4.55                                               | 7.50                                  | 11.43              | 2.56               |  |
| Terminal rates(c)                            | 2/44( 4.5)                                         | 3/40( 7.5)                            | 4/35(11.4)         | 1/39( 2.6)         |  |
| Statistical analysis<br>Peto test            |                                                    |                                       |                    |                    |  |
| Standard method(d)                           | P = 0.2447                                         |                                       |                    |                    |  |
| Prevalence method(d)                         | P = 0.8011                                         |                                       |                    |                    |  |
| Combined analysis(d)                         | P = 0.5418                                         |                                       |                    |                    |  |
| Cochran-Armitage test(e)                     | P = 0.8584                                         |                                       |                    |                    |  |
| Fisher Exact test(e)                         |                                                    | P = 0.3790                            | P = 0.1836         | P = 0.4895         |  |

STUDY NO. : 0162 ANIMAL : RAT F344 SEX : MALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                                                                                                                                                                                                      | Control                                                                                                                                     | 400 ppm               | mag 000\$            | 10000 mag             |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------------------|-----------------------|--|
|                                                                                                                                                                                                                                                                 | SITE : oral cavity                                                                                                                          |                       |                      |                       |  |
| Tumor rate                                                                                                                                                                                                                                                      | TUMOR : squamous cell carcinoma                                                                                                             |                       |                      |                       |  |
| Overall rates(a)                                                                                                                                                                                                                                                | 0/50( 0.0)                                                                                                                                  | 0/50( 0.0)            | 0/50( 0.0)           | 5/50( 10.0)           |  |
| Adjusted rates(b)                                                                                                                                                                                                                                               | 0.0                                                                                                                                         | 0.0                   | 0.0                  | 7.69                  |  |
| Terminal rates(c)                                                                                                                                                                                                                                               | 0/44( 0.0)                                                                                                                                  | 0/40( 0.0)            | 0/36( 0.0)           | 3/39( 7.7)            |  |
| Statistical analysis                                                                                                                                                                                                                                            | , , ,                                                                                                                                       |                       | , , , , ,            |                       |  |
| Peto test                                                                                                                                                                                                                                                       |                                                                                                                                             |                       |                      |                       |  |
| Standard method(d)                                                                                                                                                                                                                                              | P = 0.0161 * ?                                                                                                                              |                       |                      |                       |  |
| Prevalence method(d)                                                                                                                                                                                                                                            | P = 0.0019 * * ?                                                                                                                            |                       |                      |                       |  |
| Combined analysis(d)                                                                                                                                                                                                                                            | P = 0.0001**?                                                                                                                               |                       |                      |                       |  |
| Cochran-Armitage test(e)                                                                                                                                                                                                                                        | P = 0.0001 **                                                                                                                               | D 0 5000              |                      | D 0.0000              |  |
| Fisher Exact test(e)                                                                                                                                                                                                                                            |                                                                                                                                             | P = 0.5000            | P = 0.5000           | P = 0.0360*           |  |
|                                                                                                                                                                                                                                                                 | SITE : oral cavity                                                                                                                          |                       |                      |                       |  |
|                                                                                                                                                                                                                                                                 | TUMOR : squamous cell papilloma, so                                                                                                         | uamous cell carcinoma |                      |                       |  |
| Tumor rate                                                                                                                                                                                                                                                      |                                                                                                                                             |                       |                      |                       |  |
| Overall rates(a)                                                                                                                                                                                                                                                | 0/50( 0.0)                                                                                                                                  | 0/50( 0.0)            | 0/50( 0.0)           | 7/50(14.0)            |  |
| Adjusted rates(b)                                                                                                                                                                                                                                               | 0.0                                                                                                                                         | 0.0                   | 0.0                  | 12.82                 |  |
| Terminal rates(c)                                                                                                                                                                                                                                               | 0/44( 0.0)                                                                                                                                  | 0/40( 0.0)            | 0/36( 0.0)           | 5/39(12.8)            |  |
| Statistical analysis                                                                                                                                                                                                                                            | •<br>•                                                                                                                                      |                       |                      |                       |  |
| Peto test<br>Standard method(d)                                                                                                                                                                                                                                 | P = 0.0161 * ?                                                                                                                              |                       |                      |                       |  |
| Prevalence method(d)                                                                                                                                                                                                                                            | P < 0.0001 * ?                                                                                                                              |                       |                      |                       |  |
|                                                                                                                                                                                                                                                                 | 1 < 0.0001**!                                                                                                                               |                       |                      |                       |  |
|                                                                                                                                                                                                                                                                 | P < 0 0001**7                                                                                                                               |                       |                      |                       |  |
| Combined analysis(d)                                                                                                                                                                                                                                            | P < 0.0001**?<br>P < 0.0001**                                                                                                               |                       |                      |                       |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)                                                                                                                                                                                                                | P < 0.0001**?<br>P < 0.0001**                                                                                                               | P = 0.5000            | P = 0.5000           | P = 0.0101*           |  |
| Combined analysis(d)                                                                                                                                                                                                                                            |                                                                                                                                             | P = 0.5000            | P = 0.5000           | P = 0.0101*           |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)                                                                                                                                                                                                                | P < 0.0001**<br>SITE : pituitary gland                                                                                                      | P = 0.5000            | P = 0.5000           | P = 0.0101*           |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)                                                                                                                                                                                        | P < 0.0001**                                                                                                                                | P = 0.5000            | P = 0.5000           | P = 0.0101*           |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Tumor rate                                                                                                                                                                          | P < 0.0001**<br>SITE : pituitary gland<br>TUMOR : adenoma                                                                                   |                       |                      |                       |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Tumor rate<br>Ouerall rates(a)                                                                                                                                                      | P < 0.0001**<br>SITE : pituitary gland<br>TUMOR : adenoma<br>19/50(38.0)                                                                    | 16/50( 32.0)          | 14/50(28.0)          | 11/50( 22.0)          |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)                                                                                                                                 | P < 0.0001**<br>SITE : pituitary gland<br>TUMOR : adenoma<br>19/50(38.0)<br>36.36                                                           | 16/50( 32.0)<br>30.95 | 14/50(28.0)<br>27.78 | 11/50( 22.0)<br>23.26 |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)                                                                                                            | P < 0.0001**<br>SITE : pituitary gland<br>TUMOR : adenoma<br>19/50(38.0)                                                                    | 16/50( 32.0)          | 14/50(28.0)          | 11/50( 22.0)          |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis                                                                                    | P < 0.0001**<br>SITE : pituitary gland<br>TUMOR : adenoma<br>19/50(38.0)<br>36.36                                                           | 16/50( 32.0)<br>30.95 | 14/50(28.0)<br>27.78 | 11/50( 22.0)<br>23.26 |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test                                                                       | P < 0.0001**<br>SITE : pituitary gland<br>TUMOR : adenoma<br>19/50(38.0)<br>36.36<br>16/44(36.4)                                            | 16/50( 32.0)<br>30.95 | 14/50(28.0)<br>27.78 | 11/50( 22.0)<br>23.26 |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Fumor rate<br>Ouerall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)                                                 | P < 0.0001**<br>SITE : pituitary gland<br>TUMOR : adenoma<br>19/50(38.0)<br>36.36<br>16/44(36.4)<br>P = 0.8020                              | 16/50( 32.0)<br>30.95 | 14/50(28.0)<br>27.78 | 11/50( 22.0)<br>23.26 |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Fumor rate<br>Ouerall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)                         | <pre>P &lt; 0.0001** SITE : pituitary gland TUMOR : adenoma 19/50(38.0) 36.36 16/44(36.4) P = 0.8020 P = 0.9032</pre>                       | 16/50( 32.0)<br>30.95 | 14/50(28.0)<br>27.78 | 11/50( 22.0)<br>23.26 |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Tumor rate<br>Ouerall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d) | <pre>P &lt; 0.0001** SITE : pituitary gland TUMOR : adenoma 19/50(38.0) 36.36 16/44(36.4) P = 0.8020 P = 0.9032 P = 0.9032 P = 0.9418</pre> | 16/50( 32.0)<br>30.95 | 14/50(28.0)<br>27.78 | 11/50( 22.0)<br>23.26 |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)<br>Ouerall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)                                       | <pre>P &lt; 0.0001** SITE : pituitary gland TUMOR : adenoma 19/50(38.0) 36.36 16/44(36.4) P = 0.8020 P = 0.9032</pre>                       | 16/50( 32.0)<br>30.95 | 14/50(28.0)<br>27.78 | 11/50( 22.0)<br>23.26 |  |

STUDY No. : 0162 ANIMAL : RAT F344 SEX : MALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                       | 400 ppm             | 2000 mqq           | 10000 ppm                             |    |
|--------------------------------------------------|-------------------------------|---------------------|--------------------|---------------------------------------|----|
|                                                  | SITE : pituitary gland        |                     |                    |                                       |    |
| umor rate                                        | TUMOR : adenoma, adenocarcino | na                  |                    |                                       |    |
| Overall rates(a)                                 | 19/50( 38.0)                  | 16/50( 32.0)        | 15/50( 30.0)       | 11/50(22.0)                           |    |
| Adjusted rates(b)                                | 36.36                         | 30.95               | 29.73              | 23.26                                 |    |
| Terminal rates(c)                                | 16/44( 36.4)                  | 12/40( 30.0)        | 10/36(27.8)        | 8/39(20.5)                            |    |
| itatistical analysis                             |                               |                     |                    |                                       |    |
| Peto test                                        |                               |                     |                    |                                       |    |
| Standard method(d)                               | P = 0.8020                    |                     |                    |                                       |    |
| Prevalence method(d)                             | P = 0.9091                    |                     |                    |                                       |    |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.9453                    |                     |                    |                                       |    |
| Fisher Exact test(e)                             | P = 0.1057                    | P = 0.4055          | P = 0.3472         | P = 0.1411                            |    |
|                                                  |                               | r - 0.4055          | r = 0.3472         | P = 0.1411                            |    |
|                                                  | SITE : thyroid                |                     |                    |                                       |    |
|                                                  | TUMOR : C-cell adenoma        |                     |                    |                                       |    |
| Cumor rate                                       |                               |                     |                    |                                       |    |
| Overall rates(a)<br>Adjusted rates(b)            | 7/50(14.0)<br>15.22           | 9/49(18.4)<br>22.50 | 3/49( 6.1)<br>8.33 | 7/49(14.3)                            |    |
| Terminal rates(c)                                | 6/44(13.6)                    | 9/40(22.5)          | 2/35( 5.7)         | 17.95<br>7/39(17.9)                   |    |
| Statistical analysis                             | 0/11(10.0)                    | 0/10( 22.0)         | 2/00( 0.1)         | 7/00(11:0)                            |    |
| Peto test                                        |                               |                     |                    |                                       |    |
| Standard method(d)                               | P =                           |                     |                    |                                       |    |
| Prevalence method(d)                             | P = 0.4844                    |                     |                    |                                       |    |
| Combined analysis(d)                             | P =                           | ·                   |                    |                                       |    |
| Cochran-Armitage test(e)                         | P = 0.9755                    |                     |                    |                                       |    |
| Fisher Exact test(e)                             |                               | P = 0.4089          | P = 0.2004         | P = 0.4019                            |    |
|                                                  | SITE : thyroid                |                     |                    | · · · · · · · · · · · · · · · · · · · |    |
|                                                  | TUMOR : C-cell adenoma, C-cel | l carcinoma         |                    |                                       |    |
| umor rate                                        |                               |                     |                    |                                       | Ν. |
| Overall rates(a)                                 | 8/50(16.0)                    | 11/49(22.4)         | 5/49( 10.2)        | 7/49(14.3)                            |    |
| Adjusted rates(b)                                | 17.39                         | 27,50               | 11.90              | 17.95                                 |    |
| Terminal rates(c)<br>Statistical analysis        | 7/44(15,9)                    | 11/40(27.5)         | 3/35( 8.6)         | 7/39(17.9)                            |    |
| Peto test                                        |                               |                     |                    |                                       |    |
| Standard method(d)                               | P =                           |                     |                    |                                       |    |
| Prevalence method(d)                             | P = 0.7025                    |                     |                    |                                       |    |
| Combined analysis(d)                             | P =                           |                     |                    |                                       |    |
| Cochran-Armitage test(e)                         | P = 0.5880                    |                     |                    |                                       |    |
| Fisher Exact test(e)                             |                               | P = 0.3379          | P = 0.3267         | P = 0.4706                            |    |

STUDY No. : 0162 ANIMAL : RAT F344 SEX : MALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                      | Control                                             | 400 mag                          | 2000 mag                        | 10000 ppm                        |
|---------------------------------------------------------------------------------|-----------------------------------------------------|----------------------------------|---------------------------------|----------------------------------|
| umor rate                                                                       | SITE : thyroid<br>TUMOR : follicular adenoma,foll   | icular adenocarcinoma            |                                 |                                  |
| Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)                      | 0/50( 0.0)<br>0.0<br>0/44( 0.0)                     | 3/49( 6.1)<br>6.38<br>2/40( 5.0) | 0/49( 0.0)<br>0.0<br>0/35( 0.0) | 1/49( 2.0)<br>2.56<br>1/39( 2.6) |
| tatistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)  | P =<br>P = 0.5241                                   | 2, 10( 010)                      | 0,00( 0.0)                      | 1,00( 2.0)                       |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e)        | P =<br>P = 0.8872                                   | P = 0.1287                       | P = 0.5000                      | P = 0.5000                       |
|                                                                                 | SITE : pancreas islet<br>TUMOR : islet cell adenoma |                                  |                                 |                                  |
| .mor rate<br>Dverall rates(a)                                                   | 6/50(12.0)                                          | 5/50( 10.0)                      | 4/50( 8.0)                      | 3/50( 6.0)                       |
| djusted rates(b)<br>erminal rates(c)<br>ratistical analysis                     | 13.04<br>5/44( 11.4)                                | 12.50<br>5/40(12.5)              | 11.11<br>4/36(11.1)             | 6.12<br>2/39( 5.1)               |
| Peto test<br>Standard method(d)<br>Pre∪alence method(d)<br>Combined analysis(d) | P =<br>P = 0.8427<br>P =                            |                                  |                                 |                                  |
| Cochran-Armitage test(e)<br>Visher Exact test(e)                                | P = 0.3355                                          | P = 0.4872                       | P = 0.3944                      | P = 0.2728                       |
|                                                                                 | SITE : adrenal gland<br>TUMOR : pheochromocytoma    |                                  |                                 |                                  |
| mor rate<br>Duerall rates(a)                                                    | 8/50(16.0)                                          | 4/50( 8.0)                       | 9/50(18.0)                      | 7/50( 14.0)                      |
| djusted rates(b)<br>Yerminal rates(c)<br>Satistical analysis<br>Yeto test       | 17.78<br>7/44(15.9)                                 | 10.00<br>4/40( 10.0)             | 23.68<br>8/36(22.2)             | 15.38<br>6/39(15.4)              |
| Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)              | P =<br>P = 0.4493<br>P =                            |                                  |                                 |                                  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e)                                | P = 0.8881                                          | P = 0.2169                       | P = 0.4846                      | P = 0.4854                       |

STUDY No. : 0162 ANIMAL : RAT F344

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

SEX : MALE

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| Group Name                             | Control                     | 400 mag                  | 2000 ppm                              | 10000 ppm    |           |
|----------------------------------------|-----------------------------|--------------------------|---------------------------------------|--------------|-----------|
|                                        | SITE : adrenal gland        |                          |                                       |              |           |
| Tumor rate                             | TUMOR : pheachromocytoma,ph | eochromocytoma:malignant |                                       |              |           |
| Overall rates(a)                       | 9/50(18.0)                  | 4/50( 8.0)               | 10/50( 20,0)                          | 7/50(14.0)   |           |
| Adjusted rates(b)                      | 20.00                       | 4/50( 8.0)<br>10.00      | 23.81                                 | 15.38        |           |
| Terminal rates(c)                      | 8/44(18.2)                  | 4/40( 10.0)              | 8/36(22,2)                            | 6/39(15.4)   |           |
| Statistical analysis                   | 0/44( 10.2)                 | 4/40( 10.0)              | 0/30(22.2)                            | 0/39(13:4)   |           |
| Peto test                              |                             |                          |                                       |              |           |
| Standard method(d)                     | P =                         |                          |                                       |              |           |
| Prevalence method(d)                   | P = 0.5452                  |                          |                                       |              |           |
| Combined analysis(d)                   | P =                         |                          |                                       |              |           |
| Cochran-Armitage test(e)               | P = 0.9455                  |                          |                                       |              |           |
| Fisher Exact test(e)                   | 1 - 0.0400                  | P = 0.1562               | P = 0.4839                            | P = 0.4234   |           |
|                                        | SITE : testis               |                          | · · · · · · · · · · · · · · · · · · · |              | - <u></u> |
|                                        | TUMOR : interstitial cell t | umor                     |                                       |              |           |
| Tumor rate                             |                             |                          |                                       |              |           |
| Overall rates(a)                       | 42/50( 84.0)<br>88.89       | 40/50( 80.0)             | 44/50(88.0)                           | 47/50(94.0)  |           |
| Adjusted rates(b)<br>Terminal rates(c) | 39/44(88.6)                 | 86.05                    | 94.59                                 | 100.00       |           |
| Statistical analysis                   | 39/44( 88.6)                | 34/40( 85.0)             | 34/36(94.4)                           | 39/39(100.0) |           |
| Peto test                              |                             |                          |                                       |              |           |
| Standard method(d)                     | P =                         |                          |                                       |              |           |
| Prevalence method(d)                   | P = 0.0188*                 |                          |                                       |              |           |
| Combined analysis(d)                   | P =                         |                          |                                       |              |           |
| Cochran-Armitage test(e)               | P = 0.0543                  |                          |                                       |              |           |
| Fisher Exact test(e)                   |                             | P = 0.4942               | P = 0.4956                            | P = 0.4053   |           |

(HPT360A)

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire 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 probabities 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 :  $*: P \leq 0.05$   $**: P \leq 0.01$ 

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# APPENDIX O 2

### NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : FEMALE

(2-YEAR STUDY)

#### STUDY No. : 0162 ANIMAL : RAT F344

SEX : FENALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                                                      | Cantrol                                                 | 400 ppm     | 2000 maa   | 10000 mag                              |     |  |  |  |
|-----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|-------------|------------|----------------------------------------|-----|--|--|--|
|                                                                                                                 | SITE : spleen                                           |             |            |                                        |     |  |  |  |
| The second se | TUMOR : mononuclear cell leukemia                       |             |            |                                        |     |  |  |  |
| Tumor rate<br>Overall rates(a)                                                                                  | 4/50( 8.0)                                              | 5/50( 10.0) | 8/50(16.0) | 7/50(14.0)                             |     |  |  |  |
| Adjusted rates(b)                                                                                               | 4,30( 3.0)                                              | 6.98        | 12.20      | 8,11                                   |     |  |  |  |
| Terminal rates(c)                                                                                               | 2/41( 4.9)                                              | 2/40( 5.0)  | 5/41(12.2) | 3/37( 8.1)                             |     |  |  |  |
| Statistical analysis                                                                                            |                                                         | _, _, _, _, |            |                                        |     |  |  |  |
| Peto test                                                                                                       |                                                         |             |            |                                        |     |  |  |  |
| Standard method(d)                                                                                              | P = 0.1657                                              |             |            |                                        |     |  |  |  |
| Prevalence method(d)                                                                                            | P = 0.4001                                              |             |            |                                        |     |  |  |  |
| Combined analysis(d)                                                                                            | P = 0.2003                                              |             |            |                                        |     |  |  |  |
| Cochran-Armitage test(e)                                                                                        | P = 0.4653                                              | D 0 1000    | D 0 0100   | P = 0.9050                             |     |  |  |  |
| Fisher Exact test(e)                                                                                            |                                                         | P = 0.4883  | P = 0.2169 | P = 0.2958                             |     |  |  |  |
|                                                                                                                 | SITE : oral cavity                                      |             |            |                                        |     |  |  |  |
|                                                                                                                 | TUMOR : squamous cell carcinoma                         |             |            |                                        |     |  |  |  |
| Tumor rate                                                                                                      |                                                         |             |            |                                        |     |  |  |  |
| Overall rates(a)                                                                                                | 0/50( 0.0)                                              | 1/50( 2.0)  | 1/50( 2.0) | 3/50( 6.0)                             |     |  |  |  |
| Adjusted rates(b)                                                                                               | 0.0                                                     | 2.50        | 2,44       | 8.11                                   |     |  |  |  |
| Terminal rates(c)                                                                                               | 0/41( 0.0)                                              | 1/40( 2.5)  | 1/41( 2.4) | 3/37( 8.1)                             |     |  |  |  |
| Statistical analysis                                                                                            |                                                         |             |            |                                        |     |  |  |  |
| Peto test                                                                                                       | 2                                                       |             |            |                                        |     |  |  |  |
| Standard method(d)<br>Prevalence method(d)                                                                      | P =<br>P = 0.0342*                                      |             |            |                                        |     |  |  |  |
| Combined analysis(d)                                                                                            | P =                                                     |             |            |                                        |     |  |  |  |
| Cochran-Armitage test(e)                                                                                        | P = 0.0590                                              |             |            |                                        |     |  |  |  |
| Fisher Exact test(e)                                                                                            |                                                         | P = 0.4950  | P = 0.4950 | P = 0.1325                             |     |  |  |  |
|                                                                                                                 |                                                         |             |            |                                        |     |  |  |  |
|                                                                                                                 | SITE : oral cavity                                      |             |            |                                        |     |  |  |  |
|                                                                                                                 | TUMOR : squamous cell papilloma,squamous cell carcinoma |             |            |                                        |     |  |  |  |
| Tumor rate                                                                                                      |                                                         |             |            |                                        |     |  |  |  |
| Overall rates(a)                                                                                                | 0/50( 0.0)                                              | 1/50( 2.0)  | 1/50( 2.0) | 3/50( 6.0)                             |     |  |  |  |
| Adjusted rates(b)                                                                                               | 0.0                                                     | 2.50        | 2.44       | 8.11<br>3/37( 8.1)                     |     |  |  |  |
| Terminal rates(c)<br>Statistical analysis                                                                       | 0/41( 0.0)                                              | 1/40( 2.5)  | 1/41( 2.4) | 0/0/( 0.1)                             |     |  |  |  |
| Peto test                                                                                                       |                                                         |             |            |                                        |     |  |  |  |
| Standard method(d)                                                                                              | P =                                                     |             |            |                                        |     |  |  |  |
| Prevalence method(d)                                                                                            | P = 0.0342*                                             |             |            |                                        |     |  |  |  |
| Combined analysis(d)                                                                                            | P =                                                     |             |            |                                        |     |  |  |  |
| Cochran-Armitage test(e)                                                                                        | P = 0.0590                                              |             |            |                                        |     |  |  |  |
| Fisher Exact test(e)                                                                                            |                                                         | P = 0.4950  | P = 0.4950 | P = 0.1325                             |     |  |  |  |
| (HPT360A)                                                                                                       |                                                         |             |            | ······································ | BAI |  |  |  |

