Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

Lab: BAT

Final 1\_Rats

NTP Study Number: C03038

**Lock Date:** 05/25/2016

Cage Range: ALL

Date Range: ALL

Reasons For Removal: ALL

Removal Date Range: ALL

Treatment Groups: Include ALL

Study Gender: Both

**TDMSE Version:** 3.0.2.3\_002

PWG Approval Date: NONE

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

# P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE  | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |
|----------------------------------|------------|--------------|--------------|---------------|
| Disposition Summary              |            |              |              |               |
| Animals Initially In Study       | 50         | 50           | 50           | 50            |
| Early Deaths                     |            |              |              |               |
| Moribund Sacrifice               | 17         | 14           | 10           | 8             |
| Natural Death                    | 21         | 10           | 16           | 13            |
| Survivors                        |            |              |              |               |
| Natural Death                    |            |              | 1            |               |
| Terminal Sacrifice               | 12         | 26           | 23           | 29            |
| Animals Examined Microscopically | 50         | 50           | 50           | 50            |
| ALIMENTARY SYSTEM                |            |              |              |               |
| Esophagus                        | (50)       | (50)         | (50)         | (50)          |
| Adventitia, Polyarteritis Nodosa | ,          | ,            | ,            | 1 (2%)        |
| Muscularis, Atrophy              |            |              | 1 (2%)       | , ,           |
| Intestine Large, Cecum           | (50)       | (50)         | (49)         | (50)          |
| Edema                            | ` ,        | 2 (4%)       | 2 (4%)       | ` ,           |
| Erosion                          | 1 (2%)     | ,            | ,            |               |
| Inflammation, Suppurative        | 1 (2%)     | 1 (2%)       |              |               |
| Inflammation, Acute              | 1 (2%)     | 2 (4%)       |              |               |
| Inflammation, Chronic            | 4 (8%)     | 2 (4%)       | 1 (2%)       |               |
| Inflammation, Chronic Active     | 1 (2%)     | 1 (2%)       | . ,          |               |
| Mineral                          | 4 (8%)     | 6 (12%)      |              |               |
| Lymphoid Tissue, Hyperplasia     | . ,        | . ,          |              | 1 (2%)        |
| Intestine Large, Colon           | (50)       | (50)         | (50)         | (50)          |
| Cyst, Multiple                   | 1 (2%)     |              | . ,          |               |
| Edema                            | . ,        | 1 (2%)       | 1 (2%)       |               |
| Inflammation, Acute              | 1 (2%)     | 1 (2%)       |              |               |
| Inflammation, Chronic            |            | 1 (2%)       |              |               |
| Inflammation, Chronic Active     |            | 1 (2%)       |              |               |
| Mineral                          |            | 1 (2%)       |              |               |
| Parasite Metazoan                | 2 (4%)     |              | 2 (4%)       | 2 (4%)        |
| Polyarteritis Nodosa             |            |              |              | 2 (4%)        |
| Lymphoid Tissue, Hyperplasia     |            |              | 1 (2%)       |               |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

# P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE                 | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |
|---|------------|--------------|--------------|---------------|
| Lymphoid Tissue, Inflammation,<br>Granulomatous |            |              | 1 (2%)       |               |
| Intestine Large, Rectum                         | (50)       | (50)         | (50)         | (50)          |
| Inflammation, Chronic                           | ,          | 1 (2%)       | ,            | ,             |
| Parasite Metazoan                               | 2 (4%)     | 5 (10%)      | 6 (12%)      | 8 (16%)       |
| Polyarteritis Nodosa                            | ,          | ,            | ,            | 1 (2%)        |
| Intestine Small, Duodenum                       | (50)       | (50)         | (50)         | (50)          |
| Inflammation, Chronic                           | 1 (2%)     | 1 (2%)       | ,            | 1 (2%)        |
| Inflammation, Chronic Active                    | ( /        | ( )          | 1 (2%)       | ( /           |
| Polyarteritis Nodosa                            |            |              | 1 (2%)       |               |
| Epithelium, Hyperplasia                         |            |              | ,            | 1 (2%)        |
| Intestine Small, Ileum                          | (50)       | (50)         | (49)         | (50)          |
| Inflammation, Chronic                           | 2 (4%)     | ν/           | ( - /        | · /           |
| Inflammation, Chronic Active                    | ,          | 1 (2%)       |              |               |
| Polyarteritis Nodosa                            | 1 (2%)     | ,            |              |               |
| Peyer's Patch, Hyperplasia                      | , ,        | 1 (2%)       |              |               |
| Intestine Small, Jejunum                        | (50)       | (50)         | (50)         | (50)          |
| Diverticulum                                    | ,          | 1 (2%)       | ,            | ,             |
| Peyer's Patch, Hyperplasia                      |            | 2 (4%)       | 3 (6%)       | 1 (2%)        |
| Liver   | (50)       | (50)         | (50)         | (50)          |
| Angiectasis                                     | ,          | ,            | 1 (2%)       | ,             |
| Basophilic Focus                                | 2 (4%)     | 2 (4%)       | ,            | 1 (2%)        |
| Clear Cell Focus                                | 14 (28%)   | 23 (46%)     | 21 (42%)     | 25 (50%)      |
| Congestion                                      | 1 (2%)     | , ,          | ` ,          | , ,           |
| Degeneration, Cystic                            | . ,        |              | 2 (4%)       |               |
| Eosinophilic Focus                              | 3 (6%)     |              | . ,          |               |
| Extramedullary Hematopoiesis                    |            | 1 (2%)       |              | 2 (4%)        |
| Fatty Change, Diffuse                           | 1 (2%)     |              | 1 (2%)       | 1 (2%)        |
| Hepatodiaphragmatic Nodule                      | 1 (2%)     | 1 (2%)       |              |               |
| Inclusion Body Intracytoplasmic                 | 1 (2%)     |              |              |               |
| Infiltration Cellular, Plasma Cell              | . ,        | 1 (2%)       |              |               |
| Inflammation, Chronic                           | 1 (2%)     |              | 1 (2%)       | 2 (4%)        |
| Inflammation, Chronic Active                    |            |              | •            | 2 (4%)        |
| Mixed Cell Focus                                | 3 (6%)     |              | 4 (8%)       | 4 (8%)        |
| Pigment   |            |              | 2 (4%)       | 1 (2%)        |
| Polyarteritis Nodosa                            |            | 1 (2%)       |              | 2 (4%)        |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

# P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

**Date Report Requested:** 02/28/2019 **Time Report Requested:** 13:33:08 **First Dose M/F:** 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE         | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |
|---|------------|--------------|--------------|---------------|
| Thrombus                                | 1 (2%)     |              |              |               |
| Artery, Hyperplasia                     | ,          | 1 (2%)       |              |               |
| Bile Duct, Cyst                         | 1 (2%)     | 1 (2%)       |              |               |
| Bile Duct, Hyperplasia                  | 42 (84%)   | 38 (76%)     | 43 (86%)     | 41 (82%)      |
| Centrilobular, Hepatocyte, Degeneration | ,          | ,            | ,            | 1 (2%)        |
| Hepatocyte, Degeneration                |            |              |              | 1 (2%)        |
| Hepatocyte, Fatty Change, Focal         | 4 (8%)     | 1 (2%)       |              | 1 (2%)        |
| Hepatocyte, Fatty Change, Diffuse       | , ,        | 1 (2%)       |              | , ,           |
| Hepatocyte, Hyperplasia                 |            |              | 1 (2%)       |               |
| Hepatocyte, Hypertrophy                 |            |              | 1 (2%)       | 1 (2%)        |
| Hepatocyte, Karyomegaly                 |            |              | , ,          | 1 (2%)        |
| Hepatocyte, Necrosis                    | 4 (8%)     | 2 (4%)       | 1 (2%)       | , ,           |
| Hepatocyte, Vacuolation, Cytoplasmic    |            |              | 2 (4%)       |               |
| Oval Cell, Hyperplasia                  | 1 (2%)     |              | 1 (2%)       | 2 (4%)        |
| Mesentery                               | (2)        | (5)          | (2)          | (3)           |
| Hemorrhage                              |            |              | 1 (50%)      |               |
| Polyarteritis Nodosa                    | 2 (100%)   | 3 (60%)      | 1 (50%)      | 2 (67%)       |
| Thrombus                                |            | 1 (20%)      |              |               |
| Artery, Inflammation                    |            | 1 (20%)      |              |               |
| Pancreas                                | (50)       | (50)         | (50)         | (50)          |
| Basophilic Focus                        |            | 1 (2%)       |              |               |
| Cytoplasmic Alteration                  |            | 1 (2%)       |              |               |
| Inflammation, Chronic Active            |            | 1 (2%)       |              |               |
| Polyarteritis Nodosa                    | 5 (10%)    | 1 (2%)       | 4 (8%)       | 4 (8%)        |
| Thrombus                                | 1 (2%)     |              |              | 1 (2%)        |
| Acinus, Atrophy                         | 5 (10%)    | 1 (2%)       | 3 (6%)       | 3 (6%)        |
| Acinus, Hyperplasia                     | 22 (44%)   | 19 (38%)     | 22 (44%)     | 21 (42%)      |
| Artery, Mineral                         |            |              |              | 1 (2%)        |
| Duct, Cyst                              | 1 (2%)     |              | 1 (2%)       |               |
| Salivary Glands                         | (50)       | (50)         | (50)         | (50)          |
| Mineral                                 | 1 (2%)     |              |              |               |
| Stomach, Forestomach                    | (50)       | (50)         | (50)         | (50)          |
| Edema                                   |            | 1 (2%)       |              | 1 (2%)        |
| Inflammation, Acute                     | 2 (4%)     |              |              |               |
| Inflammation, Chronic                   | 1 (2%)     | 1 (2%)       |              | 1 (2%)        |
| Inflammation, Chronic Active            | 1 (2%)     |              | 1 (2%)       | 1 (2%)        |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |  |
|---------------------------------|------------|--------------|--------------|---------------|--|
| Mineral                         | 2 (4%)     | 1 (2%)       |              |               |  |
| Ulcer                           | 2 (4%)     | 3 (6%)       |              |               |  |
| Epithelium, Hyperplasia         | 3 (6%)     |              | 1 (2%)       | 1 (2%)        |  |
| Stomach, Glandular              | (50)       | (50)         | (50)         | (50)          |  |
| Mineral                         | 20 (40%)   | 21 (42%)     | 8 (16%)      | 11 (22%)      |  |
| Polyarteritis Nodosa            | 1 (2%)     | ,            | ,            | 1 (2%)        |  |
| Glands, Ectasia                 | ,          |              | 1 (2%)       | ,             |  |
| Tongue                          | (0)        | (1)          | (1)          | (0)           |  |
| Epithelium, Hyperplasia         | ( )        | 1 (100%)     | ( )          | ( )           |  |
| CARDIOVASCULAR SYSTEM           |            |              |              |               |  |
| Blood Vessel                    | (50)       | (50)         | (49)         | (49)          |  |
| Inflammation, Chronic Active    | , ,        | 1 (2%)       | ,            | ,             |  |
| Mineral                         | 15 (30%)   | 9 (18%)      | 1 (2%)       |               |  |
| Polyarteritis Nodosa            | 1 (2%)     | ,            | ,            |               |  |
| Heart                           | (50)       | (50)         | (50)         | (50)          |  |
| Cardiomyopathy                  | 47 (94%)   | 45 (90%)     | 44 (88%)     | 45 (90%)      |  |
| Hemorrhage                      | (          | ()           | (/           | 1 (2%)        |  |
| Inflammation, Suppurative       |            | 1 (2%)       |              | ( /           |  |
| Inflammation, Chronic           |            | (-/-/        |              | 1 (2%)        |  |
| Inflammation, Chronic Active    |            |              |              | 1 (2%)        |  |
| Mineral                         | 13 (26%)   | 6 (12%)      |              | 1 (2%)        |  |
| Polyarteritis Nodosa            | 1 (2%)     | 0 (1270)     |              | 2 (4%)        |  |
| Thrombus                        | . (=/3)    | 2 (4%)       |              | 1 (2%)        |  |
| ENDOCRINE SYSTEM                |            |              |              |               |  |
| Adrenal Cortex                  | (50)       | (50)         | (50)         | (50)          |  |
| Atrophy                         | , ,        | . ,          | , ,          | 2 (4%)        |  |
| Degeneration, Cystic            | 2 (4%)     | 1 (2%)       | 1 (2%)       | 1 (2%)        |  |
| Hyperplasia, Focal              | 21 (42%)   | 28 (56%)     | 17 (34%)     | 27 (54%)      |  |
| Hypertrophy, Focal              | 20 (40%)   | 17 (34%)     | 21 (42%)     | 18 (36%)      |  |
| Karyomegaly                     | 2 (4%)     | 3 (6%)       | 5 (10%)      | ,             |  |
| Mineral                         | 1 (2%)     | , ,          | ,            |               |  |

a - Number of animals examined microscopically at site and number of animals with lesion

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

Experiment Number: 03038 - 03

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| larian Sprague Dawley RATS MALE         | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |
|---|------------|--------------|--------------|---------------|
| Necrosis                                | 2 (4%)     | 4 (8%)       |              |               |
| Pigment                                 | 1 (2%)     | 1 (2%)       |              | 1 (2%)        |
| Thrombus                                |            | 2 (4%)       | 2 (4%)       | 1 (2%)        |
| Vacuolation, Cytoplasmic                | 1 (2%)     | , ,          | , ,          | 1 (2%)        |
| Bilateral, Hyperplasia, Focal           | 5 (10%)    | 3 (6%)       | 6 (12%)      | 10 (20%)      |
| Bilateral, Hypertrophy, Focal           | 1 (2%)     | 4 (8%)       | 2 (4%)       | 5 (10%)       |
| Adrenal Medulla                         | (50)       | (50)         | (50)         | (50)          |
| Hyperplasia, Focal                      | 18 (36%)   | 11 (22%)     | 13 (26%)     | 13 (26%)      |
| Infiltration Cellular, Mononuclear Cell |            | 1 (2%)       |              |               |
| Necrosis                                |            | 1 (2%)       |              |               |
| Thrombus                                | 1 (2%)     | 1 (2%)       |              |               |
| Vacuolation, Cytoplasmic                |            |              | 1 (2%)       |               |
| Bilateral, Hyperplasia, Focal           | 4 (8%)     | 3 (6%)       | 5 (10%)      | 2 (4%)        |
| Islets, Pancreatic                      | (50)       | (50)         | (50)         | (50)          |
| Hyperplasia                             |            | 1 (2%)       |              |               |
| Parathyroid Gland                       | (43)       | (45)         | (45)         | (45)          |
| Hyperplasia, Focal                      |            | 3 (7%)       |              | 4 (9%)        |
| Hyperplasia, Diffuse                    | 39 (91%)   | 34 (76%)     | 34 (76%)     | 28 (62%)      |
| Polyarteritis Nodosa                    |            |              |              | 1 (2%)        |
| Pituitary Gland                         | (50)       | (50)         | (50)         | (50)          |
| Pars Distalis, Atrophy                  |            |              |              | 2 (4%)        |
| Pars Distalis, Cyst                     | 1 (2%)     |              | 1 (2%)       |               |
| Pars Distalis, Hyperplasia              | 14 (28%)   | 18 (36%)     | 21 (42%)     | 14 (28%)      |
| Pars Distalis, Hypertrophy              |            | 2 (4%)       |              |               |
| Pars Distalis, Karyomegaly              | 1 (2%)     |              |              |               |
| Pars Distalis, Pigment                  |            |              |              | 1 (2%)        |
| Pars Intermedia, Hyperplasia            |            |              | 1 (2%)       |               |
| Pars Nervosa, Degeneration              |            | 1 (2%)       |              |               |
| Pars Nervosa, Vacuolation, Cytoplasmic  | 1 (2%)     |              |              |               |
| Rathke's Cleft, Cyst                    | 1 (2%)     |              |              |               |
| Thyroid Gland                           | (50)       | (50)         | (50)         | (50)          |
| Infiltration Cellular, Mononuclear Cell |            | 1 (2%)       |              |               |
| C-cell, Hyperplasia                     | 5 (10%)    | 12 (24%)     | 9 (18%)      | 7 (14%)       |
| Epithelium, Follicle, Hyperplasia       | 1 (2%)     |              |              |               |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE                           | 0mg/L male          | 250mg/L male        | 500mg/L male        | 1000mg/L male      |  |
|---|---------------------|---------------------|---------------------|--------------------|--|
| GENERAL BODY SYSTEM                                       |                     |                     |                     |                    |  |
| None  |                     |                     |                     |                    |  |
| GENITAL SYSTEM  |                     |                     |                     |                    |  |
| Epididymis<br>Granuloma Sperm                             | (50)                | (50)                | (50)<br>1 (2%)      | (49)               |  |
| Hypospermia<br>Mesothelium, Cyst                          | 14 (28%)            | 14 (28%)            | 11 (22%)<br>1 (2%)  | 12 (24%)           |  |
| Penis Congestion  | (0)                 | (0)                 | (1)<br>1 (100%)     | (0)                |  |
| Preputial Gland<br>Cyst                                   | (50)                | (50)                | (50)<br>1 (2%)      | (50)               |  |
| Inflammation, Suppurative Inflammation, Chronic Active    | 1 (2%)              | 1 (2%)              |                     |                    |  |
| Prostate Decreased Secretory Fluid                        | (50)<br>2 (4%)      | (50)                | (50)                | (50)<br>4 (8%)     |  |
| Inflammation, Chronic Active Epithelium, Hyperplasia      | 3 (6%)              | 1 (2%)<br>4 (8%)    | 3 (6%)              | 1 (2%)<br>3 (6%)   |  |
| Seminal Vesicle Decreased Secretory Fluid                 | (50)<br>9 (18%)     | (50)<br>5 (10%)     | (50)<br>5 (10%)     | (50)<br>7 (14%)    |  |
| Inflammation, Chronic Inflammation, Chronic Active Testis | (50)                | 1 (2%)<br>1 (2%)    | 1 (2%)<br>(50)      | 2 (4%)<br>(49)     |  |
| Edema<br>Hemorrhage                                       | (50)<br>1 (2%)      | (50)                | (50)                | 1 (2%)             |  |
| Polyarteritis Nodosa Germ Cell, Degeneration              | 28 (56%)<br>8 (16%) | 31 (62%)<br>6 (12%) | 26 (52%)<br>9 (18%) | 24 (49%)<br>4 (8%) |  |
| HEMATOPOIETIC SYSTEM                                      |                     |                     |                     |                    |  |
| Bone Marrow Hypercellularity                              | (50)<br>1 (2%)      | (50)                | (50)                | (50)               |  |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER

Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| larlan Sprague Dawley RATS MALE           | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |  |
|---|------------|--------------|--------------|---------------|--|
| Lymph Node                                | (3)        | (5)          | (3)          | (3)           |  |
| Bronchial, Hemorrhage                     |            | 1 (20%)      |              |               |  |
| Lumbar, Hemorrhage                        |            | 2 (40%)      |              |               |  |
| Lumbar, Hyperplasia, Plasma Cell          |            | 1 (20%)      |              |               |  |
| Lumbar, Infiltration Cellular, Histiocyte |            | 1 (20%)      |              |               |  |
| Lumbar, Lymphatic Sinus, Dilation         |            |              |              | 2 (67%)       |  |
| Lymphatic Sinus, Mediastinal, Dilation    | 1 (33%)    |              |              |               |  |
| Mediastinal, Hemorrhage                   |            | 2 (40%)      | 1 (33%)      |               |  |
| Mediastinal, Pigment                      |            |              | 1 (33%)      |               |  |
| Pancreatic, Hyperplasia, Lymphocyte       | 1 (33%)    |              | 1 (33%)      | 1 (33%)       |  |
| Pancreatic, Inflammation, Suppurative     | 1 (33%)    |              |              |               |  |
| Pancreatic, Necrosis                      | 1 (33%)    |              |              |               |  |
| Renal, Hyperplasia, Plasma Cell           |            | 1 (20%)      |              |               |  |
| Lymph Node, Mandibular                    | (50)       | (50)         | (50)         | (50)          |  |
| Atrophy                                   | 1 (2%)     |              |              |               |  |
| Congestion                                |            |              |              | 1 (2%)        |  |
| Hyperplasia, Lymphocyte                   |            | 2 (4%)       |              |               |  |
| Hyperplasia, Plasma Cell                  | 24 (48%)   | 35 (70%)     | 40 (80%)     | 40 (80%)      |  |
| Infiltration Cellular, Histiocyte         |            |              |              | 1 (2%)        |  |
| Inflammation, Chronic                     | 1 (2%)     |              |              |               |  |
| Inflammation, Chronic Active              | 1 (2%)     |              |              |               |  |
| Pigment                                   | 1 (2%)     | 1 (2%)       |              |               |  |
| Lymphatic Sinus, Dilation                 | 4 (8%)     | 13 (26%)     | 8 (16%)      | 6 (12%)       |  |
| Lymph Node, Mesenteric                    | (50)       | (50)         | (50)         | (49)          |  |
| Hemorrhage                                | 1 (2%)     | 1 (2%)       | 1 (2%)       | 1 (2%)        |  |
| Hyperplasia, Plasma Cell                  |            | 1 (2%)       | 1 (2%)       |               |  |
| Infiltration Cellular, Histiocyte         | 3 (6%)     | 3 (6%)       | 1 (2%)       |               |  |
| Inflammation, Suppurative                 |            |              | 1 (2%)       |               |  |
| Pigment                                   |            |              | 1 (2%)       | 1 (2%)        |  |
| Lymphatic Sinus, Dilation                 |            |              | 1 (2%)       | 1 (2%)        |  |
| Spleen                                    | (50)       | (50)         | (50)         | (50)          |  |
| Atrophy                                   | 1 (2%)     |              |              |               |  |
| Extramedullary Hematopoiesis              | 5 (10%)    | 9 (18%)      | 7 (14%)      | 4 (8%)        |  |
| Lymphocyte, Hyperplasia                   | 1 (2%)     | 7 (14%)      | 2 (4%)       | 2 (4%)        |  |
| White Pulp, Atrophy                       | 2 (4%)     | 4 (8%)       | 6 (12%)      | 2 (4%)        |  |
| Thymus                                    | (48)       | (48)         | (49)         | (50)          |  |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |  |
|---------------------------------|------------|--------------|--------------|---------------|--|
|                                 |            |              |              |               |  |
| Atrophy                         | 1 (2%)     |              |              |               |  |
| NTEGUMENTARY SYSTEM             |            |              |              |               |  |
| Mammary Gland                   | (48)       | (47)         | (50)         | (49)          |  |
| Inflammation, Chronic           |            | 1 (2%)       |              |               |  |
| Mineral                         | 1 (2%)     |              |              |               |  |
| Duct, Dilation                  | 1 (2%)     | 1 (2%)       | 1 (2%)       | 1 (2%)        |  |
| Skin                            | (50)       | (50)         | (50)         | (50)          |  |
| Congestion                      |            |              | 1 (2%)       |               |  |
| Cyst Epithelial Inclusion       | 3 (6%)     | 2 (4%)       | 2 (4%)       | 3 (6%)        |  |
| Fibrosis                        | 1 (2%)     |              | 1 (2%)       |               |  |
| Inflammation, Suppurative       |            |              | 1 (2%)       |               |  |
| Inflammation, Chronic           |            | 1 (2%)       | 1 (2%)       | 1 (2%)        |  |
| Inflammation, Chronic Active    | 1 (2%)     | 1 (2%)       | 1 (2%)       | 1 (2%)        |  |
| Ulcer                           | 1 (2%)     | , ,          | 1 (2%)       | 2 (4%)        |  |
| Epithelium, Hyperkeratosis      | , ,        |              | 1 (2%)       | , ,           |  |
| Epithelium, Hyperplasia         |            | 1 (2%)       | 2 (4%)       |               |  |
| Sebaceous Gland, Cyst           |            | , ,          | 1 (2%)       |               |  |
| MUSCULOSKELETAL SYSTEM          |            |              |              |               |  |
| Bone                            | (50)       | (50)         | (50)         | (50)          |  |
| Fibrous Osteodystrophy          | 1 (2%)     | ()           | ()           | ()            |  |
| Inflammation, Chronic Active    | ( - / 3 /  |              | 1 (2%)       |               |  |
| Maxilla, Cyst                   |            |              | 1 (2%)       |               |  |
| Skeletal Muscle                 | (0)        | (1)          | (0)          | (0)           |  |
| Inflammation, Chronic           | (-)        | 1 (100%)     | (-)          | (-)           |  |
| NERVOUS SYSTEM                  |            |              |              |               |  |
| Brain                           | (50)       | (50)         | (50)         | (50)          |  |
| Cyst Epithelial Inclusion       | 1 (2%)     | (30)         | (00)         | (50)          |  |
| Hemorrhage                      | 1 (270)    |              |              | 1 (2%)        |  |
| петногтаде                      |            |              |              | 1 (2%)        |  |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

# P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE                        | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |
|--|------------|--------------|--------------|---------------|
| Glial Cell, Hyperplasia                                | 1 (2%)     |              |              |               |
| Meninges, Fibrosis                                     | , ,        | 1 (2%)       |              |               |
| Neuron, Degeneration                                   |            | , ,          | 1 (2%)       |               |
| Peripheral Nerve                                       | (1)        | (3)          | (0)          | (0)           |
| Spinal Cord  | (1)        | (1)          | (0)          | (0)           |
| Axon, Degeneration                                     | 1 (100%)   | · ,          | , ,          | . ,           |
| RESPIRATORY SYSTEM                                     |            |              |              |               |
| Lung   | (50)       | (50)         | (50)         | (50)          |
| Congestion   | 2 (4%)     | •            |              | •             |
| Hemorrhage   | 5 (10%)    | 3 (6%)       |              | 1 (2%)        |
| Infiltration Cellular, Histiocyte                      | 21 (42%)   | 23 (46%)     | 17 (34%)     | 20 (40%)      |
| Inflammation, Acute                                    |            |              | 1 (2%)       |               |
| Inflammation, Chronic                                  | 12 (24%)   | 15 (30%)     | 16 (32%)     | 8 (16%)       |
| Inflammation, Chronic Active                           | 2 (4%)     |              | 1 (2%)       | 1 (2%)        |
| Mineral  | 2 (4%)     | 1 (2%)       | ·            | 1 (2%)        |
| Polyarteritis Nodosa                                   | •          | 1 (2%)       |              | •             |
| Alveolar Epithelium, Hyperplasia                       | 1 (2%)     |              | 2 (4%)       | 3 (6%)        |
| Arteriole, Hyperplasia                                 | •          |              | 1 (2%)       | ·             |
| Nose   | (50)       | (50)         | (50)         | (50)          |
| Edema  |            | 1 (2%)       |              |               |
| Inflammation, Suppurative                              |            |              | 1 (2%)       |               |
| Inflammation, Acute                                    |            | 2 (4%)       | 1 (2%)       | 1 (2%)        |
| Inflammation, Chronic Active                           | 1 (2%)     |              |              |               |
| Metaplasia, Osseous, Focal                             |            |              | 1 (2%)       |               |
| Glands, Respiratory Epithelium, Inflammation, Acute    |            |              | 1 (2%)       |               |
| Goblet Cell, Nasopharyngeal Duct, Hyperplasia          | 4 (8%)     | 14 (28%)     | 7 (14%)      | 10 (20%)      |
| Goblet Cell, Respiratory Epithelium,<br>Hyperplasia    | 16 (32%)   | 19 (38%)     | 14 (28%)     | 17 (34%)      |
| Nasolacrimal Duct, Inflammation, Acute                 |            | 1 (2%)       |              |               |
| Olfactory Epithelium, Accumulation, Hyaline<br>Droplet | 42 (84%)   | 46 (92%)     | 46 (92%)     | 44 (88%)      |
| Olfactory Epithelium, Degeneration                     | 1 (2%)     |              |              |               |
| Olfactory Epithelium, Inflammation, Acute              |            | 2 (4%)       |              |               |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

|   | 0mg/L male                                     | 250mg/L male   | 500mg/L male               | 1000mg/L male                                |  |
|---|--|--|----------------------------|--|--|
| Olfactory Epithelium, Inflammation, Chronic Active  |  | 1 (2%)   |                            |  |  |
| Olfactory Epithelium, Necrosis  |  | 1 (2%)   |                            |  |  |
| Olfactory Epithelium, Vacuolation, Cytoplasmic  |  | 3 (6%)   |                            |  |  |
| Respiratory Epithelium, Accumulation, Hyaline<br>Droplet  |  | , ,  |                            | 1 (2%)                                       |  |
| Respiratory Epithelium, Inflammation, Acute   | 2 (4%)   | 2 (4%)   | 1 (2%)                     | 5 (10%)                                      |  |
| Respiratory Epithelium, Inflammation, Chronic   | 1 (2%)   | 1 (2%)   | 1 (2%)                     |  |  |
| Respiratory Epithelium, Inflammation, Chronic Active  |  | 2 (4%)   |                            | 1 (2%)                                       |  |
| Respiratory Epithelium, Necrosis  |  |  |                            | 1 (2%)                                       |  |
| Respiratory Epithelium, Vacuolation, Cytoplasmic  | 1 (2%)   |  |                            |  |  |
| Septum, Inflammation, Chronic   | 1 (2%)   |  |                            |  |  |
| Trachea   | (50)   | (50)   | (50)                       | (50)   |  |
| Inflammation, Acute   |  |  | 1 (2%)                     |  |  |
| Inflammation, Chronic   | 1 (2%)   | 1 (2%)   |                            | 1 (2%)                                       |  |
|   |  |  |                            |  |  |
| SPECIAL SENSES SYSTEM   | (50)   | (50)   | (50)                       | (50)   |  |
| Eye   | (50)<br>1 (2%)                                 | (50)   | (50)                       | (50)   |  |
| Eye<br>Phthisis Bulbi   | (50)<br>1 (2%)                                 | , ,  | (50)                       | (50)   |  |
| Eye<br>Phthisis Bulbi<br>Cornea, Hyperplasia  | 1 (2%)   | 1 (2%)   |                            | (50)   |  |
| Eye<br>Phthisis Bulbi<br>Cornea, Hyperplasia<br>Cornea, Inflammation, Acute   | 1 (2%)<br>4 (8%)                               | 1 (2%)<br>1 (2%)   | 1 (2%)                     | ` '  |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic  | 1 (2%)<br>4 (8%)<br>3 (6%)                     | 1 (2%)<br>1 (2%)<br>1 (2%)                                       | 1 (2%)<br>3 (6%)           | 2 (4%)                                       |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic Cornea, Inflammation, Chronic Active   | 1 (2%)<br>4 (8%)                               | 1 (2%)<br>1 (2%)   | 1 (2%)                     | 2 (4%)<br>1 (2%)                             |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic Cornea, Inflammation, Chronic Active Lens, Cataract  | 1 (2%) 4 (8%) 3 (6%) 3 (6%)                    | 1 (2%)<br>1 (2%)<br>1 (2%)                                       | 1 (2%)<br>3 (6%)           | 2 (4%)                                       |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic Cornea, Inflammation, Chronic Active Lens, Cataract Retina, Dysplasia                                      | 1 (2%) 4 (8%) 3 (6%) 3 (6%) 1 (2%)             | 1 (2%)<br>1 (2%)<br>1 (2%)<br>2 (4%)                             | 1 (2%)<br>3 (6%)<br>3 (6%) | 2 (4%)<br>1 (2%)<br>2 (4%)                   |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic Cornea, Inflammation, Chronic Active Lens, Cataract  | 1 (2%) 4 (8%) 3 (6%) 3 (6%)                    | 1 (2%)<br>1 (2%)<br>1 (2%)<br>2 (4%)                             | 1 (2%)<br>3 (6%)           | 2 (4%)<br>1 (2%)                             |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic Cornea, Inflammation, Chronic Active Lens, Cataract Retina, Dysplasia Harderian Gland Fibrosis             | 1 (2%) 4 (8%) 3 (6%) 3 (6%) 1 (2%) (50)        | 1 (2%)<br>1 (2%)<br>1 (2%)<br>2 (4%)<br>(50)<br>1 (2%)           | 1 (2%)<br>3 (6%)<br>3 (6%) | 2 (4%)<br>1 (2%)<br>2 (4%)<br>(50)           |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic Cornea, Inflammation, Chronic Active Lens, Cataract Retina, Dysplasia Harderian Gland                      | 1 (2%) 4 (8%) 3 (6%) 3 (6%) 1 (2%)             | 1 (2%)<br>1 (2%)<br>1 (2%)<br>2 (4%)                             | 1 (2%)<br>3 (6%)<br>3 (6%) | 2 (4%)<br>1 (2%)<br>2 (4%)                   |  |
| Eye Phthisis Bulbi Cornea, Hyperplasia Cornea, Inflammation, Acute Cornea, Inflammation, Chronic Cornea, Inflammation, Chronic Active Lens, Cataract Retina, Dysplasia Harderian Gland Fibrosis Hyperplasia | 1 (2%) 4 (8%) 3 (6%) 3 (6%) 1 (2%) (50) 2 (4%) | 1 (2%)<br>1 (2%)<br>1 (2%)<br>2 (4%)<br>(50)<br>1 (2%)<br>1 (2%) | 1 (2%)<br>3 (6%)<br>3 (6%) | 2 (4%)<br>1 (2%)<br>2 (4%)<br>(50)<br>3 (6%) |  |

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS MALE         | 0mg/L male | 250mg/L male | 500mg/L male | 1000mg/L male |
|---|------------|--------------|--------------|---------------|
| Inflammation, Chronic                   |            | 1 (2%)       |              |               |
| