ビフェ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(混餌試験)報告書

**試験番号**：ラット/0205；マウス/0206

# APPENDIX

(K1－R2)

# APPENDIXES (CONTINUED)

# APPENDIXES (CONTINUED)

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# APPENDIX K 1

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

## RAT : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Integumentary system/appandage] | | | | | | | | | | | | | | | | | | |
| skin/app | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | inflammation | | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | epidermal cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | thrombus | | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 3 ( 25) | 0 ( 0) | 3 ( 16) | 3 ( 16) | 2 ( 11) | 0 ( 0) |
| | mineralization | | 11 ( 85) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 56) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 ( 83) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 ( 53) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:olfactory epithelium | | 12 ( 92) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 89) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 26) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:respiratory epithelium | | 5 ( 38) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 56) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammation:foreign body | | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 8 ( 42) | 1 ( 5) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | respiratory metaplasia:olfactory epithelium | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 16) | ( 0) | ( 0) | ( 0) |
| | respiratory metaplasia:gland | | 12 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 15 | 0 | 0 | 0 |
| | | | ( 92) | ( 0) | ( 0) | ( 0) | ( 89) | ( 0) | ( 0) | ( 0) | ( 75) | ( 0) | ( 0) | ( 0) | ( 79) | ( 0) | ( 0) | ( 0) |
| lung | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | congestion | | 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) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | inflammatory infiltration | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 4 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 0) | ( 21) | ( 0) | ( 0) |
| | bronchiolar-alveolar 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) | ( 5) | ( 0) | ( 0) | ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | angiectasis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 17) | ( 0) | ( 0) | ( 0) | ( 11) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | increased hematopoiesis | | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 22) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | decreased hematopoiesis | | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | erythropoiesis:increased | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spleen | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) |
| | deposit of hemosiderin | | 0 ( 0) | 3 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 22) | 0 ( 0) | 0 ( 0) | 3 ( 25) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | extramedullary hematopoiesis | | 1 ( 8) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 1 ( 11) | 0 ( 0) | 1 ( 8) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | myocardial fibrosis | | 3 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 22) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 25) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 16) | 1 ( 5) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | erosion:forestomach | | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | ulcer:forestomach | | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammation:forestomach | | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | ulcer:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hemorrhage:glandular stomach | | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | herniation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | necrosis:central | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | fatty change:peripheral | | 0 ( 0) | 2 ( 15) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) |
| | acidophilic cell focus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | basophilic cell focus | | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | spongiosis hepatis | | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 21) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | bile duct hyperplasia | | 3 ( 23) | 9 ( 69) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 7 ( 78) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 11 ( 92) | 0 ( 0) | 0 ( 0) | 6 ( 32) | 9 ( 47) | 1 ( 5) | 0 ( 0) |
| | biliary cyst | | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| pancreas | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | atrophy | | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 8) | ( 0) | ( 0) | ( 11) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | deposit of hemosiderin | | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | ( 0) | ( 15) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 11) | ( 5) | ( 0) | ( 0) |
| | squamous cell metaplasia | | 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) | ( 5) | ( 0) | ( 0) | ( 0) |
| | chronic nephropathy | | 0 | 3 | 3 | 3 | 0 | 4 | 1 | 0 | 1 | 4 | 0 | 1 | 3 | 4 | 1 | 0 |
| | | | ( 0) | ( 23) | ( 23) | ( 23) | ( 0) | ( 44) | ( 11) | ( 0) | ( 8) | ( 33) | ( 0) | ( 8) | ( 16) | ( 21) | ( 5) | ( 0) |
| | tubular necrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 0 | 1 | 2 | 2 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 25) | ( 0) | ( 5) | ( 11) | ( 11) | ( 0) |
| | papillary necrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 16) | ( 5) | ( 0) |
| | mineralization:cortico-medullary junction | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 5) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 13 | | | | 500ppm 9 | | | | 1500ppm 12 | | | | 4500ppm 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | mineralization:papilla | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 32) | 2 ( 11) | 0 ( 0) | 0 ( 0) |
| | mineralization:pelvis | | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 26) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortex | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 11) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 26) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | simple hyperplasia:transitional epithelium | | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 21) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| | calculus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 26) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| ureter | | | < 6> | | | | < 1> | | | | < 3> | | | | < 2> | | | |
| | dilatation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 13 | | | | 500ppm 9 | | | | 1500ppm 12 | | | | 4500ppm 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| urin bladd | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | hemorrhage | | 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) | ( 21) | ( 0) | ( 0) |
| | squamous cell metaplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 2 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 16) | ( 11) | ( 0) | ( 0) |
| | squamous cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) |
| | inflammatory polyp | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 1 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 16) | ( 5) |
| | simple hyperplasia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 26) | ( 5) | ( 0) | ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 6 | 1 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 42) | ( 32) | ( 5) | ( 0) |
| | papillary hyperplasia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 5 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 26) | ( 0) | ( 0) |
| | basal cell hyperplasia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 5) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| | hyperplasia:gland | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | Rathke pouch | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| thyroid | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | C-cell hyperplasia | | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 11) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| adrenal | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | hypertrophy | | 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) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | hyperplasia:medulla | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | atrophy | | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 23) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 13 | | | | 500ppm 9 | | | | 1500ppm 12 | | | | 4500ppm 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | arteritis | | 1 ( 8) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | interstitial cell hyperplasia | | 4 ( 31) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| prostate | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| | hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| mammary gl | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | hyperplasia | | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | galactocele | | 1 ( 8) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| brain | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | hemorrhage | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 1 ( 5) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 13 | | | | 500ppm 9 | | | | 1500ppm 12 | | | | 4500ppm 19 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| spinal cord | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | hemorrhage | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 11) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | retinal atrophy | | 8 ( 62) | 2 ( 15) | 0 ( 0) | 0 ( 0) | 3 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 50) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 7 ( 37) | 5 ( 26) | 1 ( 5) | 0 ( 0) |
| | keratitis | | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) |
| Harder gl | | | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | degeneration | | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) |
| | lymphocytic infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hyperplasia | | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 13 | | | | 9 | | | | 12 | | | | 19 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| nasolacr d | | <a> | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | inflammation | b | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (c) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | | <a> | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | mineralization | b | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (c) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Body cavities] | | | | | | | | | | | | | | | | | | |
| peritoneum | | <a> | <13> | | | | < 9> | | | | <12> | | | | <19> | | | |
| | peritonitis | b | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (c) | ( 8) | ( 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

# APPENDIX K 2

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

## RAT : FEMALE : DEAD AND MORIBUND ANIMALS

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | thrombus | | 1 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 1 | 0 |
| | | | ( 17) | ( 33) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 31) | ( 0) | ( 8) | ( 0) |
| | necrosis | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 17) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | mineralization | | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 |
| | | | ( 17) | ( 0) | ( 0) | ( 0) | ( 33) | ( 0) | ( 0) | ( 0) | ( 33) | ( 0) | ( 0) | ( 0) | ( 38) | ( 0) | ( 0) | ( 0) |
| | eosinophilic change:olfactory epithelium | | 1 | 4 | 1 | 0 | 4 | 7 | 1 | 0 | 2 | 4 | 0 | 0 | 5 | 5 | 0 | 0 |
| | | | ( 17) | ( 67) | ( 17) | ( 0) | ( 33) | ( 58) | ( 8) | ( 0) | ( 33) | ( 67) | ( 0) | ( 0) | ( 38) | ( 38) | ( 0) | ( 0) |
| | eosinophilic change:respiratory epithelium | | 2 | 1 | 0 | 0 | 12 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 10 | 0 | 0 | 0 |
| | | | ( 33) | ( 17) | ( 0) | ( 0) | (100) | ( 0) | ( 0) | ( 0) | ( 83) | ( 0) | ( 0) | ( 0) | ( 77) | ( 0) | ( 0) | ( 0) |
| | inflammation:foreign body | | 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) | ( 0) | ( 0) | ( 0) | ( 0) |
| | inflammation:olfactory epithelium | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 17) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | respiratory metaplasia:gland | | 4 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 10 | 0 | 0 | 0 |
| | | | ( 67) | ( 0) | ( 0) | ( 0) | ( 83) | ( 0) | ( 0) | ( 0) | (100) | ( 0) | ( 0) | ( 0) | ( 77) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasopharynx | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | inflammation:foreign body | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| larynx | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | inflammatory infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) |
| lung | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | congestion | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hemorrhage | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) |
| | inflammatory infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 2 ( 15) | 0 ( 0) | 0 ( 0) |
| | bronchiolar-alveolar cell hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | increased hematopoiesis | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 23) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | atrophy | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 15) | ( 0) |
| | deposit of hemosiderin | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 17) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) |
| | fibrosis | | 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) | ( 0) | ( 0) | ( 0) | ( 0) |
| | extramedullary hematopoiesis | | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 4 | 1 | 0 |
| | | | ( 0) | ( 0) | ( 33) | ( 0) | ( 17) | ( 0) | ( 0) | ( 0) | ( 0) | ( 17) | ( 0) | ( 0) | ( 8) | ( 31) | ( 8) | ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | thrombus | | 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) | ( 0) | ( 0) | ( 0) |
| | mineralization | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 15) | ( 0) |
| | myocardial fibrosis | | 0 | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 17) | ( 0) | ( 0) | ( 17) | ( 8) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 6 1 (%) | Control 6 2 (%) | Control 6 3 (%) | Control 6 4 (%) | 500ppm 12 1 (%) | 500ppm 12 2 (%) | 500ppm 12 3 (%) | 500ppm 12 4 (%) | 1500ppm 6 1 (%) | 1500ppm 6 2 (%) | 1500ppm 6 3 (%) | 1500ppm 6 4 (%) | 4500ppm 13 1 (%) | 4500ppm 13 2 (%) | 4500ppm 13 3 (%) | 4500ppm 13 4 (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | ulcer:forestomach | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | ulcer:glandular stomach | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| large intes | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | inflammation | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | herniation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | fatty change:central | | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | degeneration:central | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 1 ( 17) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | basophilic cell focus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | bile duct hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 25) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | biliary cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| pancreas | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 15) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | infarct | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | deposit of hemosiderin | | 0 ( 0) | 2 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 67) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 31) | 0 ( 0) | 0 ( 0) |
| | chronic nephropathy | | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 15) | 1 ( 8) | 0 ( 0) |
| | tubular necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 25) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 1 ( 8) | 0 ( 0) |
| | papillary necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 2 ( 15) | 3 ( 23) | 0 ( 0) |
| | mineralization:cortico-medullary junction | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 50) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 4 ( 31) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:papilla | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:pelvis | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortex | | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 2 ( 15) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | simple hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 38) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | calculus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:inner stripe,outer medulla | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) |
| urin bladd | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | squamous cell metaplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | papillary hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 23) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| thyroid | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | C-cell hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 2 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) |
| adrenal | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | peliosis-like lesion | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hyperplasia:medulla | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | focal fatty change:cortex | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| uterus | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | cystic endometrial hyperplasia | | 3 ( 50) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 3 ( 25) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| mammary gl | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | galactocele | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| brain | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | hemorrhage | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spinal cord | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | hemorrhage | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | <6> | | | | <12> | | | | <6> | | | | <13> | | | |
| | hemorrhage | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | retinal atrophy | | 3 ( 50) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 4 ( 33) | 4 ( 33) | 0 ( 0) | 0 ( 0) | 4 ( 67) | 2 ( 33) | 0 ( 0) | 0 ( 0) | 7 ( 54) | 1 ( 8) | 0 ( 0) | 0 ( 0) |
| | keratitis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| Harder gl | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | degeneration | | 2 ( 33) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | lymphocytic infiltration | | 1 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| nasolacr d | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 17) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 17) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 2 ( 15) | 0 ( 0) | 0 ( 0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | mineralization | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | | | | 12 | | | | 6 | | | | 13 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| bone | | | < 6> | | | | <12> | | | | < 6> | | | | <13> | | | |
| | osteosclerosis | | 1 ( 17) | 1 ( 17) | 2 ( 33) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 1 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 8) | 1 ( 8) | 0 ( 0) |

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

APPENDIX K 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Integumentary system/appandage] | | | | | | | | | | | | | | | | | | |
| skin/app | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | inflammation | | 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) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | epidermal cyst | | 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) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | thrombus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| | mineralization | | 18 | 0 | 0 | 0 | 17 | 0 | 0 | 0 | 29 | 0 | 0 | 0 | 16 | 1 | 0 | 0 |
| | | | ( 49) | ( 0) | ( 0) | ( 0) | ( 41) | ( 0) | ( 0) | ( 0) | ( 76) | ( 0) | ( 0) | ( 0) | ( 52) | ( 3) | ( 0) | ( 0) |
| | eosinophilic change:olfactory epithelium | | 34 | 2 | 0 | 0 | 33 | 3 | 0 | 0 | 18 | 0 | 0 | 0 | 10 | 0 | 0 | 0 |
| | | | ( 92) | ( 5) | ( 0) | ( 0) | ( 80) | ( 7) | ( 0) | ( 0) | ( 47) | ( 0) | ( 0) | ( 0) | ( 32) | ( 0) | ( 0) | ( 0) |
| | eosinophilic change:respiratory epithelium | | 26 | 0 | 0 | 0 | 26 | 0 | 0 | 0 | 14 | 0 | 0 | 0 | 10 | 0 | 0 | 0 |
| | | | ( 70) | ( 0) | ( 0) | ( 0) | ( 63) | ( 0) | ( 0) | ( 0) | ( 37) | ( 0) | ( 0) | ( 0) | ( 32) | ( 0) | ( 0) | ( 0) |
| | inflammation:foreign body | | 8 | 2 | 1 | 0 | 5 | 5 | 0 | 0 | 7 | 4 | 0 | 0 | 4 | 4 | 1 | 0 |
| | | | ( 22) | ( 5) | ( 3) | ( 0) | ( 12) | ( 12) | ( 0) | ( 0) | ( 18) | ( 11) | ( 0) | ( 0) | ( 13) | ( 13) | ( 3) | ( 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

| Organ | Findings | Grade | Control (37) | 500ppm (41) | 1500ppm (38) | 4500ppm (31) |
|---|---|---|---|---|---|---|
| | | | 1 (%) | 1 (%) | 1 (%) | 1 (%) |
| | | | 2 (%) | 2 (%) | 2 (%) | 2 (%) |
| | | | 3 (%) | 3 (%) | 3 (%) | 3 (%) |
| | | | 4 (%) | 4 (%) | 4 (%) | 4 (%) |
| [Respiratory system] | | | | | | |
| nasal cavit | | | <37> | <41> | <38> | <31> |
| | inflammation:respiratory epithelium | | 2 ( 5) | 3 ( 7) | 2 ( 5) | 1 ( 3) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:olfactory epithelium | | 1 ( 3) | 10 ( 24) | 6 ( 16) | 2 ( 6) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:gland | | 36 ( 97) | 39 ( 95) | 32 ( 84) | 29 ( 94) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| nasopharynx | | | <37> | <41> | <38> | <31> |
| | inflammation:foreign body | | 3 ( 8) | 0 ( 0) | 1 ( 3) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| larynx | | | <37> | <41> | <38> | <31> |
| | inflammation:foreign body | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lung | | | <37> | <41> | <38> | <31> |
| | inflammatory infiltration | | 0 ( 0) | 1 ( 2) | 1 ( 3) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | accumulation of foamy cells | | 1 ( 3) | 0 ( 0) | 1 ( 3) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 37 | | | | 41 | | | | 38 | | | | 31 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| lung | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | bronchopneumonia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | bronchiolar-alveolar cell hyperplasia | | 2 ( 5) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | angiectasis | | 3 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 19) | 3 ( 10) | 0 ( 0) | 0 ( 0) |
| | thrombus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 4 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 12) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 3 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | increased hematopoiesis | | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | decreased hematopoiesis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 37 | | | | 41 | | | | 38 | | | | 31 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | erythropoiesis:increased | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lymph node | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | lymphadenitis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spleen | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | deposit of hemosiderin | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | fibrosis | | 0 ( 0) | 3 ( 8) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 2 ( 6) | 0 ( 0) | 0 ( 0) |
| | extramedullary hematopoiesis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 2 ( 6) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | thrombus | | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | myocardial degeneration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | myocardial fibrosis | | 10 ( 27) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 14 ( 34) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 24) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 2 ( 6) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tongue | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | arteritis | | 3 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| stomach | | | <36> | | | | <41> | | | | <37> | | | | <31> | | | |
| | ulcer:forestomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | erosion:glandular stomach | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | herniation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 37 | | | | 41 | | | | 38 | | | | 31 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | necrosis:focal | | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | granulation | | 4 | 2 | 1 | 0 | 1 | 6 | 1 | 0 | 2 | 4 | 0 | 0 | 2 | 4 | 0 | 0 |
| | | | ( 11) | ( 5) | ( 3) | ( 0) | ( 2) | ( 15) | ( 2) | ( 0) | ( 5) | ( 11) | ( 0) | ( 0) | ( 6) | ( 13) | ( 0) | ( 0) |
| | clear cell focus | | 8 | 2 | 0 | 0 | 4 | 1 | 1 | 1 | 4 | 4 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 22) | ( 5) | ( 0) | ( 0) | ( 10) | ( 2) | ( 2) | ( 2) | ( 11) | ( 11) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| | acidophilic cell focus | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| | basophilic cell focus | | 6 | 2 | 0 | 0 | 5 | 0 | 1 | 0 | 4 | 1 | 0 | 0 | 5 | 2 | 0 | 0 |
| | | | ( 16) | ( 5) | ( 0) | ( 0) | ( 12) | ( 0) | ( 2) | ( 0) | ( 11) | ( 3) | ( 0) | ( 0) | ( 16) | ( 6) | ( 0) | ( 0) |
| | vacuolated cell focus | | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 3) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| | mixed cell focus | | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 0 |
| | | | ( 3) | ( 3) | ( 0) | ( 0) | ( 2) | ( 0) | ( 2) | ( 0) | ( 3) | ( 0) | ( 3) | ( 0) | ( 3) | ( 3) | ( 0) | ( 0) |
| | spongiosis hepatis | | 2 | 1 | 0 | 0 | 3 | 1 | 0 | 0 | 16 | 2 | 0 | 0 | 8 | 5 | 0 | 0 |
| | | | ( 5) | ( 3) | ( 0) | ( 0) | ( 7) | ( 2) | ( 0) | ( 0) | ( 42) | ( 5) | ( 0) | ( 0) | ( 26) | ( 16) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | bile duct hyperplasia | | 1 ( 3) | 35 ( 95) | 1 ( 3) | 0 ( 0) | 3 ( 7) | 37 ( 90) | 1 ( 2) | 0 ( 0) | 2 ( 5) | 33 ( 87) | 2 ( 5) | 0 ( 0) | 4 ( 13) | 24 ( 77) | 3 ( 10) | 0 ( 0) |
| pancreas | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | atrophy | | 6 ( 16) | 4 ( 11) | 1 ( 3) | 0 ( 0) | 6 ( 15) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 6 ( 16) | 3 ( 8) | 0 ( 0) | 0 ( 0) | 5 ( 16) | 3 ( 10) | 0 ( 0) | 0 ( 0) |
| | hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | infarct | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 0 ( 0) | 0 ( 0) |
| | hyaline droplet | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | deposit of hemosiderin | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | squamous cell metaplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | chronic nephropathy | | 6 ( 16) | 14 ( 38) | 12 ( 32) | 4 ( 11) | 5 ( 12) | 17 ( 41) | 14 ( 34) | 3 ( 7) | 3 ( 8) | 12 ( 32) | 18 ( 47) | 4 ( 11) | 10 ( 32) | 7 ( 23) | 8 ( 26) | 3 ( 10) |
| | hydronephrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) |
| | pyelitis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | papillary necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 2 ( 6) | 0 ( 0) |
| | mineralization:cortico-medullary junction | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 19) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | mineralization:papilla | | 9 ( 24) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 ( 26) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 12 ( 39) | 2 ( 6) | 1 ( 3) | 0 ( 0) |
| | mineralization:pelvis | | 6 ( 16) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 5 ( 12) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 6 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 26) | 4 ( 13) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | desquamation:pelvis | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 19) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | simple hyperplasia:transitional epithelium | | 4 ( 11) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 7 ( 17) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 4 ( 11) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 11 ( 35) | 4 ( 13) | 1 ( 3) | 0 ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 26) | 7 ( 23) | 1 ( 3) | 0 ( 0) |
| | calculus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 7 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| ureter | | | <35> | | | | <38> | | | | <35> | | | | <27> | | | |
| | dilatation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 33) | 4 ( 15) | 0 ( 0) | 0 ( 0) |
| | simple hyperplasia:transitional epithelium | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) |
| urin bladd | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | squamous cell metaplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 12 ( 39) | 2 ( 6) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| urin bladd | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | squamous cell hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 6 ( 19) | 1 ( 3) | 0 ( 0) |
| | inflammatory polyp | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 4 ( 13) | 0 ( 0) |
| | simple hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 19) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 16) | 15 ( 48) | 5 ( 16) | 0 ( 0) |
| | papillary hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 10) | 6 ( 19) | 1 ( 3) | 0 ( 0) |
| | basal cell hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 26) | 12 ( 39) | 4 ( 13) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | angiectasis | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 37 | | | | 41 | | | | 38 | | | | 31 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hyperplasia | | 8 ( 22) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 7 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 11) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hyperplasia:gland | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | Rathke pouch | | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| thyroid | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | ultimibranchial body remanet | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | C-cell hyperplasia | | 3 ( 8) | 3 ( 8) | 0 ( 0) | 0 ( 0) | 7 ( 17) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 3 ( 10) | 2 ( 6) | 0 ( 0) | 0 ( 0) |
| parathyroid | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | cyst | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hyperplasia:medulla | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 15) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | focal fatty change:cortex | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | arteritis | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 10) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | interstitial cell hyperplasia | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| prostate | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 1 ( 3) | 1 ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| prostate | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | hyperplasia | | 6 | 1 | 0 | 0 | 8 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 16) | ( 3) | ( 0) | ( 0) | ( 20) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| mammary gl | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | galactocele | | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| prep/cli gl | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | duct ectasia | | 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) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | cataract | | 1 | 0 | 1 | 0 | 1 | 1 | 2 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 2 | 0 |
| | | | ( 3) | ( 0) | ( 3) | ( 0) | ( 2) | ( 2) | ( 5) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 0) | ( 6) | ( 0) |
| | retinal atrophy | | 23 | 6 | 3 | 0 | 23 | 5 | 5 | 1 | 18 | 6 | 3 | 1 | 17 | 6 | 3 | 0 |
| | | | ( 62) | ( 16) | ( 8) | ( 0) | ( 56) | ( 12) | ( 12) | ( 2) | ( 47) | ( 16) | ( 8) | ( 3) | ( 55) | ( 19) | ( 10) | ( 0) |
| | keratitis | | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 2) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 37 | | | | 500ppm 41 | | | | 1500ppm 38 | | | | 4500ppm 31 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | degeneration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | lymphocytic infiltration | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| nasolacr d | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | inflammation | | 1 ( 3) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| bone | | | <37> | | | | <41> | | | | <38> | | | | <31> | | | |
| | osteosclerosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 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

# APPENDIX K 4

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

## RAT : FEMALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 44 | | | | 500ppm 38 | | | | 1500ppm 44 | | | | 4500ppm 37 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Integumentary system/appandage] | | | | | | | | | | | | | | | | | | |
| skin/app | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | epidermal cyst | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | thrombus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | mineralization | | 10 | 0 | 0 | 0 | 13 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 20 | 0 | 0 | 0 |
| | | | ( 23) | ( 0) | ( 0) | ( 0) | ( 34) | ( 0) | ( 0) | ( 0) | ( 20) | ( 0) | ( 0) | ( 0) | ( 54) | ( 0) | ( 0) | ( 0) |
| | goblet cell hyperplasia | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | eosinophilic change:olfactory epithelium | | 4 | 16 | 23 | 0 | 2 | 22 | 13 | 1 | 7 | 24 | 12 | 0 | 6 | 24 | 5 | 0 |
| | | | ( 9) | ( 36) | ( 52) | ( 0) | ( 5) | ( 58) | ( 34) | ( 3) | ( 16) | ( 55) | ( 27) | ( 0) | ( 16) | ( 65) | ( 14) | ( 0) |
| | eosinophilic change:respiratory epithelium | | 38 | 0 | 0 | 0 | 35 | 2 | 0 | 0 | 36 | 1 | 0 | 0 | 32 | 1 | 0 | 0 |
| | | | ( 86) | ( 0) | ( 0) | ( 0) | ( 92) | ( 5) | ( 0) | ( 0) | ( 82) | ( 2) | ( 0) | ( 0) | ( 86) | ( 3) | ( 0) | ( 0) |
| | inflammation:foreign body | | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 1 | 0 | 0 | 4 | 0 | 0 | 1 |
| | | | ( 9) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 11) | ( 2) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 3) |

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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | inflammation:respiratory epithelium | | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | ( 9) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 3) | ( 3) | ( 0) | ( 0) |
| | respiratory metaplasia:olfactory epithelium | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| | respiratory metaplasia:gland | | 37 | 0 | 0 | 0 | 35 | 2 | 0 | 0 | 37 | 0 | 0 | 0 | 33 | 0 | 0 | 0 |
| | | | ( 84) | ( 0) | ( 0) | ( 0) | ( 92) | ( 5) | ( 0) | ( 0) | ( 84) | ( 0) | ( 0) | ( 0) | ( 89) | ( 0) | ( 0) | ( 0) |
| nasopharynx | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | inflammation:foreign body | | 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) |
| larynx | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | inflammation:foreign body | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| lung | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | inflammatory infiltration | | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | accumulation of foamy cells | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 2) | ( 2) | ( 0) | ( 0) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| lung | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | bronchiolar-alveolar cell hyperplasia | | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | inflammation:foreign body | | 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) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | angiectasis | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | granulation | | 4 | 0 | 0 | 0 | 6 | 1 | 0 | 0 | 4 | 3 | 0 | 0 | 11 | 0 | 0 | 0 |
| | | | ( 9) | ( 0) | ( 0) | ( 0) | ( 16) | ( 3) | ( 0) | ( 0) | ( 9) | ( 7) | ( 0) | ( 0) | ( 30) | ( 0) | ( 0) | ( 0) |
| | increased hematopoiesis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) |
| | decreased hematopoiesis | | 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) | ( 0) | ( 0) | ( 0) | ( 0) |
| | erythropoiesis:increased | | 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) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | reticulosis | | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| spleen | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | deposit of hemosiderin | | 4 | 1 | 0 | 0 | 6 | 0 | 0 | 0 | 6 | 1 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | ( 9) | ( 2) | ( 0) | ( 0) | ( 16) | ( 0) | ( 0) | ( 0) | ( 14) | ( 2) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) |
| | fibrosis | | 0 | 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) | ( 0) | ( 0) | ( 0) |
| | extramedullary hematopoiesis | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 5) | ( 2) | ( 0) | ( 0) | ( 5) | ( 3) | ( 0) | ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | myocardial fibrosis | | 1 | 0 | 0 | 0 | 4 | 2 | 0 | 0 | 5 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 11) | ( 5) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tongue | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | arteritis | | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 7) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | ulcer:forestomach | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | erosion:glandular stomach | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| liver | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | herniation | | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 7) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | necrosis:focal | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| | granulation | | 20 | 11 | 1 | 0 | 17 | 5 | 0 | 0 | 20 | 6 | 1 | 0 | 18 | 6 | 4 | 0 |
| | | | ( 45) | ( 25) | ( 2) | ( 0) | ( 45) | ( 13) | ( 0) | ( 0) | ( 45) | ( 14) | ( 2) | ( 0) | ( 49) | ( 16) | ( 11) | ( 0) |
| | clear cell focus | | 3 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | | | ( 7) | ( 2) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 0) | ( 3) | ( 3) | ( 0) |
| | acidophilic cell focus | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | basophilic cell focus | | 14 | 1 | 0 | 0 | 16 | 2 | 0 | 0 | 19 | 1 | 0 | 0 | 15 | 2 | 0 | 0 |
| | | | ( 32) | ( 2) | ( 0) | ( 0) | ( 42) | ( 5) | ( 0) | ( 0) | ( 43) | ( 2) | ( 0) | ( 0) | ( 41) | ( 5) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | vacuolated cell focus | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | mixed cell focus | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | bile duct hyperplasia | | 5 | 2 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 11) | ( 5) | ( 0) | ( 0) | ( 13) | ( 0) | ( 0) | ( 0) | ( 11) | ( 2) | ( 2) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| pancreas | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | atrophy | | 5 | 3 | 0 | 0 | 3 | 4 | 0 | 0 | 3 | 1 | 0 | 0 | 3 | 1 | 0 | 0 |
| | | | ( 11) | ( 7) | ( 0) | ( 0) | ( 8) | ( 11) | ( 0) | ( 0) | ( 7) | ( 2) | ( 0) | ( 0) | ( 8) | ( 3) | ( 0) | ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | infarct | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 2 | 0 | 0 |
| | | | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 14) | ( 5) | ( 0) | ( 0) |
| | deposit of hemosiderin | | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 1 | 17 | 0 | 0 | 0 | 21 | 0 | 0 |
| | | | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 2) | ( 39) | ( 0) | ( 0) | ( 0) | ( 57) | ( 0) | ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | chronic nephropathy | | 12 | 15 | 5 | 0 | 25 | 7 | 1 | 0 | 19 | 6 | 3 | 1 | 10 | 9 | 2 | 2 |
| | | | ( 27) | ( 34) | ( 11) | ( 0) | ( 66) | ( 18) | ( 3) | ( 0) | ( 43) | ( 14) | ( 7) | ( 2) | ( 27) | ( 24) | ( 5) | ( 5) |
| | papillary necrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 8 | 5 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 22) | ( 14) | ( 0) |
| | mineralization:cortico-medullary junction | | 20 | 0 | 0 | 0 | 20 | 0 | 0 | 0 | 20 | 2 | 0 | 0 | 14 | 0 | 0 | 0 |
| | | | ( 45) | ( 0) | ( 0) | ( 0) | ( 53) | ( 0) | ( 0) | ( 0) | ( 45) | ( 5) | ( 0) | ( 0) | ( 38) | ( 0) | ( 0) | ( 0) |
| | mineralization:papilla | | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 10 | 1 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 27) | ( 3) | ( 0) | ( 0) |
| | mineralization:pelvis | | 11 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 15 | 1 | 0 | 0 | 22 | 2 | 0 | 0 |
| | | | ( 25) | ( 0) | ( 0) | ( 0) | ( 26) | ( 0) | ( 0) | ( 0) | ( 34) | ( 2) | ( 0) | ( 0) | ( 59) | ( 5) | ( 0) | ( 0) |
| | desquamation:pelvis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| | simple hyperplasia:transitional epithelium | | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 16 | 4 | 0 | 0 |
| | | | ( 7) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 23) | ( 0) | ( 0) | ( 0) | ( 43) | ( 11) | ( 0) | ( 0) |
| | nodular hyperplasia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 7 | 4 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 19) | ( 11) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | calculus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| | mineralization:inner stripe,outer medulla | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| ureter | | | <29> | | | | <30> | | | | <38> | | | | <31> | | | |
| | dilatation | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 2 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 13) | ( 6) | ( 0) | ( 0) |
| | simple hyperplasia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 6) | ( 0) | ( 0) | ( 0) |
| urin bladd | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | squamous cell metaplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) |
| | squamous cell hyperplasia | | 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) |
| | simple hyperplasia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 44 | | | | 500ppm 38 | | | | 1500ppm 44 | | | | 4500ppm 37 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| urin bladd | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | nodular hyperplasia:transitional epithelium | | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 2 ( 5) | 0 ( 0) | 0 ( 0) |
| | papillary hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 1 ( 3) | 0 ( 0) |
| | basal cell hyperplasia:transitional epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 2 ( 5) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | angiectasis | | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 7) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 3 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | cyst | | 6 ( 14) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 24) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 18) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 8) | 2 ( 5) | 0 ( 0) | 0 ( 0) |
| | hyperplasia | | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 18) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 14) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | Rathke pouch | | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 44 | | | | 500ppm 38 | | | | 1500ppm 44 | | | | 4500ppm 37 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| thyroid | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | ultimibranchial body remanet | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | C-cell hyperplasia | | 2 | 3 | 0 | 0 | 5 | 0 | 0 | 0 | 6 | 1 | 0 | 0 | 3 | 2 | 0 | 0 |
| | | | ( 5) | ( 7) | ( 0) | ( 0) | ( 13) | ( 0) | ( 0) | ( 0) | ( 14) | ( 2) | ( 0) | ( 0) | ( 8) | ( 5) | ( 0) | ( 0) |
| adrenal | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | peliosis-like lesion | | 9 | 0 | 0 | 0 | 14 | 1 | 0 | 0 | 13 | 1 | 0 | 0 | 16 | 1 | 1 | 0 |
| | | | ( 20) | ( 0) | ( 0) | ( 0) | ( 37) | ( 3) | ( 0) | ( 0) | ( 30) | ( 2) | ( 0) | ( 0) | ( 43) | ( 3) | ( 3) | ( 0) |
| | hyperplasia:cortical cell | | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | ( 9) | ( 0) | ( 0) | ( 0) | ( 13) | ( 0) | ( 0) | ( 0) | ( 14) | ( 0) | ( 0) | ( 0) | ( 5) | ( 3) | ( 0) | ( 0) |
| | hyperplasia:medulla | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 2) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| | focal fatty change:cortex | | 6 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 6 | 0 | 0 | 0 |
| | | | ( 14) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 16) | ( 0) | ( 0) | ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| ovary | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | granulation | | 0 | 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) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| uterus | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | cystic endometrial hyperplasia | | 10 | 4 | 2 | 0 | 13 | 1 | 2 | 0 | 11 | 2 | 1 | 0 | 12 | 5 | 0 | 0 |
| | | | ( 23) | ( 9) | ( 5) | ( 0) | ( 34) | ( 3) | ( 5) | ( 0) | ( 25) | ( 5) | ( 2) | ( 0) | ( 32) | ( 14) | ( 0) | ( 0) |
| mammary gl | | | <44> | | | | <37> | | | | <44> | | | | <37> | | | |
| | hyperplasia | | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 2) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | galactocele | | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 9) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | cataract | | 1 | 3 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 2) | ( 7) | ( 5) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 2) | ( 2) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) |
| | retinal atrophy | | 21 | 11 | 8 | 0 | 21 | 7 | 4 | 0 | 24 | 10 | 2 | 0 | 24 | 10 | 1 | 0 |
| | | | ( 48) | ( 25) | ( 18) | ( 0) | ( 55) | ( 18) | ( 11) | ( 0) | ( 55) | ( 23) | ( 5) | ( 0) | ( 65) | ( 27) | ( 3) | ( 0) |
| | keratitis | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 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

| Organ | Findings | Group Name | Control | | | | 500ppm | | | | 1500ppm | | | | 4500ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 44 | | | | 38 | | | | 44 | | | | 37 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | degeneration | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | lymphocytic infiltration | | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | ( 7) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) |
| nasolacr d | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | inflammation | | 4 | 2 | 0 | 0 | 0 | 1 | 2 | 0 | 7 | 1 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | ( 9) | ( 5) | ( 0) | ( 0) | ( 0) | ( 3) | ( 5) | ( 0) | ( 16) | ( 2) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| bone | | | <44> | | | | <38> | | | | <44> | | | | <37> | | | |
| | osteosclerosis | | 7 | 2 | 5 | 0 | 2 | 3 | 1 | 0 | 2 | 0 | 3 | 0 | 2 | 3 | 3 | 0 |
| | | | ( 16) | ( 5) | ( 11) | ( 0) | ( 5) | ( 8) | ( 3) | ( 0) | ( 5) | ( 0) | ( 7) | ( 0) | ( 5) | ( 8) | ( 8) | ( 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

# APPENDIX K 5

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

## MOSUE : MALE : DEAD AND MORIBUND ANIMALS

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 15 | | | | 9 | | | | 9 | | | | 11 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | mineralization | | 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) | ( 9) | ( 0) | ( 0) | ( 0) |
| | inflammation | | 0 | 0 | 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) |
| | eosinophilic change:olfactory epithelium | | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 13) | ( 0) | ( 0) | ( 0) | ( 22) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | eosinophilic change:respiratory epithelium | | 3 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 20) | ( 0) | ( 0) | ( 0) | ( 22) | ( 11) | ( 0) | ( 0) | ( 33) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) |
| | respiratory metaplasia:olfactory epithelium | | 3 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 2 | 0 | 0 |
| | | | ( 20) | ( 0) | ( 0) | ( 0) | ( 22) | ( 11) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 36) | ( 18) | ( 0) | ( 0) |
| | respiratory metaplasia:gland | | 3 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 6 | 2 | 0 | 0 |
| | | | ( 20) | ( 7) | ( 0) | ( 0) | ( 11) | ( 11) | ( 0) | ( 0) | ( 33) | ( 0) | ( 0) | ( 0) | ( 55) | ( 18) | ( 0) | ( 0) |
| | atrophy:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 7 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 33) | ( 11) | ( 0) | ( 0) | ( 64) | ( 9) | ( 0) | ( 0) |
| | necrosis:olfactory epithelium | | 0 | 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) |

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

| Organ | Findings | Grade | Control 15 | | | | 667ppm 9 | | | | 2000ppm 9 | | | | 6000ppm 11 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasopharynx | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | eosinophilic change:respiratory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lung | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | congestion | | 0 ( 0) | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammatory infiltration | | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 18) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | increased hematopoiesis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | megakaryocyte:increased | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 0 ( 0) | 0 ( 0) |
| | granulopoiesis:increased | | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 15 | | | | 667ppm 9 | | | | 2000ppm 9 | | | | 6000ppm 11 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | deposit of melanin | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) |
| | extramedullary hematopoiesis | | 1 | 3 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 3 | 0 | 0 |
| | | | ( 7) | ( 20) | ( 0) | ( 0) | ( 11) | ( 11) | ( 0) | ( 0) | ( 0) | ( 22) | ( 0) | ( 0) | ( 9) | ( 27) | ( 0) | ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | thrombus | | 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) | ( 9) | ( 0) | ( 0) |
| | mineralization | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | arteritis | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | cyst | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 15 | | | | 9 | | | | 9 | | | | 11 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | dysplasia | | 5 | 1 | 0 | 1 | 2 | 1 | 1 | 0 | 4 | 0 | 0 | 0 | 4 | 2 | 0 | 0 |
| | | | ( 33) | ( 7) | ( 0) | ( 7) | ( 22) | ( 11) | ( 11) | ( 0) | ( 44) | ( 0) | ( 0) | ( 0) | ( 36) | ( 18) | ( 0) | ( 0) |
| tongue | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | mineralization | | 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) | ( 9) | ( 0) | ( 0) | ( 0) |
| | arteritis | | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 13) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| salivary gl | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | arteritis | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| stomach | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | mineralization | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 13) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | ulcer:forestomach | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 7) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | hyperplasia:forestomach | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 15 | | | | 9 | | | | 9 | | | | 11 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | angiectasis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | necrosis:central | | 0 ( 0) | 2 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 0 ( 0) |
| | necrosis:focal | | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | degeneration:central | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mixed cell focus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| pancreas | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 15 | | | | 667ppm 9 | | | | 2000ppm 9 | | | | 6000ppm 11 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | necrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | hyaline droplet | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 7) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) |
| | basophilic change | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 7) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 22) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) |
| | hydronephrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | pyelonephritis | | 0 | 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) | ( 9) | ( 0) |
| | mineralization:papilla | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | mineralization:pelvis | | 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) | ( 9) | ( 0) | ( 0) | ( 0) |
| | mineralization:cortex | | 8 | 3 | 0 | 0 | 5 | 2 | 0 | 0 | 5 | 3 | 0 | 0 | 5 | 2 | 0 | 0 |
| | | | ( 53) | ( 20) | ( 0) | ( 0) | ( 56) | ( 22) | ( 0) | ( 0) | ( 56) | ( 33) | ( 0) | ( 0) | ( 45) | ( 18) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 15 | | | | 9 | | | | 9 | | | | 11 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 18) | 1 ( 9) | 0 ( 0) | 0 ( 0) |
| | mineralization:inner stripe,outer medulla | | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 44) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 27) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| urin bladd | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | simple hyperplasia:transitional epithelium | | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <15> | | | | < 9> | | | | < 9> | | | | <10> | | | |
| | Rathke pouch | | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| adrenal | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 9) | 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 15 | | | | 9 | | | | 9 | | | | 11 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | necrosis | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | mineralization | | 9 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 60) | ( 0) | ( 0) | ( 0) | ( 44) | ( 11) | ( 0) | ( 0) | ( 78) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| epididymis | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | spermatogenic granuloma | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| semin ves | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | hemorrhage | | 0 | 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) |
| prostate | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | 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) | ( 9) | ( 0) | ( 0) |
| prep/cli gl | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | duct cell | | 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) | ( 9) | ( 0) | ( 0) |
| | inflammation | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 9) | ( 9) | ( 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

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 15 | | | | 667ppm 9 | | | | 2000ppm 9 | | | | 6000ppm 11 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| brain | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | mineralization | | 5 ( 33) | 4 ( 27) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 6 ( 67) | 0 ( 0) | 0 ( 0) | 5 ( 56) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 3 ( 27) | 5 ( 45) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| nasolacr d | | | <15> | | | | < 9> | | | | < 9> | | | | <11> | | | |
| | inflammation | | 1 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 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

# APPENDIX K 6

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

## MOSUE : FEMALE : DEAD AND MORIBUND ANIMALS

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 19 | | | | 667ppm 28 | | | | 2000ppm 25 | | | | 6000ppm 17 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | thrombus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | catarrh | | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | basal cell hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:olfactory epithelium | | 5 ( 26) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 21) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:respiratory epithelium | | 11 ( 58) | 1 ( 5) | 1 ( 5) | 0 ( 0) | 15 ( 54) | 3 ( 11) | 1 ( 4) | 0 ( 0) | 9 ( 36) | 2 ( 8) | 2 ( 8) | 0 ( 0) | 4 ( 24) | 1 ( 6) | 0 ( 0) | 0 ( 0) |
| | inflammation:foreign body | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammation:respiratory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 19 | | | | 667ppm 28 | | | | 2000ppm 25 | | | | 6000ppm 17 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | respiratory metaplasia:olfactory epithelium | | 3 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 12) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:gland | | 5 ( 26) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 24) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | atrophy:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 36) | 2 ( 8) | 0 ( 0) | 0 ( 0) | 8 ( 47) | 3 ( 18) | 1 ( 6) | 0 ( 0) |
| nasopharynx | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | eosinophilic change:respiratory epithelium | | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 7) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 2 ( 12) | 1 ( 6) | 0 ( 0) | 0 ( 0) |
| lung | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | hemorrhage | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammatory infiltration | | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | congestion | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 8) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 19 | | | | 28 | | | | 25 | | | | 17 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | increased hematopoiesis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulopoiesis:increased | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lymph node | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | lymphadenitis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spleen | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | deposit of hemosiderin | | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | extramedullary hematopoiesis | | 1 ( 5) | 4 ( 21) | 0 ( 0) | 0 ( 0) | 8 ( 29) | 4 ( 14) | 0 ( 0) | 0 ( 0) | 4 ( 16) | 5 ( 20) | 0 ( 0) | 0 ( 0) | 4 ( 24) | 2 ( 12) | 0 ( 0) | 0 ( 0) |
| | engorgement of erythrocyte | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | follicular hyperplasia | | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 19 | | | | 28 | | | | 25 | | | | 17 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | mineralization | | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 6) | ( 6) | ( 0) | ( 0) |
| | arteritis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 6) | ( 0) | ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | inflammation | | 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) | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | dysplasia | | 1 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 3 | 1 | 1 | 0 | 1 | 0 | 1 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 7) | ( 4) | ( 0) | ( 0) | ( 12) | ( 4) | ( 4) | ( 0) | ( 6) | ( 0) | ( 6) | ( 0) |
| | inflammation:foreign body | | 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) | ( 6) | ( 0) | ( 0) |
| tongue | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | arteritis | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 6) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 19 | | | | 667ppm 28 | | | | 2000ppm 25 | | | | 6000ppm 17 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | mineralization | | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 14) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 6) | ( 0) | ( 0) | ( 0) |
| | hyperplasia:glandular stomach | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 12) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| large intes | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | necrosis | | 0 | 0 | 0 | 0 | 0 | 1 | 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) |
| liver | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | angiectasis | | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 5) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | necrosis:central | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | necrosis:focal | | 0 | 1 | 0 | 0 | 1 | 3 | 0 | 0 | 1 | 3 | 1 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 5) | ( 0) | ( 0) | ( 4) | ( 11) | ( 0) | ( 0) | ( 4) | ( 12) | ( 4) | ( 0) | ( 12) | ( 0) | ( 0) | ( 0) |
| | fatty change | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 5) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 19 | | | | 28 | | | | 25 | | | | 17 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | inflammatory infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | clear cell focus | | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | acidophilic cell focus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | basophilic cell focus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 12) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | hyaline droplet | | 4 ( 21) | 2 ( 11) | 0 ( 0) | 0 ( 0) | 5 ( 18) | 3 ( 11) | 0 ( 0) | 0 ( 0) | 9 ( 36) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 47) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 1 ( 6) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 19 | | | | 667ppm 28 | | | | 2000ppm 25 | | | | 6000ppm 17 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | deposit of amyloid | | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammatory infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammatory polyp | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hydronephrosis | | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 1 ( 4) | 3 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | tubular necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:papilla | | 2 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 14) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortex | | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 12) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 24) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 19 | | | | 28 | | | | 25 | | | | 17 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | mineralization:inner stripe,outer medulla | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 7) | ( 0) | ( 0) | ( 0) | ( 12) | ( 0) | ( 0) | ( 0) | ( 24) | ( 0) | ( 0) | ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <19> | | | | <27> | | | | <25> | | | | <17> | | | |
| | cyst | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 6) | ( 0) | ( 0) | ( 0) |
| | hyperplasia | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| adrenal | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | hyperplasia:cortical cell | | 0 | 0 | 0 | 0 | 1 | 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) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| ovary | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | cyst | | 0 | 0 | 0 | 0 | 1 | 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) |

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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 19 | | | | 28 | | | | 25 | | | | 17 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| ovary | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | lymphocytic infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| uterus | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | cystic endometrial hyperplasia | | 4 ( 21) | 3 ( 16) | 0 ( 0) | 0 ( 0) | 5 ( 18) | 3 ( 11) | 0 ( 0) | 0 ( 0) | 3 ( 12) | 3 ( 12) | 0 ( 0) | 0 ( 0) | 2 ( 12) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| brain | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | mineralization | | 1 ( 5) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 9 ( 32) | 5 ( 18) | 0 ( 0) | 0 ( 0) | 4 ( 16) | 5 ( 20) | 0 ( 0) | 0 ( 0) | 3 ( 18) | 3 ( 18) | 0 ( 0) | 0 ( 0) |
| spinal cord | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 6) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | degeneration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 19 | | | | 28 | | | | 25 | | | | 17 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | inflammation | | 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) |
| nasolacr d | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | inflammation | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | mineralization | | 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) |
| [Body cavities] | | | | | | | | | | | | | | | | | | |
| adipose | | | <19> | | | | <28> | | | | <25> | | | | <17> | | | |
| | granulation | | 0 | 0 | 0 | 0 | 0 | 1 | 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) |

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

# APPENDIX K 7

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

## MOSUE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 35 | | | | 667ppm 41 | | | | 2000ppm 41 | | | | 6000ppm 39 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | mineralization | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | catarrh | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | epidermal cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:olfactory epithelium | | 10 ( 29) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 22) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 12) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:respiratory epithelium | | 16 ( 46) | 8 ( 23) | 0 ( 0) | 0 ( 0) | 13 ( 32) | 2 ( 5) | 1 ( 2) | 0 ( 0) | 13 ( 32) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | inflammation:foreign body | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:olfactory epithelium | | 9 ( 26) | 6 ( 17) | 0 ( 0) | 0 ( 0) | 13 ( 32) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 11 ( 27) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 16 ( 41) | 5 ( 13) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:gland | | 13 ( 37) | 6 ( 17) | 0 ( 0) | 0 ( 0) | 13 ( 32) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 17 ( 41) | 3 ( 7) | 0 ( 0) | 0 ( 0) | 28 ( 72) | 4 ( 10) | 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 35 | | | | 41 | | | | 41 | | | | 39 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | desquamation:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) |
| | atrophy:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 29 | 5 | 0 | 0 | 16 | 21 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 71) | ( 12) | ( 0) | ( 0) | ( 41) | ( 54) | ( 0) | ( 0) |
| | necrosis:olfactory epithelium | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| nasopharynx | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | eosinophilic change:respiratory epithelium | | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 14) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| lung | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | inflammatory 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) | ( 3) | ( 0) | ( 0) | ( 0) |
| | lymphocytic infiltration | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| | bronchiolar-alveolar cell hyperplasia | | 0 | 0 | 0 | 0 | 3 | 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) |

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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 35 | 667ppm 41 | 2000ppm 41 | 6000ppm 39 |
|---|---|---|---|---|---|---|
| | | | 1 (%) | 1 (%) | 1 (%) | 1 (%) |
| | | | 2 (%) | 2 (%) | 2 (%) | 2 (%) |
| | | | 3 (%) | 3 (%) | 3 (%) | 3 (%) |
| | | | 4 (%) | 4 (%) | 4 (%) | 4 (%) |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <35> | <41> | <41> | <39> |
| | granulation | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | increased hematopoiesis | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulopoiesis:increased | | 0 ( 0) | 1 ( 2) | 0 ( 0) | 2 ( 5) |
| | | | 0 ( 0) | 0 ( 0) | 3 ( 7) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lymph node | | | <35> | <41> | <41> | <39> |
| | xanthogranuloma | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spleen | | | <35> | <40> | <41> | <39> |
| | deposit of melanin | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 1 ( 3) |
| | | | 1 ( 3) | 1 ( 3) | 1 ( 2) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | extramedullary hematopoiesis | | 1 ( 3) | 1 ( 3) | 1 ( 2) | 0 ( 0) |
| | | | 1 ( 3) | 2 ( 5) | 1 ( 2) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | follicular hyperplasia | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 1 ( 3) | 3 ( 8) | 3 ( 7) | 2 ( 5) |
| | | | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 35 | | | | 667ppm 41 | | | | 2000ppm 41 | | | | 6000ppm 39 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | arteritis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | aplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | dysplasia | | 21 ( 60) | 2 ( 6) | 1 ( 3) | 0 ( 0) | 25 ( 61) | 1 ( 2) | 2 ( 5) | 0 ( 0) | 32 ( 78) | 3 ( 7) | 0 ( 0) | 0 ( 0) | 25 ( 64) | 0 ( 0) | 2 ( 5) | 0 ( 0) |
| tongue | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | arteritis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| stomach | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | mineralization | | 3 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 8) | 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 35 | | | | 41 | | | | 41 | | | | 39 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | ulcer:forestomach | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | hyperplasia:glandular stomach | | 6 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | ( 17) | ( 0) | ( 0) | ( 0) | ( 12) | ( 0) | ( 0) | ( 0) | ( 12) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| liver | | | <35> | | | | <40> | | | | <41> | | | | <39> | | | |
| | necrosis:focal | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | granulation | | 12 | 6 | 0 | 0 | 13 | 9 | 0 | 0 | 8 | 8 | 0 | 0 | 8 | 5 | 0 | 0 |
| | | | ( 34) | ( 17) | ( 0) | ( 0) | ( 33) | ( 23) | ( 0) | ( 0) | ( 20) | ( 20) | ( 0) | ( 0) | ( 21) | ( 13) | ( 0) | ( 0) |
| | clear cell focus | | 0 | 1 | 0 | 0 | 2 | 4 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 3) | ( 0) | ( 0) | ( 5) | ( 10) | ( 0) | ( 0) | ( 2) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | acidophilic cell focus | | 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) |
| | basophilic cell focus | | 0 | 0 | 0 | 0 | 3 | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 5) | ( 3) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
| | vacuolated cell focus | | 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) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 35 | | | | 667ppm 41 | | | | 2000ppm 41 | | | | 6000ppm 39 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <35> | | | | <40> | | | | <41> | | | | <39> | | | |
| | mixed cell focus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | spongiosis hepatis | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | biliary cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| pancreas | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | infarct | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 10) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 35 | | | | 667ppm 41 | | | | 2000ppm 41 | | | | 6000ppm 39 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | basophilic change | | 17 ( 49) | 5 ( 14) | 0 ( 0) | 0 ( 0) | 19 ( 46) | 10 ( 24) | 0 ( 0) | 0 ( 0) | 20 ( 49) | 11 ( 27) | 0 ( 0) | 0 ( 0) | 21 ( 54) | 5 ( 13) | 0 ( 0) | 0 ( 0) |
| | inflammatory polyp | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | vacuolization of proximal tubule | | 3 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hydronephrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | pyelonephritis | | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortico-medullary junction | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:papilla | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:pelvis | | 6 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 7) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 12) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 35 | | | | 41 | | | | 41 | | | | 39 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | mineralization:cortex | | 14 ( 40) | 19 ( 54) | 0 ( 0) | 0 ( 0) | 17 ( 41) | 21 ( 51) | 0 ( 0) | 0 ( 0) | 12 ( 29) | 28 ( 68) | 0 ( 0) | 0 ( 0) | 21 ( 54) | 14 ( 36) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 15) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | mineralization:inner stripe,outer medulla | | 8 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 7 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 ( 24) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 11 ( 28) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <34> | | | | <41> | | | | <41> | | | | <39> | | | |
| | cyst | | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | Rathke pouch | | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| adrenal | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | hyperplasia:cortical cell | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 7) | 1 ( 2) | 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 35 | | | | 667ppm 41 | | | | 2000ppm 41 | | | | 6000ppm 39 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | atrophy | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization | | 32 ( 91) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 34 ( 83) | 3 ( 7) | 0 ( 0) | 0 ( 0) | 38 ( 93) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 9 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| epididymis | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | spermatogenic granuloma | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| prep/cli gl | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | duct cell | | 2 ( 6) | 6 ( 17) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 14 ( 34) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 ( 24) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 7 ( 18) | 0 ( 0) | 0 ( 0) |
| | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 2) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| brain | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | mineralization | | 9 ( 26) | 14 ( 40) | 0 ( 0) | 0 ( 0) | 8 ( 20) | 21 ( 51) | 0 ( 0) | 0 ( 0) | 9 ( 22) | 17 ( 41) | 0 ( 0) | 0 ( 0) | 7 ( 18) | 23 ( 59) | 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 35 | | | | 41 | | | | 41 | | | | 39 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | | | <35> | | | | <41> | | | | <39> | | | | <39> | | | |
| | hyperplasia | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| nasolacr d | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | inflammation | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 2) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Body cavities] | | | | | | | | | | | | | | | | | | |
| adipose | | | <35> | | | | <41> | | | | <41> | | | | <39> | | | |
| | granulation | | 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) | ( 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

# APPENDIX K 8

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

## MOSUE : FEMALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 31 | | | | 22 | | | | 25 | | | | 32 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | catarrh | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 2 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 16) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:olfactory epithelium | | 11 ( 35) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 14) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 19) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:respiratory epithelium | | 18 ( 58) | 7 ( 23) | 0 ( 0) | 1 ( 3) | 11 ( 50) | 2 ( 9) | 0 ( 0) | 0 ( 0) | 13 ( 52) | 2 ( 8) | 0 ( 0) | 0 ( 0) | 21 ( 66) | 2 ( 6) | 0 ( 0) | 0 ( 0) |
| | inflammation:respiratory epithelium | | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:olfactory epithelium | | 3 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 24) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 25) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:gland | | 10 ( 32) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 24) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 6 ( 19) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | desquamation:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulopoiesis:increased | | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 31 | | | | 667ppm 22 | | | | 2000ppm 25 | | | | 6000ppm 32 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | atrophy:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 16 ( 64) | 3 ( 12) | 0 ( 0) | 0 ( 0) | 15 ( 47) | 16 ( 50) | 0 ( 0) | 0 ( 0) |
| | necrosis:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| nasopharynx | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | eosinophilic change:respiratory epithelium | | 1 ( 3) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| lung | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | lymphocytic infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | bronchiolar-alveolar cell hyperplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | increased hematopoiesis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 31 | | | | 22 | | | | 25 | | | | 32 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | myelofibrosis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | granulopoiesis:increased | | 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) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| spleen | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | deposit of melanin | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 6) | ( 0) | ( 0) | ( 0) |
| | extramedullary hematopoiesis | | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 5 | 2 | 0 | 0 |
| | | | ( 10) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) | ( 4) | ( 4) | ( 0) | ( 0) | ( 16) | ( 6) | ( 0) | ( 0) |
| | follicular hyperplasia | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 20) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | arteritis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 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
b b : Number of animals with lesion
( c ) c : b / a * 100

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 31 1 (%) | Control 31 2 (%) | Control 31 3 (%) | Control 31 4 (%) | 667ppm 22 1 (%) | 667ppm 22 2 (%) | 667ppm 22 3 (%) | 667ppm 22 4 (%) | 2000ppm 25 1 (%) | 2000ppm 25 2 (%) | 2000ppm 25 3 (%) | 2000ppm 25 4 (%) | 6000ppm 32 1 (%) | 6000ppm 32 2 (%) | 6000ppm 32 3 (%) | 6000ppm 32 4 (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) |
| | dysplasia | | 7 ( 23) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 27) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 5 ( 20) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 4 ( 13) | 4 ( 13) | 1 ( 3) | 0 ( 0) |
| | inflammation:foreign body | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| tongue | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | arteritis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| salivary gl | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | lymphocytic infiltration | | 4 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 18) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 8) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| stomach | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | mineralization | | 9 ( 29) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 14) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 24) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 19) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 31 | | | | 22 | | | | 25 | | | | 32 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | hyperplasia:glandular stomach | | 8 ( 26) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 4 ( 18) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 4 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | angiectasis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 2 ( 9) | 0 ( 0) | 0 ( 0) | 3 ( 12) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | granulation | | 7 ( 23) | 15 ( 48) | 3 ( 10) | 0 ( 0) | 3 ( 14) | 9 ( 41) | 1 ( 5) | 0 ( 0) | 11 ( 44) | 7 ( 28) | 1 ( 4) | 0 ( 0) | 7 ( 22) | 10 ( 31) | 0 ( 0) | 0 ( 0) |
| | clear cell focus | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 12) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 1 ( 3) | 0 ( 0) | 0 ( 0) |
| | basophilic cell focus | | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 20) | 3 ( 12) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 1 ( 3) | 1 ( 3) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | hyaline droplet | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 4) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 6) | 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 31 | | | | 22 | | | | 25 | | | | 32 | | | |
| | | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | basophilic change | | 5 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 5) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 7 ( 22) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | lymphocytic infiltration | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 9) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hydronephrosis | | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortico-medullary junction | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:papilla | | 6 ( 19) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 14) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 32) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 3) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortex | | 5 ( 16) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 14) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 32) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 28) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 4 ( 13) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 11 ( 34) | 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

| Organ | Findings | Group Name | Control | | | | 667ppm | | | | 2000ppm | | | | 6000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 31 | | | | 22 | | | | 25 | | | | 32 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | mineralization:inner stripe,outer medulla | | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 22 | 0 | 0 | 0 |
| | | | ( 10) | ( 0) | ( 0) | ( 0) | ( 14) | ( 0) | ( 0) | ( 0) | ( 36) | ( 0) | ( 0) | ( 0) | ( 69) | ( 0) | ( 0) | ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | cyst | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 6 | 2 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 8) | ( 0) | ( 0) | ( 0) | ( 19) | ( 6) | ( 0) | ( 0) |
| | hyperplasia | | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 |
| | | | ( 13) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 16) | ( 0) | ( 0) | ( 0) |
| | Rathke pouch | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| adrenal | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | fatty change | | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | hyperplasia:cortical cell | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 3) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 4) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 31 | | | | 667ppm 22 | | | | 2000ppm 25 | | | | 6000ppm 32 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | hyperplasia:medulla | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | | | 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) | ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| ovary | thrombus | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | | | 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) |
| | cyst | | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 3) | ( 3) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
| uterus | cystic endometrial hyperplasia | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | | | 9 | 16 | 1 | 0 | 6 | 10 | 0 | 0 | 6 | 12 | 1 | 0 | 10 | 5 | 1 | 0 |
| | | | ( 29) | ( 52) | ( 3) | ( 0) | ( 27) | ( 45) | ( 0) | ( 0) | ( 24) | ( 48) | ( 4) | ( 0) | ( 31) | ( 16) | ( 3) | ( 0) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| brain | mineralization | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | | | 12 | 8 | 0 | 0 | 4 | 9 | 0 | 0 | 7 | 9 | 0 | 0 | 2 | 7 | 0 | 0 |
| | | | ( 39) | ( 26) | ( 0) | ( 0) | ( 18) | ( 41) | ( 0) | ( 0) | ( 28) | ( 36) | ( 0) | ( 0) | ( 6) | ( 22) | ( 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

| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 31 | | | | 667ppm 22 | | | | 2000ppm 25 | | | | 6000ppm 32 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | cataract | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| Harder gl | | | <31> | | | | <22> | | | | <25> | | | | <32> | | | |
| | degeneration | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 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
b b : Number of animals with lesion
( c ) c : b / a * 100

APPENDIX L 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

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE



| Time-related Weeks | Items / Groupe Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|
| 0-52 | NO. OF EXAMINED ANIMALS | 0 | 1 | 1 | 1 |
| | NO. OF ANIMALS WITH TUMORS | 0 | 1 | 1 | 0 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 0 | 1 | 1 | 0 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 0 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | 0 | 1 | 1 | 0 |
| | NO. OF TOTAL TUMORS | 0 | 1 | 1 | 0 |
| 53-78 | NO. OF EXAMINED ANIMALS | 2 | 2 | 1 | 5 |
| | NO. OF ANIMALS WITH TUMORS | 2 | 2 | 1 | 5 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 1 | 1 | 0 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 1 | 1 | 1 | 4 |
| | NO. OF BENIGN TUMORS | 2 | 1 | 1 | 4 |
| | NO. OF MALIGNANT TUMORS | 1 | 2 | 1 | 5 |
| | NO. OF TOTAL TUMORS | 3 | 3 | 2 | 9 |
| 79-105 | NO. OF EXAMINED ANIMALS | 11 | 6 | 10 | 13 |
| | NO. OF ANIMALS WITH TUMORS | 11 | 6 | 10 | 13 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 2 | 0 | 1 | 2 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 9 | 6 | 9 | 11 |
| | NO. OF BENIGN TUMORS | 22 | 11 | 15 | 18 |
| | NO. OF MALIGNANT TUMORS | 7 | 5 | 7 | 14 |
| | NO. OF TOTAL TUMORS | 29 | 16 | 22 | 32 |
| AT SACRIFICED | NO. OF EXAMINED ANIMALS | 37 | 41 | 38 | 31 |
| | NO. OF ANIMALS WITH TUMORS | 37 | 41 | 37 | 31 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 10 | 14 | 12 | 4 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 27 | 27 | 25 | 27 |
| | NO. OF BENIGN TUMORS | 70 | 66 | 80 | 63 |
| | NO. OF MALIGNANT TUMORS | 8 | 16 | 15 | 28 |
| | NO. OF TOTAL TUMORS | 78 | 82 | 95 | 91 |

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

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE



| Time-related Weeks | Items | Groupe Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| TOTAL | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 50 | 50 | 49 | 49 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 13 | 16 | 14 | 7 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 37 | 34 | 35 | 42 |
| | NO. OF BENIGN TUMORS | | 94 | 78 | 82 | 85 |
| | NO. OF MALIGNANT TUMORS | | 16 | 24 | 22 | 47 |
| | NO. OF TOTAL TUMORS | | 110 | 102 | 104 | 132 |

APPENDIX L 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

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE



| Time-related Weeks | Items | Groupe Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| 0-52 | NO. OF EXAMINED ANIMALS | | 0 | 0 | 0 | 3 |
| | 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 TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF TOTAL TUMORS | | 0 | 0 | 0 | 0 |
| 53-78 | NO. OF EXAMINED ANIMALS | | 2 | 3 | 2 | 1 |
| | NO. OF ANIMALS WITH TUMORS | | 2 | 3 | 2 | 1 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 3 | 2 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 1 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 2 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 1 | 3 | 2 | 1 |
| | NO. OF TOTAL TUMORS | | 3 | 3 | 2 | 1 |
| 79-104 | NO. OF EXAMINED ANIMALS | | 4 | 9 | 4 | 9 |
| | NO. OF ANIMALS WITH TUMORS | | 4 | 8 | 4 | 58 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 2 | 3 | 3 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 4 | 6 | 1 | 5 |
| | NO. OF BENIGN TUMORS | | 4 | 9 | 2 | 6 |
| | NO. OF MALIGNANT TUMORS | | 4 | 6 | 4 | 11 |
| | NO. OF TOTAL TUMORS | | 8 | 15 | 6 | |
| AT SACRIFICED | NO. OF EXAMINED ANIMALS | | 44 | 38 | 44 | 37 |
| | NO. OF ANIMALS WITH TUMORS | | 36 | 30 | 34 | 25 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 22 | 16 | 18 | 12 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 14 | 14 | 16 | 13 |
| | NO. OF BENIGN TUMORS | | 41 | 34 | 42 | 33 |
| | NO. OF MALIGNANT TUMORS | | 14 | 14 | 12 | 8 |
| | NO. OF TOTAL TUMORS | | 55 | 48 | 54 | 41 |

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

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE



| Time-related Weeks | Items | Groupe Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| TOTAL | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 50 | 50 | 49 | 49 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 13 | 16 | 14 | 7 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 37 | 34 | 35 | 42 |
| | NO. OF BENIGN TUMORS | | 94 | 78 | 82 | 85 |
| | NO. OF MALIGNANT TUMORS | | 16 | 24 | 22 | 47 |
| | NO. OF TOTAL TUMORS | | 110 | 102 | 104 | 132 |

APPENDIX L 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. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE



| Time-related Weeks | Items / Groupe Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|
| 0-52 | NO. OF EXAMINED ANIMALS | 1 | 0 | 1 | 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 TUMORS | 0 | 0 | 0 | 0 |
| | NO. OF TOTAL TUMORS | 0 | 0 | 0 | 0 |
| 53-78 | NO. OF EXAMINED ANIMALS | 3 | 2 | 2 | 4 |
| | NO. OF ANIMALS WITH TUMORS | 2 | 1 | 2 | 2 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 2 | 1 | 2 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 0 | 0 | 0 | 1 |
| | NO. OF BENIGN TUMORS | 1 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | 1 | 1 | 2 | 3 |
| | NO. OF TOTAL TUMORS | 2 | 1 | 2 | 3 |
| 79-105 | NO. OF EXAMINED ANIMALS | 11 | 7 | 6 | 7 |
| | NO. OF ANIMALS WITH TUMORS | 9 | 5 | 6 | 8 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 5 | 2 | 2 | 5 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 4 | 3 | 4 | 1 |
| | NO. OF BENIGN TUMORS | 2 | 2 | 2 | 0 |
| | NO. OF MALIGNANT TUMORS | 14 | 7 | 8 | 8 |
| | NO. OF TOTAL TUMORS | 16 | 9 | 10 | 8 |
| AT SACRIFICED | NO. OF EXAMINED ANIMALS | 35 | 41 | 41 | 39 |
| | NO. OF ANIMALS WITH TUMORS | 18 | 32 | 26 | 18 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 12 | 22 | 21 | 12 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 6 | 10 | 5 | 6 |
| | NO. OF BENIGN TUMORS | 10 | 20 | 14 | 11 |
| | NO. OF MALIGNANT TUMORS | 14 | 24 | 23 | 14 |
| | NO. OF TOTAL TUMORS | 24 | 44 | 37 | 25 |

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

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE



| Time-related Weeks | Items | Groupe Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| TOTAL | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 29 | 38 | 34 | 26 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 19 | 25 | 25 | 18 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 10 | 13 | 9 | 8 |
| | NO. OF BENIGN TUMORS | | 13 | 22 | 16 | 11 |
| | NO. OF MALIGNANT TUMORS | | 29 | 32 | 33 | 25 |
| | NO. OF TOTAL TUMORS | | 42 | 54 | 49 | 36 |

APPENDIX L4

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

MOUSE: FEMALE

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

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE



| Time-related Weeks | Items | Groupe Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| 0-52 | NO. OF EXAMINED ANIMALS | | 2 | 0 | 1 | 1 |
| | NO. OF ANIMALS WITH TUMORS | | 1 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 1 | 0 | 0 | 0 |
| | NO. OF TOTAL TUMORS | | 1 | 0 | 0 | 0 |
| 53-78 | NO. OF EXAMINED ANIMALS | | 1 | 5 | 5 | 2 |
| | NO. OF ANIMALS WITH TUMORS | | 1 | 2 | 5 | 2 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 2 | 4 | 2 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 1 | 0 |
| | NO. OF BENIGN TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 1 | 2 | 6 | 2 |
| | NO. OF TOTAL TUMORS | | 1 | 2 | 6 | 2 |
| 79-104 | NO. OF EXAMINED ANIMALS | | 16 | 23 | 19 | 14 |
| | NO. OF ANIMALS WITH TUMORS | | 16 | 21 | 17 | 14 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 11 | 16 | 12 | 11 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 5 | 5 | 5 | 3 |
| | NO. OF BENIGN TUMORS | | 1 | 3 | 2 | 4 |
| | NO. OF MALIGNANT TUMORS | | 20 | 27 | 20 | 14 |
| | NO. OF TOTAL TUMORS | | 21 | 30 | 22 | 18 |
| AT SACRIFICED | NO. OF EXAMINED ANIMALS | | 31 | 22 | 25 | 32 |
| | NO. OF ANIMALS WITH TUMORS | | 24 | 16 | 21 | 27 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 17 | 7 | 9 | 16 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 7 | 9 | 12 | 11 |
| | NO. OF BENIGN TUMORS | | 16 | 15 | 24 | 17 |
| | NO. OF MALIGNANT TUMORS | | 18 | 15 | 15 | 23 |
| | NO. OF TOTAL TUMORS | | 34 | 30 | 39 | 40 |

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

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE



| Time-related Weeks | Items / Groupe Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|
| TOTAL | NO. OF EXAMINED ANIMALS | 50 | 50 | 50 | 49 |
| | NO. OF ANIMALS WITH TUMORS | 42 | 39 | 43 | 43 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | 30 | 25 | 25 | 29 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | 12 | 14 | 18 | 14 |
| | NO. OF BENIGN TUMORS | 17 | 18 | 26 | 21 |
| | NO. OF MALIGNANT TUMORS | 40 | 44 | 41 | 39 |
| | NO. OF TOTAL TUMORS | 57 | 62 | 67 | 60 |

APPENDIX M 1

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

RAT : MALE :

| Organ | Findings | Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | No. of animals on Study | 50 | 50 | 50 | 50 |
| [Integumentary system/appandage] | | | | | | |
| skin/app | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 2 ( 4%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| | keratoacanthoma | | 1 ( 2%) | 2 ( 4%) | 0 ( 0%) | 1 ( 2%) |
| | sebaceous adenoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | squamous cell carcinoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| subcutis | | | <50> | <50> | <50> | <50> |
| | fibroma | | 5 ( 10%) | 5 ( 10%) | 2 ( 4%) | 2 ( 4%) |
| | lipoma | | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| | fibrosarcoma | | 1 ( 2%) | 1 ( 2%) | 1 ( 2%) | 1 ( 2%) |
| [Respiratory system] | | | | | | |
| nasal cavit | | | <50> | <50> | <50> | <50> |
| | chondroma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| nasopharynx | | | <50> | <50> | <50> | <50> |
| | squamous cell carcinoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| lung | | | <50> | <50> | <50> | <50> |
| | bronchiolar-alveolar adenoma | | 1 ( 2%) | 2 ( 4%) | 2 ( 4%) | 2 ( 4%) |
| [Hematopoietic system] | | | | | | |
| lymph node | | | <50> | <50> | <50> | <50> |
| | malignant lymphoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |

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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Hematopoietic system] | | | | | | |
| spleen | | | <50> | <50> | <50> | <50> |
| | histiocytic sarcoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | mononuclear cell leukemia | | 7 ( 14%) | 12 ( 24%) | 10 ( 20%) | 9 ( 18%) |
| | hemangiosarcoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| [Digestive system] | | | | | | |
| oral cavity | | | <50> | <50> | <50> | <50> |
| | squamous cell carcinoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| tongue | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 0 ( 0%) | 0 ( 0%) | 2 ( 4%) | 0 ( 0%) |
| salivary gl | | | <50> | <50> | <50> | <50> |
| | schwannoma:malignant | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| stomach | | | <49> | <50> | <49> | <50> |
| | squamous cell carcinoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| liver | | | <50> | <50> | <50> | <50> |
| | hepatocellular adenoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| | histiocytic sarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| pancreas | | | <50> | <50> | <50> | <50> |
| | acinar cell adenoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| | sarcoma:NOS | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| [Urinary system] | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | renal cell adenoma | | 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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Urinary system] | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | sarcoma:NOS | | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) |
| | nephroblastoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| urin bladd | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | transitional cell papilloma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 10 ( 20%) |
| | squamous cell carcinoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | transitional cell carcinoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 24 ( 48%) |
| [Endocrine system] | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | adenoma | | 14 ( 28%) | 12 ( 24%) | 10 ( 20%) | 8 ( 16%) |
| thyroid | | | <50> | <50> | <50> | <50> |
| | C-cell adenoma | | 3 ( 6%) | 3 ( 6%) | 7 ( 14%) | 3 ( 6%) |
| | C-cell carcinoma | | 0 ( 0%) | 3 ( 6%) | 1 ( 2%) | 0 ( 0%) |
| | follicular adenocarcinoma | | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 2 ( 4%) |
| panc islet | | | <50> | <50> | <50> | <50> |
| | islet cell adenoma | | 7 ( 14%) | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) |
| adrenal | | | <50> | <50> | <50> | <50> |
| | pheochromocytoma | | 5 ( 10%) | 4 ( 8%) | 8 ( 16%) | 7 ( 14%) |

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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Endocrine system] | | | | | | |
| adrenal | | | <50> | <50> | <50> | <50> |
| | cortical adenoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | pheochromocytoma:malignant | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| [Reproductive system] | | | | | | |
| testis | | | <50> | <50> | <50> | <50> |
| | interstitial cell tumor | | 44 ( 88%) | 44 ( 88%) | 45 ( 90%) | 48 ( 96%) |
| mammary gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 ( 0%) | 2 ( 4%) | 0 ( 0%) | 0 ( 0%) |
| | fibroadenoma | | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| | adenocarcinoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| prep/cli gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 6 ( 12%) | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) |
| [Nervous system] | | | | | | |
| brain | | | <50> | <50> | <50> | <50> |
| | meningioma:benign | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| | malignant reticulosis | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | glioma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Special sense organs/appandage] | | | | | | |
| Zymbal gl | | | <50> | <50> | <50> | <50> |
| | sebaceous adenoma | | 0 ( 0%) | 1 ( 2%) | 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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Special sense organs/appandage] | | | | | | |
| Zymbal gl | | | <50> | <50> | <50> | <50> |
| | squamous cell carcinoma | | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Musculoskeletal system] | | | | | | |
| muscle | | | <50> | <50> | <50> | <50> |
| | fibroma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| bone | | | <50> | <50> | <50> | <50> |
| | osteosarcoma | | 0 ( 0%) | 2 ( 4%) | 0 ( 0%) | 0 ( 0%) |
| vertebra | | | <50> | <50> | <50> | <50> |
| | sarcoma:NOS | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Body cavities] | | | | | | |
| pleura | | | <50> | <50> | <50> | <50> |
| | mesothelioma | | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| peritoneum | | | <50> | <50> | <50> | <50> |
| | mesothelioma | | 1 ( 2%) | 1 ( 2%) | 2 ( 4%) | 4 ( 8%) |
| retroperit | | | <50> | <50> | <50> | <50> |
| | paraganglioma:benign | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| | malignant fibrous histiocytoma | | 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

APPENDIX M 2

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

RAT : FEMALE :

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Integumentary system/appandage] | | | | | | |
| skin/app | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| subcutis | | | <50> | <50> | <50> | <50> |
| | fibroma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) |
| | fibrosarcoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| [Respiratory system] | | | | | | |
| lung | | | <50> | <50> | <50> | <50> |
| | bronchiolar-alveolar adenoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <50> | <50> | <50> | <50> |
| | malignant histiocytosis | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| lymph node | | | <50> | <49> | <50> | <50> |
| | malignant lymphoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| spleen | | | <50> | <50> | <50> | <50> |
| | mononuclear cell leukemia | | 7 ( 14%) | 16 ( 32%) | 12 ( 24%) | 8 ( 16%) |
| [Circulatory system] | | | | | | |
| heart | | | <50> | <50> | <50> | <50> |
| | schwannoma:malignant | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| [Digestive system] | | | | | | |
| oral cavity | | | <50> | <50> | <50> | <50> |
| | squamous cell carcinoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |

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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Digestive system] | | | | | | |
| tongue | | | <50> | <50> | <50> | <50> |
| | squamous cell carcinoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| liver | | | <50> | <50> | <50> | <50> |
| | hepatocellular adenoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 4%) |
| | histiocytic sarcoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| [Urinary system] | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | sarcoma:NOS | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| [Endocrine system] | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | adenoma | | 23 ( 46%) | 18 ( 36%) | 19 ( 38%) | 16 ( 32%) |
| | adenocarcinoma | | 2 ( 4%) | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) |
| thyroid | | | <50> | <50> | <50> | <50> |
| | C-cell adenoma | | 6 ( 12%) | 4 ( 8%) | 2 ( 4%) | 2 ( 4%) |
| | follicular adenoma | | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) |
| | C-cell carcinoma | | 4 ( 8%) | 1 ( 2%) | 2 ( 4%) | 1 ( 2%) |
| | follicular adenocarcinoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| panc islet | | | <50> | <50> | <50> | <50> |
| | islet cell adenoma | | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) |

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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Endocrine system] | | | | | | |
| adrenal | | | <50> | <50> | <50> | <50> |
| | pheochromocytoma | | 0 ( 0%) | 3 ( 6%) | 2 ( 4%) | 1 ( 2%) |
| | cortical adenoma | | 0 ( 0%) | 0 ( 0%) | 2 ( 4%) | 0 ( 0%) |
| | pheochromocytoma:malignant | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| [Reproductive system] | | | | | | |
| ovary | | | <50> | <50> | <50> | <50> |
| | granulosa-theca cell tumor:malignant | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| uterus | | | <50> | <50> | <50> | <50> |
| | hemangioma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | endometrial stromal polyp | | 5 ( 10%) | 2 ( 4%) | 8 ( 16%) | 8 ( 16%) |
| | adenocarcinoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | endometrial stromal sarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) |
| vagina | | | <50> | <50> | <50> | <50> |
| | squamous cell carcinoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| mammary gl | | | <50> | <49> | <50> | <50> |
| | adenoma | | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) |
| | fibroadenoma | | 8 ( 16%) | 7 ( 14%) | 6 ( 12%) | 6 ( 12%) |
| | adenocarcinoma | | 2 ( 4%) | 1 ( 2%) | 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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 500ppm 50 | 1500ppm 50 | 4500ppm 50 |
|---|---|---|---|---|---|---|
| [Reproductive system] | | | | | | |
| prep/cli gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 3 ( 6%) | 2 ( 4%) | 2 ( 4%) | 0 ( 0%) |
| [Nervous system] | | | | | | |
| brain | | | <50> | <50> | <50> | <50> |
| | meningioma:benign | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| [Musculoskeletal system] | | | | | | |
| bone | | | <50> | <50> | <50> | <50> |
| | osteosarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Body cavities] | | | | | | |
| retroperit | | | <50> | <50> | <50> | <50> |
| | hemangiosarcoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| adipose | | | <50> | <50> | <50> | <50> |
| | lipoma | | 1 ( 2%) | 1 ( 2%) | 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

# APPENDIX M 3

# HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

# MOUSE: MALE

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 667ppm 50 | 2000ppm 50 | 6000ppm 50 |
|---|---|---|---|---|---|---|
| [Integumentary system/appandage] | | | | | | |
| subcutis | | | <50> | <50> | <50> | <50> |
| | leiomyosarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Respiratory system] | | | | | | |
| lung | | | <50> | <50> | <50> | <50> |
| | bronchiolar-alveolar adenoma | | 3 ( 6%) | 8 ( 16%) | 5 ( 10%) | 3 ( 6%) |
| | bronchiolar-alveolar carcinoma | | 2 ( 4%) | 4 ( 8%) | 5 ( 10%) | 1 ( 2%) |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <50> | <50> | <50> | <50> |
| | hemangioma | | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) |
| | mastcytoma:malignant | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | hemangiosarcoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| lymph node | | | <50> | <50> | <50> | <50> |
| | mastcytoma:benign | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | malignant lymphoma | | 4 ( 8%) | 7 ( 14%) | 6 ( 12%) | 7 ( 14%) |
| spleen | | | <50> | <49> | <50> | <50> |
| | malignant lymphoma | | 2 ( 4%) | 0 ( 0%) | 2 ( 4%) | 3 ( 6%) |
| | hemangiosarcoma | | 3 ( 6%) | 3 ( 6%) | 5 ( 10%) | 3 ( 6%) |
| [Circulatory system] | | | | | | |
| heart | | | <50> | <50> | <50> | <50> |
| | hemangiosarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |

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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 667ppm 50 | 2000ppm 50 | 6000ppm 50 |
|---|---|---|---|---|---|---|
| [Digestive system] | | | | | | |
| salivary gl | | | <50> | <50> | <50> | <50> |
| | histiocytic sarcoma | | 1 ( 2%) | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) |
| stomach | | | <50> | <50> | <50> | <50> |
| | neuroendocrine cell tumor:malignant | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | mastcytoma:malignant | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| liver | | | <50> | <49> | <50> | <50> |
| | hemangioma | | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) |
| | hepatocellular adenoma | | 8 ( 16%) | 6 ( 12%) | 7 ( 14%) | 3 ( 6%) |
| | histiocytic sarcoma | | 2 ( 4%) | 2 ( 4%) | 0 ( 0%) | 1 ( 2%) |
| | hemangiosarcoma | | 4 ( 8%) | 2 ( 4%) | 2 ( 4%) | 1 ( 2%) |
| | hepatocellular carcinoma | | 8 ( 16%) | 8 ( 16%) | 5 ( 10%) | 4 ( 8%) |
| [Urinary system] | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | hemangioma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | adenocarcinoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 1 ( 2%) |
| | transitional cell carcinoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| urin bladd | | | <50> | <50> | <50> | <50> |
| | histiocytic sarcoma | | 0 ( 0%) | 2 ( 4%) | 1 ( 2%) | 0 ( 0%) |

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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 667ppm 50 | 2000ppm 50 | 6000ppm 50 |
|---|---|---|---|---|---|---|
| [Endocrine system] | | | | | | |
| pituitary | | | <49> | <50> | <50> | <49> |
| | adenoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) |
| [Reproductive system] | | | | | | |
| testis | | | <50> | <50> | <50> | <50> |
| | interstitial cell tumor | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| epididymis | | | <50> | <50> | <50> | <50> |
| | lipoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| | histiocytic sarcoma | | 1 ( 2%) | 0 ( 0%) | 2 ( 4%) | 0 ( 0%) |
| prostate | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Nervous system] | | | | | | |
| periph nerv | | | <50> | <50> | <50> | <50> |
| | histiocytic sarcoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| [Special sense organs/appandage] | | | | | | |
| Harder gl | | | <50> | <50> | <48> | <50> |
| | adenoma | | 0 ( 0%) | 5 ( 10%) | 2 ( 4%) | 0 ( 0%) |
| [Musculoskeletal system] | | | | | | |
| muscle | | | <50> | <50> | <50> | <50> |
| | hemangiosarcoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 4%) |
| [Body cavities] | | | | | | |
| retroperit | | | <50> | <50> | <50> | <50> |
| | hemangiosarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |

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

# APPENDIX M 4

# HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YERA STUDY: SUMMARY)

# MOUSE: FEMALE

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 667ppm 50 | 2000ppm 50 | 6000ppm 49 |
|---|---|---|---|---|---|---|
| [Integumentary system/appandage] | | | | | | |
| skin/app | | | <50> | <50> | <50> | <49> |
| | squamous cell papilloma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| subcutis | | | <50> | <50> | <50> | <49> |
| | mastcytoma:benign | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | histiocytic sarcoma | | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| | sarcoma:NOS | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Respiratory system] | | | | | | |
| lung | | | <50> | <50> | <50> | <49> |
| | bronchiolar-alveolar adenoma | | 3 ( 6%) | 1 ( 2%) | 1 ( 2%) | 1 ( 2%) |
| | bronchiolar-alveolar carcinoma | | 4 ( 8%) | 2 ( 4%) | 1 ( 2%) | 2 ( 4%) |
| [Hematopoietic system] | | | | | | |
| lymph node | | | <50> | <50> | <50> | <49> |
| | mastcytoma:benign | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| | malignant lymphoma | | 14 ( 28%) | 15 ( 30%) | 11 ( 22%) | 7 ( 14%) |
| thymus | | | <49> | <49> | <48> | <49> |
| | malignant lymphoma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| spleen | | | <50> | <50> | <50> | <49> |
| | malignant lymphoma | | 6 ( 12%) | 4 ( 8%) | 3 ( 6%) | 4 ( 8%) |
| | hemangiosarcoma | | 1 ( 2%) | 1 ( 2%) | 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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 667ppm 50 | 2000ppm 50 | 6000ppm 49 |
|---|---|---|---|---|---|---|
| [Digestive system] | | | | | | |
| salivary gl | | | <50> | <50> | <50> | <49> |
| | histiocytic sarcoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| stomach | | | <50> | <50> | <50> | <49> |
| | squamous cell papilloma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| large intes | | | <50> | <50> | <50> | <49> |
| | leiomyoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| liver | | | <50> | <50> | <50> | <49> |
| | hemangioma | | 0 ( 0%) | 1 ( 2%) | 3 ( 6%) | 1 ( 2%) |
| | hepatocellular adenoma | | 2 ( 4%) | 3 ( 6%) | 12 ( 24%) | 10 ( 20%) |
| | histiocytic sarcoma | | 2 ( 4%) | 1 ( 2%) | 1 ( 2%) | 1 ( 2%) |
| | hemangiosarcoma | | 2 ( 4%) | 0 ( 0%) | 1 ( 2%) | 4 ( 8%) |
| | hepatocellular carcinoma | | 1 ( 2%) | 5 ( 10%) | 7 ( 14%) | 5 ( 10%) |
| [Urinary system] | | | | | | |
| kidney | | | <50> | <50> | <50> | <49> |
| | adenocarcinoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| [Endocrine system] | | | | | | |
| pituitary | | | <50> | <49> | <50> | <49> |
| | adenoma | | 5 ( 10%) | 6 ( 12%) | 5 ( 10%) | 4 ( 8%) |
| [Reproductive system] | | | | | | |
| ovary | | | <50> | <50> | <50> | <49> |
| | cystadenoma | | 3 ( 6%) | 1 ( 2%) | 1 ( 2%) | 0 ( 0%) |

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

| Organ | Findings | Group Name / No. of animals on Study | Control 50 | 667ppm 50 | 2000ppm 50 | 6000ppm 49 |
|---|---|---|---|---|---|---|
| [Reproductive system] | | | | | | |
| uterus | | | <50> | <50> | <50> | <49> |
| | schwannoma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | hemangioma | | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) |
| | endometrial stromal polyp | | 1 ( 2%) | 0 ( 0%) | 2 ( 4%) | 1 ( 2%) |
| | histiocytic sarcoma | | 8 ( 16%) | 13 ( 26%) | 12 ( 24%) | 15 ( 31%) |
| vagina | | | <50> | <50> | <50> | <49> |
| | squamous cell papilloma | | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| mammary gl | | | <50> | <50> | <50> | <49> |
| | adenocarcinoma | | 0 ( 0%) | 2 ( 4%) | 0 ( 0%) | 0 ( 0%) |
| [Nervous system] | | | | | | |
| spinal cord | | | <50> | <50> | <50> | <49> |
| | histiocytic sarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |
| periph nerv | | | <50> | <50> | <50> | <49> |
| | histiocytic sarcoma | | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| [Special sense organs/appandage] | | | | | | |
| Harder gl | | | <50> | <50> | <50> | <49> |
| | adenoma | | 1 ( 2%) | 4 ( 8%) | 1 ( 2%) | 1 ( 2%) |
| [Body cavities] | | | | | | |
| retroperit | | | <50> | <50> | <50> | <49> |
| | histiocytic sarcoma | | 0 ( 0%) | 0 ( 0%) | 1 ( 2%) | 0 ( 0%) |

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

# APPENDIX N 1

# NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

# RAT : MALE

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : skin/appendage | | | |
| | TUMOR : squamous cell papilloma,squamous cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 0/50( 0.0) | 1/50( 2.0) | 0/50( 0.0) |
| Adjusted rates(b) | 8.11 | 0.0 | 2.44 | 0.0 |
| Terminal rates(c) | 3/37( 8.1) | 0/41( 0.0) | 0/38( 0.0) | 0/31( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9329 | | | |
| Combined analysis(d) | P = ------- | | | |
| Cochran-Armitage test(e) | P = 0.1480 | | | |
| Fisher Exact test(e) | | P = 0.1325 | P = 0.3235 | P = 0.1325 |
| | SITE : subcutis | | | |
| | TUMOR : fibroma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50( 10.0) | 5/50( 10.0) | 2/50( 4.0) | 2/50( 4.0) |
| Adjusted rates(b) | 9.09 | 7.32 | 5.26 | 6.45 |
| Terminal rates(c) | 3/37( 8.1) | 3/41( 7.3) | 2/38( 5.3) | 2/31( 6.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9106 | | | |
| Prevalence method(d) | P = 0.7364 | | | |
| Combined analysis(d) | P = 0.8837 | | | |
| Cochran-Armitage test(e) | P = 0.1902 | | | |
| Fisher Exact test(e) | | P = 0.3710 | P = 0.2425 | P = 0.2425 |
| | SITE : subcutis | | | |
| | TUMOR : fibroma,fibrosarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50( 12.0) | 6/50( 12.0) | 3/50( 6.0) | 2/50( 4.0) |
| Adjusted rates(b) | 11.36 | 7.32 | 7.89 | 6.45 |
| Terminal rates(c) | 4/37( 10.8) | 3/41( 7.3) | 3/38( 7.9) | 2/31( 6.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9380 | | | |
| Prevalence method(d) | P = 0.8019 | | | |
| Combined analysis(d) | P = 0.9332 | | | |
| Cochran-Armitage test(e) | P = 0.1061 | | | |
| Fisher Exact test(e) | | P = 0.3807 | P = 0.2728 | P = 0.1606 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : spleen<br>TUMOR : mononuclear cell leukemia | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50( 14.0) | 12/50( 24.0) | 10/50( 20.0) | 9/50( 18.0) |
| Adjusted rates(b) | 10.81 | 24.39 | 19.05 | 16.13 |
| Terminal rates(c) | 4/37( 10.8) | 10/41( 24.4) | 7/38( 18.4) | 5/31( 16.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1956 | | | |
| Prevalence method(d) | P = 0.5566 | | | |
| Combined analysis(d) | P = 0.3523 | | | |
| Cochran-Armitage test(e) | P = 0.9794 | | | |
| Fisher Exact test(e) | | P = 0.2119 | P = 0.3417 | P = 0.4234 |
| | SITE : urinary bladder<br>TUMOR : transitional cell papilloma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 0/50( 0.0) | 0/50( 0.0) | 10/50( 20.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 25.81 |
| Terminal rates(c) | 0/37( 0.0) | 0/41( 0.0) | 0/38( 0.0) | 8/31( 25.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P < 0.0001**? | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P < 0.0001** | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.0016** |
| | SITE : urinary bladder<br>TUMOR : transitional cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 0/50( 0.0) | 0/50( 0.0) | 24/50( 48.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 51.52 |
| Terminal rates(c) | 0/37( 0.0) | 0/41( 0.0) | 0/38( 0.0) | 15/31( 48.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P < 0.0001**? | | | |
| 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** |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : urinary bladder | | | |
| | TUMOR : transitional cell papilloma,transitional cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 0/50( 0.0) | 0/50( 0.0) | 31/50( 62.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 66.67 |
| Terminal rates(c) | 0/37( 0.0) | 0/41( 0.0) | 0/38( 0.0) | 20/31( 64.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P < 0.0001**? | | | |
| 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 : urinary bladder | | | |
| | TUMOR : transitional cell papilloma,transitional cell carcinoma,squamous cell papilloma,squamous cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 0/50( 0.0) | 0/50( 0.0) | 31/50( 62.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 66.67 |
| Terminal rates(c) | 0/37( 0.0) | 0/41( 0.0) | 0/38( 0.0) | 20/31( 64.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P < 0.0001**? | | | |
| 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 : pituitary gland | | | |
| | TUMOR : adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 14/50( 28.0) | 12/50( 24.0) | 10/50( 20.0) | 8/50( 16.0) |
| Adjusted rates(b) | 23.81 | 24.39 | 15.79 | 25.81 |
| Terminal rates(c) | 8/37( 21.6) | 10/41( 24.4) | 6/38( 15.8) | 8/31( 25.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9555 | | | |
| Prevalence method(d) | P = 0.5913 | | | |
| Combined analysis(d) | P = 0.8513 | | | |
| Cochran-Armitage test(e) | P = 0.1562 | | | |
| Fisher Exact test(e) | | P = 0.4489 | P = 0.3071 | P = 0.1781 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : pituitary gland<br>TUMOR : adenoma,adenocarcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 14/50( 28.0) | 12/50( 24.0) | 10/50( 20.0) | 8/50( 16.0) |
| Adjusted rates(b) | 23.81 | 24.39 | 15.79 | 25.81 |
| Terminal rates(c) | 8/37( 21.6) | 10/41( 24.4) | 6/38( 15.8) | 8/31( 25.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9555 | | | |
| Prevalence method(d) | P = 0.5913 | | | |
| Combined analysis(d) | P = 0.8513 | | | |
| Cochran-Armitage test(e) | P = 0.1562 | | | |
| Fisher Exact test(e) | | P = 0.4489 | P = 0.3071 | P = 0.1781 |
| | SITE : thyroid<br>TUMOR : C-cell adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 3/50( 6.0) | 7/50( 14.0) | 3/50( 6.0) |
| Adjusted rates(b) | 6.98 | 7.32 | 16.67 | 9.68 |
| Terminal rates(c) | 1/37( 2.7) | 3/41( 7.3) | 5/38( 13.2) | 3/31( 9.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.4912 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.9405 | | | |
| Fisher Exact test(e) | | P = 0.3392 | P = 0.1917 | P = 0.3392 |
| | SITE : thyroid<br>TUMOR : C-cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 3/50( 6.0) | 1/50( 2.0) | 0/50( 0.0) |
| Adjusted rates(b) | 0.0 | 6.98 | 2.63 | 0.0 |
| Terminal rates(c) | 0/37( 0.0) | 1/41( 2.4) | 1/38( 2.6) | 0/31( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.8033 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.3112 | | | |
| Fisher Exact test(e) | | P = 0.1325 | P = 0.4950 | P = 0.5000 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : thyroid<br>TUMOR : C-cell adenoma,C-cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 6/50( 12.0) | 8/50( 16.0) | 3/50( 6.0) |
| Adjusted rates(b) | 6.98 | 13.95 | 19.05 | 9.68 |
| Terminal rates(c) | 1/37( 2.7) | 4/41( 9.8) | 6/38( 15.8) | 3/31( 9.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.6601 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.5891 | | | |
| Fisher Exact test(e) | | P = 0.2728 | P = 0.1322 | P = 0.3392 |
| | SITE : pancreas islet<br>TUMOR : islet cell adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50( 14.0) | 0/50( 0.0) | 1/50( 2.0) | 1/50( 2.0) |
| Adjusted rates(b) | 15.38 | 0.0 | 2.50 | 3.23 |
| Terminal rates(c) | 5/37( 13.5) | 0/41( 0.0) | 0/38( 0.0) | 1/31( 3.2) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9564 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.0919 | | | |
| Fisher Exact test(e) | | P = 0.0101* | P = 0.0430* | P = 0.0430* |
| | SITE : adrenal gland<br>TUMOR : pheochromocytoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50( 10.0) | 4/50( 8.0) | 8/50( 16.0) | 7/50( 14.0) |
| Adjusted rates(b) | 10.81 | 8.33 | 21.05 | 19.35 |
| Terminal rates(c) | 4/37( 10.8) | 3/41( 7.3) | 8/38( 21.1) | 6/31( 19.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.1375 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.4178 | | | |
| Fisher Exact test(e) | | P = 0.4883 | P = 0.3141 | P = 0.4062 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : adrenal gland<br>TUMOR : pheochromocytoma,pheochromocytoma:malignant | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50( 10.0) | 5/50( 10.0) | 8/50( 16.0) | 7/50( 14.0) |
| Adjusted rates(b) | 10.81 | 10.42 | 21.05 | 19.35 |
| Terminal rates(c) | 4/37( 10.8) | 3/41( 7.3) | 8/38( 21.1) | 6/31( 19.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.1874 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.5103 | | | |
| Fisher Exact test(e) | | P = 0.3710 | P = 0.3141 | P = 0.4062 |
| | SITE : testis<br>TUMOR : interstitial cell tumor | | | |
| Tumor rate | | | | |
| Overall rates(a) | 44/50( 88.0) | 44/50( 88.0) | 45/50( 90.0) | 48/50( 96.0) |
| Adjusted rates(b) | 97.67 | 95.35 | 97.37 | 100.00 |
| Terminal rates(c) | 36/37( 97.3) | 39/41( 95.1) | 37/38( 97.4) | 31/31(100.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.0017** | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.1161 | | | |
| Fisher Exact test(e) | | P = 0.4419 | P = 0.4726 | P = 0.4379 |
| | SITE : preputial/clitoral gland<br>TUMOR : adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50( 12.0) | 1/50( 2.0) | 0/50( 0.0) | 1/50( 2.0) |
| Adjusted rates(b) | 14.63 | 2.44 | 0.0 | 3.23 |
| Terminal rates(c) | 4/37( 10.8) | 1/41( 2.4) | 0/38( 0.0) | 1/31( 3.2) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9590 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.0982 | | | |
| Fisher Exact test(e) | | P = 0.0724 | P = 0.0190* | P = 0.0724 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : peritoneum<br>TUMOR : mesothelioma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50( 2.0) | 1/50( 2.0) | 2/50( 4.0) | 4/50( 8.0) |
| Adjusted rates(b) | 2.70 | 2.44 | 0.0 | 10.00 |
| Terminal rates(c) | 1/37( 2.7) | 1/41( 2.4) | 0/38( 0.0) | 3/31( 9.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.4590 | | | |
| Prevalence method(d) | P = 0.0229* | | | |
| Combined analysis(d) | P = 0.0430* | | | |
| Cochran-Armitage test(e) | P = 0.0789 | | | |
| Fisher Exact test(e) | | P = 0.2475 | P = 0.4926 | P = 0.1998 |



(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 ≦ 0.05 ** : P ≦ 0.01

# APPENDIX N 2

# NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

# RAT : FEMALE

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : spleen | | | |
| | TUMOR : mononuclear cell leukemia | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50( 14.0) | 16/50( 32.0) | 12/50( 24.0) | 8/50( 16.0) |
| Adjusted rates(b) | 11.36 | 23.68 | 18.18 | 18.92 |
| Terminal rates(c) | 5/44( 11.4) | 9/38( 23.7) | 8/44( 18.2) | 7/37( 18.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8946 | | | |
| Prevalence method(d) | P = 0.3421 | | | |
| Combined analysis(d) | P = 0.6636 | | | |
| Cochran-Armitage test(e) | P = 0.4374 | | | |
| Fisher Exact test(e) | | P = 0.0704 | P = 0.2119 | P = 0.4854 |
| | SITE : pituitary gland | | | |
| | TUMOR : adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 23/50( 46.0) | 18/50( 36.0) | 19/50( 38.0) | 16/50( 32.0) |
| Adjusted rates(b) | 45.45 | 41.03 | 40.91 | 39.47 |
| Terminal rates(c) | 20/44( 45.5) | 15/38( 39.5) | 18/44( 40.9) | 14/37( 37.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5949 | | | |
| Prevalence method(d) | P = 0.7418 | | | |
| Combined analysis(d) | P = 0.7645 | | | |
| Cochran-Armitage test(e) | P = 0.2426 | | | |
| Fisher Exact test(e) | | P = 0.3187 | P = 0.3695 | P = 0.2231 |
| | SITE : pituitary gland | | | |
| | TUMOR : adenoma,adenocarcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 25/50( 50.0) | 19/50( 38.0) | 20/50( 40.0) | 16/50( 32.0) |
| Adjusted rates(b) | 50.00 | 43.59 | 43.18 | 39.47 |
| Terminal rates(c) | 22/44( 50.0) | 16/38( 42.1) | 19/44( 43.2) | 14/37( 37.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5949 | | | |
| Prevalence method(d) | P = 0.8458 | | | |
| Combined analysis(d) | P = 0.8581 | | | |
| Cochran-Armitage test(e) | P = 0.1261 | | | |
| Fisher Exact test(e) | | P = 0.2836 | P = 0.3304 | P = 0.1586 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : thyroid<br>TUMOR : C-cell adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50( 12.0) | 4/50( 8.0) | 2/50( 4.0) | 2/50( 4.0) |
| Adjusted rates(b) | 13.64 | 8.89 | 4.55 | 5.41 |
| Terminal rates(c) | 6/44( 13.6) | 3/38( 7.9) | 2/44( 4.5) | 2/37( 5.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9038 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.1648 | | | |
| Fisher Exact test(e) | | P = 0.3944 | P = 0.1606 | P = 0.1606 |
| | SITE : thyroid<br>TUMOR : C-cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50( 8.0) | 1/50( 2.0) | 2/50( 4.0) | 1/50( 2.0) |
| Adjusted rates(b) | 8.70 | 2.63 | 4.55 | 2.22 |
| Terminal rates(c) | 3/44( 6.8) | 1/38( 2.6) | 2/44( 4.5) | 0/37( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.8312 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.3013 | | | |
| Fisher Exact test(e) | | P = 0.1998 | P = 0.3574 | P = 0.1998 |
| | SITE : thyroid<br>TUMOR : C-cell adenoma,C-cell carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 10/50( 20.0) | 5/50( 10.0) | 4/50( 8.0) | 3/50( 6.0) |
| Adjusted rates(b) | 21.74 | 11.11 | 9.09 | 6.67 |
| Terminal rates(c) | 9/44( 20.5) | 4/38( 10.5) | 4/44( 9.1) | 2/37( 5.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9597 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.0750 | | | |
| Fisher Exact test(e) | | P = 0.1771 | P = 0.1108 | P = 0.0604 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : adrenal gland<br>TUMOR : pheochromocytoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 3/50( 6.0) | 2/50( 4.0) | 1/50( 2.0) |
| Adjusted rates(b) | 0.0 | 7.89 | 4.55 | 2.70 |
| Terminal rates(c) | 0/44( 0.0) | 3/38( 7.9) | 2/44( 4.5) | 1/37( 2.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.4964 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.8586 | | | |
| Fisher Exact test(e) | | P = 0.1325 | P = 0.2574 | P = 0.4950 |
| | SITE : adrenal gland<br>TUMOR : pheochromocytoma,pheochromocytoma:malignant | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50( 2.0) | 3/50( 6.0) | 2/50( 4.0) | 1/50( 2.0) |
| Adjusted rates(b) | 2.27 | 7.89 | 4.55 | 2.70 |
| Terminal rates(c) | 1/44( 2.3) | 3/38( 7.9) | 2/44( 4.5) | 1/37( 2.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.6337 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.6006 | | | |
| Fisher Exact test(e) | | P = 0.3235 | P = 0.4926 | P = 0.2475 |
| | SITE : uterus<br>TUMOR : endometrial stromal polyp | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50( 10.0) | 2/50( 4.0) | 8/50( 16.0) | 8/50( 16.0) |
| Adjusted rates(b) | 11.36 | 2.63 | 17.02 | 18.92 |
| Terminal rates(c) | 5/44( 11.4) | 1/38( 2.6) | 7/44( 15.9) | 7/37( 18.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.2219 | | | |
| Prevalence method(d) | P = 0.0541 | | | |
| Combined analysis(d) | P = 0.0391* | | | |
| Cochran-Armitage test(e) | P = 0.1399 | | | |
| Fisher Exact test(e) | | P = 0.2425 | P = 0.3141 | P = 0.3141 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : uterus | | | |
| | TUMOR : endometrial stromal polyp,endometrial stromal sarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50( 10.0) | 2/50( 4.0) | 9/50( 18.0) | 9/50( 18.0) |
| Adjusted rates(b) | 11.36 | 2.63 | 19.15 | 18.82 |
| Terminal rates(c) | 5/44( 11.4) | 1/38( 2.6) | 8/44( 18.2) | 7/37( 18.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0721 | | | |
| Prevalence method(d) | P = 0.0577 | | | |
| Combined analysis(d) | P = 0.0211* | | | |
| Cochran-Armitage test(e) | P = 0.0783 | | | |
| Fisher Exact test(e) | | P = 0.2425 | P = 0.2379 | P = 0.2379 |
| | SITE : mammary gland | | | |
| | TUMOR : fibroadenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50( 16.0) | 7/49( 14.3) | 6/50( 12.0) | 6/50( 12.0) |
| Adjusted rates(b) | 16.33 | 16.28 | 13.64 | 13.64 |
| Terminal rates(c) | 6/44( 13.6) | 4/37( 10.8) | 6/44( 13.6) | 4/37( 10.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.6530 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.5919 | | | |
| Fisher Exact test(e) | | P = 0.4706 | P = 0.4157 | P = 0.4157 |
| | SITE : mammary gland | | | |
| | TUMOR : adenoma,fibroadenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50( 16.0) | 8/49( 16.3) | 7/50( 14.0) | 6/50( 12.0) |
| Adjusted rates(b) | 16.33 | 18.60 | 15.91 | 13.64 |
| Terminal rates(c) | 6/44( 13.6) | 5/37( 13.5) | 7/44( 15.9) | 4/37( 10.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.6993 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.5058 | | | |
| Fisher Exact test(e) | | P = 0.4089 | P = 0.4854 | P = 0.4157 |

| Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|
| | SITE : mammary gland<br>TUMOR : adenoma,fibroadenoma,adenocarcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 10/50( 20.0) | 9/49( 18.4) | 7/50( 14.0) | 6/50( 12.0) |
| Adjusted rates(b) | 20.41 | 20.93 | 15.91 | 13.64 |
| Terminal rates(c) | 7/44( 15.9) | 6/37( 16.2) | 7/44( 15.9) | 4/37( 10.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------- | | | |
| Prevalence method(d) | P = 0.8400 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.2611 | | | |
| Fisher Exact test(e) | | P = 0.4676 | P = 0.3417 | P = 0.2557 |
| | SITE : preputial/clitoral gland<br>TUMOR : adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 2/50( 4.0) | 2/50( 4.0) | 0/50( 0.0) |
| Adjusted rates(b) | 6.67 | 5.26 | 4.55 | 0.0 |
| Terminal rates(c) | 2/44( 4.5) | 2/38( 5.3) | 2/44( 4.5) | 0/37( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------- | | | |
| Prevalence method(d) | P = 0.9504 | | | |
| Combined analysis(d) | P = ------- | | | |
| Cochran-Armitage test(e) | P = 0.1040 | | | |
| Fisher Exact test(e) | | P = 0.4909 | P = 0.4909 | P = 0.1325 |



(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 ≦ 0.05 ** : P ≦ 0.01

# APPENDIX N 3

# NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

# MOSUE : MALE

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 8/50( 16.0) | 5/50( 10.0) | 3/50( 6.0) |
| Adjusted rates(b) | 6.12 | 19.51 | 11.36 | 7.69 |
| Terminal rates(c) | 2/35( 5.7) | 8/41( 19.5) | 4/41( 9.8) | 3/39( 7.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.7957 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.4170 | | | |
| Fisher Exact test(e) | | P = 0.1322 | P = 0.3790 | P = 0.3392 |
| | SITE : lung<br>TUMOR : bronchiolar-alveolar carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50( 4.0) | 4/50( 8.0) | 5/50( 10.0) | 1/50( 2.0) |
| Adjusted rates(b) | 2.86 | 9.76 | 9.09 | 2.56 |
| Terminal rates(c) | 1/35( 2.9) | 4/41( 9.8) | 3/41( 7.3) | 1/39( 2.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7164 | | | |
| Prevalence method(d) | P = 0.7705 | | | |
| Combined analysis(d) | P = 0.8412 | | | |
| Cochran-Armitage test(e) | P = 0.3482 | | | |
| Fisher Exact test(e) | | P = 0.3574 | P = 0.2425 | P = 0.4926 |
| | SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50( 8.0) | 12/50( 24.0) | 9/50( 18.0) | 4/50( 8.0) |
| Adjusted rates(b) | 6.25 | 29.27 | 18.18 | 10.26 |
| Terminal rates(c) | 2/35( 5.7) | 12/41( 29.3) | 7/41( 17.1) | 4/39( 10.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7164 | | | |
| Prevalence method(d) | P = 0.8437 | | | |
| Combined analysis(d) | P = 0.8821 | | | |
| Cochran-Armitage test(e) | P = 0.2682 | | | |
| Fisher Exact test(e) | | P = 0.0539 | P = 0.1562 | P = 0.3579 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : lymph node | | | |
| | TUMOR : malignant lymphoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50( 8.0) | 7/50( 14.0) | 6/50( 12.0) | 7/50( 14.0) |
| Adjusted rates(b) | 5.71 | 13.64 | 12.20 | 10.26 |
| Terminal rates(c) | 2/35( 5.7) | 5/41( 12.2) | 5/41( 12.2) | 4/39( 10.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1953 | | | |
| Prevalence method(d) | P = 0.4534 | | | |
| Combined analysis(d) | P = 0.2831 | | | |
| Cochran-Armitage test(e) | P = 0.5331 | | | |
| Fisher Exact test(e) | | P = 0.2958 | P = 0.3944 | P = 0.2958 |
| | SITE : spleen | | | |
| | TUMOR : malignant lymphoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50( 4.0) | 0/49( 0.0) | 2/50( 4.0) | 3/50( 6.0) |
| Adjusted rates(b) | 5.41 | 0.0 | 2.44 | 7.69 |
| Terminal rates(c) | 1/35( 2.9) | 0/40( 0.0) | 1/41( 2.4) | 3/39( 7.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.3798 | | | |
| Prevalence method(d) | P = 0.1222 | | | |
| Combined analysis(d) | P = 0.1458 | | | |
| Cochran-Armitage test(e) | P = 0.2630 | | | |
| Fisher Exact test(e) | | P = 0.2626 | P = 0.3088 | P = 0.4909 |
| | SITE : spleen | | | |
| | TUMOR : hemangiosarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 3/49( 6.1) | 5/50( 10.0) | 3/50( 6.0) |
| Adjusted rates(b) | 6.82 | 7.50 | 12.20 | 6.38 |
| Terminal rates(c) | 0/35( 0.0) | 3/40( 7.5) | 5/41( 12.2) | 1/39( 2.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.5091 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.9584 | | | |
| Fisher Exact test(e) | | P = 0.3483 | P = 0.3790 | P = 0.3392 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : liver<br>TUMOR : hepatocellular adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50( 16.0) | 6/49( 12.2) | 7/50( 14.0) | 3/50( 6.0) |
| Adjusted rates(b) | 20.00 | 15.00 | 16.67 | 7.69 |
| Terminal rates(c) | 7/35( 20.0) | 6/40( 15.0) | 6/41( 14.6) | 3/39( 7.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9468 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.1307 | | | |
| Fisher Exact test(e) | | P = 0.4299 | P = 0.4854 | P = 0.1322 |
| | SITE : liver<br>TUMOR : hemangiosarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50( 8.0) | 2/49( 4.1) | 2/50( 4.0) | 1/50( 2.0) |
| Adjusted rates(b) | 0.0 | 2.50 | 2.44 | 0.0 |
| Terminal rates(c) | 0/35( 0.0) | 1/40( 2.5) | 1/41( 2.4) | 0/39( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8651 | | | |
| Prevalence method(d) | P = 0.6367 | | | |
| Combined analysis(d) | P = 0.8940 | | | |
| Cochran-Armitage test(e) | P = 0.2281 | | | |
| Fisher Exact test(e) | | P = 0.3668 | P = 0.3574 | P = 0.1998 |
| | SITE : liver<br>TUMOR : hepatocellular carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50( 16.0) | 8/49( 16.3) | 5/50( 10.0) | 4/50( 8.0) |
| Adjusted rates(b) | 22.86 | 15.22 | 6.67 | 7.69 |
| Terminal rates(c) | 8/35( 22.9) | 6/40( 15.0) | 2/41( 4.9) | 3/39( 7.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.3303 | | | |
| Prevalence method(d) | P = 0.9661 | | | |
| Combined analysis(d) | P = 0.9280 | | | |
| Cochran-Armitage test(e) | P = 0.1681 | | | |
| Fisher Exact test(e) | | P = 0.4089 | P = 0.3141 | P = 0.2169 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : liver | | | |
| | TUMOR : hemangioma,hemangiosarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50( 8.0) | 3/49( 6.1) | 3/50( 6.0) | 1/50( 2.0) |
| Adjusted rates(b) | 0.0 | 5.00 | 4.88 | 0.0 |
| Terminal rates(c) | 0/35( 0.0) | 2/40( 5.0) | 2/41( 4.9) | 0/39( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8651 | | | |
| Prevalence method(d) | P = 0.7557 | | | |
| Combined analysis(d) | P = 0.9161 | | | |
| Cochran-Armitage test(e) | P = 0.1869 | | | |
| Fisher Exact test(e) | | P = 0.4788 | P = 0.4895 | P = 0.1998 |
| | SITE : liver | | | |
| | TUMOR : hepatocellular adenoma,hepatocellular carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 16/50( 32.0) | 12/49( 24.5) | 9/50( 18.0) | 7/50( 14.0) |
| Adjusted rates(b) | 42.86 | 25.00 | 15.56 | 15.38 |
| Terminal rates(c) | 15/35( 42.9) | 10/40( 25.0) | 6/41( 14.6) | 6/39( 15.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.3303 | | | |
| Prevalence method(d) | P = 0.9922 | | | |
| Combined analysis(d) | P = 0.9833 | | | |
| Cochran-Armitage test(e) | P = 0.0426* | | | |
| Fisher Exact test(e) | | P = 0.3429 | P = 0.1514 | P = 0.0704 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : Harderian gland<br>TUMOR : adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 5/50( 10.0) | 2/48( 4.2) | 0/50( 0.0) |
| Adjusted rates(b) | 0.0 | 11.90 | 5.13 | 0.0 |
| Terminal rates(c) | 0/35( 0.0) | 4/41( 9.8) | 2/39( 5.1) | 0/39( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9158 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.1969 | | | |
| Fisher Exact test(e) | | P = 0.0360* | P = 0.2475 | 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 ≦ 0.05 ** : P ≦ 0.01

STUDY No. : 0206
ANIMAL : MOUSE BDF1
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS



| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : ALL SITE<br>TUMOR : histiocytic sarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50( 10.0) | 5/50( 10.0) | 4/50( 8.0) | 2/50( 4.0) |
| Adjusted rates(b) | 5.71 | 7.32 | 7.32 | 0.0 |
| Terminal rates(c) | 2/35( 5.7) | 3/41( 7.3) | 3/41( 7.3) | 0/39( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.6127 | | | |
| Prevalence method(d) | P = 0.9434 | | | |
| Combined analysis(d) | P = 0.9064 | | | |
| Cochran-Armitage test(e) | P = 0.2044 | | | |
| Fisher Exact test(e) | | P = 0.3710 | P = 0.4883 | P = 0.2425 |
| | SITE : ALL SITE<br>TUMOR : malignant lymphoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50( 12.0) | 7/50( 14.0) | 8/50( 16.0) | 10/50( 20.0) |
| Adjusted rates(b) | 11.11 | 13.64 | 14.63 | 17.95 |
| Terminal rates(c) | 3/35( 8.6) | 5/41( 12.2) | 6/41( 14.6) | 7/39( 17.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.2173 | | | |
| Prevalence method(d) | P = 0.2252 | | | |
| Combined analysis(d) | P = 0.1482 | | | |
| Cochran-Armitage test(e) | P = 0.2571 | | | |
| Fisher Exact test(e) | | P = 0.4863 | P = 0.4157 | P = 0.2557 |

(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 ≦ 0.05 ** : P ≦ 0.01

# APPENDIX N 4

## NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

## MOSUE :FEMALE

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : lung | | | |
| | TUMOR : bronchiolar-alveolar adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 1/50( 2.0) | 1/50( 2.0) | 1/49( 2.0) |
| Adjusted rates(b) | 7.69 | 4.55 | 4.00 | 3.13 |
| Terminal rates(c) | 2/31( 6.5) | 1/22( 4.5) | 1/25( 4.0) | 1/32( 3.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.7949 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.4505 | | | |
| Fisher Exact test(e) | | P = 0.3235 | P = 0.3235 | P = 0.3312 |
| | SITE : lung | | | |
| | TUMOR : bronchiolar-alveolar carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50( 8.0) | 2/50( 4.0) | 1/50( 2.0) | 2/49( 4.1) |
| Adjusted rates(b) | 11.76 | 2.50 | 3.57 | 6.25 |
| Terminal rates(c) | 3/31( 9.7) | 0/22( 0.0) | 0/25( 0.0) | 2/32( 6.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5184 | | | |
| Prevalence method(d) | P = 0.6677 | | | |
| Combined analysis(d) | P = 0.7397 | | | |
| Cochran-Armitage test(e) | P = 0.5566 | | | |
| Fisher Exact test(e) | | P = 0.3574 | P = 0.1998 | P = 0.3668 |
| | SITE : lung | | | |
| | TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50( 14.0) | 3/50( 6.0) | 2/50( 4.0) | 3/49( 6.1) |
| Adjusted rates(b) | 17.95 | 5.00 | 7.14 | 9.38 |
| Terminal rates(c) | 5/31( 16.1) | 1/22( 4.5) | 1/25( 4.0) | 3/32( 9.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5184 | | | |
| Prevalence method(d) | P = 0.8161 | | | |
| Combined analysis(d) | P = 0.8548 | | | |
| Cochran-Armitage test(e) | P = 0.3413 | | | |
| Fisher Exact test(e) | | P = 0.1917 | P = 0.1045 | P = 0.2004 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : lymph node<br>TUMOR : malignant lymphoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 14/50( 28.0) | 15/50( 30.0) | 11/50( 22.0) | 7/49( 14.3) |
| Adjusted rates(b) | 21.05 | 22.73 | 12.00 | 3.13 |
| Terminal rates(c) | 6/31( 19.4) | 5/22( 22.7) | 3/25( 12.0) | 1/32( 3.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7107 | | | |
| Prevalence method(d) | P = 0.9972 | | | |
| Combined analysis(d) | P = 0.9797 | | | |
| Cochran-Armitage test(e) | P = 0.0524 | | | |
| Fisher Exact test(e) | | P = 0.4810 | P = 0.3777 | P = 0.1338 |
| | SITE : spleen<br>TUMOR : malignant lymphoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50( 12.0) | 4/50( 8.0) | 3/50( 6.0) | 4/49( 8.2) |
| Adjusted rates(b) | 15.15 | 18.18 | 4.00 | 12.50 |
| Terminal rates(c) | 4/31( 12.9) | 4/22( 18.2) | 1/25( 4.0) | 4/32( 12.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.6966 | | | |
| Prevalence method(d) | P = 0.6362 | | | |
| Combined analysis(d) | P = 0.7227 | | | |
| Cochran-Armitage test(e) | P = 0.6743 | | | |
| Fisher Exact test(e) | | P = 0.3944 | P = 0.2728 | P = 0.4066 |
| | SITE : liver<br>TUMOR : hemangioma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50( 0.0) | 1/50( 2.0) | 3/50( 6.0) | 1/49( 2.0) |
| Adjusted rates(b) | 0.0 | 4.55 | 12.00 | 2.56 |
| Terminal rates(c) | 0/31( 0.0) | 1/22( 4.5) | 3/25( 12.0) | 0/32( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = -------- | | | |
| Prevalence method(d) | P = 0.4140 | | | |
| Combined analysis(d) | P = -------- | | | |
| Cochran-Armitage test(e) | P = 0.7060 | | | |
| Fisher Exact test(e) | | P = 0.4950 | P = 0.1325 | P = 0.5000 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : liver | | | |
| | TUMOR : hepatocellular adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50( 4.0) | 3/50( 6.0) | 12/50( 24.0) | 10/49( 20.4) |
| Adjusted rates(b) | 6.45 | 12.00 | 40.00 | 28.57 |
| Terminal rates(c) | 2/31( 6.5) | 2/22( 9.1) | 10/25( 40.0) | 8/32( 25.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.0178* | | | |
| Combined analysis(d) | P = ------- | | | |
| Cochran-Armitage test(e) | P = 0.0123* | | | |
| Fisher Exact test(e) | | P = 0.4909 | P = 0.0106* | P = 0.0251* |
| | SITE : liver | | | |
| | TUMOR : hemangiosarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50( 4.0) | 0/50( 0.0) | 1/50( 2.0) | 4/49( 8.2) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 12.50 |
| Terminal rates(c) | 0/31( 0.0) | 0/22( 0.0) | 0/25( 0.0) | 4/32( 12.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8757 | | | |
| Prevalence method(d) | P = 0.0013** | | | |
| Combined analysis(d) | P = 0.0714 | | | |
| Cochran-Armitage test(e) | P = 0.0686 | | | |
| Fisher Exact test(e) | | P = 0.2574 | P = 0.4926 | P = 0.3483 |
| | SITE : liver | | | |
| | TUMOR : hepatocellular carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50( 2.0) | 5/50( 10.0) | 7/50( 14.0) | 5/49( 10.2) |
| Adjusted rates(b) | 3.23 | 9.68 | 24.00 | 15.63 |
| Terminal rates(c) | 1/31( 3.2) | 2/22( 9.1) | 6/25( 24.0) | 5/32( 15.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7586 | | | |
| Prevalence method(d) | P = 0.1597 | | | |
| Combined analysis(d) | P = 0.2776 | | | |
| Cochran-Armitage test(e) | P = 0.3545 | | | |
| Fisher Exact test(e) | | P = 0.1210 | P = 0.0430* | P = 0.1163 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : liver | | | |
| | TUMOR : hemangioma,hemangiosarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50( 4.0) | 1/50( 2.0) | 4/50( 8.0) | 5/49( 10.2) |
| Adjusted rates(b) | 0.0 | 4.55 | 12.00 | 12.82 |
| Terminal rates(c) | 0/31( 0.0) | 1/22( 4.5) | 3/25( 12.0) | 4/32( 12.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8757 | | | |
| Prevalence method(d) | P = 0.0190* | | | |
| Combined analysis(d) | P = 0.1049 | | | |
| Cochran-Armitage test(e) | P = 0.0974 | | | |
| Fisher Exact test(e) | | P = 0.4926 | P = 0.3574 | P = 0.2345 |
| | SITE : liver | | | |
| | TUMOR : hepatocellular adenoma,hepatocellular carcinoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 8/50( 16.0) | 16/50( 32.0) | 14/49( 28.6) |
| Adjusted rates(b) | 9.68 | 20.00 | 52.00 | 40.00 |
| Terminal rates(c) | 3/31( 9.7) | 4/22( 18.2) | 13/25( 52.0) | 12/32( 37.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7586 | | | |
| Prevalence method(d) | P = 0.0091** | | | |
| Combined analysis(d) | P = 0.0222* | | | |
| Cochran-Armitage test(e) | P = 0.0118* | | | |
| Fisher Exact test(e) | | P = 0.1322 | P = 0.0049** | P = 0.0104* |
| | SITE : pituitary gland | | | |
| | TUMOR : adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50( 10.0) | 6/49( 12.2) | 5/50( 10.0) | 4/49( 8.2) |
| Adjusted rates(b) | 16.13 | 22.73 | 20.00 | 9.38 |
| Terminal rates(c) | 5/31( 16.1) | 5/22( 22.7) | 5/25( 20.0) | 3/32( 9.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.2817 | | | |
| Prevalence method(d) | P = 0.8671 | | | |
| Combined analysis(d) | P = 0.7989 | | | |
| Cochran-Armitage test(e) | P = 0.6045 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.3710 | P = 0.4763 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : ovary<br>TUMOR : cystadenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50( 6.0) | 1/50( 2.0) | 1/50( 2.0) | 0/49( 0.0) |
| Adjusted rates(b) | 9.68 | 4.55 | 4.00 | 0.0 |
| Terminal rates(c) | 3/31( 9.7) | 1/22( 4.5) | 1/25( 4.0) | 0/32( 0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.9654 | | | |
| Combined analysis(d) | P = ------- | | | |
| Cochran-Armitage test(e) | P = 0.1147 | | | |
| Fisher Exact test(e) | | P = 0.3235 | P = 0.3235 | P = 0.1364 |
| | SITE : uterus<br>TUMOR : histiocytic sarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50( 16.0) | 13/50( 26.0) | 12/50( 24.0) | 15/49( 30.6) |
| Adjusted rates(b) | 5.71 | 14.29 | 12.50 | 18.92 |
| Terminal rates(c) | 1/31( 3.2) | 2/22( 9.1) | 3/25( 12.0) | 5/32( 15.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.4010 | | | |
| Prevalence method(d) | P = 0.0638 | | | |
| Combined analysis(d) | P = 0.1357 | | | |
| Cochran-Armitage test(e) | P = 0.1612 | | | |
| Fisher Exact test(e) | | P = 0.2265 | P = 0.2846 | P = 0.1293 |

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : Harderian gland | | | |
| | TUMOR : adenoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50( 2.0) | 4/50( 8.0) | 1/50( 2.0) | 1/49( 2.0) |
| Adjusted rates(b) | 3.23 | 18.18 | 4.00 | 3.13 |
| Terminal rates(c) | 1/31( 3.2) | 4/22( 18.2) | 1/25( 4.0) | 1/32( 3.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ------ | | | |
| Prevalence method(d) | P = 0.8072 | | | |
| Combined analysis(d) | P = ------ | | | |
| Cochran-Armitage test(e) | P = 0.4686 | | | |
| Fisher Exact test(e) | | P = 0.1998 | P = 0.2475 | P = 0.2525 |

(HPT360A)

BAIS3

(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 ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$

| Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|
| | SITE : ALL SITE<br>TUMOR : histiocytic sarcoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 10/50( 20.0) | 15/50( 30.0) | 16/50( 32.0) | 17/49( 34.7) |
| Adjusted rates(b) | 8.57 | 14.81 | 16.22 | 24.32 |
| Terminal rates(c) | 2/31( 6.5) | 2/22( 9.1) | 4/25( 16.0) | 7/32( 21.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5816 | | | |
| Prevalence method(d) | P = 0.0358* | | | |
| Combined analysis(d) | P = 0.1823 | | | |
| Cochran-Armitage test(e) | P = 0.1904 | | | |
| Fisher Exact test(e) | | P = 0.2516 | P = 0.2039 | P = 0.1527 |
| | SITE : ALL SITE<br>TUMOR : malignant lymphoma | | | |
| Tumor rate | | | | |
| Overall rates(a) | 21/50( 42.0) | 19/50( 38.0) | 14/50( 28.0) | 11/49( 22.4) |
| Adjusted rates(b) | 34.29 | 40.91 | 16.00 | 15.63 |
| Terminal rates(c) | 10/31( 32.3) | 9/22( 40.9) | 4/25( 16.0) | 5/32( 15.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8096 | | | |
| Prevalence method(d) | P = 0.9923 | | | |
| Combined analysis(d) | P = 0.9885 | | | |
| Cochran-Armitage test(e) | P = 0.0318* | | | |
| Fisher Exact test(e) | | P = 0.4682 | P = 0.2055 | P = 0.0983 |



(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 ≦ 0.05 ** : P ≦ 0.01

APPENDIX O 1

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY: SUMMARY)

RAT: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of Animals on Study | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | | 13 | 9 | 12 | 19 |
| [Respiratory system] | | | | | | |
| nasal cavit | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |
| lung | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 2 | 2 | 1 | 4 |
| | metastasis:adrenal tumor | | 0 | 1 | 0 | 0 |
| | metastasis:pancreas tumor | | 0 | 0 | 0 | 1 |
| | metastasis:kidney tumor | | 0 | 1 | 0 | 0 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 2 | 2 | 1 | 2 |
| lymph node | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 1 | 1 | 2 | 3 |
| [Circulatory system] | | | | | | |
| heart | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 1 | 1 | 1 | 0 |
| [Digestive system] | | | | | | |
| tongue | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| stomach | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |

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

| Organ | Findings | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|
| | Group Name | Control | 500ppm | 1500ppm | 4500ppm |
| | No. of Animals on Study | 13 | 9 | 12 | 19 |
| [Digestive system] | | | | | |
| small intes | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |
| large intes | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |
| liver | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 2 | 2 | 2 | 4 |
| pancreas | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |
| [Urinary system] | | | | | |
| kidney | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 0 | 2 | 2 | 2 |
| | metastasis:pancreas tumor | 0 | 0 | 0 | 1 |
| [Endocrine system] | | | | | |
| thyroid | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| adrenal | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 2 | 0 | 2 | 1 |
| [Reproductive system] | | | | | |
| mammary gl | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 1 | 0 | 0 | 0 |
| [Nervous system] | | | | | |
| brain | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | 0 | 1 | 1 | 0 |

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

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of Animals on Study | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | | 13 | 9 | 12 | 19 |
| [Nervous system] | | | | | | |
| brain | | | <13> | < 9> | <12> | <19> |
| | metastasis:kidney tumor | | 0 | 0 | 0 | 1 |
| spinal cord | | | <13> | < 9> | <12> | <19> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |

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

APPENDIX O 2

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY: SUMMARY)

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

| Organ | Findings | Group Name / No. of Animals on Study | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | | 6 | 12 | 6 | 13 |
| [Respiratory system] | | | | | | |
| nasal cavit | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| lung | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 6 | 3 | 0 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 5 | 4 | 2 |
| | metastasis:liver tumor | | 1 | 0 | 0 | 0 |
| lymph node | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 3 | 1 | 1 |
| | metastasis:tongue tumor | | 0 | 1 | 0 | 0 |
| | metastasis:ovary tumor | | 0 | 1 | 0 | 0 |
| | metastasis:oral cavity tumor | | 0 | 0 | 0 | 1 |
| spleen | | | < 6> | <12> | < 6> | <13> |
| | metastasis:bone marrow tumor | | 0 | 0 | 0 | 1 |
| [Circulatory system] | | | | | | |
| heart | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 3 | 1 | 0 |
| [Digestive system] | | | | | | |
| tongue | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 2 | 0 | 0 |

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

| Organ | Findings | Group Name / No. of Animals on Study | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | | 6 | 12 | 6 | 13 |
| [Digestive system] | | | | | | |
| tongue | | | < 6> | <12> | < 6> | <13> |
| | metastasis:oral cavity tumor | | 0 | 0 | 0 | 1 |
| salivary gl | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| stomach | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 2 | 0 | 1 |
| small intes | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| large intes | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| liver | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 2 | 6 | 4 | 2 |
| | metastasis:bone marrow tumor | | 0 | 0 | 0 | 1 |
| pancreas | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 3 | 0 | 0 |
| [Urinary system] | | | | | | |
| kidney | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 5 | 1 | 1 |
| | metastasis:ovary tumor | | 0 | 1 | 0 | 0 |
| [Endocrine system] | | | | | | |
| pituitary | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |

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

| Organ | Findings | Group Name / No. of Animals on Study | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | | 6 | 12 | 6 | 13 |
| [Endocrine system] | | | | | | |
| adrenal | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 5 | 3 | 1 |
| | metastasis:ovary tumor | | 0 | 1 | 0 | 0 |
| [Reproductive system] | | | | | | |
| ovary | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 3 | 1 | 1 |
| uterus | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 2 | 0 | 1 |
| | metastasis:ovary tumor | | 0 | 1 | 0 | 0 |
| mammary gl | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| [Nervous system] | | | | | | |
| brain | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 4 | 1 | 1 |
| spinal cord | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 3 | 1 | 0 |
| [Special sense organs/appandage] | | | | | | |
| Harder gl | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 2 | 0 | 1 |
| | metastasis:oral cavity tumor | | 0 | 0 | 0 | 1 |

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

| Organ | Findings | Group Name | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 6 | 12 | 6 | 13 |
| [Musculoskeletal system] | | | | | | |
| muscle | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| [Body cavities] | | | | | | |
| mediastinum | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 1 | 0 | 1 | 2 |
| retroperit | | | < 6> | <12> | < 6> | <13> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| | metastasis:ovary tumor | | 0 | 1 | 0 | 0 |

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

APPENDIX O 3

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY: SUMMARY)

RAT: MALE : SACRIFICED ANIMALS

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|
| | Group Name | Control | 500ppm | 1500ppm | 4500ppm |
| | No. of Animals on Study | 37 | 41 | 38 | 31 |
| [Respiratory system] | | | | | |
| lung | | <37> | <41> | <38> | <31> |
| | leukemic cell infiltration | 1 | 1 | 4 | 1 |
| | metastasis:liver tumor | 0 | 0 | 1 | 0 |
| | metastasis:bone tumor | 0 | 1 | 0 | 0 |
| | metastasis:spleen tumor | 0 | 1 | 0 | 0 |
| [Hematopoietic system] | | | | | |
| bone marrow | | <37> | <41> | <38> | <31> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| | metastasis:liver tumor | 0 | 0 | 1 | 0 |
| | metastasis:spleen tumor | 0 | 1 | 0 | 0 |
| lymph node | | <37> | <41> | <38> | <31> |
| | leukemic cell infiltration | 0 | 1 | 1 | 1 |
| | metastasis:liver tumor | 0 | 0 | 1 | 0 |
| | metastasis:urinary bladder tumor | 0 | 0 | 0 | 1 |
| [Digestive system] | | | | | |
| liver | | <37> | <41> | <38> | <31> |
| | leukemic cell infiltration | 0 | 2 | 5 | 0 |
| | metastasis:spleen tumor | 0 | 1 | 0 | 0 |
| [Urinary system] | | | | | |
| kidney | | <37> | <41> | <38> | <31> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |

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

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of Animals on Study | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | | 37 | 41 | 38 | 31 |
| [Endocrine system] | | | | | | |
| adrenal | | | <37> | <41> | <38> | <31> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |

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

APPENDIX O 4

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY: SUMMARY)

RAT: FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name / No. of Animals on Study | Control 44 | 500ppm 38 | 1500ppm 44 | 4500ppm 37 |
|---|---|---|---|---|---|---|
| [Respiratory system] | | | | | | |
| trachea | | | <44> | <38> | <44> | <37> |
| | metastasis:thyroid tumor | | 1 | 0 | 0 | 0 |
| lung | | | <44> | <38> | <44> | <37> |
| | leukemic cell infiltration | | 1 | 1 | 2 | 1 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <44> | <38> | <44> | <37> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 1 |
| lymph node | | | <44> | <38> | <44> | <37> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 2 |
| [Circulatory system] | | | | | | |
| heart | | | <44> | <38> | <44> | <37> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| [Digestive system] | | | | | | |
| liver | | | <44> | <38> | <44> | <37> |
| | leukemic cell infiltration | | 3 | 2 | 3 | 2 |
| | metastasis:uterus tumor | | 0 | 1 | 0 | 0 |
| [Urinary system] | | | | | | |
| kidney | | | <44> | <38> | <44> | <37> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| [Reproductive system] | | | | | | |
| ovary | | | <44> | <38> | <44> | <37> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |

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

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name / No. of Animals on Study | Control | 500ppm | 1500ppm | 4500ppm |
|---|---|---|---|---|---|---|
| | | | 44 | 38 | 44 | 37 |
| [Nervous system] | | | | | | |
| brain | | | <44> | <38> | <44> | <37> |
| | metastasis:pituitary tumor | | 2 | 1 | 1 | 0 |

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

# APPENDIX O 5

## HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY: SUMMARY)

## MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|
| Group Name | | Control | 667ppm | 2000ppm | 6000ppm |
| No. of Animals on Study | | 15 | 9 | 9 | 11 |
| [Respiratory system] | | | | | |
| nasal cavit | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 0 | 2 |
| | metastasis:periferal nerve tumor | 1 | 0 | 0 | 1 |
| trachea | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| lung | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 1 | 1 | 1 | 3 |
| | metastasis:liver tumor | 0 | 1 | 0 | 1 |
| [Hematopoietic system] | | | | | |
| bone marrow | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 1 | 0 | 1 |
| lymph node | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 1 | 0 | 0 |
| | metastasis:subcutis tumor | 0 | 0 | 1 | 0 |
| spleen | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 2 | 1 | 1 | 2 |
| | metastasis:liver tumor | 1 | 0 | 0 | 0 |
| [Circulatory system] | | | | | |
| heart | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 0 | 2 |
| [Digestive system] | | | | | |
| salivary gl | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |

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

| Organ | Findings | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|
| | Group Name | Control | 667ppm | 2000ppm | 6000ppm |
| | No. of Animals on Study | 15 | 9 | 9 | 11 |
| [Digestive system] | | | | | |
| salivary gl | | <15> | < 9> | < 9> | <11> |
| | metastasis:liver tumor | 0 | 1 | 0 | 0 |
| stomach | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |
| | metastasis:liver tumor | 1 | 0 | 0 | 0 |
| liver | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 1 | 2 | 2 |
| | metastasis:epididymis tumor | 0 | 0 | 1 | 0 |
| pancreas | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| [Urinary system] | | | | | |
| kidney | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 0 | 2 |
| urin bladd | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |
| | metastasis:liver tumor | 0 | 1 | 0 | 0 |
| [Endocrine system] | | | | | |
| adrenal | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| [Reproductive system] | | | | | |
| testis | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |

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

| Organ | Findings | Group Name / No. of Animals on Study | Control<br>15 | 667ppm<br>9 | 2000ppm<br>9 | 6000ppm<br>11 |
|---|---|---|---|---|---|---|
| [Reproductive system] | | | | | | |
| epididymis | | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 1 |
| prostate | | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| [Nervous system] | | | | | | |
| brain | | | <15> | < 9> | < 9> | <11> |
| | metastasis:periferal nerve tumor | | 1 | 0 | 0 | 1 |
| [Special sense organs/appandage] | | | | | | |
| eye | | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| Harder gl | | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| | metastasis:periferal nerve tumor | | 0 | 0 | 0 | 1 |
| [Musculoskeletal system] | | | | | | |
| muscle | | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| [Body cavities] | | | | | | |
| pleura | | | <15> | < 9> | < 9> | <11> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |

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

# APPENDIX O 6

## HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY : SUMMARY)

## MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

| Organ | Findings | Group Name / No. of Animals on Study | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| | | | 19 | 28 | 25 | 17 |
| [Integumentary system/appandage] | | | | | | |
| skin/app | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 2 | 0 | 0 |
| [Respiratory system] | | | | | | |
| nasal cavit | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 1 | 1 | 1 |
| | metastasis:periferal nerve tumor | | 0 | 1 | 0 | 0 |
| trachea | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 1 | 1 | 2 |
| lung | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 7 | 7 | 9 | 4 |
| | metastasis:liver tumor | | 1 | 2 | 1 | 0 |
| | metastasis:uterus tumor | | 2 | 3 | 1 | 4 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 5 | 1 | 2 | 2 |
| | metastasis:liver tumor | | 1 | 1 | 0 | 0 |
| | metastasis:uterus tumor | | 2 | 2 | 1 | 0 |
| lymph node | | | <19> | <28> | <25> | <17> |
| | metastasis:uterus tumor | | 1 | 0 | 1 | 1 |
| spleen | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 6 | 5 | 8 | 6 |

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

| Organ | Findings | Group Name / No. of Animals on Study | Control<br>19 | 667ppm<br>28 | 2000ppm<br>25 | 6000ppm<br>17 |
|---|---|---|---|---|---|---|
| [Hematopoietic system] | | | | | | |
| spleen | | | <19> | <28> | <25> | <17> |
| | metastasis:liver tumor | | 0 | 1 | 1 | 0 |
| | metastasis:uterus tumor | | 0 | 2 | 0 | 0 |
| [Circulatory system] | | | | | | |
| heart | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 4 | 1 | 2 | 1 |
| | metastasis:uterus tumor | | 1 | 0 | 1 | 0 |
| [Digestive system] | | | | | | |
| tongue | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 1 | 2 | 1 |
| salivary gl | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 4 | 3 | 6 | 0 |
| | metastasis:uterus tumor | | 1 | 0 | 0 | 0 |
| esophagus | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| stomach | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 5 | 4 | 3 | 1 |
| | metastasis:uterus tumor | | 1 | 1 | 1 | 3 |
| small intes | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| large intes | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |

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

| Organ | Findings | Group Name / No. of Animals on Study | Control 19 | 667ppm 28 | 2000ppm 25 | 6000ppm 17 |
|---|---|---|---|---|---|---|
| [Digestive system] | | | | | | |
| liver | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 5 | 4 | 8 | 3 |
| | metastasis:uterus tumor | | 5 | 7 | 5 | 7 |
| pancreas | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 3 | 5 | 1 |
| | metastasis:uterus tumor | | 1 | 1 | 3 | 0 |
| [Urinary system] | | | | | | |
| kidney | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 6 | 5 | 8 | 4 |
| | metastasis:uterus tumor | | 1 | 3 | 1 | 4 |
| urin bladd | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 3 | 3 | 4 | 0 |
| | metastasis:uterus tumor | | 1 | 4 | 0 | 0 |
| [Endocrine system] | | | | | | |
| pituitary | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| thyroid | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 1 | 0 |
| adrenal | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 3 | 1 | 5 | 1 |
| [Reproductive system] | | | | | | |
| ovary | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 7 | 4 | 6 | 5 |

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

| Organ | Findings | Group Name / No. of Animals on Study | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| | | | 19 | 28 | 25 | 17 |
| [Reproductive system] | | | | | | |
| ovary | | | <19> | <28> | <25> | <17> |
| | metastasis:liver tumor | | 1 | 0 | 0 | 0 |
| | metastasis:uterus tumor | | 4 | 4 | 4 | 7 |
| | metastasis:retroperitoneum tumor | | 0 | 0 | 1 | 0 |
| uterus | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 2 | 5 | 0 |
| vagina | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 1 | 2 | 0 |
| mammary gl | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 2 | 0 |
| [Nervous system] | | | | | | |
| brain | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 1 | 0 |
| | metastasis:periferal nerve tumor | | 0 | 1 | 0 | 0 |
| spinal cord | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 1 | 0 |
| [Special sense organs/appandage] | | | | | | |
| eye | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 3 | 0 | 2 | 0 |
| Harder gl | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 3 | 3 | 0 |

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

| Organ | Findings | Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 19 | 28 | 25 | 17 |
| [Musculoskeletal system] | | | | | | |
| muscle | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 2 | 4 | 3 | 1 |
| | metastasis:retroperitoneum tumor | | 0 | 0 | 1 | 0 |
| [Body cavities] | | | | | | |
| mediastinum | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| peritoneum | | | <19> | <28> | <25> | <17> |
| | leukemic cell infiltration | | 1 | 0 | 1 | 0 |

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

APPENDIX O 7

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0206
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|
| | Group Name | Control | 667ppm | 2000ppm | 6000ppm |
| | No. of Animals on Study | 35 | 41 | 41 | 39 |
| [Respiratory system] | | | | | |
| lung | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 1 | 1 | 2 | 1 |
| | metastasis:liver tumor | 1 | 0 | 0 | 1 |
| [Hematopoietic system] | | | | | |
| bone marrow | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 0 | 1 | 1 | 0 |
| spleen | | <35> | <40> | <41> | <39> |
| | leukemic cell infiltration | 0 | 4 | 3 | 3 |
| [Digestive system] | | | | | |
| stomach | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| small intes | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |
| liver | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 1 | 2 | 3 | 1 |
| pancreas | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| [Urinary system] | | | | | |
| kidney | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 1 | 1 | 1 | 2 |
| urin bladd | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | 0 | 1 | 0 | 0 |

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

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



| Organ | Findings | Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 35 | 41 | 41 | 39 |
| [Reproductive system] | | | | | | |
| prostate | | | <35> | <41> | <41> | <39> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| prep/cli gl | | | <35> | <41> | <41> | <39> |
| | metastasis:salivary gland tumor | | 0 | 0 | 1 | 0 |

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

APPENDIX O 8

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YERA STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 31 | 22 | 25 | 32 |
| [Integumentary system/appandage] | | | | | | |
| skin/app | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| [Respiratory system] | | | | | | |
| trachea | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| lung | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 4 | 4 | 1 | 1 |
| | metastasis:liver tumor | | 0 | 0 | 0 | 1 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 3 | 3 | 1 | 1 |
| spleen | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 2 | 4 | 3 | 1 |
| | metastasis:liver tumor | | 0 | 0 | 0 | 1 |
| [Digestive system] | | | | | | |
| tongue | | | <31> | <22> | <25> | <32> |
| | metastasis:subcutis tumor | | 0 | 0 | 1 | 0 |
| salivary gl | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 6 | 7 | 2 | 0 |
| | metastasis:uterus tumor | | 0 | 0 | 1 | 0 |

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

| Organ | Findings | Group Name / No. of Animals on Study | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|---|
| | | | 31 | 22 | 25 | 32 |
| [Digestive system] | | | | | | |
| stomach | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 2 | 1 | 1 | 1 |
| | metastasis:uterus tumor | | 0 | 0 | 0 | 1 |
| small intes | | | <31> | <22> | <25> | <32> |
| | metastasis:uterus tumor | | 0 | 0 | 0 | 1 |
| liver | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 4 | 3 | 1 | 1 |
| | metastasis:uterus tumor | | 0 | 1 | 1 | 1 |
| pancreas | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |
| | metastasis:uterus tumor | | 0 | 1 | 0 | 1 |
| [Urinary system] | | | | | | |
| kidney | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 1 | 3 | 1 | 2 |
| | metastasis:uterus tumor | | 0 | 1 | 0 | 0 |
| urin bladd | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 3 | 4 | 1 | 1 |
| [Endocrine system] | | | | | | |
| pituitary | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| adrenal | | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |

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

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



| Organ | Findings | Control | 667ppm | 2000ppm | 6000ppm |
|---|---|---|---|---|---|
| | Group Name | Control | 667ppm | 2000ppm | 6000ppm |
| | No. of Animals on Study | 31 | 22 | 25 | 32 |
| [Reproductive system] | | | | | |
| ovary | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | 0 | 1 | 1 | 0 |
| | metastasis:uterus tumor | 0 | 1 | 0 | 1 |
| uterus | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | 0 | 4 | 1 | 1 |
| vagina | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | 0 | 3 | 0 | 0 |
| [Body cavities] | | | | | |
| mediastinum | | <31> | <22> | <25> | <32> |
| | leukemic cell infiltration | 0 | 1 | 0 | 0 |
| adipose | | <31> | <22> | <25> | <32> |
| | metastasis:uterus tumor | 1 | 0 | 0 | 0 |

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

# APPENDIX P 1

# IDENTITY OF BIPHENYL

# (TOW-YERA STUDY)

IDENTITY OF BIPHENYL(TWO-YEAR STUDIES)

Test Substance Lot No. TWN6529

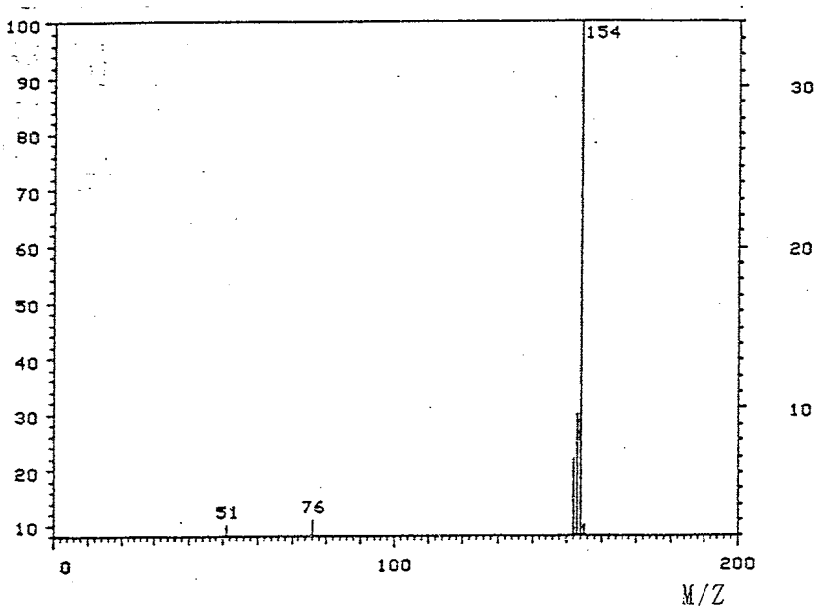
1. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV




Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with Literature spectrum.

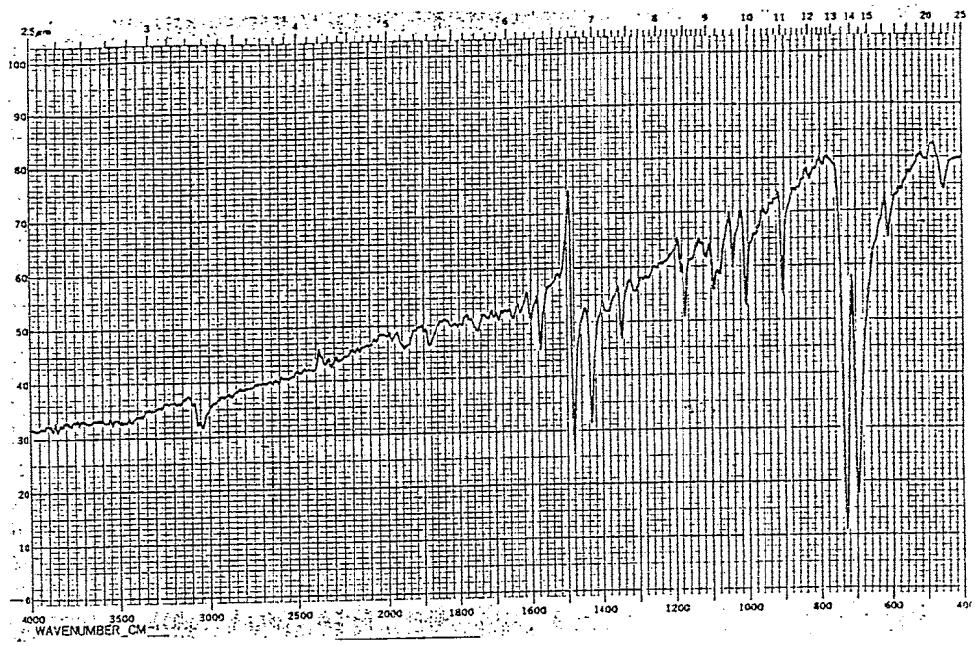
| Determined<br>Molecular and Fragment Peak(M/Z) | Literature Value*<br>Molecular and Fragment Peak(M/Z) |
|---|---|
| 154 | 154 |
| 76 | 76 |
| 51 | 51 |
| | (*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 529.) |

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium




Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| Determines | Literature Values* |
|---|---|
| Wave Number($cm^{-1}$) | Wave Number($cm^{-1}$) |
| 440～ 480 | 430～ 480 |
| 600～ 620 | 600～ 620 |
| 650～ 710 | 650～ 710 |
| 710～ 750 | 710～ 750 |
| 880～ 910 | 890～ 910 |
| 990～1020 | 990～1010 |
| 1020～1050 | 1020～1050 |
| 1050～1100 | 1050～1120 |
| 1150～1180 | 1150～1170 |
| 1330～1360 | 1330～1350 |
| 1400～1450 | 1400～1450 |
| 1460～1490 | 1460～1490 |
| 1550～1580 | 1550～1580 |
| 1730～1770 | 1730～1770 |
| 1870～1890 | 1860～1890 |
| 1930～1970 | 1930～1970 |
| 2990～3100 | 2990～3100 |
| | 3300～3500 |

(*Sadtler Handbook by Sadtler Research Laboratories, Inc. (1978) p. 68.)

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

# APPENDIX P 2

## STABILITY OF 1BIPHENYL

## (TOW-YERA STUDY)

STABILITY OF BIPHENYL(TWO-YEAR STUDIES)

Test Substance Lot No. TWN6529

1. Sample storage: This lot was used from 1992.6.1 to 1994.6.29. Test substance was stored in the dark at room temperature.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

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

| 1992.05.29(date analyzed) Wave Number($cm^{-1}$) | 1994.07.01(date analyzed) Wave Number($cm^{-1}$) |
|---|---|
| 440～ 480 | 440～ 480 |
| 600～ 620 | 600～ 620 |
| 650～ 710 | 650～ 710 |
| 710～ 750 | 710～ 750 |
| 880～ 910 | 880～ 910 |
| 990～1020 | 990～1020 |
| 1020～1050 | 1020～1050 |
| 1050～1100 | 1050～1100 |
| 1150～1180 | 1150～1180 |
| 1330～1360 | 1330～1360 |
| 1400～1450 | 1400～1450 |
| 1460～1490 | 1460～1490 |
| 1550～1580 | 1550～1580 |
| 1730～1770 | 1730～1770 |
| 1870～1890 | 1870～1890 |
| 1930～1970 | 1930～1970 |
| 2990～3100 | 2990～3100 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

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

Column Temperature : 180°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 $\mu$l

Results: Chromatogram indicated one major peak analyzed except solvent peak (acetone) at 1992.5.29 and one major peak analyzed except solvent peak(acetone) at 1994.7.1. No new trace impurity peak in the test substance analyzed at 1994.7.1 was detected.

| Date | Retention Time(min) | AREA |
|---|---|---|
| 1992.05.29 (date analyzed) | 3.752 | 682 |
| 1994.07.01 (date analyzed) | 3.752 | 675 |

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for 2 years).

# APPENDIX P 3

# CONCENTRATION OF BIPHENYL IN FORMULATED DIETS IN RAT

# (TOW-YERA STUDY)

CONCENTRATION OF BIPHENYL IN FORMULATED DIETS(TWO-YEAR STUDIES)

(Rat)

| | Target Concentration(ppm) | | |
|---|---|---|---|
| Date analyzed | 500 | 1500 | 4500 |
| 1992.05.29 | 444( 88.8)* | 1513(100.9) | 4146( 92.1) |
| 1992.08.31 | 434( 86.8) | 1362( 90.8) | 4198( 93.3) |
| 1992.11.17 | 484( 96.8) | 1425( 95.0) | 4245( 94.3) |
| 1993.02.25 | 467( 93.4) | 1438( 95.9) | 4229( 94.0) |
| 1993.05.24 | 470( 94.0) | 1371( 91.4) | 4103( 91.2) |
| 1993.09.10 | 455( 91.0) | 1380( 92.0) | 4232( 94.0) |
| 1993.12.13 | 431( 86.2) | 1417( 94.5) | 4426( 98.4) |
| 1994.03.30 | 473( 94.6) | 1436( 95.7) | 4234( 94.1) |

* : % of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mm$\phi$ × 50m)
Column Temperature: 180°C
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization detector)
Injection Volume : 1$\mu$l

# APPENDIX P 4

# CONCENTRATION OF BIPHENYL IN FORMULATED DIETS IN MOUSE

# (TOW-YERA STUDY)

CONCENTRATION OF BIPHENYL IN FORMULATED DIETS(TWO-YEAR STUDIES)

(Mouse)

| | Target Concentration(ppm) | | |
|---|---|---|---|
| Date analyzed | 667 | 2000 | 6000 |
| 1992.06.17 | 621( 93.1)* | 2236(111.8) | 5575( 92.9) |
| 1992.08.31 | 567( 85.0) | 1814( 90.7) | 5585( 93.1) |
| 1992.11.17 | 602( 90.3) | 1774( 88.7) | 5280( 88.0) |
| 1993.02.25 | 528( 79.2) | 1955( 97.8) | 5838( 97.3) |
| 1993.05.24 | 608( 91.2) | 1836( 91.8) | 5443( 90.7) |
| 1993.09.10 | 596( 89.4) | 1868( 93.4) | 5603( 93.4) |
| 1993.12.13 | 566( 84.9) | 1865( 93.3) | 5736( 95.6) |
| 1994.03.30 | 629( 94.3) | 1874( 93.7) | 5803( 96.7) |

* : % of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mm$\phi$ × 50m)
Column Temperature: 180°C
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization Detector)
Injection Volume : 1$\mu$l

# APPENDIX P 5

# STABILITY OF BIPHENYL IN FORMULATED DIETS

# (TOW-YERA STUDY)

STABILITY OF BIPHENYL IN FORMULATED DIETS(TWO-YEAR STUDIES)

(Rat)

| | Target Concentration(ppm) | | |
|---|---|---|---|
| Date analyzed | 500 | 1500 | 4500 |
| 1992.05.29(a) | 444 | 1513 | 4146 |
| 1992.10.23(b) | 458 | 1412 | 4181 |

(Mouse)

| | Target Concentration(ppm) | | |
|---|---|---|---|
| Date analyzed | 667 | 2000 | 6000 |
| 1992.06.17(a) | 621 | 2236 | 5575 |
| 1992.11.24(b) | 556 | 2152 | 5485 |

(a) Date of preparation
(b) The stability of biphenyl in formulated diets was established for 5 months when stored at 5°C.

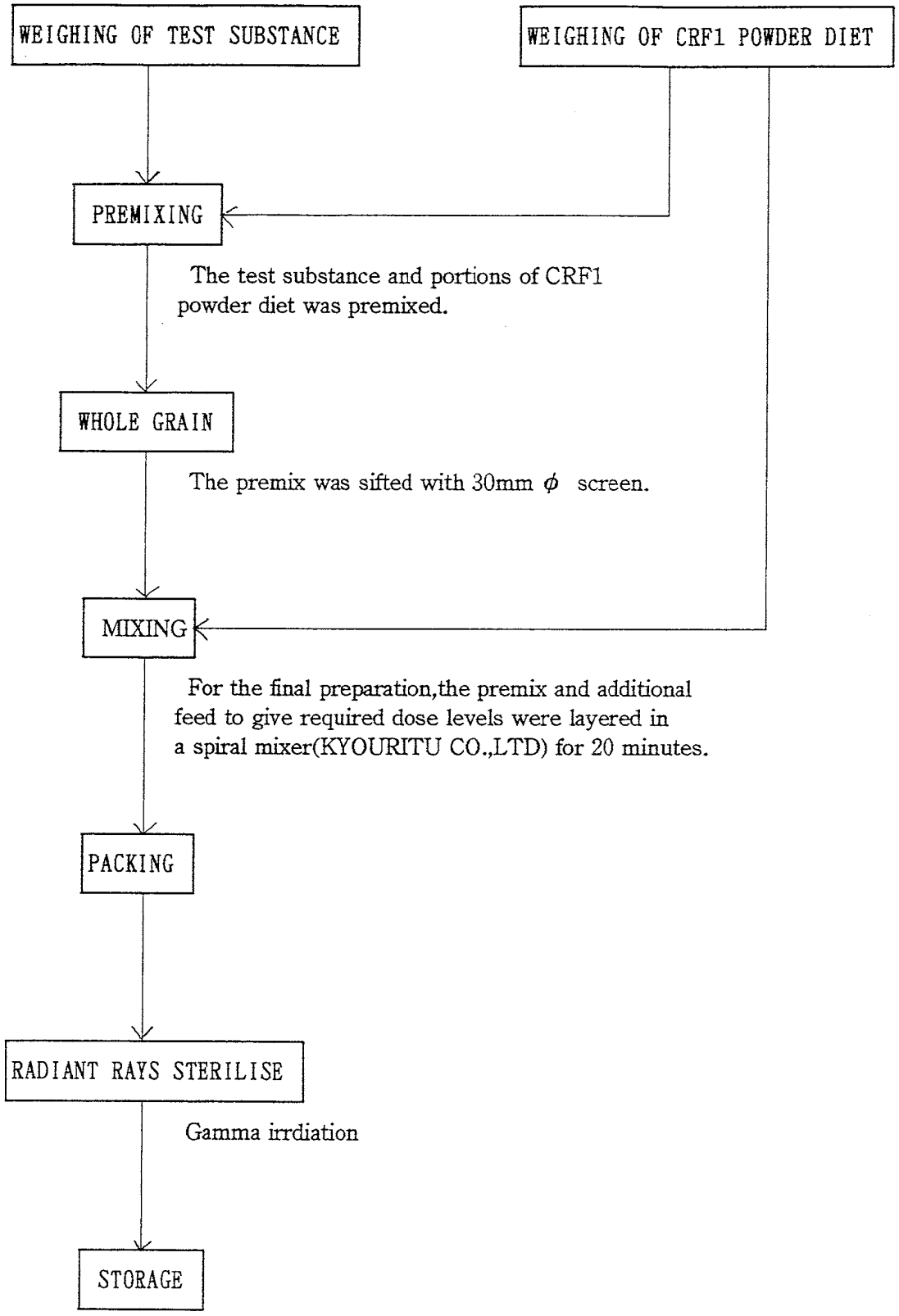
Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mm$\phi$ × 50m)
Column Temperature: 180°C
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization Detector)
Injection Volume : 1$\mu$l

# APPENDIX Q 1

# DOSE FORMULATIONS IN BIPHENYL

# DOSE FORMULATIONS OF BIPHENYL



# 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] | $\times 10^6/\mu l$ |
| Hemoglobin(Hgb) | Cyanmethohemoglobin method[1] | g/dl |
| Hematocrit(Hct) | Calculated as RBC × MCV/10[1] | % |
| Mean corpuscular volume(MCV) | Light scattering method[1] | fl |
| Mean corpuscular hemoglobin(MCHC) | Calculated as Hgb / RBC × 10[1] | pg |
| Mean corpuscular hemoglobin concentration(MCHC) | Calculated as Hgb / Hct × 100[1] | g/dl |
| Platelet | Light scattering method[1] | $\times 10^3/\mu l$ |
| Reticulocyte | Pattern recognition method[3] (New methyleneblue staining) | ‰ |
| Prothrombin time | Quick one stage method[2] | sec. |
| Activated partial thromboplastin time(APTT) | Ellagic acid activated method[2] | sec. |
| White blood cell(WBC) | Light scattering method[1] | $\times 10^3/\mu l$ |
| Differential WBC | Pattern recognition method[3] (May-Grunwald-Giemsa staining) | % |
| Biochemistry | | |
| Total protein(TP) | Biuret method[4] | g/dl |
| Albumin(Alb) | BCG method[4] | g/dl |
| A/G ratio | Calculated as Alb / (TP-Alb)[4] | |
| T-bilirubin | Alkaline azobilirubin method[4] | mg/dl |
| Glucose | Enzymatic method(GLK·G-6-PDH)[4] | mg/dl |
| T-cholesterol | Enzymatic method(CE·COD·POD)[4] | mg/dl |
| Triglyceride | Enzymatic method(LPL·GK·GPO·POD)[4] | mg/dl |
| Phospholipid | Enzymatic method(PLD·COD·POD)[4] | mg/dl |
| Glutamic oxaloacetic transaminase(GOT) | IFCC Method[4] | IU/l |
| Glutamic pyruvic transaminase(GPT) | IFCC Method[4] | IU/l |
| Lactate dehydrogenase(LDH) | Wroblewski-Ladue method[4] | IU/l |
| Alkaline phosphatase(ALP) | GSCC method[4] | IU/l |
| $\gamma$-Glutamyl transpeptidase(G-GTP) | L-$\gamma$-Glutamyl-p-nitroaniline substrate method[4] | IU/l |
| Creatine phosphokinase(CPK) | GSCC method[4] | IU/l |
| Urea nitrogen | Enzymatic method(Urease·GLDH)[4] | mg/dl |
| Creatinine | Jaffe method[4] | mg/dl |
| Sodium | Ion selective electrode method[4] | mEq/l |
| Potassium | Ion selective electrode method[4] | mEq/l |
| Chloride | Ion selective electrode method[4] | mEq/l |
| Calcium | OCPC method[4] | mg/dl |
| Inorganic phosphorus | Enzymatic method(PNP·XOD·POD)[4] | mg/dl |
| Urinalysis | | |
| pH, Protein, Glucose, Ketone body Bilirubin, Occult blood, Urobilinogen | Urinalysis reagent paper method[5] | |

1)Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation, USA)
2)Automatic coagulometer (Sysmex Ca-500 : Toa Medical Electronics Co., Ltd. , Japan)
3)Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, LTD. , Japan)
4)Automatic analyzer (Hitachi 7070 : Hitachi, LTD. , Japan)
5)Ames reagent strips for urinalysis (Multistix, Uro-Labstix : Bayer-Sankyo Co., LTD. , Japan)

# APPENDIX R 2

# UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

# UNIT AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

| | TEST ITEM | DECIMAL PLACE | UNIT |
|---|---|---|---|
| HEMATOLOGY | Red blood cell | 2 | $\times 10^6/\mu l$ |
| | Hemoglobin | 1 | g/dl |
| | Hematorcit | 1 | % |
| | MCV | 1 | fl |
| | MCH | 1 | pg |
| | MCHC | 1 | g/dl |
| | Platelet | 0 | $\times 10^3/\mu l$ |
| | Prothorombin time | 1 | sec. |
| | APTT | 1 | sec. |
| | White blood cell | 2 | $\times 10^3/\mu l$ |
| | Differential WBC | 0 | % |
| | Reticulocyte | 1 | ‰ |
| 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 | IU/l |
| | GPT | 0 | IU/l |
| | LDH | 0 | IU/l |
| | ALP | 0 | IU/l |
| | $\gamma$-GTP | 0 | IU/l |
| | CPK | 0 | IU/l |
| | Urea nitrogen | 1 | mEq/l |
| | Creatinine | 1 | mg/dl |
| | Sodium | 0 | mEq/l |
| | Potassium | 1 | mEq/l |
| | Chloride | 0 | mEq/l |
| | Calcium | 1 | mEq/l |
| | Inorganic phosphorus | 1 | mEq/l |