STUDY No. : 0162 ANIMAL : RAT F344 SEX : FEMALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                 | Control                                                  | 400 maa               | 2000 ppm            | 10000 ppm            |   |
|--------------------------------------------|----------------------------------------------------------|-----------------------|---------------------|----------------------|---|
|                                            | SITE : pituitary gland<br>TUMOR : adenoma                |                       |                     |                      |   |
| `umor rate                                 |                                                          |                       |                     |                      |   |
| Overall rates(a)                           | 8/50(16.0)                                               | 11/50(22.0)           | 9/50(18,0)          | 14/50(28.0)          |   |
| Ndjusted rates(b)<br>Ferminal rates(c)     | 17.07<br>7/41(17.1)                                      | 12.50<br>5/40(12.5)   | 17.39<br>7/41(17.1) | 27.50<br>10/37(27.0) |   |
| tatistical analysis                        | ()41(11.1)                                               | 5/40(12.5)            | //41( 1/,1/         | 10/01 ( 20:0)        |   |
| Peto test                                  |                                                          |                       |                     |                      |   |
| Standard method(d)<br>Prevalence method(d) | P = 0.4575<br>P = 0.0586                                 |                       |                     |                      |   |
| Combined analysis(d)                       | P = 0.0890                                               |                       |                     |                      |   |
| Cochran-Armitage test(e)                   | P = 0.1679                                               |                       |                     |                      |   |
| Fisher Exact test(e)                       |                                                          | P = 0.3526            | P = 0.4846          | P = 0,1781           |   |
|                                            | SITE : pituitary gland<br>TUMOR : adenoma,adenocarcinoma |                       |                     |                      |   |
| umor rate                                  |                                                          | 12/50( 24.0)          | 9/50(18.0)          | 14/50(28.0)          |   |
| Overall rates(a)<br>Adjusted rates(b)      | 8/50(16.0)<br>17.07                                      | 12/50( 24:0)<br>15.00 | 17.39               | 27.50                |   |
| Terminal rates(c)                          | 7/41(17.1)                                               | 6/40(15.0)            | 7/41(17.1)          | 10/37(27.0)          |   |
| Statistical analysis                       |                                                          |                       |                     |                      |   |
| Peto test                                  | D - A 4575                                               |                       |                     |                      |   |
| Standard method(d)<br>Prevalence method(d) | P = 0.4575<br>P = 0.0766                                 |                       |                     |                      |   |
| Combined analysis(d)                       | P = 0.1086                                               |                       |                     |                      |   |
| Cochran-Armitage test(e)                   | P = 0.2103                                               |                       |                     | B 0 4704             |   |
| Fisher Exact test(e)                       |                                                          | P = 0,2846            | P = 0.4846          | P = 0.1781           |   |
|                                            | SITE : thyraid                                           |                       |                     |                      |   |
| <b>.</b> .                                 | TUMOR : C-cell adenoma                                   |                       |                     |                      |   |
| Tumor rate<br>Overall rates(a)             | 2/50( 4.0)                                               | 7/50(14.0)            | 8/50(16.0)          | 5/50( 10.0)          |   |
| Adjusted rates(b)                          | 4.88                                                     | 15,00                 | 18.18               | 12.82                |   |
| Terminal rates(c)                          | 2/41( 4.9)                                               | 6/40(15.0)            | 7/41(17.1)          | 4/37( 10.8)          |   |
| Statistical analysis                       |                                                          |                       |                     |                      |   |
| Peto test                                  | D                                                        |                       |                     |                      |   |
| Standard method(d)<br>Prevalence method(d) | P = P = 0.4601                                           |                       |                     |                      |   |
| Combined analysis(d)                       | P =                                                      |                       |                     |                      |   |
| Cochran-Armitage test(e)                   | P = 0.9733                                               |                       |                     |                      |   |
| Fisher Exact test(e)                       |                                                          | P = 0.1045            | P = 0.0671          | P = 0.2425           |   |
| IIPT360A)                                  |                                                          |                       |                     |                      | I |

### STUDY No. : 0162

ANIMAL : RAT F344 SEX : FEMALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                                                   | 400 maa    | 2000 man    | 10000 mqq   |  |  |  |
|--------------------------------------------------|-----------------------------------------------------------|------------|-------------|-------------|--|--|--|
|                                                  | SITE : thyroid<br>TUMOR : C-cell adenoma,C-cell carcinoma |            |             |             |  |  |  |
| Tumor rate                                       | TOMOR - C-Cell adendia, C-Cell C                          |            |             |             |  |  |  |
| Overall rates(a)                                 | 2/50( 4.0)                                                | 7/50(14.0) | 9/50(18.0)  | 6/50( 12.0) |  |  |  |
| Adjusted rates(b)                                | 4.88                                                      | 15.00      | 20.45       | 15.38       |  |  |  |
| Terminal rates(c)                                | 2/41( 4.9)                                                | 6/40(15.0) | 8/41(19.5)  | 5/37(13.5)  |  |  |  |
| Statistical analysis                             |                                                           |            |             |             |  |  |  |
| Peto test                                        | P                                                         |            |             |             |  |  |  |
| Standard method(d)                               | P =P = 0.3422                                             |            |             |             |  |  |  |
| Prevalence method(d)<br>Combined analysis(d)     | P = 0.3422<br>P =                                         |            |             |             |  |  |  |
| Cochran-Armitage test(e)                         | P = 0.7312                                                |            |             |             |  |  |  |
| Fisher Exact test(e)                             |                                                           | P = 0.1045 | P = 0.0427* | P = 0.1606  |  |  |  |
|                                                  | SITE : pancreas islet                                     |            |             |             |  |  |  |
| Tumor rate                                       | TUMOR : islet cell adenoma                                |            |             |             |  |  |  |
| Overall rates(a)                                 | 0/50( 0.0)                                                | 1/50( 2.0) | 3/50( 6.0)  | 1/50( 2.0)  |  |  |  |
| Adjusted rates(b)                                | 0.0                                                       | 2.50       | 6.82        | 2.70        |  |  |  |
| Terminal rates(c)                                | 0/41( 0.0)                                                | 1/40( 2.5) | 2/41( 4.9)  | 1/37( 2.7)  |  |  |  |
| Statistical analysis                             |                                                           |            |             |             |  |  |  |
| Peto test                                        |                                                           |            |             |             |  |  |  |
| Standard method(d)                               | P =                                                       |            |             |             |  |  |  |
| Prevalence method(d)<br>Combined analysis(d)     | P = 0.4189<br>P =                                         |            |             |             |  |  |  |
| Cochran-Armitage test(e)                         | P = 0.9199                                                |            |             |             |  |  |  |
| Fisher Exact test(e)                             | 1 - 0.0100                                                | P = 0.4950 | P = 0.1325  | P = 0.4950  |  |  |  |
|                                                  |                                                           |            |             |             |  |  |  |
|                                                  |                                                           |            |             |             |  |  |  |
|                                                  | SITE : adrenal gland<br>TUMOR : pheochromocytoma          |            |             |             |  |  |  |
| Tumor rate                                       | TOMOR • priedci il dinacy tanà                            |            |             |             |  |  |  |
| Overall rates(a)                                 | 4/50( 8.0)                                                | 1/50( 2.0) | 1/50( 2.0)  | 2/50( 4.0)  |  |  |  |
| Adjusted rates(b)                                | 9.76                                                      | 2.50       | 2.44        | 5.13        |  |  |  |
| Terminal rates(c)                                | 4/41(9.8)                                                 | 1/40( 2.5) | 1/41( 2.4)  | 1/37(2.7)   |  |  |  |
| Statistical analysis                             |                                                           |            |             |             |  |  |  |
| Peto test                                        |                                                           |            |             |             |  |  |  |
| Standard method(d)                               | P =                                                       |            |             |             |  |  |  |
| Prevalence method(d)                             | P = 0.5314                                                |            |             |             |  |  |  |
| Combined analysis(d)                             | P =                                                       |            |             |             |  |  |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.8308                                                | P = 0.1998 | P = 0.1998  | P = 0.3574  |  |  |  |
| LIGHT LAGEL LOSL(D)                              |                                                           | 1 - 0.1000 |             |             |  |  |  |

STUDY No. : 0162

#### ANIMAL : RAT F344 SEX : FEMALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                                                       | 400 ppm                  | 2000 maa     | 10000 mqq          |  |  |
|--------------------------------------------------|---------------------------------------------------------------|--------------------------|--------------|--------------------|--|--|
|                                                  | SITE : admenal gland                                          |                          |              |                    |  |  |
|                                                  | TUMOR : pheachromocytoma,ph                                   | eochromocytoma:malignant |              |                    |  |  |
| umor rate<br>Charall rates(a)                    | 4/50( 8.0)                                                    | 1/50( 2.0)               | 1/50( 2.0)   | 2/50( 4.0)         |  |  |
| Overall rates(a)<br>Adjusted rates(b)            | 4/50( 8.0)<br>9.76                                            | 2.50                     | 2.44         | 5.13               |  |  |
| Terminal rates(c)                                | 4/41(9.8)                                                     | 1/40( 2.5)               | 1/41(2.4)    | 1/37( 2.7)         |  |  |
| tatistical analysis                              | 4/41( 0.0)                                                    | 1/40 ( 2:0)              | .,,          |                    |  |  |
| Peto test                                        |                                                               | <b>,</b>                 |              |                    |  |  |
| Standard method(d)                               | P =                                                           |                          |              |                    |  |  |
| Prevalence method(d)                             | P = 0.5314                                                    |                          |              |                    |  |  |
| Combined analysis(d)                             | P =                                                           |                          |              |                    |  |  |
| Cochran-Armitage test(e)                         | P = 0.8308                                                    |                          |              |                    |  |  |
| Fisher Exact test(e)                             |                                                               | P = 0.1998               | P = 0.1998   | P = 0.3574         |  |  |
|                                                  | SITE : uterus                                                 |                          |              |                    |  |  |
|                                                  | TUMOR : endometrial stromal                                   | polyp                    |              |                    |  |  |
| 'umor rate                                       |                                                               |                          |              | 4(60( 8 0)         |  |  |
| Overall rates(a)                                 | 5/50( 10.0)                                                   | 5/50(10.0)               | 10/50( 20.0) | 4/50( 8.0)<br>9.76 |  |  |
| Adjusted rates(b)                                | 10.64                                                         | 10.64                    | 20.45        | 1/37( 2.7)         |  |  |
| Terminal rates(c)                                | 4/41( 9.8)                                                    | 3/40(7.5)                | 7/41(17.1)   | 1/3/( 2.7)         |  |  |
| Statistical analysis                             |                                                               |                          |              |                    |  |  |
| Peto test                                        | P 0.0000                                                      |                          |              |                    |  |  |
| Standard method(d)                               | P = 0.3209                                                    |                          |              |                    |  |  |
| Prevalence method(d)                             | P = 0.7098<br>P = 0.7255                                      |                          |              |                    |  |  |
| Combined analysis(d)                             |                                                               |                          |              |                    |  |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.5056                                                    | P = 0.3710               | P = 0.1771   | P = 0.4883         |  |  |
| LIZHAR EXACT TAZT(A)                             |                                                               | 1 - 0.5/10               | 1 - 0+1/+1   |                    |  |  |
|                                                  | SITE : uterus                                                 |                          |              |                    |  |  |
|                                                  | TUMOR : endometrial stromal polyp,endometrial stromal sarcoma |                          |              |                    |  |  |
| 'umor rate                                       |                                                               |                          |              |                    |  |  |
| Overall rates(a)                                 | 6/50(12.0)                                                    | 5/50( 10.0)              | 11/50(22.0)  | 4/50( 8.0)         |  |  |
| Adjusted rates(b)                                | 10.87                                                         | 10.64                    | 20.45        | 9.76               |  |  |
| Terminal rates(c)                                | 4/41( 9.8)                                                    | 3/40( 7.5)               | 7/41(17.1)   | 1/37( 2.7)         |  |  |
| Statistical analysis                             |                                                               |                          |              |                    |  |  |
| Peto test                                        |                                                               |                          |              |                    |  |  |
| Standard method(d)                               | P = 0.7320                                                    |                          |              |                    |  |  |
| Prevalence method(d)                             | P = 0.7167                                                    |                          |              |                    |  |  |
| Combined analysis(d)                             | P = 0.7912                                                    |                          |              |                    |  |  |
| Cochran-Armitage test(e)                         | P = 0.3892                                                    | P = 0.4872               | P = 0.1955   | P = 0.3944         |  |  |
| Fisher Exact test(e)                             |                                                               |                          |              |                    |  |  |

### STUDY No. : 0162

ANIMAL : RAT F344 : FEMALE

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### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                                        | 400 ppm              | 2000 ppm            | 10000 mag   |  |
|--------------------------------------------------|------------------------------------------------|----------------------|---------------------|-------------|--|
|                                                  | SITE : mammary gland<br>TUMOR : adenoma        |                      |                     |             |  |
| iumor rate<br>Ouemall meter(a)                   | 1/50( 2.0)                                     | 3/50( 6.0)           | 0/50( 0.0)          | 1/50( 2.0)  |  |
| Overall rates(a)<br>Adjusted rates(b)            | 2.44                                           | 6.67                 | 0.0                 | 2.70        |  |
| Terminal rates(c)                                | 1/41(2.4)                                      | 2/40( 5.0)           | 0/41( 0.0)          | 1/37( 2.7)  |  |
| tatistical analysis                              | .,                                             |                      |                     |             |  |
| Peto test                                        |                                                |                      |                     |             |  |
| Standard method(d)                               | P =                                            |                      |                     |             |  |
| Prevalence method(d)                             | P = 0.6475                                     |                      |                     |             |  |
| Combined analysis(d)                             | P =                                            |                      |                     |             |  |
| Cochran-Armitage test(e)                         | P = 0.6309                                     |                      |                     | P = 0.2475  |  |
| Fisher Exact test(e)                             |                                                | P = 0.3235           | P = 0.4950          | P = 0.2475  |  |
|                                                  | SITE : mammary gland<br>TUMOR : fibroadenoma   |                      |                     |             |  |
| lumor rate                                       |                                                |                      |                     | 9/50(18.0)  |  |
| Overall rates(a)                                 | 9/50(18.0)                                     | 10/50( 20.0)         | 8/50(16.0)<br>18.18 | 21.62       |  |
| Adjusted rates(b)                                | 19.51                                          | 25.00<br>10/40(25.0) | 7/41(17.1)          | 8/37(21.6)  |  |
| Terminal rates(c)<br>Statistical analysis        | 8/41(19.5)                                     | 10/40( 25.0)         | (/41( 17.1)         | 0/07( 11:0) |  |
| Peto test                                        |                                                |                      |                     |             |  |
| Standard method(d)                               | P = 0.2456                                     |                      |                     |             |  |
| Prevalence method(d)                             | P = 0.5360                                     |                      |                     |             |  |
| Combined analysis(d)                             | P = 0.4628                                     |                      |                     |             |  |
| Cochran-Armitage test(e)                         | P = 0.9421                                     |                      |                     |             |  |
| Fisher Exact test(e)                             |                                                | P = 0.4839           | P = 0.4846          | P = 0.3993  |  |
|                                                  | CITE                                           |                      | · ·                 |             |  |
|                                                  | SITE : mammary gland<br>TUMOR : adenocarcinoma |                      |                     |             |  |
| Tumor rate                                       |                                                |                      |                     |             |  |
| Overall rates(a)                                 | 0/50( 0.0)                                     | 0/50( 0.0)           | 0/50( 0.0)          | 3/50( 6.0)  |  |
| Adjusted rates(b)                                | 0.0                                            | 0.0                  | 0.0                 | 5.41        |  |
| Terminal rates(c)                                | 0/41( 0.0)                                     | 0/40( 0.0)           | 0/41( 0.0)          | 2/37(5.4)   |  |
| Statistical analysis                             |                                                |                      |                     |             |  |
| Peto test                                        |                                                |                      |                     |             |  |
| Standard method(d)                               | P = 0.1723                                     |                      |                     |             |  |
| Prevalence method(d)                             | P = 0.0117*?                                   |                      |                     |             |  |
| Combined analysis(d)                             | P = 0.0017 * *?                                |                      |                     |             |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.0030 * *                                 | P = 0.5000           | P = 0.5000          | P = 0,1325  |  |
| LISHOL EXAULT LOST (0)                           |                                                | 1 - 0.0000           |                     |             |  |

#### STUDY No. : 0162 ANIMAL : RAT F344

SEX : FEMALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                       | 400 ppm            | maa 0002            | 10000 mqq            |  |
|--------------------------------------------------|-------------------------------|--------------------|---------------------|----------------------|--|
|                                                  | SITE : mammary gland          |                    |                     |                      |  |
| P                                                | TUMOR : adenoma,fibroadenoma  | 1                  |                     |                      |  |
| lumor rate<br>Overall rates(a)                   | 10/50( 20.0)                  | 12/50(24.0)        | 8/50(16.0)          | 10/50( 20.0)         |  |
| Adjusted rates(b)                                | 21.95                         | 27,50              | 18.18               | 24.32                |  |
| Terminal rates(c)                                | 9/41(22.0)                    | 11/40(27.5)        | 7/41(17.1)          | 9/37(24.3)           |  |
| Statistical analysis                             |                               |                    |                     |                      |  |
| Peto test                                        |                               |                    |                     |                      |  |
| Standard method(d)                               | P = 0.2456                    |                    |                     |                      |  |
| Prevalence method(d)                             | P = 0.5619                    |                    |                     |                      |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.4912<br>P = 0.8890      |                    |                     |                      |  |
| Fisher Exact test(e)                             | r - 0,0090                    | P = 0.4406         | P = 0.4300          | P = 0.4035           |  |
|                                                  |                               |                    |                     |                      |  |
|                                                  | SITE : mammary gland          |                    |                     |                      |  |
|                                                  | TUMOR : adenoma, adenocarcino | oma                |                     |                      |  |
| Tumor rate                                       |                               |                    | 0/50( 0.0)          | 4/50( 8.0)           |  |
| Overall rates(a)                                 | 1/50( 2.0)<br>2.44            | 3/50( 6.0)<br>6.67 | 0.0                 | 8,11                 |  |
| Adjusted rates(b)<br>Terminal rates(c)           | 1/41(2.4)                     | 2/40( 5.0)         | 0/41( 0.0)          | 3/37( 8.1)           |  |
| Statistical analysis                             | 1/41 ( 2,4)                   |                    | ·/····              |                      |  |
| Peto test                                        |                               | ·                  |                     |                      |  |
| Standard method(d)                               | P = 0.1723                    |                    |                     |                      |  |
| Prevalence method(d)                             | P = 0.1852                    |                    |                     |                      |  |
| Combined analysis(d)                             | P = 0.0832                    |                    |                     |                      |  |
| Cochran-Armitage test(e)                         | P = 0.1443                    |                    | P = 0.4950          | P = 0.1998           |  |
| Fisher Exact test(e)                             |                               | P = 0.3235         | r = 0.4950          | 1 - 0.1335           |  |
|                                                  | SITE : mammary gland          |                    |                     |                      |  |
|                                                  | TUMOR : adenoma, adenocarcino | oma,fibroadenoma   |                     |                      |  |
| Tumor rate                                       |                               |                    |                     |                      |  |
| Ouerall rates(a)                                 | 10/50( 20.0)                  | 12/50(24.0)        | 8/50(16.0)          | 13/50(26.0)          |  |
| Adjusted rates(b)                                | 21.95                         | 27.50              | 18.18<br>7/41(17.1) | 29.73<br>11/37(29.7) |  |
| Terminal rates(c)                                | 9/41(22.0)                    | 11/40(27.5)        | (/41( 1/.1)         | 11/01 20.17          |  |
| Statistical analysis<br>Peto test                |                               |                    |                     |                      |  |
| Standard method(d)                               | P = 0.0860                    |                    |                     |                      |  |
| Prevalence method(d)                             | P = 0.3179                    |                    |                     |                      |  |
| Combined analysis(d)                             | P = 0.1829                    |                    |                     |                      |  |
| Cochran-Armitage test(e)                         | P = 0.4574                    |                    |                     | P = 0.3703           |  |
| Fisher Exact test(e)                             |                               | P = 0.4406         | P = 0.4300          |                      |  |

#### STUDY No. : 0162 ANIMAL : RAT F344

SEX : FEMALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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|                          |                                                |            | 2000 maa   | 10000 maa  |  |
|--------------------------|------------------------------------------------|------------|------------|------------|--|
|                          | SITE : preputial/clitoral s<br>'UMOR : adenoma | gland      |            |            |  |
| umor rate                |                                                |            |            |            |  |
| Overall rates(a)         | 2/50( 4.0)                                     | 0/50( 0.0) | 3/50( 6.0) | 1/50( 2.0) |  |
| Adjusted rates(b)        | 4.88                                           | 0.0        | 2.44       | 2.70       |  |
| Terminal rates(c)        | 2/41( 4.9)                                     | 0/40( 0.0) | 1/41(2.4)  | 1/37( 2.7) |  |
| tatistical analysis      |                                                |            |            |            |  |
| Peto test                |                                                |            |            |            |  |
| Standard method(d)       | P = 0.5477                                     |            |            |            |  |
| Prevalence method(d)     | P = 0.4433                                     |            |            |            |  |
| Combined analysis(d)     | P = 0.5405                                     |            |            |            |  |
| Cochran-Armitage test(e) | P = 0.7903                                     |            |            |            |  |
| Fisher Exact test(e)     |                                                | P = 0.2574 | P = 0.4909 | P = 0.4926 |  |

(IIPT360A)

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire 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 probabities 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 ;  $*: P \leq 0.05$   $**: P \leq 0.01$ 

# APPENDIX O 3

# NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE : MALE

(2-YEAR STUDY)

STUDY No. : 0163 ANIMAL : MOUSE BDF1 SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                                                      | Control                     | 400 ppm                                  | 2000 ppm    | 10000 maa                    |  |
|-----------------------------------------------------------------------------------------------------------------|-----------------------------|------------------------------------------|-------------|------------------------------|--|
|                                                                                                                 | SITE : lung                 |                                          |             |                              |  |
| in the second | TUMOR : bronchiolar-alveola | - adenoma                                |             |                              |  |
| umor rate<br>Ouerall rates(a)                                                                                   | 3/50( 6.0)                  | 3/50( 6.0)                               | 4/50( 8.0)  | 3/50( 6.0)                   |  |
| Adjusted rates(b)                                                                                               | 8.57                        | 6.38                                     | 10.53       | 8.82                         |  |
| Terminal rates(c)                                                                                               | 3/35( 8.6)                  | 2/42( 4,8)                               | 4/38(10.5)  | 2/33( 6.1)                   |  |
| tatistical analysis                                                                                             | 0,00( 0,0)                  | -, (                                     | -, ( ,      |                              |  |
| Peto test                                                                                                       |                             |                                          |             |                              |  |
| Standard method(d)                                                                                              | P =                         |                                          |             |                              |  |
| Prevalence method(d)                                                                                            | P = 0.4681                  |                                          |             |                              |  |
| Combined analysis(d)                                                                                            | P =                         |                                          |             |                              |  |
| Cochran-Armitage test(e)                                                                                        | P = 0.9380                  |                                          |             | <b>D A A A A A A A A A A</b> |  |
| Fisher Exact test(e)                                                                                            |                             | P = 0.3392                               | P = 0.4895  | P = 0.3392                   |  |
|                                                                                                                 | SITE : lung                 |                                          |             |                              |  |
| • •                                                                                                             | TUMOR : bronchiolar-alveola | r carcinoma                              |             |                              |  |
| `umor rate<br>Overall rates(a)                                                                                  | 7/50(14.0)                  | 3/50( 6.0)                               | 5/50( 10.0) | 2/50( 4.0)                   |  |
| Adjusted rates(b)                                                                                               | 17.14                       | 7.14                                     | 7.89        | 3.03                         |  |
| Terminal rates(c)                                                                                               | 6/35(17.1)                  | 3/42(7.1)                                | 3/38(7.9)   | 1/33( 3.0)                   |  |
| Statistical analysis                                                                                            | 0,00(1111)                  | 0,12(111)                                | 0,00(,      |                              |  |
| Peto test                                                                                                       |                             |                                          |             |                              |  |
| Standard method(d)                                                                                              | P = 0.3806                  |                                          |             |                              |  |
| Prevalence method(d)                                                                                            | P = 0.9399                  |                                          |             |                              |  |
| Combined analysis(d)                                                                                            | P = 0.8794                  |                                          |             |                              |  |
| Cochran-Armitage test(e)                                                                                        | P = 0.1787                  |                                          |             |                              |  |
| Fisher Exact test(e)                                                                                            |                             | P = 0.1917                               | P = 0.4062  | P = 0.1045                   |  |
|                                                                                                                 |                             |                                          |             |                              |  |
|                                                                                                                 | SITE : lung                 | r adapama bropobialar-aluadar assairas   | <u>_</u>    |                              |  |
| lumor rate                                                                                                      |                             | r adenoma,bronchiolar-alveolar carcinoma | a           |                              |  |
| Overall rates(a)                                                                                                | 10/50( 20.0)                | 6/50(12.0)                               | 9/50(18.0)  | 5/50( 10.0)                  |  |
| Adjusted rates(b)                                                                                               | 25.71                       | 12.77                                    | 18.42       | 11.76                        |  |
| Terminal rates(c)                                                                                               | 9/35(25.7)                  | 5/42(11.9)                               | 7/38(18.4)  | 3/33( 9.1)                   |  |
| Statistical analysis                                                                                            |                             |                                          |             |                              |  |
| Peto test                                                                                                       |                             |                                          |             |                              |  |
| Standard method(d)                                                                                              | P = 0.3806                  |                                          |             |                              |  |
| Prevalence method(d)                                                                                            | P = 0.8587                  |                                          |             |                              |  |
| Combined analysis(d)                                                                                            | P = 0.8134                  |                                          |             |                              |  |
| Cochran-Armitage test(e)                                                                                        | P = 0.2695                  | P = 0.2557                               | P = 0.4839  | P = 0.1771                   |  |
| Fisher Exact test(e)                                                                                            |                             |                                          |             |                              |  |

STUDY No. : 0163 ANIMAL : MOUSE BDF1 Sex : Male

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                                    | 400 ppm            | 2000 maa           | 10000 maa         |  |
|--------------------------------------------------|--------------------------------------------|--------------------|--------------------|-------------------|--|
|                                                  | SITE : Lymph node                          |                    |                    |                   |  |
| `umor rate                                       | TUMOR : malignant lymphoma                 |                    |                    |                   |  |
| Overall rates(a)                                 | 5/50( 10.0)                                | 6/50(12.0)         | 6/50(12.0)         | 3/50( 6.0)        |  |
| Adjusted rates(b)                                | 11.43                                      | 7.14               | 7.89               | 6.06              |  |
| Terminal rates(c)                                | 4/35(11.4)                                 | 3/42(7.1)          | 3/38( 7.9)         | 2/33( 6.1)        |  |
| tatistical analysis                              |                                            |                    |                    |                   |  |
| Peto test<br>Standard method(d)                  | B = 0.7200                                 |                    |                    |                   |  |
| Standard method(d)<br>Prevalence method(d)       | P = 0.7299<br>P = 0.6891                   |                    |                    |                   |  |
| Combined analysis(d)                             | P = 0.7977                                 |                    |                    |                   |  |
| Cochran-Armitage test(e)                         | P = 0.3061                                 |                    |                    |                   |  |
| Fisher Exact test(e)                             |                                            | P = 0.4872         | P = 0.4872         | P = 0.3790        |  |
|                                                  |                                            | <u> </u>           |                    |                   |  |
|                                                  | SITE : spleen                              |                    |                    |                   |  |
|                                                  | TUMOR : hemangiosarcoma                    |                    |                    |                   |  |
| umor rate                                        |                                            |                    |                    |                   |  |
| Overall rates(a)                                 | 2/50( 4.0)                                 | 1/50( 2.0)         | 4/50( 8.0)         | 0/50( 0.0)        |  |
| Adjusted rates(b)<br>Terminal rates(c)           | 0.0<br>0/35( 0.0)                          | 2.38<br>1/42( 2.4) | 6.52<br>1/38( 2.6) | 0.0<br>0/33( 0.0) |  |
| tatistical analysis                              | 0/00( 0.0)                                 | 1/42( 2.4)         | 1/38( 2.0)         | 0/03( 0.0)        |  |
| Peto test                                        |                                            |                    |                    |                   |  |
| Standard method(d)                               | P = 0.8477                                 |                    |                    |                   |  |
| Prevalence method(d)                             | P = 0.7584                                 |                    |                    |                   |  |
| Combined analysis(d)                             | P = 0.9070                                 |                    |                    |                   |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.2068                                 | P = 0.4926         | P = 0.3574         | P = 0.2574        |  |
| FISHER EXACT LEST(E)                             |                                            | r = 0,4920         | r = 0.3074         | F = 0.2014        |  |
|                                                  | SITE : spleen                              |                    |                    |                   |  |
|                                                  | TUMOR : hemangioma, hemangiosarcoma        |                    |                    |                   |  |
| umor rate                                        | Tonon - Hondrig Fond y fond i Stodal obind |                    |                    |                   |  |
| Overall rates(a)                                 | 3/50( 6.0)                                 | 1/50( 2.0)         | 5/50( 10.0)        | 0/50( 0.0)        |  |
| Adjusted rates(b)                                | 2.86                                       | 2,38               | 8.70               | 0.0               |  |
| Terminal rates(c)                                | 1/35( 2.9)                                 | 1/42( 2.4)         | 2/38( 5.3)         | 0/33( 0.0)        |  |
| tatistical analysis                              |                                            |                    |                    |                   |  |
| Peto test<br>Standard method(d)                  | P = 0.8477                                 |                    |                    |                   |  |
| Prevalence method(d)                             | P = 0.8477<br>P = 0.8614                   |                    |                    |                   |  |
| Combined analysis(d)                             | P = 0.9439                                 |                    |                    |                   |  |
| Cochran-Armitage test(e)                         | P = 0.1408                                 |                    |                    |                   |  |
| Fisher Exact test(e)                             |                                            | P = 0.3235         | P = 0.3790         | P = 0.1325        |  |

STUDY No. : 0163 ANIMAL : MOUSE BDF1

#### SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                                                                       | 400 ppm               | 2000 ppm          | 10000 maa      |  |  |
|--------------------------------------------------|-------------------------------------------------------------------------------|-----------------------|-------------------|----------------|--|--|
|                                                  | SITE : oral cavity                                                            |                       |                   |                |  |  |
| Tumor rate                                       | TUMOR : squamous cell papilloma                                               |                       |                   |                |  |  |
| Overall rates(a)                                 | 0/50( 0.0)                                                                    | 0/50( 0.0)            | 0/50( 0.0)        | 4/50( 8.0)     |  |  |
| Adjusted rates(b)                                | 0.0                                                                           | 0.0                   | 0.0               | 9.76           |  |  |
| Terminal rates(c)                                | 0/35( 0.0)                                                                    | 0/42( 0.0)            | 0/38( 0.0)        | 3/33( 9.1)     |  |  |
| Statistical analysis                             |                                                                               |                       |                   |                |  |  |
| Peto test<br>Standard method(d)                  | P =                                                                           |                       |                   |                |  |  |
| Prevalence method(d)                             | P = 0.0003 * * ?                                                              |                       |                   |                |  |  |
| Combined analysis(d)                             | P =                                                                           |                       |                   |                |  |  |
| Cochran-Armitage test(e)                         | P = 0.0006 * *                                                                |                       |                   |                |  |  |
| Fisher Exact test(e)                             |                                                                               | P = 0.5000            | P = 0.5000        | P = 0.0688     |  |  |
|                                                  | SITE : oral cavity                                                            |                       |                   |                |  |  |
| _                                                | TUMOR : squamous cell carcinoma                                               |                       |                   |                |  |  |
| Tumor rate                                       |                                                                               |                       | 0(50( 0.0)        | 13/50( 26.0)   |  |  |
| Overall rates(a)<br>Adjusted rates(b)            | 0/50( 0.0)<br>0.0                                                             | 0/50( 0.0)<br>0.0     | 0/50( 0.0)<br>0.0 | 13/30(20.0)    |  |  |
| Terminal rates(c)                                | 0/35( 0.0)                                                                    | 0/42( 0.0)            | 0/38( 0.0)        | 4/33(12.1)     |  |  |
| Statistical analysis                             |                                                                               |                       |                   |                |  |  |
| Peto test                                        |                                                                               |                       |                   |                |  |  |
| Standard method(d)                               | P < 0.0001 **?                                                                |                       |                   |                |  |  |
| Prevalence method(d)<br>Combined analysis(d)     | P < 0.0001**?<br>P < 0.0001**?                                                |                       |                   |                |  |  |
| Cochran-Armitage test(e)                         | P < 0.0001**                                                                  |                       |                   |                |  |  |
| Fisher Exact test(e)                             |                                                                               | P = 0.5000            | P = 0.5000        | P = 0.0003 * * |  |  |
|                                                  |                                                                               |                       |                   |                |  |  |
|                                                  | SITE : oral cavity<br>TUMOR : squamous cell papilloma,squamous cell carcinoma |                       |                   |                |  |  |
| Tumor rate                                       | IUMUK + Squambus cell papilloma, squ                                          | Jamous cell carcinoma |                   |                |  |  |
| Overall rates(a)                                 | 0/50( 0.0)                                                                    | 0/50( 0.0)            | 0/50( 0.0)        | 16/50( 32.0)   |  |  |
| Adjusted rates(b)                                | 0.0                                                                           | 0.0                   | 0.0               | 24.39          |  |  |
| Terminal rates(c)                                | 0/35( 0.0)                                                                    | 0/42( 0.0)            | 0/38( 0.0)        | 7/33( 21.2)    |  |  |
| Statistical analysis                             |                                                                               |                       |                   |                |  |  |
| Peto test                                        |                                                                               |                       |                   |                |  |  |
| Standard method(d)<br>Prevalence method(d)       | P < 0.0001**?<br>P < 0.0001**?                                                |                       |                   |                |  |  |
|                                                  | P < 0.0001**?                                                                 |                       |                   |                |  |  |
| Combined analysis(d)                             | L N V V V V V I T T I                                                         |                       |                   |                |  |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P < 0.0001**                                                                  |                       |                   |                |  |  |

STUDY No. : 0163 ANIMAL : MOUSE BDF1 SEX : MALE

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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                                           | 400 maa                                | 2000 maa          | maq 00001            |  |
|--------------------------------------------------|---------------------------------------------------|----------------------------------------|-------------------|----------------------|--|
|                                                  | SITE : esophagus                                  |                                        |                   |                      |  |
| Tumor rate                                       | TUMOR : squamous cell carcinoma                   | a                                      |                   |                      |  |
| Overall rates(a)                                 | 0/50( 0.0)                                        | 0/50( 0.0)                             | 0/50( 0.0)        | 7/50(14.0)           |  |
| Adjusted rates(b)                                | 0.0                                               | 0.0                                    | 0.0               | 15.15                |  |
| Terminal rates(c)                                | 0/35( 0.0)                                        | 0/42( 0.0)                             | 0/38( 0.0)        | 5/33(15.2)           |  |
| Statistical analysis                             |                                                   |                                        |                   |                      |  |
| Peto test<br>Standard method(d)                  | P = 0.1801                                        |                                        |                   |                      |  |
| Prevalence method(d)                             | P < 0.0001 **?                                    |                                        |                   |                      |  |
| Combined analysis(d)                             | P < 0.0001**?                                     |                                        |                   |                      |  |
| Cochran-Armitage test(e)                         | P < 0.0001**                                      |                                        |                   |                      |  |
| Fisher Exact test(e)                             |                                                   | P = 0.5000                             | P = 0.5000        | P = 0.0101*          |  |
|                                                  | SITE : stomach                                    |                                        |                   |                      |  |
|                                                  | TUMOR : squamous cell carcinoma                   | 3                                      |                   |                      |  |
| Tumor rate                                       |                                                   |                                        |                   |                      |  |
| Overall rates(a)<br>Adjusted rates(b)            | 1/50( 2.0)                                        | 0/50( 0.0)                             | 0/50( 0.0)        | 7/50(14.0)           |  |
| Terminal rates(c)                                | 2.86<br>1/35(2.9)                                 | 0.0<br>0/42( 0.0)                      | 0.0<br>0/38( 0.0) | 18.18<br>6/33( 18.2) |  |
| Statistical analysis                             |                                                   | 0,42( 0.0)                             | 0,00( 0.0)        | 0/00( 10:2)          |  |
| Peto test                                        |                                                   |                                        |                   |                      |  |
| Standard method(d)                               | P = 0.1821                                        |                                        |                   |                      |  |
| Prevalence method(d)<br>Combined analysis(d)     | P = 0.0001**<br>P < 0.0001**                      |                                        |                   |                      |  |
| Cochran-Armitage test(e)                         | P = 0.0001 **                                     |                                        |                   |                      |  |
| Fisher Exact test(e)                             |                                                   | P = 0.4950                             | P = 0.4950        | P = 0.0430*          |  |
|                                                  |                                                   | ······································ |                   |                      |  |
|                                                  | SITE : stomach<br>TUMOR : squamous cell papilloma |                                        |                   |                      |  |
| Tumor rate                                       | TOTON · SQUANDUS CALL PAPILLUNA                   | aysquamuus Gert Gal Giriullia          |                   |                      |  |
| Overall rates(a)                                 | 1/50( 2.0)                                        | 0/50( 0.0)                             | 0/50( 0.0)        | 9/50(18.0)           |  |
| Adjusted rates(b)                                | 2.86                                              | 0.0                                    | 0.0               | 24.24                |  |
| Terminal rates(c)                                | 1/35( 2.9)                                        | 0/42( 0.0)                             | 0/38( 0.0)        | 8/33(24.2)           |  |
| Statistical analysis<br>Peto test                |                                                   |                                        |                   |                      |  |
| Standard method(d)                               | P = 0.1821                                        |                                        |                   |                      |  |
| Prevalence method(d)                             | P < 0.0001**                                      |                                        |                   |                      |  |
| Combined analysis(d)                             | P < 0.0001**                                      |                                        |                   |                      |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P < 0.0001**                                      | D 0 1050                               | 5 4 1074          |                      |  |
|                                                  |                                                   | P = 0.4950                             | P = 0.4950        | P = 0.0150*          |  |

(HPT360A)

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STUDY No. : 0163 ANIMAL : MOUSE BDF1

SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                               | 400 ppm                                | 2000 ppm            | 10000 maa           |
|--------------------------------------------------|---------------------------------------|----------------------------------------|---------------------|---------------------|
|                                                  | SITE : liver                          |                                        |                     |                     |
| Tumor rate                                       | TUMOR : hepatocellular adenoma        |                                        |                     |                     |
| Overali rates(a)                                 | 2/50( 4.0)                            | 6/50(12.0)                             | 4/50( 8.0)          | 3/50( 6.0)          |
| Adjusted rates(b)                                | 5.56                                  | 14.29                                  | 10.00               | 6.06                |
| Terminal rates(c)                                | 1/35( 2.9)                            | 6/42(14.3)                             | 3/38(7,9)           | 2/33( 6.1)          |
| Statistical analysis                             |                                       |                                        |                     |                     |
| Peto test                                        |                                       |                                        |                     |                     |
| Standard method(d)                               | P = 0.1705                            |                                        |                     |                     |
| Prevalence method(d)                             | P = 0.7427                            |                                        |                     |                     |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.5537<br>P = 0.6862              |                                        |                     |                     |
| Fisher Exact test(e)                             | $1^{-} = 0.0002$                      | P = 0.1606                             | P = 0.3574          | P = 0.4909          |
|                                                  |                                       | 1 - 0,1000                             | 1 - 0.0074          | 1 0,1000            |
|                                                  | SITE : Liver                          |                                        |                     |                     |
|                                                  | TUMOR : hemangiosarcoma               |                                        |                     |                     |
| Tumor rate                                       |                                       |                                        |                     |                     |
| Overall rates(a)                                 | 4/50( 8.0)                            | 5/50( 10.0)                            | 5/50( 10.0)         | 4/50( 8.0)          |
| Adjusted rates(b)                                | 9.09                                  | 9.52                                   | 7.89                | 9.09                |
| Terminal rates(c)                                | 2/35( 5.7)                            | 4/42( 9.5)                             | 3/38( 7.9)          | 3/33( 9.1)          |
| Statistical analysis<br>Peto test                |                                       |                                        |                     |                     |
| Standard method(d)                               | P = 0.3769                            |                                        |                     |                     |
| Prevalence method(d)                             | P = 0.6249                            |                                        |                     |                     |
| Combined analysis(d)                             | P = 0.5650                            |                                        |                     |                     |
| Cochran-Armitage test(e)                         | P = 0.8168                            |                                        |                     |                     |
| Fisher Exact test(e)                             |                                       | P = 0.4883                             | P = 0.4883          | P = 0.3579          |
|                                                  |                                       | ····· ···· ···· ··· ··· ··· ··· ··· ·· |                     |                     |
|                                                  | SITE : Liver                          |                                        |                     |                     |
| 71                                               | TUMOR : hepatocellular carcinoma      |                                        |                     |                     |
| Tumor rate                                       | 10/50/ 20 0)                          | 10/50/ 00 0)                           | 0/50( 10 0)         | 4/50/ 8 0)          |
| Overall rates(a)<br>Adjusted rates(b)            | 13/50(26.0)                           | 10/50(20.0)<br>23.26                   | 9/50(18.0)          | 4/50( 8.0)<br>11.76 |
| Terminal rates(c)                                | 31.43<br>11/35( 31.4)                 | 23.26<br>9/42(21.4)                    | 23.68<br>9/38(23.7) | 3/33(9.1)           |
| Statistical analysis                             | 11/00( 01.4)                          | 0/42( 21.4)                            | 0/00( 20:1)         | 0,00( 0,1)          |
| Peto test                                        |                                       |                                        |                     |                     |
| Standard method(d)                               | P = 1.0000 ?                          |                                        |                     |                     |
| Prevalence method(d)                             | P = 0.9783                            |                                        |                     |                     |
| Combined analysis(d)                             | P = 0.9837                            |                                        |                     |                     |
| Cochran-Armitage test(e)                         | P = 0.0243*                           |                                        |                     |                     |
| Fisher Exact test(e)                             |                                       | P = 0.3703                             | P = 0.2965          | P = 0.0371*         |
| (IIPT360A)                                       | · · · · · · · · · · · · · · · · · · · |                                        |                     | ]                   |

STUDY No. : 0163 ANIMAL : MOUSE BDF1 SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                               | Control                                        | 400 ppm                   | 2000 ppm           | 10000 ppm          |  |
|--------------------------------------------------------------------------|------------------------------------------------|---------------------------|--------------------|--------------------|--|
|                                                                          | SITE : Liver                                   |                           |                    |                    |  |
|                                                                          | TUMOR : hemangioma,hemangiosaro                | coma                      |                    |                    |  |
| umor rate<br>Ouerall water(a)                                            | 4/50( 9.0)                                     |                           |                    | 4/50( 8.0)         |  |
| Overall rates(a)<br>Adjusted rates(b)                                    | 4/50( 8.0)<br>9.09                             | 5/50(10.0)<br>9.52        | 5/50(10.0)<br>7.89 | 4/50( 8.0)<br>9.09 |  |
| Terminal rates(c)                                                        | 2/35( 5,7)                                     | 9.52<br>4/42( 9.5)        | 3/38(7,9)          | 3/33( 9.1)         |  |
| tatistical analysis                                                      | 2/33( 3.7)                                     | 4/42( 5.5)                | 5/58( 7,5)         | 0/00( 0.1)         |  |
| Peto test                                                                |                                                |                           |                    |                    |  |
| Standard method(d)                                                       | P = 0.3769                                     |                           |                    |                    |  |
| Prevalence method(d)                                                     | P = 0.6249                                     |                           |                    |                    |  |
| Combined analysis(d)                                                     | P = 0.5650                                     |                           |                    |                    |  |
| Cochran-Armitage test(e)                                                 | P = 0.8168                                     |                           |                    |                    |  |
| Fisher Exact test(e)                                                     |                                                | P = 0.4883                | P = 0.4883         | P = 0.3579         |  |
|                                                                          | SITE : liver<br>TVMOR : hepatocellular adenoma | ,hepatocellular carcinoma |                    |                    |  |
| umor rate                                                                |                                                | ,                         |                    |                    |  |
| Overall rates(a)                                                         | 14/50(28.0)                                    | 13/50(26.0)               | 13/50(26.0)        | 7/50(14.0)         |  |
| Adjusted rates(b)                                                        | 34.29                                          | 30.23                     | 32,50              | 17.65              |  |
| Terminal rates(c)                                                        | 12/35( 34.3)                                   | 12/42(28.6)               | 12/38( 31.6)       | 5/33(15.2)         |  |
| tatistical analysis                                                      |                                                |                           |                    |                    |  |
| Peto test                                                                |                                                |                           |                    |                    |  |
| Standard method(d)                                                       | P = 0.2361                                     |                           |                    |                    |  |
| Prevalence method(d)                                                     | P = 0.9639                                     |                           |                    |                    |  |
| Combined analysis(d)                                                     | P = 0.9400                                     |                           |                    |                    |  |
| Cochran-Armitage test(e)                                                 | P = 0.0671                                     | B 0 4015                  | D 0 4015           | D 0 1040           |  |
| Fisher Exact test(e)                                                     |                                                | P = 0.4815                | P = 0.4815         | P = 0.1246         |  |
|                                                                          | SITE : Harderian gland                         |                           |                    |                    |  |
|                                                                          | TUMOR : adenoma                                |                           |                    |                    |  |
| lumor rate                                                               |                                                |                           |                    |                    |  |
| Overall rates(a)                                                         | 3/50( 6.0)                                     | 4/50( 8.0)                | 6/50(12.0)         | 2/50( 4.0)         |  |
| Adjusted rates(b)                                                        | 8.57                                           | 8.51                      | 14.29              | 6.06               |  |
| Terminal rates(c)                                                        | 3/35( 8.6)                                     | 3/42( 7.1)                | 4/38(10.5)         | 2/33( 6.1)         |  |
| Statistical analysis                                                     |                                                |                           |                    |                    |  |
| Peto test                                                                | D.                                             |                           |                    |                    |  |
| Standard method(d)                                                       | P =                                            |                           |                    |                    |  |
| Prevalence method(d)                                                     | P = 0.7794                                     |                           |                    |                    |  |
| Contributed and train (-1)                                               | P =                                            |                           |                    |                    |  |
| Combined analysis(d)                                                     |                                                |                           |                    |                    |  |
| Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.3929                                     | P = 0,4895                | P = 0.2728         | P = 0.4909         |  |

STUDY No. : 0163

#### ANIMAL : MOUSE BDF1

SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name               | Control                         | 400 ppm     | 2000 ppm    | 10000 maa  |       |
|--------------------------|---------------------------------|-------------|-------------|------------|-------|
|                          | SITE : Harderian gland          |             |             |            |       |
| <b>T</b>                 | TUMOR : adenoma, adenocarcinoma |             |             |            |       |
| Tumor rate               |                                 |             |             |            |       |
| Overall rates(a)         | 4/50( 8.0)                      | 5/50( 10.0) | 6/50( 12.0) | 2/50( 4.0) |       |
| Adjusted rates(b)        | 11.43                           | 10.64       | 14.29       | 6.06       |       |
| Terminal rates(c)        | 4/35(11.4)                      | 3/42( 7.1)  | 4/38( 10.5) | 2/33( 6.1) |       |
| Statistical analysis     |                                 |             |             |            |       |
| Peto test                |                                 |             |             |            |       |
| Standard method(d)       | P =                             |             |             |            |       |
| Prevalence method(d)     | P = 0.8679                      |             |             |            |       |
| Combined analysis(d)     | P =                             |             |             |            |       |
| Cochran-Armitage test(e) | P = 0.2421                      |             |             |            |       |
| Fisher Exact test(e)     |                                 | P = 0.4883  | P = 0.3944  | P = 0.3574 |       |
| (IIPT360A)               |                                 | ······      |             |            | BAIS2 |

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Neire 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 probabities 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 ;  $*: P \leq 0.05$   $**: P \leq 0.01$ 

STUDY No. : 0163 ANINAL : MOUSE BDF1 SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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PAGE: 1

| Group Name                                 | Control                                       | 400 ppm           | 2000 pm                 | 10000 ppm  |  |
|--------------------------------------------|-----------------------------------------------|-------------------|-------------------------|------------|--|
|                                            | SITE : ALL SITE                               |                   |                         |            |  |
| www.wata                                   | TUMOR : hemangioma                            |                   |                         |            |  |
| umor rate<br>Nuerall rates(a)              | 2/50/ 6 0)                                    | 0/50( 0 0)        | $\rho(F_0(-\Lambda_0))$ | 0/50( 0.0) |  |
| Adjusted rates(b)                          | 3/50( 6.0)<br>6.82                            | 0/50( 0.0)<br>0.0 | 2/50( 4.0)<br>5,26      | 0.0        |  |
| Terminal rates(c)                          | 1/35( 2,9)                                    | 0/42( 0.0)        | 2/38( 5.3)              | 0/33( 0.0) |  |
| tatistical analysis                        | 1/03( 2:0)                                    | 0/42( 0:0)        | 2/08( 0,0)              | 0/00( 0.0/ |  |
| Peto test                                  |                                               |                   |                         |            |  |
| Standard method(d)                         | P =                                           |                   |                         |            |  |
| Prevalence method(d)                       | P = 0.9182                                    |                   |                         |            |  |
| Combined analysis(d)                       | P =                                           |                   |                         |            |  |
| Cochran-Armitage test(e)                   | P = 0.1988                                    |                   |                         |            |  |
| Fisher Exact test(e)                       |                                               | P = 0.1325        | P = 0.4909              | P = 0.1325 |  |
| umor rate                                  | SITE : ALL SITE<br>TUMOR : malignant lymphoma |                   |                         |            |  |
| Overall rates(a)                           | 6/50( 12.0)                                   | 7/50(14.0)        | 8/50(16.0)              | 3/50( 6.0) |  |
| Adjusted rates(b)                          | 14.29                                         | 9.52              | 13.16                   | 6.06       |  |
| Terminal rates(c)                          | 5/35(14.3)                                    | 4/42( 9.5)        | 5/38(13.2)              | 2/33( 6.1) |  |
| tatistical analysis                        | 0,00(1100)                                    | .,                | 0,00(1012)              |            |  |
| Peto test                                  | х.                                            |                   |                         |            |  |
|                                            | P = 0.7299                                    |                   |                         |            |  |
| Standard method(d)                         |                                               |                   |                         |            |  |
| Standard method(d)<br>Prevalence method(d) | P = 0.8266                                    |                   |                         |            |  |
|                                            | P = 0.8266<br>P = 0.8800                      |                   |                         |            |  |
| Prevalence method(d)                       |                                               |                   |                         |            |  |

(IIPT360A)

BAIS2

STUDY No. : 0163 ANIMAL : MOUSE BDF1

#### SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name               | Control                 | 400 maa     | 2000 ppm                              | 10000 maa  |       |
|--------------------------|-------------------------|-------------|---------------------------------------|------------|-------|
|                          | SITE : ALL SITE         |             |                                       |            |       |
| There are the            | TUMOR : hemangiosarcoma |             |                                       |            |       |
| Tumor rate               |                         |             |                                       | 4/50/ 0.0) |       |
| Overall rates(a)         | 6/50(12.0)              | 7/50(14.0)  | 7/50(14.0)                            | 4/50( 8.0) |       |
| Adjusted rates(b)        | 8.57                    | 11.90       | 7.89                                  | 9.09       |       |
| Terminal rates(c)        | 3/35( 8.6)              | 5/42( 11.9) | 3/38( 7.9)                            | 3/33( 9.1) |       |
| Statistical analysis     |                         |             |                                       |            |       |
| Peto test                |                         |             |                                       |            |       |
| Standard method(d)       | P = 0.8258              |             |                                       |            |       |
| Prevalence method(d)     | P = 0.5365              |             |                                       |            |       |
| Combined analysis(d)     | P = 0.7672              |             |                                       |            |       |
| Cochran-Armitage test(e) | P = 0.3448              |             |                                       |            |       |
| Fisher Exact test(e)     |                         | P = 0.4863  | P = 0.4863                            | P = 0.3944 |       |
| (IIPT360A)               |                         | ,           | · · · · · · · · · · · · · · · · · · · |            | BAIS2 |

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire 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 probabities 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 ;  $*: P \leq 0.05$   $**: P \leq 0.01$ 

# APPENDIX O 4

# NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

(2-YEAR STUDY)

STUDY No. : 0163

#### ANIMAL : NOUSE BDF1

SEX : FEMALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control                     | 400 ppm                                  | 2000 ppm           | 10000 mag                             |   |
|--------------------------------------------------|-----------------------------|------------------------------------------|--------------------|---------------------------------------|---|
|                                                  | SITE : lung                 |                                          |                    | · · · · · · · · · · · · · · · · · · · |   |
| Thursday and the                                 | TUMOR : bronchiolar-alveola | r adenoma                                |                    |                                       |   |
| Tumor rate<br>Overall rates(a)                   | 1/50( 2.0)                  | 3/50( 6.0)                               | 1/50( 9.0)         | 9/40( 4 1)                            |   |
| Adjusted rates(b)                                | 2.56                        | 3750( 8.0)<br>11.11                      | 1/50( 2.0)<br>4.00 | 2/49( 4.1)<br>8.70                    |   |
| Terminal rates(c)                                | 0/26( 0.0)                  | 3/27(11.1)                               | 1/25( 4.0)         | 2/23(8.7)                             |   |
| Statistical analysis                             |                             | -,,                                      | 1,40( 110)         | 2,20( 011)                            |   |
| Peto test                                        |                             |                                          |                    |                                       |   |
| Standard method(d)                               | P =                         |                                          |                    |                                       |   |
| Prevalence method(d)                             | P = 0.3856                  |                                          |                    |                                       | • |
| Combined analysis(d)                             | P =                         |                                          |                    |                                       |   |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.8680                  |                                          | D 0.0477           | D 0 5000                              |   |
|                                                  |                             | P = 0.3235                               | P = 0.2475         | P = 0.5000                            |   |
|                                                  | SITE : Lung                 |                                          |                    |                                       |   |
|                                                  | TUMOR : bronchiplar-alveola | r carcinoma                              |                    |                                       |   |
| Tumor rate                                       |                             |                                          |                    |                                       |   |
| Overall rates(a)                                 | 2/50( 4.0)                  | 3/50( 6.0)                               | 1/50( 2.0)         | 1/49( 2.0)                            |   |
| Adjusted rates(b)                                | 4.26                        | 5.41                                     | 4.00               | 4.35                                  |   |
| Terminal rates(c)                                | 1/26( 3.8)                  | 1/27( 3.7)                               | 1/25( 4.0)         | 1/23( 4.3)                            |   |
| Statistical analysis                             |                             |                                          |                    |                                       |   |
| Peto test                                        | P 1 0000 P                  |                                          |                    |                                       |   |
| Standard method(d)<br>Prevalence method(d)       | P = 1.0000 ?<br>P = 0.6925  |                                          |                    |                                       |   |
| Combined analysis(d)                             | P = 0.6925<br>P = 0.7720    |                                          |                    |                                       |   |
| Cochran-Armitage test(e)                         | P = 0.4309                  |                                          |                    |                                       |   |
| Fisher Exact test(e)                             | 1 - 0,4505                  | P = 0.4909                               | P = 0.4926         | P = 0.4851                            |   |
|                                                  |                             | 1 - 0.4303                               | r - 0.4820         | r = 0.4651                            |   |
|                                                  | SITE : Lung                 |                                          |                    |                                       |   |
|                                                  |                             | r adenoma,bronchiolar-alveolar carcinoma |                    |                                       |   |
| Tumor rate                                       |                             |                                          |                    |                                       |   |
| Overall rates(a)                                 | 3/50( 6.0)                  | 6/50(12.0)                               | 2/50( 4.0)         | 3/49(6.1)                             |   |
| Adjusted rates(b)                                | 6.38                        | 14.81                                    | 8.00               | 13.04                                 |   |
| Terminal rates(c)                                | 1/26( 3.8)                  | 4/27(14.8)                               | 2/25( 8.0)         | 3/23(13.0)                            |   |
| Statistical analysis                             |                             |                                          |                    |                                       |   |
| Peto test                                        |                             |                                          |                    |                                       |   |
| Standard method(d)                               | P = 1.0000 ?                |                                          |                    |                                       |   |
| Prevalence method(d)<br>Combined analysis(d)     | P = 0.5740                  |                                          |                    |                                       |   |
| Compined analysis(d)<br>Cochran-Armitage test(e) | P = 0.6444<br>P = 0.6544    |                                          |                    |                                       |   |
| Fisher Exact test(e)                             | 1 - 0.0044                  | P = 0,2728                               | P = 0.4909         | P = 0.3483                            |   |
|                                                  |                             | 1 - V, 2120                              | 1 - 0.4000         | r = 0.5400                            |   |

STUDY No. : 0163 ANIMAL : MOUSE BDF1 SEX : FEMALE

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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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|                                                  |                                                 | 400 ppm             | 2000 ppm            | 10000 ppm           |  |
|--------------------------------------------------|-------------------------------------------------|---------------------|---------------------|---------------------|--|
|                                                  | SITE : Lymph node<br>TUMOR : malignant Lymphoma |                     |                     |                     |  |
| 'umor rate                                       |                                                 |                     |                     |                     |  |
| Overall rates(a)                                 | 11/50( 22.0)                                    | 10/50( 20.0)        | 17/50( 34.0)        | 10/49( 20.4)        |  |
| Adiusted rates(b)<br>Terminal rates(c)           | 15.38<br>4/26(15.4)                             | 16.67<br>4/27(14.8) | 24.00<br>6/25(24.0) | 8.70<br>2/23( 8.7)  |  |
| tatistical analysis                              | 1,00(1011)                                      | 4/2/(14.0)          | 0720(24.0)          | 2/20( 0.1)          |  |
| Peto test                                        |                                                 |                     |                     |                     |  |
| Standard method(d)<br>Prevalence method(d)       | P = 0.3556<br>P = 0.8661                        |                     |                     |                     |  |
| Combined analysis(d)                             | P = 0.6221                                      |                     |                     |                     |  |
| Cochran-Armitage test(e)                         | P = 0.7075                                      | <b>D</b>            |                     |                     |  |
| Fisher Exact test(e)                             |                                                 | P = 0.4833          | P = 0.2154          | P = 0.4662          |  |
|                                                  | SITE : spleen                                   |                     |                     |                     |  |
|                                                  | TUMOR : malignant lymphoma                      |                     |                     |                     |  |
| umor rate                                        |                                                 |                     |                     |                     |  |
| Overall rates(a)<br>Adjusted rates(b)            | 0/50( 0.0)<br>0.0                               | 5/50( 10.0)<br>7.41 | 1/50( 2.0)<br>4.00  | 1/49( 2.0)<br>4.35  |  |
| Terminal rates(c)                                | 0/26( 0.0)                                      | 2/27(7.4)           | 1/25( 4.0)          | 4.35                |  |
| tatistical analysis                              |                                                 |                     |                     |                     |  |
| Peto test<br>Standard method(d)                  | P = 0.8889                                      |                     |                     |                     |  |
| Prevalence method(d)                             | P = 0.3952                                      |                     |                     |                     |  |
| Combined analysis(d)                             | P = 0.7198                                      |                     |                     |                     |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.4769                                      | P = 0.0360*         | P = 0.4950          | P = 0.5000          |  |
|                                                  |                                                 |                     | 1 - 0.4800          | r - 0.5000          |  |
|                                                  | SITE : oral cavity                              |                     |                     |                     |  |
| · ·                                              | TUMOR : squamous cell papilloma                 |                     |                     |                     |  |
| iumor rate<br>Overall rates(a)                   | 0/50( 0.0)                                      | 0/50( 0.0)          | 0/50( 0.0)          | 3/49( 6.1)          |  |
| Adjusted rates(b)                                | 0.0                                             | 0.0                 | 0,50( 0.0)<br>0.0   | 3/49( 6.1)<br>12.50 |  |
| Terminal rates(c)                                | 0/26( 0.0)                                      | 0/27( 0.0)          | 0/25( 0.0)          | 2/23( 8.7)          |  |
| Statistical analysis<br>Peto test                |                                                 |                     |                     |                     |  |
| Standard method(d)                               | P =                                             |                     |                     |                     |  |
| Prevalence method(d)                             | P = 0.0014 **?                                  |                     |                     |                     |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P =<br>P = 0.0027**                             |                     |                     |                     |  |
| Fisher Exact test(e)                             |                                                 | P = 0.5000          | P = 0.5000          | P = 0.1287          |  |

(HPT360A)

STUDY No. : 0163 ANIMAL : MOUSE BDF1

SEX

: FEMALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                             | Control                                                   | 400 ppm              | 2000 maa          | 10000 mag          |  |
|----------------------------------------|-----------------------------------------------------------|----------------------|-------------------|--------------------|--|
|                                        | SITE : oral cavity                                        |                      |                   |                    |  |
| n                                      | TUMOR : squamous cell carcinoma                           |                      |                   |                    |  |
| Tumor rate<br>Overall rates(a)         |                                                           |                      |                   |                    |  |
| Adjusted rates(b)                      | 0/50( 0.0)<br>0.0                                         | 0/50( 0.0)           | 0/50( 0.0)        | 15/49( 30.6)       |  |
| Terminal rates(c)                      | 0/26( 0.0)                                                | 0.0<br>0/27( 0.0)    | 0.0<br>0/25( 0.0) | 35,48              |  |
| Statistical analysis                   | 0,20( 0.0)                                                | 0/2/( 0.0)           | 0/20( 0.0)        | 8/23(34.8)         |  |
| Peto test                              |                                                           |                      |                   |                    |  |
| Standard method(d)                     | P = 0.0004 * * ?                                          |                      |                   |                    |  |
| Prevalence method(d)                   | P < 0.0001**?                                             |                      |                   |                    |  |
| Combined analysis(d)                   | P < 0.0001**?                                             |                      |                   |                    |  |
| Cochran-Armitage test(e)               | P < 0.0001**                                              |                      |                   |                    |  |
| Fisher Exact test(e)                   |                                                           | P = 0.5000           | P = 0.5000        | P = 0.0001 **      |  |
|                                        | SITE : oral cavity<br>TUMOR : squamous cell papilloma,squ | amous cell carcinoma |                   |                    |  |
| l'umor rate                            | - <b>b</b> - <b>b</b> - <b>b</b>                          |                      |                   |                    |  |
| Overall rates(a)                       | 0/50( 0.0)                                                | 0/50( 0.0)           | 0/50( 0.0)        | 18/49( 36.7)       |  |
| Adjusted rates(b)<br>Terminal rates(c) | 0.0                                                       | 0.0                  | 0.0               | 45.83              |  |
| Statistical analysis<br>Peto test      | 0/26( 0.0)                                                | 0/27( 0.0)           | 0/25( 0.0)        | 10/23( 43.5)       |  |
| Standard method(d)                     | P = 0.0004 * * ?                                          |                      |                   |                    |  |
| Prevalence method(d)                   | P < 0.0001**?                                             |                      |                   |                    |  |
| Combined analysis(d)                   | P < 0.0001**?                                             |                      |                   |                    |  |
| Cochran-Armitage test(e)               | P < 0.0001**                                              |                      |                   |                    |  |
| Fisher Exact test(e)                   |                                                           | P = 0.5000           | P = 0.5000        | P < 0.0001**       |  |
|                                        |                                                           |                      |                   |                    |  |
|                                        | SITE : stomach<br>TUMOR : squamous cell carcinoma         |                      |                   |                    |  |
| lumor rate                             | TOTON · SQUAINUUS COLL CALCINDINA                         |                      |                   |                    |  |
| Overall rates(a)                       | 0/50( 0.0)                                                | 0/50( 0.0)           | 0/50( 0.0)        | 3/49( 6.1)         |  |
| Adjusted rates(b)                      | 0.0                                                       | 0.0                  | 0.0               | 3/49( 6.1)<br>4.35 |  |
| Terminal rates(c)                      | 0/26( 0.0)                                                | 0/27( 0.0)           | 0/25( 0.0)        | 1/23( 4.3)         |  |
| Statistical analysis                   |                                                           |                      |                   | 1,00( 1+0)         |  |
| Peto test                              |                                                           |                      |                   |                    |  |
| Standard method(d)                     | P = 0.0146* ?                                             |                      |                   |                    |  |
| Provid and mathematical                | P = 0.1561                                                |                      |                   |                    |  |
| Prevalence method(d)                   | P = 0.0019 * * ?                                          |                      |                   |                    |  |
| Combined analysis(d)                   |                                                           |                      |                   |                    |  |
|                                        | P = 0.0027 **                                             | P = 0.5000           | P = 0.5000        | P = 0.1287         |  |

#### STUDY No. : 0163 ANIMAL : MOUSE BDF1

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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                | Control                                        | 400 mada                 | 2000 ppm   | 10000 maa          |   |
|-------------------------------------------|------------------------------------------------|--------------------------|------------|--------------------|---|
|                                           | SITE : stomach                                 |                          |            |                    |   |
| Tumor rate                                | TUMOR : squamous cell papilloma                | ,squamous cell carcinoma |            |                    |   |
| Overall rates(a)                          | 0/50( 0.0)                                     | 0/50( 0.0)               | 0/50( 0.0) | 4/49( 8.2)         |   |
| Adjusted rates(b)                         | . 0.0                                          | 0.0                      | 0.0        | 4/43( 8.2)<br>8.70 |   |
| Terminal rates(c)                         | 0/26( 0.0)                                     | 0/27( 0.0)               | 0/25( 0.0) | 2/23(8,7)          |   |
| Statistical analysis                      |                                                |                          | 0,000      | 2,20( 0,1)         |   |
| Peto test                                 |                                                |                          |            |                    |   |
| Standard method(d)                        | P = 0.0146 * ?                                 |                          |            |                    |   |
| Prevalence method(d)                      | P = 0.0103 * ?                                 |                          |            |                    |   |
| Combined analysis(d)                      | P = 0,0002**?                                  |                          |            |                    |   |
| Cochran-Armitage test(e)                  | P = 0.0005**                                   |                          |            |                    |   |
| Fisher Exact test(e)                      |                                                | P = 0.5000               | P = 0.5000 | P = 0.0662         |   |
| _                                         | SITE : liver<br>TUMOR : hepatocellular adenoma |                          |            |                    |   |
| Tumor rate                                |                                                |                          |            |                    |   |
| Overall rates(a)                          | 3/50( 6.0)                                     | 1/50( 2.0)               | 4/50( 8.0) | 0/49( 0.0)         |   |
| Adjusted rates(b)                         | 11.54                                          | 3.70                     | 15.38      | 0.0                |   |
| Terminal rates(c)<br>Statistical analysis | 3/26( 11.5)                                    | 1/27( 3.7)               | 3/25(12.0) | 0/23( 0.0)         |   |
| Peto test                                 |                                                |                          |            |                    |   |
| Standard method(d)                        | P =                                            |                          |            |                    |   |
| Prevalence method(d)                      | P = 0.9402                                     |                          |            |                    |   |
| Combined analysis(d)                      | P =                                            |                          |            |                    |   |
| Cochran-Armitage test(e)                  | P = 0.1492                                     |                          |            |                    |   |
| Fisher Exact test(e)                      |                                                | P = 0.3235               | P = 0.4895 | P = 0.1364         |   |
|                                           |                                                |                          |            |                    |   |
|                                           | SITE : Liver                                   |                          |            |                    |   |
|                                           | TUMOR : hemangiosarcoma                        |                          |            |                    |   |
| Tumor rate                                |                                                |                          |            |                    |   |
| Overall rates(a)                          | 3/50( 6.0)                                     | 3/50( 6.0)               | 0/50( 0.0) | 1/49( 2.0)         |   |
| Adjusted rates(b)                         | 9.38                                           | 6.45                     | 0.0        | 3.23               |   |
| Terminal rates(c)                         | 2/26(7.7)                                      | 1/27( 3.7)               | 0/25( 0.0) | 0/23( 0.0)         |   |
| Statistical analysis                      |                                                |                          | · · ·      |                    |   |
| Peto test                                 |                                                |                          |            |                    |   |
| Standard method(d)                        | P = 1.0000 ?                                   |                          |            |                    |   |
| Prevalence method(d)                      | P = 0.7676                                     |                          |            |                    |   |
| Combined analysis(d)                      | P = 0.8309                                     |                          |            |                    |   |
| Cochran-Armitage test(e)                  | P = 0.3279                                     | B 0.0000                 | B 0 4005   | B 4 6515           |   |
| Fisher Exact test(e)                      |                                                | P = 0.3392               | P = 0.1325 | P = 0.3312         |   |
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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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 $\frac{1}{2} = \frac{1}{2} \sum_{i=1}^{n} \frac{1}{2} \sum_{i=1$ 

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| Group Name                             | Control                           | 400 ppm                               | 2000 ppm   | 10000 maa          |
|----------------------------------------|-----------------------------------|---------------------------------------|------------|--------------------|
|                                        | SITE : Liver                      |                                       |            |                    |
| umor rate                              | TUMOR : hemangioma, hemangiosarco | oma                                   |            |                    |
| Overall rates(a)                       | 3/50( 6.0)                        | 3/50( 6.0)                            | 0/50( 0.0) | 2/49( 4.1)         |
| Adjusted rates(b)                      | 9,38                              | 6.45                                  | 0.0        | 2/45( 4.1)<br>6.45 |
| Terminal rates(c)                      | 2/26(7.7)                         | 1/27( 3.7)                            | 0/25( 0.0) | 1/23( 4.3)         |
| tatistical analysis                    | 2,20( 111)                        | 1/11( 0.1)                            | 0,20( 0.0) | 1/20( 4.0)         |
| Peto test                              |                                   |                                       |            |                    |
| Standard method(d)                     | P = 1.0000 ?                      |                                       |            |                    |
| Prevalence method(d)                   | P = 0.4983                        |                                       |            |                    |
| Combined analysis(d)                   | P = 0.5906                        |                                       |            |                    |
| Cochran-Armitage test(e)               | P = 0.7663                        |                                       |            |                    |
| Fisher Exact test(e)                   |                                   | P = 0.3392                            | P = 0.1325 | P = 0.4816         |
|                                        | SITE : liver                      | · · · · · · · · · · · · · · · · · · · |            |                    |
|                                        | TUMOR : hepatocellular adenoma,   | nepatocellular carcinoma              |            |                    |
| umor rate                              |                                   |                                       |            |                    |
| Overall rates(a)                       | 4/50( 8.0)                        | 1/50( 2.0)                            |            | 0/49( 0.0)         |
| Adjusted rates(b)                      | 15.38                             | 3.70                                  | 15.38      | 0.0                |
| Terminal rates(c)                      | 4/26(15.4)                        | 1/27( 3.7)                            | 3/25(12.0) | 0/23( 0.0)         |
| tatistical analysis<br>Peto test       |                                   |                                       |            |                    |
| Standard method(d)                     | P =                               |                                       |            |                    |
| Prevalence method(d)                   | P = 0.9635                        |                                       |            |                    |
| Combined analysis(d)                   | P =                               |                                       |            |                    |
| Cochran-Armitage test(e)               | P = 0.1047                        |                                       |            |                    |
| Fisher Exact test(e)                   |                                   | P = 0.1998                            | P = 0.3579 | P = 0.0715         |
|                                        |                                   |                                       |            |                    |
|                                        | SITE : pituitary gland            |                                       |            |                    |
|                                        | TUMOR : adenoma                   |                                       |            |                    |
| umor rate                              |                                   |                                       |            |                    |
| Overall rates(a)                       | 10/50(20.0)                       | 6/49(12.2)                            | 8/49(16.3) | 7/49(14.3)         |
| Adjusted rates(b)<br>Terminal rates(c) | 22.86<br>5/26(19.2)               | 18.52                                 | 29.17      | 30.43              |
| Statistical analysis                   | 0/20( 10.2)                       | 5/27(18.5)                            | 7/24(29.2) | 7/23( 30.4)        |
| Peto test                              |                                   |                                       |            |                    |
| Standard method(d)                     | P = 0.8435                        |                                       |            |                    |
| Prevalence method(d)                   | P = 0.4523                        |                                       |            |                    |
| Combined analysis(d)                   | P = 0.5960                        |                                       |            |                    |
| Cochran-Armitage test(e)               | P = 0.7275                        |                                       |            |                    |
|                                        |                                   | P = 0.2683                            | P = 0.4459 | P = 0.3564         |
| Fisher Exact test(e)                   |                                   | 1 - 0.2000                            | 1 = 0.4400 | r = 0.0004         |

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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                             | Control                                      | 400 ppm      | mqq 0002   | 10000 mag    |  |
|--------------------------------------------------------|----------------------------------------------|--------------|------------|--------------|--|
|                                                        | SITE : pituitary gland                       |              |            |              |  |
| Tumor rate                                             | TUMOR : adenoma, adenocarcinoma              |              |            |              |  |
| Overall rates(a)                                       | 10/50( 20.0)                                 | 6/49(12.2)   | 8/49(16.3) | 8/49(16.3)   |  |
| Adjusted rates(b)                                      | 22.86                                        | 18.52        | 29.17      | 30.43        |  |
| Terminal rates(c)<br>Statistical analysis<br>Peto test | 5/26(19.2)                                   | 5/27(18.5)   | 7/24(29,2) | 7/23( 30.4)  |  |
| Standard method(d)                                     | P = 0.4700                                   |              |            |              |  |
| Prevalence method(d)                                   | P = 0.4523                                   |              |            |              |  |
| Combined analysis(d)                                   | P = 0.4612                                   |              |            |              |  |
| Cochran-Armitage test(e)                               | P = 0.9887                                   |              |            |              |  |
| Fisher Exact test(e)                                   |                                              | P = 0.2683   | P = 0.4459 | P = 0.4459   |  |
| There and                                              | SITE : uterus<br>TUNOR : histiocytic sarcoma |              |            |              |  |
| Tumor rate<br>Overall rates(a)                         | 10/50( 20.0)                                 | 11/50( 22.0) | 8/50(16.0) | 10/48( 20.8) |  |
| Adjusted rates(b)                                      | 7.69                                         | 10.81        | 4.00       | 23.08        |  |
| Terminal rates(c)                                      | 2/26(7,7)                                    | 2/27(7.4)    | 1/25( 4.0) | 5/23(21.7)   |  |
| Statistical analysis                                   |                                              |              |            | 0,00(000)    |  |
| Peto test                                              | D 4 4745                                     |              |            |              |  |
| Standard method(d)<br>Prevalence method(d)             | P = 0.8738<br>P = 0.0656                     |              |            |              |  |
| Combined analysis(d)                                   | P = 0.0000<br>P = 0.5100                     |              |            |              |  |
| Cochran-Armitage test(e)                               | P = 0.9213                                   |              |            |              |  |
| Fisher Exact test(e)                                   |                                              | P = 0.4833   | P = 0.4300 | P = 0.4361   |  |
| · · · · · · · · · · · · · · · · · · ·                  |                                              |              |            |              |  |
|                                                        | SITE : mammary gland                         |              |            |              |  |
| Tumor rate                                             | TUMOR : adenoma,adenocarcinoma               |              |            |              |  |
| Overall rates(a)                                       | 2/50( 4.0)                                   | 1/50( 2.0)   | 3/50( 6.0) | 0/49( 0.0)   |  |
| Adjusted rates(b)                                      | 3.85                                         | 0.0          | 8.00       | 0.0          |  |
| Terminal rates(c)                                      | 1/26( 3.8)                                   | 0/27( 0.0)   | 2/25( 8.0) | 0/23( 0.0)   |  |
| Statistical analysis                                   |                                              |              |            |              |  |
| Peto test                                              |                                              |              |            |              |  |
| Standard method(d)<br>Prevalence method(d)             | P = 0.8447<br>P = 0.7509                     |              |            |              |  |
| Combined analysis(d)                                   | P = 0.7509<br>P = 0.8959                     |              |            |              |  |
| Cochran-Armitage test(e)                               | P = 0.2178                                   |              |            |              |  |
| Fisher Exact test(e)                                   |                                              | P = 0.4926   | P = 0.4909 | P = 0.2626   |  |
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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                            | Control                                                  | 400 ppm    | 2000 mag   | 10000 maa         |  |
|---------------------------------------|----------------------------------------------------------|------------|------------|-------------------|--|
|                                       | SITE : Harderian gland                                   |            |            |                   |  |
| were secto                            | TUNOR : adenoma                                          |            |            |                   |  |
| umor rate<br>Orionalli rater(a)       |                                                          | 1/50/ 0.0) |            |                   |  |
| Overall rates(a)<br>Adjusted rates(b) | 0/50( 0.0)<br>0.0                                        | 4/50( 8.0) | 3/50( 6.0) | 0/49( 0.0)        |  |
| Terminal rates(c)                     | 0/26( 0.0)                                               | 12.90      | 12.00      | 0.0<br>0/23( 0.0) |  |
| tatistical analysis                   | 0/28( 0.0)                                               | 3/27(11.1) | 3/25(12.0) | 0/23( 0.0)        |  |
| Peto test                             |                                                          |            |            |                   |  |
| Standard method(d)                    | P =                                                      |            |            |                   |  |
| Prevalence method(d)                  | P = 0.9268                                               |            |            |                   |  |
| Combined analysis(d)                  | P =                                                      |            |            |                   |  |
| Cochran-Armitage test(e)              | P = 0.1862                                               |            |            |                   |  |
| Fisher Exact test(e)                  |                                                          | P = 0.0688 | P = 0.1325 | P = 0.5000        |  |
| umor rate                             | SITE : Narderian gland<br>TUMOR : adenoma,adenocarcinoma |            |            |                   |  |
| Overall rates(a)                      | 0/50( 0.0)                                               | 4/50( 8.0) | 3/50( 6.0) | 1/49( 2.0)        |  |
| Adjusted rates(b)                     | 0.0                                                      | 12.90      | 12.00      | 4.35              |  |
| Terminal rates(c)                     | 0/26( 0.0)                                               | 3/27(11.1) | 3/25(12.0) | 1/23( 4.3)        |  |
| tatistical analysis                   |                                                          | -, - , , , | -,,        |                   |  |
| Peto test                             |                                                          |            |            |                   |  |
| Standard method(d)                    | P =                                                      |            |            |                   |  |
| Prevalence method(d)                  | P = 0.7267                                               |            |            |                   |  |
| Combined analysis(d)                  | P =                                                      |            |            |                   |  |
| Cochran-Armitage test(e)              | P = 0.5357                                               |            |            |                   |  |
| Fisher Exact test(e)                  |                                                          | P = 0.0688 | P = 0.1325 | P = 0.5000        |  |
| _                                     |                                                          |            |            |                   |  |

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire 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 probabities 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$ 

#### STUDY No. : 0163

ANIMAL : MOUSE BDF1

SEX : FEMALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                | Control                                       | 400 ppm     | 2000 ppm     | 10000 mqq   |
|-------------------------------------------|-----------------------------------------------|-------------|--------------|-------------|
|                                           | SITE : ALL SITE<br>TUMOR : malignant lymphoma |             |              |             |
| Tumor rate                                |                                               |             |              |             |
| Overall rates(a)                          | 11/50( 22,0)                                  | 16/50(32.0) | 18/50( 36.0) | 11/49(22.4) |
| Adjusted rates(b)                         | 15.38                                         | 24.14       | 28,00        | 13,04       |
| Terminal rates(c)                         | 4/26(15.4)                                    | 6/27(22.2)  | 7/25(28.0)   | 3/23(13.0)  |
| Statistical analysis                      |                                               |             |              |             |
| Peta test                                 |                                               |             |              |             |
| Standard method(d)                        | P = 0.5370                                    |             |              |             |
| Prevalence method(d)                      | P = 0.8304                                    |             |              |             |
| Combined analysis(d)                      | P = 0.7371                                    |             |              |             |
| Cochran-Armitage test(e)                  | P = 0.4517                                    |             |              | ·           |
| Fisher Exact test(e)                      |                                               | P = 0.2625  | P = 0.1751   | P = 0.4239  |
|                                           | SITE : ALL SITE                               |             |              |             |
| <b>_</b>                                  | TUMOR : hemangiosarcoma                       |             |              |             |
| Tumor rate                                |                                               |             |              |             |
| Overall rates(a)                          | 4/50( 8.0)                                    | 5/50( 10.0) | 1/50( 2.0)   | 1/49( 2.0)  |
| Adjusted rates(b)                         | 12.50                                         | 9.68        | 0.0          | 3.23        |
| Terminal rates(c)<br>Statistical analysis | 2/26(7.7)                                     | 2/27(7.4)   | 0/25( 0.0)   | 0/23( 0.0)  |
| Peto test                                 |                                               |             |              |             |
| Standard method(d)                        | P = 0.7972                                    |             |              |             |
| Prevalence method(d)                      | P = 0.8907                                    |             |              |             |
| Combined analysis(d)                      | P = 0.9444                                    |             |              |             |
| Cochran-Armitage test(e)                  | P = 0.1294                                    |             |              |             |
| Fisher Exact test(e)                      |                                               | P = 0.4883  | P = 0.1998   | P = 0.2063  |

(IIPT360A)

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire 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 probabities 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 :  $*: P \leq 0.05$   $**: P \leq 0.01$ 

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# APPENDIX P 1

# HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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PAGE: 1

| Organ          | Findings                        | Group Name<br>No. of Animals on Study | Control<br>6 | 400 מסק<br>10 | 2000 ppm<br>14 | מכוס 10000<br>11 |
|----------------|---------------------------------|---------------------------------------|--------------|---------------|----------------|------------------|
| [Respiratory : | system]                         |                                       |              |               |                |                  |
| nasal cavit    |                                 |                                       | < 6>         | <10>          | <14>           | <11>             |
|                | leukemic cell infiltration      |                                       | 0            | 0             | 0              | 2                |
| lung           | leukemic cell infiltration      |                                       | < 6><br>1    | <10><br>3     | <14><br>3      | <11><br>3        |
|                | metastasis:liver tumor          |                                       | 0            | 0             | 1              | 0                |
|                | metastasis:subcutis tumor       |                                       | 1            | 1             | 0              | 1                |
|                | metastasis:skin/appendage tumor |                                       | 0            | 1             | 0              | 0                |
| llematopoieti  | c system]                       |                                       |              |               |                |                  |
| xone marrow    | leukemic cell infiltration      |                                       | < 6><br>0    | <10><br>2     | <14><br>2      | <11><br>3        |
|                | metastasis:liver tumor          |                                       | 0            | 0             | 1              | 0                |
| ymph nade      | leukemic cell infiltration      |                                       | < 6><br>1    | <10><br>0     | <14><br>0      | <11> 1           |
|                | metastasis:liver tumor          | ,                                     | 0            | 0             | 1              | 0                |
|                | metastasis:skin/appendage tumor |                                       | 0            | i             | 0              | 0                |
| spleen         | metastasis:liver tumor          |                                       | < 6><br>0    | <10><br>0     | <14><br>1      | <11><br>0        |
| [Circulatory   | system]                         |                                       |              |               |                |                  |
| heart          | leukemic cell infiltration      |                                       | < 6><br>1    | <10>          | <14><br>0      | <11><br>0        |

STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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PAGE : 2

| )rgan       | Findings                     | Group Name<br>No. of Animals on Study | Contral<br>6 | 400 ppm<br>10 | 2000 ppm<br>14 | 10000 ppm<br>11 |
|-------------|------------------------------|---------------------------------------|--------------|---------------|----------------|-----------------|
| )igestive s | vstem]                       |                                       |              |               |                |                 |
| ONGUE       | leukemic cell infiltration   |                                       | < 6>         | <10><br>0     | <14><br>0      | <10><br>1       |
|             | metastasis:oral cavity tumor |                                       | 0            | 0             | 0              | 1               |
| :omach      | leukemic cell infiltration   |                                       | < 6><br>0    | <10><br>1     | <14><br>0      | <11><br>0       |
| arge intes  | leukemic cell infiltration   |                                       | < 6><br>0    | <10><br>1     | <14><br>0      | <11><br>0       |
| iver        | leukemic cell infiltration   |                                       | < 6><br>1    | <10><br>3     | <14><br>3      | <11><br>3       |
|             | metastasis:subcutis tumor    |                                       | 0            | 1             | . 0            | 0               |
| ancreas     | leukemic cell infiltration   |                                       | < 6><br>1    | <10><br>1     | <14><br>0      | <11><br>1       |
|             | metastasis:liver tumor       |                                       | 0            | 0             | 1              | 0               |
| lrinary sys | tem]                         |                                       |              |               |                |                 |
| i dney      | leukemic cell infiltration   |                                       | < 6><br>0    | <10><br>0     | <14><br>3      | <11><br>3       |
|             | metastasis:liver tumor       |                                       | 0            | 0             | 1              | 0               |
| Endocrine s | ystem]                       |                                       |              |               |                |                 |
| ituitary    | leukemic cell infiltration   |                                       | < 6><br>1    | <10><br>0     | <14><br>0      | <11><br>0       |
| drenal      | leukemic cell infiltration   |                                       | < 6>         | <10><br>1     | <14><br>2      | <11>2           |

b b: Number of animals with lesion

| STUDY NO.   | : | 0162     |
|-------------|---|----------|
| ANIMAL.     | : | RAT F344 |
| REPORT TYPE | : | ۸1       |
| SEX         |   | MALE     |

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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| SEX            | : MALE                                                                 |                                       |              |               |                | PAGE :          |
|----------------|------------------------------------------------------------------------|---------------------------------------|--------------|---------------|----------------|-----------------|
| 0rgan          | Findings                                                               | Group Name<br>No. of Animals on Study | Control<br>6 | 400 ppm<br>10 | 2000 maa<br>14 | 10000 ppm<br>11 |
| [Endocrine s;  | vstem]                                                                 |                                       |              |               |                |                 |
| adrenal        | metastasis:liver tumor                                                 |                                       | < 6><br>0    | <10><br>0     | <14><br>1      | <11><br>0       |
| [Reproductive  | e system]                                                              |                                       |              |               |                |                 |
| epididymis     | leukemic cell infiltration                                             |                                       | < 6><br>0    | <10><br>0     | <14><br>0      | <11><br>1       |
| semin ves      | leukemic cell infiltration                                             |                                       | < 6><br>0    | <10><br>1     | <14><br>0      | <11><br>0       |
| prostate       | leukemic cell infiltration                                             |                                       | < 6><br>0    | <10><br>1     | <14><br>0      | <11><br>1       |
| [Special sen   | se organs/appandage]                                                   |                                       |              |               |                |                 |
| өуө            | leukemic cell infiltration                                             |                                       | < 6><br>0    | <10><br>0     | <14><br>0      | <11><br>1       |
| llarder gl     | loukomic cell infiltration                                             |                                       | < 6>         | <10><br>0     | <14><br>0      | <11><br>1       |
| (Musculoskel   | etal system]                                                           |                                       |              |               |                |                 |
| muscle         | metastasis:liver tumor                                                 |                                       | < 6>         | <10><br>0     | <14><br>1      | <11><br>0       |
| [Body cavition | es]                                                                    |                                       |              |               |                |                 |
| pleura         | mətastasis:livər tumor                                                 |                                       | < 6><br>0    | <10><br>0     | <14><br>1      | <11><br>0       |
| <a>b</a>       | a : Number of animals examined at<br>b : Number of animals with lesion |                                       |              |               |                |                 |

PAGE : 3

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| rgan          | Findings               | Group Name<br>No. of Animals on Study | Control<br>6 | 400 ppm<br>10 | 2000 ppm<br>14 | 10000 ppm<br>11 |
|---------------|------------------------|---------------------------------------|--------------|---------------|----------------|-----------------|
| Body cavities | 5]                     |                                       |              |               |                |                 |
| ediastinum    | metastasis:liver tumor |                                       | < 6>         | <10><br>0     | <14><br>1      | <11><br>0       |
| eritaneum     | metastasis:liver tumor |                                       | < 6><br>0    | <10><br>0     | <14><br>1      | <11><br>0       |

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# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)

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# STUDY NO. : 0162 ANIMAL : RAT F344

### APPENDIX P 2

# HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

| SEX : FEMALE |                            |                                       |              |               |               |                 |
|--------------|----------------------------|---------------------------------------|--------------|---------------|---------------|-----------------|
| gan          | Findings                   | Group Name<br>No. of Animals on Study | Control<br>9 | 400 ppm<br>10 | mqq 0002<br>9 | 10000 maa<br>13 |
| Jai (        |                            |                                       |              |               |               |                 |
| ntegumentar  | y system/appandage]        |                                       |              |               |               |                 |
| in/app       | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>0     | < 9><br>0     | <13><br>0       |
|              | metastasis:subcutis tumor  |                                       | 1            | 0             | 0             | 0               |
| bcutis       | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>0     | < 9><br>0     | <13><br>0       |
| espiratory   | system]                    |                                       |              |               |               |                 |
| sal cavit    | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>0     | < 9><br>0     | <13><br>0       |
| achea        | metastasis:subcutis tumor  |                                       | < 9><br>1    | <10><br>0     | < 9><br>0     | <13><br>0       |
| 9            | leukemic cell infiltration |                                       | < 9><br>2    | <10><br>3     | < 9><br>3     | <13><br>4       |
|              | metastasis:liver tumor     |                                       | 0            | 1             | 0             | 1               |
|              | metastasis:uterus tumor    |                                       | 0            | 0             | 1             | 0               |
| matopoieti   | c system]                  |                                       |              |               |               |                 |
| e marrow     | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>2     | < 9><br>2     | <13><br>1       |
|              | metastasis:liver tumor     |                                       | 0            | 0             | 0             | 1               |
| ph node      | leukemic cell infiltration |                                       | < 9><br>2    | <10><br>1     | < 9><br>1     | <13><br>3       |
|              | metastasis:subcutis tumor  |                                       | 1            | 0             | 0             | 0               |

# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0162

| EPORT TYPE :<br>EX : | FEMALE                             |                                       |              |               |               | PAGE :          |
|----------------------|------------------------------------|---------------------------------------|--------------|---------------|---------------|-----------------|
| irgan                | Findings                           | Group Name<br>No. of Animals on Study | Control<br>9 | 400 mag<br>10 | 2000 ppm<br>9 | 10000 ppm<br>13 |
|                      |                                    |                                       |              |               |               |                 |
| llematopoieti        | c system]                          |                                       |              |               |               | (12)            |
| ymph node            | metastasis:bone marrow tumor       |                                       | < 9><br>0    | <10><br>0     | < 9><br>1     | <13><br>0       |
| pleen                |                                    |                                       | < 9>         | <10>          | < 9>          | <13>            |
|                      | metastasis:liver tumor             |                                       | 0            | 0             | 0             | 1               |
|                      | metastasis:bone marrow tumor       |                                       | 0            | 0             | 1             | 0               |
| Circulatory          | system]                            |                                       |              |               |               |                 |
| eart                 | la tania anti in <b>f</b> ilmanian |                                       | < 9>         | <10><br>0     | < 9><br>0     | <13><br>1       |
|                      | leukemic cell infiltration         |                                       | -            | 1             | 0             | 0               |
|                      | metastasis:liver tumor             |                                       | 0            | 1             | U             | v               |
| Digestive s          | vstem]                             |                                       |              |               |               |                 |
| ali∪ary gl           |                                    |                                       | < 9><br>1    | <10><br>0     | < 9>          | <13><br>0       |
|                      | leukemic cell infiltration         |                                       |              | <10>          | < 9>          | <13>            |
| tomach               | leukemic cell infiltration         |                                       | < 9><br>1    | 0             | 0             | 0               |
|                      | metastasis;subcutis tumor          |                                       | 1            | 0             | 0             | 0               |
| iver                 |                                    |                                       | < 9>         | <10>          | < 9>          | <13>            |
|                      | leukemic cell infiltration         |                                       | 2            | 3             | 3             | 4               |
|                      | metastasis:uterus tumor            |                                       | 0            | 0             | 1             | 0               |
|                      | metastasis:bone marrow tumor       |                                       | 0            | 0             | 1             | 0               |
| ancreas              | leukemic cell infiltration         |                                       | < 9><br>1    | <10><br>2     | < 9>          | <13><br>0       |

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#### (JPT150)

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| EPORT TYPE :<br>EX : | : AI<br>; FEMALE           |                                       |              |               |               |                 |  |  |
|----------------------|----------------------------|---------------------------------------|--------------|---------------|---------------|-----------------|--|--|
| rgan                 | Findings                   | Group Name<br>No. of Animals on Study | Control<br>9 | 400 ppm<br>10 | 2000 ppm<br>9 | 10000 ppm<br>13 |  |  |
| Digestive sy         | rstem]                     |                                       |              |               |               |                 |  |  |
| ancreas              | metastasis:uterus tumor    |                                       | < 9>         | <10><br>0     | < 9><br>1     | <13><br>0       |  |  |
|                      | metastasis:subcutis tumor  |                                       | 1            | 0             | 0             | 0               |  |  |
| Urinary syst         | cem]                       |                                       |              |               |               |                 |  |  |
| i dney               | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>1     | < 9><br>0     | <13><br>3       |  |  |
|                      | metastasis:uterus tumor    |                                       | 0            | 0             | 1             | 0               |  |  |
| rin bladd            | leukemic cell infiltration |                                       | < 9>         | <10><br>0     | < 9><br>0     | <13><br>1       |  |  |
| Indocrine sy         | vstem]                     |                                       |              |               |               |                 |  |  |
| drenal               | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>0     | < 9><br>1     | <13><br>0       |  |  |
| Reproductive         | ə system]                  |                                       |              |               |               |                 |  |  |
| ∪агу                 | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>1     | < 9><br>1     | <13><br>0       |  |  |
|                      | metastasis:uterus tumor    |                                       | 0            | 1             | 0             | 0               |  |  |
| terus                | loukemic cell infiltration |                                       | < 9><br>1    | <10><br>0     | < 9><br>0     | <13><br>1       |  |  |
| agina                | leukemic cell infiltration |                                       | < 9><br>1    | <10><br>0     | < 9><br>0     | <13><br>0       |  |  |

# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0162 ANIMAI : RAT E344

| STUDY NO. : 0162<br>ANIMAL : RAT F344<br>REPORT TYPE : A1<br>SEX : FENALE | HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0-105W)<br>PAGE : |              |               |               |                 |  |
|---------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|--------------|---------------|---------------|-----------------|--|
| Organ Findings                                                            | Group Name<br>No. of Animals on Study                                                                 | Control<br>9 | 400 ppm<br>10 | מקק 2000<br>9 | 10000 mag<br>13 |  |
| [Special sense organs/appandage]                                          |                                                                                                       |              |               |               |                 |  |
|                                                                           |                                                                                                       |              | (10)          | ( 0)          | <13>            |  |
| eye<br>leukemic cell infiltration                                         |                                                                                                       | < 9><br>1    | <10><br>0     | < 9> 0        | 0               |  |
| Narder gl<br>leukemic cell infiltration                                   |                                                                                                       | < 9><br>1    | <10><br>1     | 0             | <13><br>0       |  |
| [Musculoskeletal system]                                                  |                                                                                                       |              |               |               |                 |  |
| muscle<br>leukemic cell infiltration                                      |                                                                                                       | < 9><br>1    | <10><br>0     | 0<br>( 9>     | <13><br>0       |  |
| [Body cavities]                                                           |                                                                                                       |              |               |               |                 |  |
| peritoneum<br>metastasis:uterus tumor                                     |                                                                                                       | < 9><br>1    | <10><br>0     | < 9>          | <13><br>0       |  |
| metastasis:subcutis tumor                                                 |                                                                                                       | 1            | 0             | 0             | 0               |  |
| retroperit<br>metastasis:uterus tumor                                     |                                                                                                       | < 9>         | <10><br>0     | < 9><br>1     | <13><br>0       |  |
| metastasis:uterus tumor                                                   |                                                                                                       | < 9>         | <10><br>0     | < 9>          | <13><br>0       |  |

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### APPENDIX P 3

# HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

| 0rgan          | Findings                      | Group Name<br>No. of Animals on Study | Control<br>41 | 400 ppm<br>40 | מכס 2000<br>41 |
|----------------|-------------------------------|---------------------------------------|---------------|---------------|----------------|
| [Respiratory : | system]                       |                                       |               |               |                |
| lung           | leukemic cell infiltration    |                                       | <41> 1        | <40><br>0     | <41><br>0      |
|                | metastasis:adrenal tumor      |                                       | 0             | 0             | 0              |
|                | metastasis:thyroid tumor      |                                       | 0             | 0             | 1              |
| [llematopoieti | c system]                     |                                       |               |               |                |
| lymph node     | metastasis:zymbal gland tumor |                                       | <41><br>0     | <40><br>0     | <41><br>1      |
| spleen         | metastasis:bone marrow tumor  |                                       | <41><br>1     | <40><br>0     | <41><br>0      |
| [Digesti∪e sy  | stem]                         |                                       |               |               |                |
| saliuary gl    | metastasis:zymbal gland tumor |                                       | <41><br>0     | <40><br>0     | <41><br>1      |

# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

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STUDY NO. : 0162 ANIMAL : RAT F344 REPORT TYPE : A1 SEX ; FEMALE

PAGE : 2

10000 ppm 37

**<**37**>** 0

|               | metastasis:adrenal tumor                                                        | 0         | 0         | 0         | 1         |
|---------------|---------------------------------------------------------------------------------|-----------|-----------|-----------|-----------|
|               | metastasis:thyroid tumor                                                        | 0         | 0         | 1         | 0         |
| [Hematopoieti | c system]                                                                       |           |           |           |           |
| lymph nade    | metastasis:zymbal gland tumor                                                   | <41><br>0 | <40><br>0 | <41><br>1 | <37><br>0 |
| spleen        | metastasis:bone marrow tumor                                                    | <41><br>1 | <40><br>0 | <41><br>0 | <37><br>0 |
| [Digesti∪e sy | /stem]                                                                          |           |           |           |           |
| saliuary gl   | metastasis:zymbal gland tumor                                                   | <41><br>0 | <40><br>0 | <41><br>1 | <37><br>0 |
| liver         | leukemic cell infiltration                                                      | <41><br>2 | <40><br>1 | <41><br>5 | <37><br>2 |
| [Urinary syst | tem]                                                                            |           |           |           |           |
| k i dney      | leukemic cell infiltration                                                      | <41><br>0 | <40><br>0 | <41><br>2 | <37><br>0 |
| (Neruous syst | tem]                                                                            |           |           |           |           |
| brain         | metastasis:pituitary tumor                                                      | <41><br>0 | <40><br>1 | <41><br>0 | <37><br>0 |
| <a>b</a>      | a : Number of animals examined at the site<br>b : Number of animals with lesion |           |           |           |           |

### APPENDIX P 4

# HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

| REPORT TYPE :<br>SEX : | AI<br>NALE                      |                                       |               |                                               |                | PAG             |
|------------------------|---------------------------------|---------------------------------------|---------------|-----------------------------------------------|----------------|-----------------|
| )rgan                  | Findings                        | Group Name<br>No. of Animals on Study | Control<br>44 | 400 maa<br>40                                 | 2000 ppm<br>36 | 10000 ppm<br>39 |
| [Respiratory :         | system]                         |                                       |               | <u>,, , , , , , , , , , , , , , , , , , ,</u> |                |                 |
| trachea                | metastasis:thyroid tumor        |                                       | <44> 1        | <40><br>0                                     | <36><br>0      | <39><br>0       |
| ung                    | leukemic cell infiltration      |                                       | <44> 1        | <40><br>2                                     | <36><br>1      | <39><br>1       |
|                        | metastasis:thyroid tumor        |                                       | 1             | 0                                             | 0              | 0               |
|                        | metastasis:skin/appendage tumor |                                       | 0             | 0                                             | 0              | 1               |
| llematopoieti          | c system]                       |                                       |               |                                               |                |                 |
| xone marrow            | leukemic cell infiltration      |                                       | <44>0         | <40><br>0                                     | <36><br>0      | <39><br>1       |
| ymph node              | leukomic coll infiltration      |                                       | <44>0         | <40><br>1                                     | <36><br>1      | <39><br>0       |
|                        | metastasis:thyroid tumor        |                                       | 1             | 0                                             | 0              | 0               |
| Digestive sy           | rstem]                          |                                       |               |                                               |                |                 |
| liver                  | leukemic cell infiltration      |                                       | <44> 1        | <40><br>2                                     | <36><br>4      | <39><br>1       |
| (Urinary syst          | tem]                            |                                       |               |                                               |                |                 |
| kidney                 | leukemic cell infiltration      |                                       | <44><br>0     | <40><br>0                                     | <36><br>2      | <39><br>1       |
|                        | metastasis:skin/appendage tumor |                                       | 0             | 0                                             | 0              | 1               |
| Endocrine sy           | vstem]                          |                                       |               |                                               |                |                 |
| Idrenal                | leukemic cell infiltration      |                                       | <44><br>0     | <40><br>1                                     | <36><br>0      | <39><br>0       |
|                        |                                 |                                       |               |                                               |                |                 |

STUDY NO. : 0162 ANIMAL : RAT F344

# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

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

b b : Number of animals with lesion

### APPENDIX P 5

# HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0163 ANIMAI. : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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| rgan           | Findings                         | Group Name<br>No. of Animals on Study | Control<br>15 | 400 ppm<br>8 | 2000 ppm<br>12 | 10000 ppm<br>17 |
|----------------|----------------------------------|---------------------------------------|---------------|--------------|----------------|-----------------|
|                |                                  |                                       |               |              |                |                 |
| [Respiratory   | system]                          |                                       |               |              |                |                 |
| nasal cavit    | metastasis:periferal nerve tumor |                                       | <15><br>1     | < 8><br>0    | <12><br>0      | <17><br>0       |
| lung           | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>2    | <12><br>2      | <17><br>0       |
|                | metastasis:liver tumor           |                                       | 0             | 1            | 0              | 1               |
|                | metastasis:spleen tumpr          |                                       | 0             | 0            | 1              | 0               |
|                | metastasis:oral cavity tumor     |                                       | 0             | 0            | 0              | 2               |
|                | metastasis:esophagus tumor       |                                       | 0             | 0            | 0              | 1               |
| [llematopoieti | c system]                        |                                       |               |              |                |                 |
| oone marrow    | metastasis:liver tumor           |                                       | <15><br>0     | < 8><br>0    | <12><br>0      | <17><br>1       |
| lymph node     | metastasis:liver tumor           |                                       | <15><br>0     | < 8><br>1    | <12><br>0      | <17><br>0       |
|                | metastasis:oral cavity tumor     |                                       | 0             | 0            | 0              | 2               |
|                | metastasis:epididymis tumor      |                                       | 0             | 1            | 0              | 0               |
| spleen         | leukemic cell infiltration       |                                       | <15><br>1     | < 8><br>2    | <12><br>3      | <17><br>1       |
|                | metastasis:liver tumor           |                                       | 0             | 1            | 0              | 0               |
| [Circulatory   | system]                          |                                       |               |              |                |                 |
| heart          | leukemic cell infiltration       |                                       | <15><br>1     | < 8><br>0    | <12><br>1      | <17><br>0       |

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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| )rgan          | Findings                         | Group Name<br>No. of Animals on Study | Control<br>15 | 400 mag<br>8 | 2000 ppm<br>12 | 10000 m<br>17        |
|----------------|----------------------------------|---------------------------------------|---------------|--------------|----------------|----------------------|
| [Circulatory : | system]                          |                                       |               |              |                |                      |
| neart          | metastasis:liver tumor           |                                       | <15><br>0     | < 8><br>0    | <12><br>0      | <1 <b>7&gt;</b><br>1 |
| Digestive sy   | stem]                            |                                       |               |              |                |                      |
| mal cavity     | loukemic cell infiltration       |                                       | <15><br>0     | < 8><br>0    | <12><br>1      | <17><br>0            |
| ongue          | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>0    | <12><br>1      | <17><br>0            |
| aliuary gl     | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>0    | <12><br>2      | <17><br>0            |
| tomach         | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>1    | <12><br>2      | <17><br>0            |
|                | metastasis:epididymis tumor      |                                       | 0             | 1            | 0              | 0                    |
|                | metastasis:seminal vesicle tumor |                                       | 0             | 0            | 1              | 0                    |
| mall intes     | metastasis:epididymis tumor      |                                       | <15><br>0     | < 8><br>1    | <12><br>0      | <17><br>0            |
| large intes    | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>0    | <12><br>1      | <17><br>0            |
| iver           | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>2    | <12><br>3      | <17><br>0            |
|                | metastasis:epididymis tumor      |                                       | 0             | 1            | 0              | 0                    |
| gall bladd     | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>1    | <12><br>0      | <17><br>0            |

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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| )rgan        | Findings                         | Group Name<br>No. of Animals on Study | Control<br>15 | 400 ppm<br>8 | 2000 ppm<br>12 | 10000 ppm<br>17 |
|--------------|----------------------------------|---------------------------------------|---------------|--------------|----------------|-----------------|
|              |                                  |                                       |               |              |                |                 |
| Digestive sy | vstem]                           |                                       |               |              |                |                 |
| ancreas      | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>1    | <12><br>2      | <17><br>0       |
|              | metastasis:epididymis tumor      |                                       | 0             | 1            | 0              | 0               |
| Urinary syst | tem]                             |                                       |               |              |                |                 |
| i dney       | leukemic cell infiltration       |                                       | <15><br>0     | < 8>         | <12><br>2      | <17><br>0       |
|              | metastasis:liver tumor           |                                       | 0             | 0            | 0              | 1               |
| -            | metastasis;lung tumor            |                                       | 0             | 0            | 1              | 0               |
| in bladd     | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>2    | <12><br>1      | <17><br>0       |
|              | metastasis:epididymis tumor      |                                       | 1             | 1            | 0              | 0               |
| Indocrine sy | /stem]                           |                                       |               |              |                |                 |
| ituitary     | metastasis:periferal nerve tumor |                                       | <15><br>1     | < 8><br>0    | <12><br>0      | <17><br>0       |
| renal        | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>0    | <12><br>1      | <17><br>0       |
| Reproductive | ə system]                        |                                       |               |              |                |                 |
| ostis        | leukemic cell infiltration       |                                       | <15><br>0     | < 8><br>1    | <12><br>0      | <17><br>0       |
| ididymis     | leukemic cell infiltration       |                                       | <15><br>0     | < 8>         | <12><br>1      | <17><br>0       |

b b : Number of animals with lesion

BAIS2

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

## HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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| Organ        | Findings                                                               | Group Name<br>No. of Animals on Study | Contral<br>15 | 400 mag<br>8 | 2000 maa<br>12 | 10000 ppm<br>17 |
|--------------|------------------------------------------------------------------------|---------------------------------------|---------------|--------------|----------------|-----------------|
|              |                                                                        |                                       |               |              |                |                 |
| [Reproductiv | e system]                                                              |                                       |               |              |                |                 |
| semin ves    | leukemic cell infiltration                                             |                                       | <15><br>0     | < 8><br>2    | <12><br>0      | <17><br>0       |
|              | metastasis:epididymis tumor                                            |                                       | 0             | 1            | 0              | 0               |
| prostate     | loukemic cell infiltration                                             |                                       | <15><br>0     | < 8>         | <12><br>2      | <17><br>0       |
|              | metastasis:epididymis tumor                                            |                                       | 1             | 1            | 0              | 1               |
| (Nervous sys | tem]                                                                   |                                       |               |              |                |                 |
| brain        | leukemic cell infiltration                                             |                                       | <15><br>0     | < 8><br>0    | <12><br>1      | <17><br>0       |
|              | metastasis:pituitary tumor                                             |                                       | 1             | 0            | 0              | 0               |
| [Special ser | ise organs/appandage]                                                  |                                       |               |              |                |                 |
| ilarder gl   | leukemic cell infiltration                                             |                                       | <15><br>0     | < 8><br>0    | <12><br>2      | <17><br>0       |
|              | metastasis:pituitary tumor                                             |                                       | 1             | 0            | 0              | 0               |
| [Musculaskel | etal system]                                                           |                                       |               |              |                |                 |
| muscle       | leukemic cell infiltration                                             |                                       | <15><br>0     | < 8><br>0    | <12><br>1      | <17><br>0       |
|              | mətastasis:epididymis tumor                                            |                                       | 0             | 1            | 0              | 0               |
| [Body caviti | ies]                                                                   |                                       |               |              |                |                 |
| mediastinum  | metastasis:liver tumor                                                 |                                       | <15><br>0     | < 8><br>0    | <12><br>0      | <17><br>1       |
| <a>b</a>     | a : Number of animals examined at<br>b : Number of animals with lesion | the site                              |               |              |                |                 |

| ANIMAL<br>REPORT TYPE | : 0163<br>: NOUSE BDF1<br>: A1<br>: MALE                                  |                                       | CAL FINDINGS : METASTA<br>AORIBUND ANIMALS (0-10 | SIS OF TUMOR (SUMMARY)<br>5W) |                | PAGE : 5        |
|-----------------------|---------------------------------------------------------------------------|---------------------------------------|--------------------------------------------------|-------------------------------|----------------|-----------------|
| 0rgan                 | Findings                                                                  | Group Name<br>No. of Animals on Study | Control<br>15                                    | 400 maa<br>8                  | 2000 ppm<br>12 | 10000 ppm<br>17 |
| [Body caviti          | es]                                                                       |                                       |                                                  |                               |                |                 |
| peritoneum            | metastasis:seminal vesicle tumor                                          |                                       | <15><br>0                                        | < 8><br>0                     | <12><br>1      | <17><br>0       |
| <a>b</a>              | a : Number of animals examined at th<br>b : Number of animals with lesion | ne site                               | ```````````````````````````````                  |                               |                |                 |
| (JPT150)              |                                                                           |                                       |                                                  |                               |                | BAIS2           |

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## APPENDIX P 6

### HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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| STUDY NO.   | : | 0163       |
|-------------|---|------------|
| ANIMAL      | : | MOUSE BDF1 |
| REPORT TYPE | ; | ۸1         |
| SEX         | : | FENALE     |

STUDY

| Irgan          | Findings                     | Group Name<br>No. of Animals on Study | Control<br>24 | 400 ppm<br>23 | 2000 pom<br>25 | 10000 ppm<br>26 |
|----------------|------------------------------|---------------------------------------|---------------|---------------|----------------|-----------------|
|                |                              | · · · · · · · · · · · · · · · · · · · |               |               |                |                 |
| Integumentar   | y system/appandage]          |                                       |               |               |                |                 |
| skin/app       | leukemic cell infiltration   |                                       | <24>          | <23><br>1     | <25><br>0      | <26><br>0       |
| ubcutis        | loukomic coll infiltration   |                                       | <24><br>0     | <23><br>2     | <25> 0         | <26><br>0       |
| [Respiratory   | system]                      |                                       |               |               |                |                 |
| nasal cavit    | leukemic cell infiltration   |                                       | <24><br>1     | <23><br>1     | <25><br>1      | <26><br>1       |
|                | metastasis:uterus tumor      |                                       | 3             | 2             | 1              | 0               |
| larynx         | leukemic cell infiltration   |                                       | <24><br>0     | <23><br>0     | <25><br>1      | <26><br>0       |
| trachea        | leukemic cell infiltration   |                                       | <24><br>0     | <23><br>0     | <25><br>0      | <26><br>1       |
| ung            | leukemic cell infiltration   |                                       | <24><br>6     | <23><br>6     | <25><br>8      | <26><br>6       |
|                | metastasis:liver tumor       |                                       | 0             | 0             | 1              | 0               |
|                | metastasis:uterus tumor      |                                       | 6             | 6             | 2              | 3               |
|                | metastasis:oral cavity tumor |                                       | 0             | 0             | 0              | 2               |
| [llematopoieti | c system]                    |                                       |               |               |                |                 |
| bone marrow    | leukemic cell infiltration   |                                       | <24><br>2     | <23><br>5     | <25><br>3      | <26><br>1       |
|                | metastasis;uterus tumor      |                                       | 1             | 1             | 1              | 1               |

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| EPORT TYPE<br>EX | : A1<br>: FEMALE                                      |                                       | PAGE :        |               |                |                 |
|------------------|-------------------------------------------------------|---------------------------------------|---------------|---------------|----------------|-----------------|
| rgan             | Findings                                              | Group Name<br>No. of Animals on Study | Control<br>24 | 400 maa<br>23 | 2000 maa<br>25 | 10000 maa<br>26 |
| llematopoiet     | ic system]                                            |                                       |               |               |                |                 |
| ymph node        | leukemic cell infiltration                            |                                       | <24><br>0     | <23><br>2     | <25><br>0      | <26><br>0       |
|                  | metastasis:liver tumor                                |                                       | 0             | 0             | 1              | 0 .             |
|                  | metastasis:uterus tumor                               |                                       | 1             | 2             | 2              | 0               |
|                  | metastasis:stomach tumor                              |                                       | 0             | 0             | 0              | 1               |
|                  | metastasis:oral cavity tumor                          |                                       | 0             | 0             | 0              | 2               |
| spleen           | leukemic cell infiltration                            |                                       | <24><br>6     | <23><br>6     | <25><br>6      | <26><br>7       |
|                  | metastasis:liver tumor                                |                                       | 0             | 0             | 1              | 0               |
|                  | metastasis:uterus tumor                               |                                       | 1             | 1             | 0              | 0               |
| Circulatory      | y system]                                             |                                       |               |               |                |                 |
| neart            | leukemic cell infiltration                            |                                       | <24><br>2     | <23><br>5     | <25><br>0      | <26><br>3       |
|                  | metastasis:uterus tumor                               |                                       | 1             | 0             | 0              | 0               |
| [Digestive :     | system}                                               |                                       |               |               |                |                 |
| oral cavity      |                                                       |                                       | <24><br>1     | <23><br>4     | <25><br>0      | <26><br>1       |
|                  | leukemic cell infiltration<br>metastasis:uterus tumor |                                       | 0             | 1             | 2              | 0               |
|                  | MULASLASTS LILU US LUMUA                              |                                       | <24>          | <23>          | <25>           | <26>            |
| tongue           | leukemic cell infiltration                            |                                       | 0             | 3             | 0              | 1               |

## AL EINDINGE . METACTACIC OF THMOR (CHMMARV)

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|               |                              | Group Name<br>No. of Animals on Study | Control<br>24 | 400 ppm<br>23 | 2000 maga<br>25 | 10000 ppm<br>26 |  |
|---------------|------------------------------|---------------------------------------|---------------|---------------|-----------------|-----------------|--|
| gan           | Findings                     |                                       |               |               |                 |                 |  |
| ligesti∪e sys | tem]                         |                                       |               |               |                 |                 |  |
| livary gl     | leukemic coll infiltration   |                                       | <24><br>3     | <23><br>6     | <25><br>5       | <26><br>4       |  |
|               | metastasis:oral cavity tumor |                                       | 0             | 0             | 0               | 1               |  |
| tomach        | leukemic cell infiltration   |                                       | <24><br>3     | <23><br>4     | <25><br>2       | <26><br>2       |  |
|               | metastasis:uterus tumor      |                                       | 1             | 0             | 2               | 0               |  |
| all intes     | metastasis:uterus tumor      |                                       | <24><br>0     | <23><br>1     | <25><br>1       | <26><br>0       |  |
| iver          | leukemic cell infiltration   |                                       | <24><br>7     | <23><br>8     | <25><br>8       | <26><br>8       |  |
|               | metastasis:uterus tumor      |                                       | 7             | 7             | 6               | 5               |  |
|               | metastasis:subcutis tumor    |                                       | 0             | 1             | 0               | 0               |  |
|               | metastasis:stomach tumor     |                                       | 0             | 0             | 0               | 1               |  |
| ancreas       | leukemic cell infiltration   |                                       | <24><br>2     | <23><br>3     | <25><br>5       | <26><br>6       |  |
|               | metastasis:uterus tumor      |                                       | 2             | 0             | 2               | 0               |  |
|               | metastasis:stomach tumor     |                                       | 0             | 0             | 0               | 1               |  |
| Irinary syste |                              |                                       |               |               |                 |                 |  |
| i dney        | leukemic cell infiltration   |                                       | <24><br>5     | <23><br>5     | <25><br>2       | <26><br>6       |  |
|               | mətastasis:uterus tumor      |                                       | 1             | 2             | 2               | 1               |  |

a : Number of animals examined at the site

≺a> b b : Number of animals with lesion HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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### STUDY NO. : 0163 : MOUSE BDF1 AN I MAL

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| EX :         | FEMALE                     |                                       |               |              |                | PAGE :          |
|--------------|----------------------------|---------------------------------------|---------------|--------------|----------------|-----------------|
| )rgan        | Findings                   | Group Name<br>No. of Animals on Study | Control<br>24 | 400 pm<br>23 | 2000 ppm<br>25 | 10000 ppm<br>26 |
| Urinary syst | tem]                       |                                       |               |              |                |                 |
| idney        | metastasis:stomach tumor   |                                       | <24><br>0     | <23><br>0    | <25><br>0      | <26><br>1       |
| rin bladd    | leukemic cell infiltration |                                       | <24><br>4     | <23><br>6    | <25><br>5      | <25><br>2       |
|              | metastasis:uterus tumor    |                                       | 1             | 0            | 1              | 0               |
| Endocrine sy | vstem]                     |                                       |               |              |                |                 |
| vituitary    | leukemic cell infiltration |                                       | <24><br>1     | <23><br>1    | <25><br>1      | <26><br>0       |
| hyroid       | leukemic cell infiltration |                                       | <24>          | <23><br>2    | <25><br>0      | <26>            |
| drenal       | leukemic cell infiltration |                                       | <24><br>4     | <23><br>4    | <25><br>2      | <26><br>1       |
|              | metastasis:uterus tumor    |                                       | 1             | 0            | 0              | 1               |
| Reproductiv  | e system]                  |                                       |               |              |                |                 |
| Dary         | leukemic cell infiltration |                                       | <24><br>6     | <23><br>7    | <25><br>7      | <26><br>5       |
|              | metastasis:uterus tumor    |                                       | 6             | 5            | 6              | 5               |
| iterus       | leukemic cell infiltration |                                       | <24><br>4     | <23><br>6    | <25><br>4      | <26><br>4       |
| vagina       | leukemic cell infiltration |                                       | <24><br>2     | <23><br>0    | <25><br>0      | <26>            |

### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)

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(JPT150)

| ANIMAL :             | 0163<br>MOUSE BDF1                                                         | HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0-105W) |               |               |                |                                       |  |  |
|----------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|---------------|---------------|----------------|---------------------------------------|--|--|
| EPORT TYPE :<br>EX : | A1<br>FEMALE                                                               | PAC                                                                                         |               |               |                |                                       |  |  |
| )rgan                | Findings                                                                   | Group Name<br>No. of Animals on Study                                                       | Control<br>24 | 400 maa<br>23 | 2000 maa<br>25 | 10000 maa<br>26                       |  |  |
| Reproductive         | system]                                                                    |                                                                                             |               |               |                |                                       |  |  |
| ammary gl .          | leukemic cell infiltration                                                 |                                                                                             | <24><br>1     | <23><br>2     | <25><br>3      | <26><br>2                             |  |  |
| (Nervous syste       | em]                                                                        |                                                                                             |               |               |                |                                       |  |  |
| brain                | leukemic cell infiltration                                                 |                                                                                             | <24><br>1     | <23><br>0     | <25><br>1      | <26><br>1                             |  |  |
| pinal cord           | leukemic cell infiltration                                                 |                                                                                             | <24><br>1     | <23><br>0     | <25><br>0      | <26><br>1                             |  |  |
| Special sense        | e organs/appandage]                                                        |                                                                                             |               |               |                |                                       |  |  |
| уе                   | leukemic cell infiltration                                                 |                                                                                             | <24><br>0     | <23><br>1     | <25><br>1      | <26><br>3                             |  |  |
| arder gl             | leukemic cell infiltration                                                 |                                                                                             | <24><br>3     | <23><br>3     | <25><br>2      | <26><br>2                             |  |  |
| Musculoskele         | tal system]                                                                |                                                                                             |               |               |                |                                       |  |  |
| nuscle               | leukemic cell infiltration                                                 |                                                                                             | <24><br>0     | <23><br>3     | <25><br>0      | <26><br>3                             |  |  |
| [Body cavitie        | s]                                                                         |                                                                                             |               |               |                |                                       |  |  |
| peritoneum           | leukemic cell infiltration                                                 |                                                                                             | <24>          | <23><br>1     | <25><br>1      | <26><br>0                             |  |  |
|                      | metastasis:uterus tumor                                                    |                                                                                             | 1             | 2             | 3              | 0                                     |  |  |
| <a>b</a>             | a : Number of animals examined at the<br>b : Number of animals with lesion | site                                                                                        |               |               |                | · · · · · · · · · · · · · · · · · · · |  |  |
| (107150)             |                                                                            |                                                                                             |               |               |                | B                                     |  |  |

## HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)

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### APPENDIX P 7

### HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

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| Organ          | Findings                   | Group Name<br>No. of Animals on Study | Control<br>35 | 400 maaa<br>42 | 2000 ppm<br>38 | 10000 maa<br>33 |
|----------------|----------------------------|---------------------------------------|---------------|----------------|----------------|-----------------|
|                |                            |                                       |               |                |                |                 |
| [Integumentar: | y system/appandage]        |                                       |               |                |                |                 |
| subcutis       | leukemic cell infiltration |                                       | <35><br>0     | <42><br>1      | <38><br>0      | <33><br>0       |
| [Respiratory : | system]                    |                                       |               |                |                |                 |
| nasal cavit    | leukemic cell infiltration |                                       | <35><br>1     | <42><br>0      | <38><br>1      | <33><br>0       |
| lung           | leukemic cell infiltration |                                       | <35><br>0     | <42><br>1      | <38><br>2      | <33><br>0       |
|                | metastasis:liver tumor     |                                       | 1             | , <b>0</b>     | 3              | 0               |
| [Hematopoieti  | c system]                  |                                       |               |                |                |                 |
| bone marrow    | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0      | <38><br>2      | <32><br>0       |
| lymph node     | leukemic cell infiltration |                                       | <35><br>1     | <42><br>0      | <38><br>0      | <33><br>0       |
| spleen         | leukemic cell infiltration |                                       | <35><br>3     | <42><br>2      | <38><br>2      | <33><br>3       |
| [Circulatory   | system]                    |                                       |               |                |                |                 |
| heart          | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0      | <38><br>1      | <33><br>0       |
| (Digestive sy  | stem]                      |                                       |               |                |                |                 |
| oral cavity    | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0      | <38><br>1      | <33><br>0       |

STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

 $\overline{\phantom{a}}$ 

| · · · · · · · · · · · · · · · · · · · |                            |                                       |               |               |                |                 |
|---------------------------------------|----------------------------|---------------------------------------|---------------|---------------|----------------|-----------------|
| Organ                                 | Findings                   | Group Name<br>No. of Animals on Study | Control<br>35 | 400 maa<br>42 | 2000 ppm<br>38 | 10000 ppm<br>33 |
| Digestive sy                          | stem]                      |                                       |               |               |                |                 |
| salivary gl                           | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0     | <38><br>2      | <33><br>0       |
| tomach                                | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0     | <38><br>2      | <33><br>0       |
| iver                                  | leukemic cell infiltration |                                       | <35><br>1     | <42><br>0     | <38><br>3      | <33><br>1       |
|                                       | metastasis:stomach tumor   |                                       | 0             | 0             | 0              | 1               |
| pancreas                              | leukemic cell infiltration |                                       | <35><br>1     | <42><br>1     | <38><br>2      | <33><br>1       |
| Urinary syst                          | em]                        |                                       |               |               |                |                 |
| idney                                 | leukemic cell infiltration |                                       | <35><br>1     | <42><br>0     | <38><br>2      | <33><br>0       |
| rin bladd                             | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0     | <38><br>2      | <33><br>0       |
| Reproductive                          | system]                    |                                       |               |               |                |                 |
| epididymis                            | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0     | <38><br>2      | <33><br>0       |
| omin ves                              | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0     | <38><br>1      | <33><br>0       |
| rostate                               | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0     | <38><br>2      | <33><br>0       |
| Musculaskele                          | tal system]                |                                       |               |               |                |                 |
| nuscle                                | leukemic cell infiltration |                                       | <35><br>0     | <42><br>0     | <38><br>1      | <33><br>0       |

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

b : Number of animals with lesion

### APPENDIX P 8

### HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

| STUDY NO. : 0163<br>ANIMAL : NOUSE BDF1 |                            | HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)<br>SACRIFICED ANIMALS (105W) |                        |                |                |                  |
|-----------------------------------------|----------------------------|------------------------------------------------------------------------------------|------------------------|----------------|----------------|------------------|
| REPORT TYPE :<br>SEX :                  | : A1<br>: FEMALE           |                                                                                    |                        |                |                | PAGE : 3         |
| Organ                                   | Findings                   | Group Name<br>No. of Animals on Study                                              | Control<br>26          | 400 מכוס<br>27 | 2000 ppm<br>25 | מכוס 10000<br>23 |
| [Integumentar                           | y system/appandage]        |                                                                                    |                        |                |                |                  |
| skin/app                                | leukemic cell infiltration |                                                                                    | <26><br>0              | <27><br>0      | <25><br>1      | <23><br>0        |
| [Respiratory                            | system]                    |                                                                                    |                        |                |                |                  |
| nasal cavit                             | leukemic cell infiltration |                                                                                    | <26><br>0              | <27><br>1      | <25><br>0      | <23><br>0        |
|                                         | metastasis:uterus tumor    |                                                                                    | 0                      | 0              | 0              | 1                |
| lung                                    | leukemic cell infiltration |                                                                                    | <26> 1                 | <27><br>4      | <25><br>1      | <23><br>1        |
|                                         | metastasis:liver tumor     |                                                                                    | 0                      | 1              | 0              | 0                |
| [Hematopoiet                            | ic system]                 |                                                                                    |                        |                |                |                  |
| bone marrow                             | leukemic cell infiltration |                                                                                    | <b>&lt;26&gt;</b><br>1 | <27><br>2      | <25><br>1      | <23><br>0        |
| lymph node                              | metastasis:uterus tumor    |                                                                                    | <26><br>0              | <27><br>0      | <25><br>0      | <23><br>1        |
| spleen                                  | leukemic cell infiltration |                                                                                    | <26><br>4              | <27><br>3      | <25><br>3      | <23><br>2        |
| [Circulatory                            | ′system]                   |                                                                                    |                        |                |                |                  |
| heart                                   | leukemic cell infiltration |                                                                                    | <26><br>0              | <27><br>2      | <25><br>1      | <23><br>0        |
| [Digestive s                            | system]                    |                                                                                    |                        |                |                |                  |
| oral cavity                             | leukemic cell infiltration |                                                                                    | <26><br>0              | <27><br>2      | <25><br>2      | <23><br>0        |

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

b : Number of animals with lesion b

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

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STUDY NO. : 0163 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

|              |                            | Group Name<br>No. of Animals on Study | Control<br>26 | 400 ppm<br>27 | 2000 ppm<br>25 | 10000 ppm<br>23 |
|--------------|----------------------------|---------------------------------------|---------------|---------------|----------------|-----------------|
| -gan         | Findings                   |                                       |               |               |                |                 |
| igestive sys | aton]                      |                                       |               |               |                |                 |
| NGESTIVE SY  | stenj                      |                                       |               |               |                |                 |
| ongue        | leukemic cell infiltration |                                       | <26><br>0     | <27><br>1     | <25><br>1      | <23><br>0       |
| aliuary gl   |                            |                                       | <26>          | <27>          | <25>           | <23>            |
|              | leukemic cell infiltration |                                       | 0             | 3             | 0              | 0               |
| omach        |                            |                                       | <26>          | <27>          | <25>           | <23>            |
|              | leukemic cell infiltration |                                       | 0             | 1             | 1              | 0               |
| all intes    |                            |                                       | <26>          | <27>          | <25>           | <23>            |
|              | leukemic cell infiltration |                                       | 0             | 1             | 0              | 0               |
| Ver          |                            |                                       | <26>          | <27>          | <25>           | <23>            |
| .01          | leukemic cell infiltration |                                       | 1             | 3             | 2              | 0               |
|              | metastasis;uterus tumor    |                                       | 1             | 1             | 0              | 2               |
| ncreas       |                            |                                       | <26>          | <27>          | <25>           | <23>            |
|              | leukemic cell infiltration |                                       | 0             | 2             | 0              | 0               |
|              | metastasis:uterus tumor    |                                       | 1             | 0             | 0              | 0               |
| Jrinary syst | em]                        |                                       |               |               |                |                 |
| idney        |                            |                                       | <26>          | <27>          | <25>           | <23>            |
|              | leukemic cell infiltration |                                       | 2             | 1             | 1              | 0               |
| in bladd     |                            |                                       | <26>          | <27>          | <25>           | <23>            |
| in pruod     | leukemic cell infiltration |                                       | 1             | 2             | 1              | 0               |
| Endocrine sy | vstem]                     |                                       |               |               |                |                 |
| drenal       |                            |                                       | <26>          | <27>          | <25>           | <23>            |
|              | leukemic cell infiltration |                                       | 0             | 1             | 0              | 0               |

| STUDY NO. : 0163<br>ANIMAL : MOUSE BDF1<br>REPORT TYPE : A1 |                                                                      |                                       | HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)<br>SACRIFICED ANIMALS (105W) |               |                                       |                 |  |
|-------------------------------------------------------------|----------------------------------------------------------------------|---------------------------------------|------------------------------------------------------------------------------------|---------------|---------------------------------------|-----------------|--|
|                                                             | FEMALE                                                               | •                                     |                                                                                    |               |                                       | PAGE :          |  |
| )rgan                                                       | Findings                                                             | Group Name<br>No. of Animals on Study | Control<br>26                                                                      | 400 ppm<br>27 | 2000 ppm<br>25                        | 10000 ppm<br>23 |  |
| Reproductive                                                | system]                                                              | · · · · · · · · · · · · · · · · · · · |                                                                                    |               |                                       |                 |  |
| DUALA                                                       | leukemic cell infiltration                                           |                                       | <26><br>1                                                                          | <27><br>3     | <25><br>2                             | <23><br>0       |  |
|                                                             | metastasis:uterus tumor                                              |                                       | 1                                                                                  | 0             | 0                                     | 2               |  |
| iterus                                                      | leukemic cell infiltration                                           |                                       | <26><br>0                                                                          | <27><br>2     | <25><br>0                             | <23><br>0       |  |
| nammary gl                                                  | leukemic cell infiltration                                           |                                       | <26><br>0                                                                          | <27><br>0     | <25><br>1                             | <23><br>0       |  |
| [Special sense                                              | e organs/appandage]                                                  |                                       |                                                                                    |               |                                       |                 |  |
| ЭУӨ                                                         | leukemic cell infiltration                                           |                                       | <26><br>0                                                                          | <27><br>1     | <25><br>1                             | <23><br>0       |  |
| larder gl                                                   | leukemic cell infiltration                                           |                                       | <26><br>0                                                                          | <27><br>1     | <25><br>1                             | <23><br>0       |  |
| (Musculoskele                                               | tal system]                                                          |                                       |                                                                                    |               |                                       |                 |  |
| muscle                                                      | leukemic cell infiltration                                           |                                       | <26><br>0                                                                          | <27><br>2     | <25><br>1                             | <23><br>0       |  |
| [Body cavitie                                               | [20                                                                  |                                       |                                                                                    |               |                                       |                 |  |
| mediastinum                                                 | leukemic cell infiltration                                           |                                       | <26><br>0                                                                          | <27><br>1     | <25><br>0                             | <23><br>0       |  |
| peritaneum                                                  | metastasis:uterus tumor                                              |                                       | <26><br>1                                                                          | <27><br>0     | <25><br>0                             | <23><br>1       |  |
| <a>b</a>                                                    | a : Number of animals examined a<br>b : Number of animals with lesio |                                       |                                                                                    |               | · · · · · · · · · · · · · · · · · · · |                 |  |
|                                                             |                                                                      |                                       |                                                                                    |               |                                       | ·····           |  |

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APPENDIX Q 1

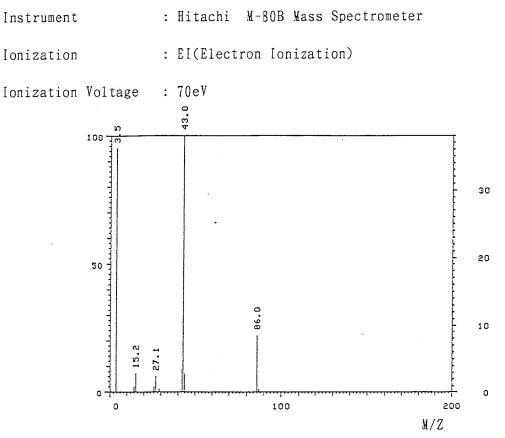
IDENTITY OF VINYL ACETATE

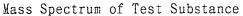
(2-YEAR STUDY)

IDENTITY OF VINYL ACETATE(TWO-YEAR STUDIES)

A. Test Substance Lot No. SAG5318

- 1. Spectral data
- (1) Mass Spectrometry





Results: <u>Determined</u>

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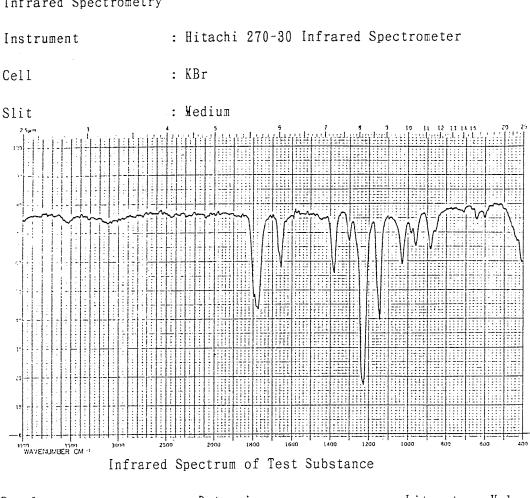
Molecular and Fragment Peak(M/Z)

| 86.0 |  |
|------|--|
| 43.0 |  |
| 27.1 |  |
| 15.2 |  |

Literature Value\* Molecular and Fragment Peak(M/Z)

> 86 43 27 15 (\*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(2) Infrared Spectrometry



Results

Determines Wave Number(cm<sup>-1</sup>)

840~ 920

940~1000 1000~1060

1120~1180

1200~1260

1280~1320

1360~1410

1630~1690 1740~1820

Literature Values\* Wave Number( $cm^{-1}$ )

> 830~ 910 930~ 990 1000~1060 1110~1170  $1180 \sim 1260$ 1280~1320 1340~1400 1630~1680 1730~1820 (\*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD. )

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

Consequently, the test substance was identified as Vinyl acetate.

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B. Test Substance Lot No. LKP4386

1. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

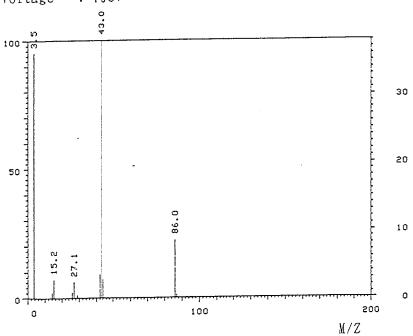
Ionization

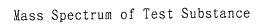
)

)

: EI(Electron Ionization)

Ionization Voltage : 70eV





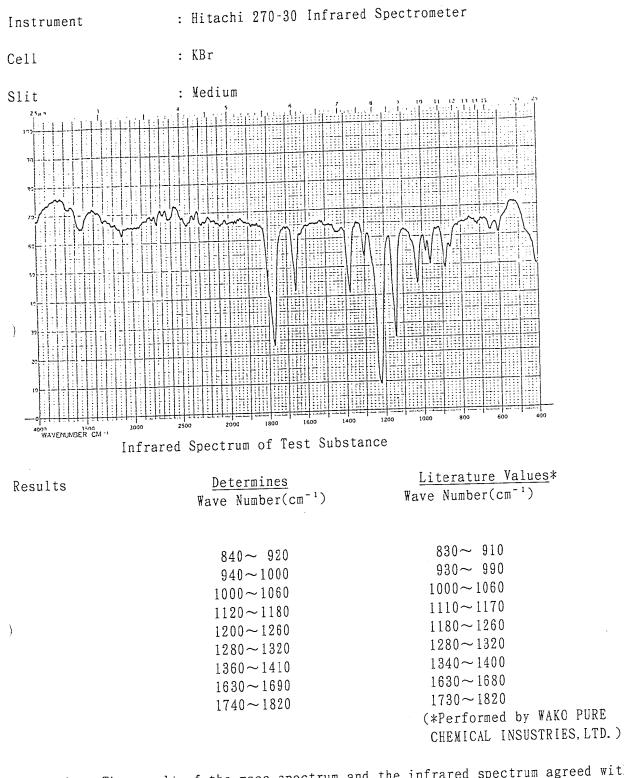
Results: <u>Determined</u> <u>Molecular</u> and Fragment Peak(M/Z)

> 86.0 43.0 27.1 15.2

Literature Value\* Molecular and Fragment Peak(M/Z)

86 43 27 15 (\*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

### (2) Infrared Spectrometry



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

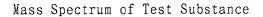
Consequently, the test substance was identified as Vinyl acetate.

C. Test Substance Lot No. WDP4895

1. Spectral data

(1) Mass Spectrometry

: Hitachi M-80B Mass Spectrometer Instrument : EI(Electron Ionization) Ionization : 70eV Ionization Voltage 43.0 100 10 30 20 50 86.0 10 15.2 27.1 0 0 200 100 0 M/Z



Results: <u>Determined</u> Molecular and Fragment Peak(M/Z)

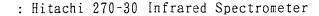
| 86.0 |  |  |  |
|------|--|--|--|
| 43.0 |  |  |  |
| 27.1 |  |  |  |
| 15.2 |  |  |  |
|      |  |  |  |

Literature Value\* Molecular and Fragment Peak(M/Z)

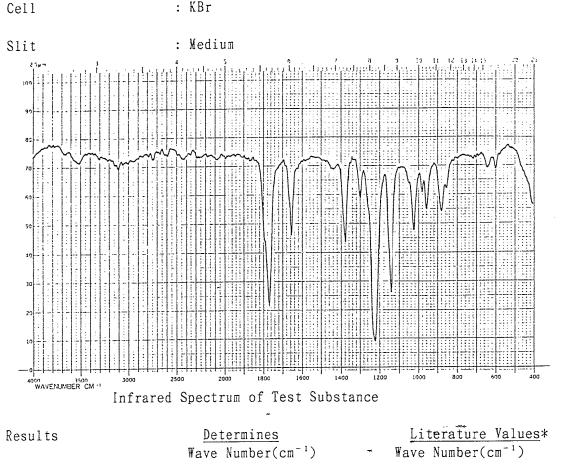
> 86 43 27 15 (\*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(2) Infrared Spectrometry





: KBr



840~ 920 940~1000 1000~1060 1120~1180 1200~1260 1280~1320 1360~1410 1630~1690  $1740 \sim 1820$ 

1110~1170 1180~1260 1280~1320  $1340 \sim 1400$  $1630 \sim 1680$ 1730~1820 (\*Performed by WAKO PURE

830~ 910

930~ 990

1000~1060

CHEMICAL INSUSTRIES, LTD. )

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Vinyl acetate.

)

D. Test Substance Lot No. WDP4894

1. Spectral data

)

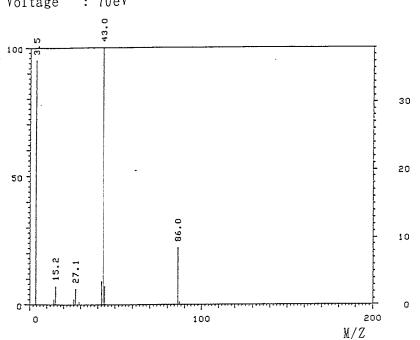
)

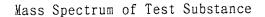
(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV





Results: <u>Determined</u> Molecular and Fragment Peak(M/Z)

| 86.0 |  |  |
|------|--|--|
| 43.0 |  |  |
| 27.1 |  |  |
| 15.2 |  |  |
|      |  |  |

<u>Literature Value\*</u> Molecular and Fragment Peak(M/Z)

> 86 43 27 15 (\*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

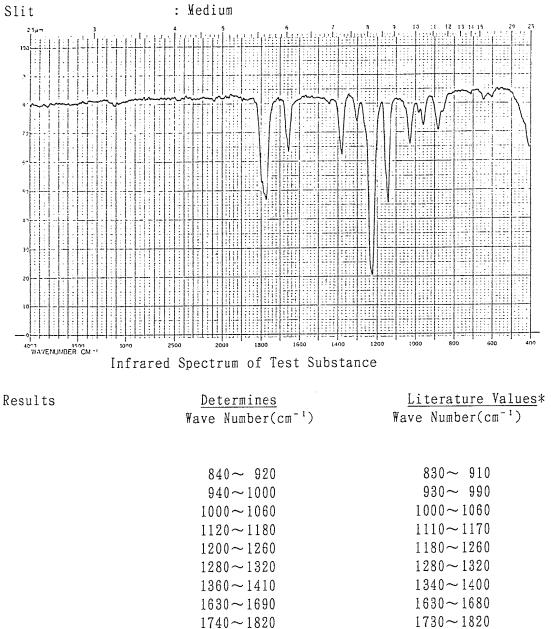
(2) Infrared Spectrometry





Cell

: KBr



1730~1820 (\*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD. )

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Vinyl acetate.

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E. Test Substance Lot No. WDP4895

1. Spectral data

(1) Mass Spectrometry

Ionization

)

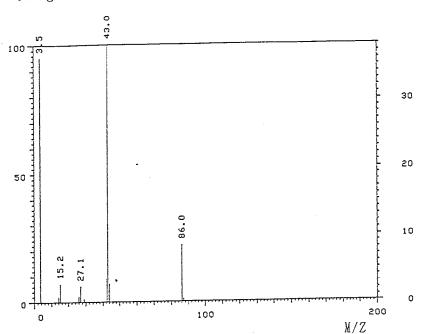
)

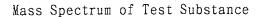
Instrument

: EI(Electron Ionization)

: Hitachi M-80B Mass Spectrometer

Ionization Voltage : 70eV





Results: <u>Determined</u> <u>L</u> Molecular and Fragment Peak(M/Z) M

> 86. 0 43. 0 27. 1 15. 2

Literature Value\* Molecular and Fragment Peak(M/Z)

> 86 43 27 15 (\*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

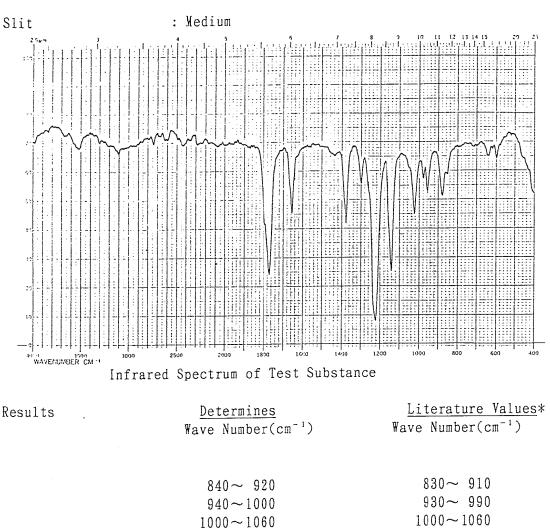
#### (2) Infrared Spectrometry



Cell

### : Hitachi 270-30 Infrared Spectrometer

: KBr



1000~1060 1110~1170 1180~1260 1280~1320 1340~1400 1630~1680  $1730 \sim 1820$ (\*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD. )

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

1120~1180

1200~1260

1280~1320

1360~1410

1630~1690

 $1740 \sim 1820$ 

Consequently, the test substance was identified as Vinyl acetate.

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- F. Test Substance Lot No. WDM5220
- 1. Spectral data
- (1) Mass Spectrometry

Instrument

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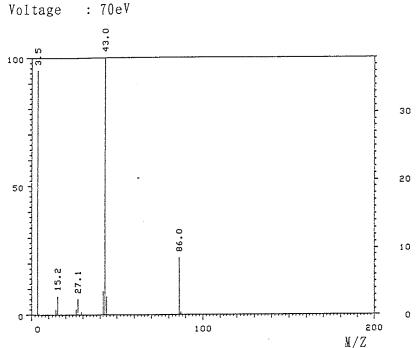
)

Ionization

: EI(Electron Ionization)

: Hitachi M-80B Mass Spectrometer

Ionization Voltage



Mass Spectrum of Test Substance

| Results: | Determined | 1   |          |           |
|----------|------------|-----|----------|-----------|
|          | Molecular  | and | Fragment | Peak(M/Z) |

86.0 43.0 27.1 15.2 Literature Value\* Molecular and Fragment Peak(M/Z)

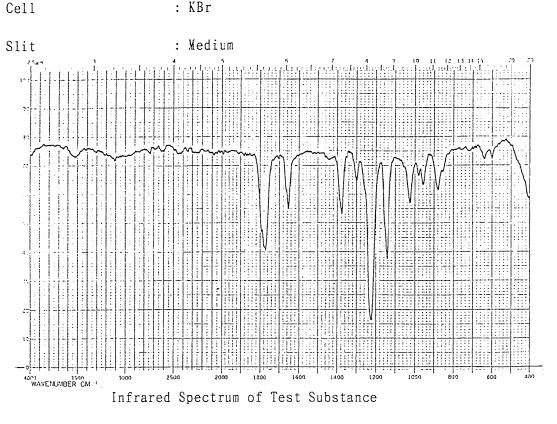
86 43 27 15 (\*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(2) Infrared Spectrometry



: Hitachi 270-30 Infrared Spectrometer

: KBr



Results

Determines Wave Number(cm<sup>-1</sup>)

840~ 920

940~1000

1000~1060

1120~1180

1200~1260

1280~1320

1360~1410

1630~1690

1740~1820

Literature Values\* Wave Number( $cm^{-1}$ ) 830~ 910 930~ 990 1000~1060 1110~1170 1180~1260 1280~1320 1340~1400  $1630 \sim 1680$ 1730~1820 (\*Performed by WAKO PURE

CHEMICAL INSUSTRIES, LTD. )

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

Consequently, the test substance was identified as Vinyl acetate.

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APPENDIX Q 2

## STABILITY OF VINYL ACETATE IN DRIKING WATER

(2-YEAR STUDY)

### STABILITY OF VINYL ACETATE(TWO-YEAR STUDIES)

A. Test Substance Lot No. SAG5318

1. Sample storage: This lot was used from 1991. 3.26 to 1991. 7.19. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

| Instrument | : Hitachi 270-30 Infrared Spectrometer                                  |             |
|------------|-------------------------------------------------------------------------|-------------|
| Cell       | : KBr                                                                   |             |
| Slit       | : Medium                                                                | =           |
| Results    | : The result of the infrared spectrum did not before and after studies. | change when |

| <u>1991.02.15(date_analyze</u><br>Wave_Number(cm <sup>-1</sup> ) | d) <u>1991.07.19(date analyzed)</u><br>Wave Number(cm <sup>-1</sup> ) |
|------------------------------------------------------------------|-----------------------------------------------------------------------|
| 840~ 920                                                         | 840~ 920                                                              |
| 940~1000                                                         | 940~1000                                                              |
| $1000 \sim 1060$                                                 | 1000~1060                                                             |
| 1120~1180                                                        | 1120~1180                                                             |
| 1200~1260                                                        | 1200~1260                                                             |
| 1280~1320                                                        | 1280~1320                                                             |
| $1360 \sim 1410$                                                 | $1360 \sim 1410$                                                      |
| $1630 \sim 1690$                                                 | $1630 \sim 1690$                                                      |
| $1740 \sim 1820$                                                 | 1740~1820                                                             |

3. Gas Chromatography

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| Instrument         | : Hewlett Packard 5890A Gass Chromatograph  |
|--------------------|---------------------------------------------|
| Column             | : Methyl Silicone(0.2mm $\phi \times 38m$ ) |
| Column Temperature | : 40°C                                      |
| Flow Rate          | : 1 ml/min                                  |
| Detector           | : FID(Flame Ionization Detector)            |
| Injection Volume   | : 1 µ l                                     |

Results: Chromatogram indicated one major peak analyzed at 1991.2.15 and one major peak analyzed at 1991.7.19. The new trace impurity peak in the test substance analyzed at 1991.7.19 was not detected.

| Date                          | Retention<br>Time(min) | AREA   |  |
|-------------------------------|------------------------|--------|--|
| 1991.02.15<br>(date analyzed) | 3.308                  | 227600 |  |
| 1991.07.19<br>(date analyzed) | 3.307                  | 224462 |  |

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 5 months).

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B. Test Substance Lot No. LKP4386

1. Sample storage: This lot was used from 1991.7.19 to 1992.3.31. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

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: The result of the infrared spectrum did not change when before and after studies.

| <u>1991.07.19(d</u><br>Wave Number( | ate analyzed)1992.03.31(date analyzed)cm <sup>-1</sup> )Wave Number(cm <sup>-1</sup> ) |
|-------------------------------------|----------------------------------------------------------------------------------------|
| 840~ 920                            | 840~ 920                                                                               |
| 940~1000                            | 940~1000                                                                               |
| 1000~1060                           | 1000~1060                                                                              |
| 1120~1180                           | 1120~1180                                                                              |
| 1200~1260                           | 1200~1260                                                                              |
| 1280~1320                           | 1280~1320                                                                              |
| $1360 \sim 1410$                    | 1360~1410                                                                              |
| $1630 \sim 1690$                    | $1630 \sim 1690$                                                                       |
| 1740~1820                           | $1740 \sim 1820$                                                                       |

3. Gas Chromatography

| Instrument         | : Hewlett Packard 5890A Gass Chromatograph  |
|--------------------|---------------------------------------------|
| Column             | : Methyl Silicone(0.2mm $\phi \times 38m$ ) |
| Column Temperature | : 40°C                                      |
| Flow Rate          | : 1 ml/min                                  |
| Detector           | : FID(Flame Ionization Detector)            |
| Injection Volume   | : 1 µ 1                                     |

Results: Chromatogram indicated one major peak analyzed at 1991.7.19 and one major peak analyzed at 1992.3.31. The new trace impurity peak in the test substance analyzed at 1992.3.31 was not detected.

| Date                          | Retention<br>Time(min) | AREA   |  |
|-------------------------------|------------------------|--------|--|
| 1991.07.19<br>(date analyzed) | 3. 3                   | 227380 |  |
| 1992.03.31<br>(date analyzed) | 3. 3                   | 227349 |  |

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 9 months).

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C. Test Substance Lot No. WDP4895

1. Sample storage: This lot was used from 1992. 3. 31 to 1992. 9. 15. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

| Instrument : | Hitachi | 270-30 | Infrared | Spectrometer |
|--------------|---------|--------|----------|--------------|
|--------------|---------|--------|----------|--------------|

Cell : KBr

Slit : Medium

Results

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: The result of the infrared spectrum did not change when before and after studies.

| <u>1992.03.27(date_analyzed)</u> | <u>1992.09.15(date analyzed)</u> |
|----------------------------------|----------------------------------|
| Wave Number(cm <sup>-1</sup> )   | Wave Number(cm <sup>-1</sup> )   |
| 0.10 0.00                        | <u></u>                          |
| 840~ 920                         | 840~ 920                         |
| 940~1000                         | 940~1000                         |
| $1000 \sim 1060$                 | 1000~1060                        |
| 1120~1180                        | 1120~1180                        |
| 1200~1260                        | 1200~1260                        |
| 1280~1320                        | 1280~1320                        |
| 1360~1410                        | $1360 \sim 1410$                 |
| 1630~1690                        | $1630 \sim 1690$                 |
| $1740 \sim 1820$                 | $1740 \sim 1820$                 |

3. Gas Chromatography

| Instrument         | : Hewlett Packard 5890A Gass Chromatograph |
|--------------------|--------------------------------------------|
| Column             | : Methyl Silicone(0.2mm $\phi$ × 38m)      |
| Column Temperature | : 40°C                                     |
| Flow Rate          | : 1 ml/min                                 |
| Detector           | : FID(Flame Ionization Detector)           |
| Injection Volume   | : 1 μ1                                     |

Results: Chromatogram indicated one major peak analyzed at 1992.3.27 and one major peak analyzed at 1992.9.15. The new trace impurity peak in the test substance analyzed at 1992.9.15 was not detected.

| Date                          | Retention<br>Time(min) | AREA   |  |
|-------------------------------|------------------------|--------|--|
| 1992.03.27<br>(date analyzed) | 3.305                  | 230886 |  |
| 1992.09.15<br>(date analyzed) | 3.307                  | 230247 |  |

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 6 months).

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D. Test Substance Lot No. WDP4894

1. Sample storage: This lot was used from 1992.9.15 to 1992.12.22. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

| Instrument : Hitachi 2 | 270-30 Infrared | Spectrometer |
|------------------------|-----------------|--------------|
|------------------------|-----------------|--------------|

- Cell : KBr
- Slit : Medium

Results

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۲ ۲ ۲ : The result of the infrared spectrum did not change when before and after studies.

| <u>1992.09.01(date_analyzed)</u><br>\#ave_Number(cm <sup>-1</sup> ) | <u>1992.12.22(date_analyzed)</u><br>Wave_Number(cm <sup>-1</sup> ) |
|---------------------------------------------------------------------|--------------------------------------------------------------------|
| 840~ 920                                                            | 840~ 920                                                           |
| 940~1000                                                            | 940~1000                                                           |
| 1000~1060                                                           | 1000~1060                                                          |
| 1120~1180                                                           | 1120~1180                                                          |
| 1200~1260                                                           | 1200~1260                                                          |
| 1280~1320                                                           | 1280~1320                                                          |
| 1360~1410                                                           | $1360 \sim 1410$                                                   |
| $1630 \sim 1690$                                                    | 1630~1690                                                          |
| 1740~1820                                                           | 1740~1820                                                          |

3. Gas Chromatography

| Instrument         | : Hewlett Packard 5890A Gass Chromatograph  |
|--------------------|---------------------------------------------|
| Column             | : Methyl Silicone(0.2mm $\phi \times 38$ m) |
| Column Temperature | : 40°C                                      |
| Flow Rate          | : 1 ml/min                                  |
| Detector           | : FID(Flame Ionization Detector)            |
| Injection Volume   | : 1 µ 1                                     |

Results: Chromatogram indicated one major peak analyzed at 1992.9.1 and one major peak analyzed at 1992.12.22. The new trace impurity peak in the test substance analyzed at 1992.12.22 was not detected.

| Date                          | Retention<br>Time(min) | AREA   |  |
|-------------------------------|------------------------|--------|--|
| 1992.09.01<br>(date analyzed) | 3. 3                   | 230304 |  |
| 1992.12.22<br>(date analyzed) | 3.3                    | 229084 |  |

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 4 months).

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E. Test Substance Lot No. WDP4895

1. Sample storage: This lot was used from 1992.12.22 to 1993.4.6. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

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| Instrument          | : Hitachi 270-30 Infrared Spec                                                                                                                                                             | trometer                                                                                                                                                                                   |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cell                | ; KBr                                                                                                                                                                                      |                                                                                                                                                                                            |
| Slit                | : Medium                                                                                                                                                                                   |                                                                                                                                                                                            |
| Results             | : The result of the infrared spectrum did not change when before and after studies.                                                                                                        |                                                                                                                                                                                            |
|                     | <u>1992.09.15(date analyzed)</u><br>Wave Number(cm <sup>-1</sup> )                                                                                                                         | <u>1993.04.06(date analyzed)</u><br>Wave Number(cm <sup>-1</sup> )                                                                                                                         |
|                     | $\begin{array}{r} 840 \sim 920 \\ 940 \sim 1000 \\ 1000 \sim 1060 \\ 1120 \sim 1180 \\ 1200 \sim 1250 \\ 1280 \sim 1320 \\ 1360 \sim 1410 \\ 1630 \sim 1690 \\ 1740 \sim 1820 \end{array}$ | $\begin{array}{r} 840 \sim 920 \\ 940 \sim 1000 \\ 1000 \sim 1060 \\ 1120 \sim 1180 \\ 1200 \sim 1260 \\ 1280 \sim 1320 \\ 1360 \sim 1410 \\ 1630 \sim 1690 \\ 1740 \sim 1820 \end{array}$ |
| .Gas Chromatography |                                                                                                                                                                                            |                                                                                                                                                                                            |
| Instrument          | : Hewlett Packard 5890A Gass Chr                                                                                                                                                           | romatograph                                                                                                                                                                                |
| Column              | : Methyl Silicone(0.2mm $\phi \times 38$ m)                                                                                                                                                |                                                                                                                                                                                            |
| Column Temperature  | : 40°C                                                                                                                                                                                     |                                                                                                                                                                                            |
| Flow Rate           | : 1 ml/min                                                                                                                                                                                 |                                                                                                                                                                                            |
| Detector            | : FID(Flame Ionization Detector)                                                                                                                                                           |                                                                                                                                                                                            |
| Injection Volume    | : 1 μl                                                                                                                                                                                     |                                                                                                                                                                                            |

Results: Chromatogram indicated one major peak analyzed at 1992.9.1 and one major peak analyzed at 1993.4.6. The new trace impurity peak in the test substance analyzed at 1993.4.6 was not detected.

| Date                          | Retention<br>Time(min) | AREA   |  |
|-------------------------------|------------------------|--------|--|
| 1992.09.01<br>(date analyzed) | 3. 3                   | 230613 |  |
| 1993.04.06<br>(date analyzed) | 3. 3                   | 230757 |  |

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 7 months).

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F. Test Substance Lot No. WDM5220

1. Sample storage: This lot was used from 1993.4.6 to 1993.4.16. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

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: The result of the infrared spectrum did not change when before and after studies.

| 1993.03.01(date analyzed) | <u>1993.04.16(date analyzed)</u> |
|---------------------------|----------------------------------|
| $Wave Number(cm^{-1})$    | ₩ave Number(cm <sup>-1</sup> )   |
|                           |                                  |
| 840~ 920                  | 840~ 920                         |
| 940~1000                  | 940~1000                         |
| 1000~1060                 | 1000~1060                        |
| 1120~1180                 | 1120~1180                        |
| 1200~1260                 | 1200~1260                        |
| 1280~1320                 | 1280~1320                        |
| $1360 \sim 1410$          | $1360 \sim 1410$                 |
| $1630 \sim 1690$          | $1630 \sim 1690$                 |
| 1740~1820                 | 1740~1820                        |

3. Gas Chromatography

| Instrument         | : Hewlett Packard 5890A Gass Chromatograph  |
|--------------------|---------------------------------------------|
| Column             | : Methyl Silicone(0.2mm $\phi \times 38$ m) |
| Column Temperature | : 40°C                                      |
| Flow Rate          | : 1 ml/min                                  |
| Detector           | : FID(Flame Ionization Detector)            |
| Injection Volume   | : 1 µ 1                                     |

Results: Chromatogram indicated one major peak analyzed at 1993.3.1 and one major peak analyzed at 1993.4.16. The new trace impurity peak in the test substance analyzed at 1993.4.16 was not detected.

| Date                          | Retention<br>Time(min) | AREA   |  |
|-------------------------------|------------------------|--------|--|
| 1993.03.01<br>(date analyzed) | 3.307                  | 232010 |  |
| 1993.04.16<br>(date analyzed) | 3.305                  | 231946 |  |

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 6 weeks).

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# APPENDIX Q 3

### CONDETRATION OF VINYL ACETATE IN DRINKING WATER

(2-YEAR STUDY)

### CONCENTRATION OF VINYL ACETATE IN DRINKING WATER(TWO-YEAR STUDIES)

(Rat)

|               | Target Co     | ncentration(ppm) |                |
|---------------|---------------|------------------|----------------|
| Date analyzed | 400           | 2000             | 10000          |
| 1991.03.26    | 412.5(103.1)* | 1910.5( 95.5)    | 9611.5( 96.1)  |
| 991.07.05     | 430.2(107.5)  | 2038.4(101.9)    | 10254.8(102.5) |
| 1991.10.11    | 370.1(92.5)   | 1791.6(89.6)     | 7137.3(71.4)   |
| 992.01.24     | 483.0(120.8)  | 1990.9(99.5)     | 10519.4(105.2) |
| 992.04.03     | 398.0(99.5)   | 2053.3(102.7)    | 10025.6(100.3) |
| 992.06.19     | 372.4(93.1)   | 1998.3(99.9)     | 10843.8(108.4) |
| 992.09.18     | 349.3( 87.3)  | 1779.4(89.0)     | 9144.7( 91.4)  |
| 1992.12.18    | 409.3(102.3)  | 1953.1(97.7)     | 11204.3(112.0) |
| 1993.03.19    | 323.9( 81.0)  | 1826.4(91.3)     | 9225.6(92.3)   |

(\*) % of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument: Hewlett Packard 5890AColumn: METHYL SILICONE(0.2mm φ × 38m)Column Temperature:40°CCarrier: He

Flow Rate: Iml/minDetector: FID(Flame Ionization)Injection Volume: 10 μ 1

### CONCENTRATION OF VINYL ACETATE IN DRINKING WATER(TWO-YEAR STUDIES)

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#### (Mouse)

| Target Concentration(ppm) |               |               |                |
|---------------------------|---------------|---------------|----------------|
| Date analyzed `           | 400           | 2000          | 10000          |
| 1991.04.16                | 371.3( 92.8)* | 1898.8(94.9)  | 9881.1( 98.8)  |
| 991.07.05                 | 409.8(102.4)  | 1990.9( 99.5) | 9791.5( 97.9)  |
| 991.10.11                 | 374.9(93.7)   | 1911.3(95.6)  | 7409.6(74.1)   |
| 992.01.24                 | 453.1(113.3)  | 1899.1( 95.0) | 9629.1( 96.3)  |
| 992.04.03                 | 352.2( 88.0)  | 1905.8(95.3)  | 9410.1( 94.1)  |
| 992.06.19                 | 430.0(107.5)  | 2367.2(118.4) | 11996.2(120.0) |
| 992.09.18                 | 349.8(87.5)   | 1767.2(88.4)  | 9166.8( 91.7)  |
| 992.12.18                 | 399.1(99.8)   | 1921.9(96.1)  | 9950.1(99.5)   |
| 993.03.19                 | 323.8(81.0)   | 1791.0(89.6)  | 9327.8(93.3)   |

(\*) % of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument: Hewlett Packard 5890AColumn: METHYL SILICONE(0.2mm φ × 38m)Column Temperature:40 ℃Carrier: He

Flow Rate: lml/minDetector: FID(Flame Ionization)Injection Volume: 10 μ l

## APPENDIX Q 4

## STABILITY OF $\beta$ -CHLOROPROPIONIC ACID IN DRINKING WATER

(2-YEAR STUDY)

#### STABILITY OF VINYL ACETATE IN DRINKING WATER(TWO-YEAR STUDIES)

(Rat)

| Target Concentration(ppm) |                           |        |         |  |
|---------------------------|---------------------------|--------|---------|--|
| Date analyzed             | 400                       | 2000   | 10000   |  |
| 1991.03.29(a)             | 369.6                     | 1959.1 | 10083.4 |  |
| 1991.04.02(b)             | 318.5                     | 1444.8 | 7391.3  |  |
| (Mouse)                   |                           |        |         |  |
|                           | Target Concentration(ppm) |        |         |  |
| Date analyzed             | 400                       | 2000   | 10000   |  |
| 1991.04.26(a)             | 433.1                     | 1975.4 | 10274.3 |  |
| 1991.04.30(b)             | 374.6                     | 1929.1 | 8608.8  |  |

(a) Date of preparation

(b) The stability of vinyl acetate in drinking water was established for 4 days when stored at 25°C.

Analytical method: The sample were analyzed by the GC.

| Instrument        | : Hewlett Packard 5890A                     | Flow Rate        | : 1ml/min               |
|-------------------|---------------------------------------------|------------------|-------------------------|
| Column            | : METHYL SILICONE(0.2mm $\phi \times 38$ m) | Detector         | : FID(Flame Ionization) |
| Column Temperatur | e: 40℃                                      | Injection Volume | $: 10 \mu 1$            |
| Carrier           | : He                                        |                  |                         |

# APPENDIX R 1

# METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

### METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

| Item                                      | Method                                                           | Unit                               |
|-------------------------------------------|------------------------------------------------------------------|------------------------------------|
| Hematology                                |                                                                  |                                    |
| Red blood cell (RBC)                      | Light scattering method 1)                                       | $\times 10^{6} / \mu 1$            |
| Hemoglobin (Hgb)                          | Cyanmethemoglobin method <sup>1)</sup>                           | g/d1                               |
| Hematocrit (Hct)                          | Calculated as RBC $\times$ MCV/10 <sup>-1</sup>                  | %                                  |
| Mean corpuscular volume (MCV)             | Light scattering method <sup>1)</sup>                            | fl                                 |
| Mean corpuscular hemoglobin (MCH)         | Calculated as Hgb/RBC $\times$ 10 <sup>-1)</sup>                 | pg                                 |
| Mean corpuscular hemoglobin               | Calculated as Hgb/Hct $\times$ 10 <sup>-1)</sup>                 | g/d1                               |
| concentration (MCHC)                      |                                                                  | 3                                  |
| Platelet                                  | Light scattering method 1)                                       | $\times 10^{3}/\mu 1$              |
| White blood cell (WBC)                    | Light scattering method <sup>1)</sup>                            | $\times$ 10 <sup>3</sup> / $\mu$ 1 |
| Differential WBC                          | Pattern recognition method <sup>2)</sup>                         | %                                  |
| Differential WDC                          | (May-Grunwald-Giemsa staining)                                   | 10                                 |
|                                           | (inay Granwald Greensa samme)                                    |                                    |
| Biochemistry                              |                                                                  |                                    |
| Total protein (TP)                        | Biuret method <sup>3)</sup>                                      | g/d1                               |
| Albumin (Alb)                             | BCG method <sup>3)</sup>                                         | g/dl                               |
| A/G ratio                                 | Calculated as Alb/(TP-Alb) <sup>3)</sup>                         | -                                  |
| T-bilirubin                               | Michaelson method <sup>3)</sup>                                  | mg/dl                              |
| Glucose                                   | Enzymatic method (HK $\cdot$ G-6-PDH) <sup>3)</sup>              | mg/dl                              |
| T-cholesterol                             | Enzymatic method (CEH $\cdot$ COD $\cdot$ POD) <sup>3)</sup>     | mg/dl                              |
| Triglyceride                              | Enzymatic method (GK · GPO · POD) <sup>3)</sup>                  | mg/dl                              |
| Phospholipid                              | Enzymatic method (PLD $\cdot$ COD $\cdot$ POD) <sup>3)</sup>     | mg/dl                              |
| Glutamic oxaloacetic transaminase         | Karmen method <sup>3)</sup>                                      | IU/1                               |
| (GOT)                                     |                                                                  |                                    |
| Glutamic pyruvic transaminase (GPT)       | Karmen method <sup>3)</sup>                                      | IU/I                               |
| Lactate dehydrogenase (LDH)               | Wroblewski-LaDue method <sup>3)</sup>                            | IU/1                               |
| Alkaline phosphatase (ALP)                | GSCC method <sup>3)</sup>                                        | IU/1                               |
| $\gamma$ -Glutamyl transpeptidase (G-GTP) | $L-\gamma$ -Glutamyl-p-nitroanilide substrate                    | IU/1                               |
|                                           | method <sup>3)</sup>                                             |                                    |
| Creatine phosphokinase (CPK)              | GSCC method <sup>3)</sup>                                        | IU/1                               |
| Urea nitrogen                             | Enzymatic method (Urease · GLDH) <sup>3)</sup>                   | mg/dl                              |
| Creatinine                                | Jaffe metod <sup>3)</sup>                                        | mg/dl                              |
| Sodium                                    | Flame photometry 4)                                              | mEq/1                              |
| Potassium                                 | Flame photometry <sup>4</sup>                                    | mEq/1                              |
| Chloride                                  | Coulometric titration <sup>4)</sup>                              | mEq/1                              |
| Calcium                                   | OCPC method 3)                                                   | mg/dl                              |
| Inorganic phosphorus                      | Enzymatic method (SPL $\cdot$ PGM $\cdot$ G-6-PDH) <sup>3)</sup> | mg/dl                              |
| Urinalysis                                |                                                                  |                                    |
| pH, Protein, Glucose, Ketone body,        | Urinalysis reagent paper metod <sup>5)</sup>                     |                                    |
| Bilirubin,                                |                                                                  |                                    |
| Occult Blood, Urobilinogen                |                                                                  |                                    |

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

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

3) Automatic analyzer (Hitachi 705 : Hitachi, Ltd., Japan)

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4) Flame photometer (Hitachi 750 : Hitachi, Ltd., Japan)

5) Ames reagent strips for urinalysis (Multistix, Uro-Labstix : Miles Sankyo Co., Ltd., Japan)

# APPENDIX R 2

### UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

### UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

|              | TEST ITEM            | DECIMAL PLACE | UNIT                  |
|--------------|----------------------|---------------|-----------------------|
| HEMATOLOGY   | Red blood cell       | 2             | $10^{6}/\mu 1$        |
|              | Hemoglobin           | 1             | g/dl                  |
|              | Hematocrit           | 1             | %                     |
|              | MCV                  | 1             | fl                    |
|              | MCH                  | 1             | pg                    |
|              | MCHC                 | 1             | g/dl                  |
|              | Platelet             | 0             | $\times 10^3/\mu$ l   |
|              |                      |               | 107,011               |
|              | White blood cell     | 2             | $\times 10^{3}/\mu$ l |
|              | Differential WBC     | 0             | %                     |
|              |                      |               | 70                    |
| BIOCHEMISTRY | Total protein        | 1             | g/dl                  |
|              | Albumin              | 1             | g/dl                  |
|              | A/G ratio            | 1             |                       |
|              | T-bilirubin          | 2             | mg/dl                 |
|              | Glucose              | 0             | mg/dl                 |
|              | T-cholesterol        | 0             | mg/dl                 |
|              | Triglyceride         | 0             | mg/dl                 |
|              | Phospholipid         | 0             | mg/dl                 |
|              | GOT                  | 0             | ΙŬΛ                   |
|              | GPT                  | 0             | IU/I                  |
|              | LDH                  | 0             | IU/l                  |
|              | ALP                  | 0             | IU/l                  |
|              | $\gamma$ -GTP        | 0             | IU/I                  |
|              | CPK                  | 0             | IU/l                  |
|              | Urea nitrogen        | 1             | mg/dl                 |
|              | Creatinine           | 1             | mg/dl                 |
|              | Sodium               | 0             | mĔq/l                 |
|              | Potassium            | 1             | mEq/l                 |
|              | Chloride             | 0             | mEq/l                 |
|              | Calcium              | 1             | mg/dl                 |
|              | Inorganic phosphorus | 1             | mg/dl                 |
| L            |                      |               | -                     |

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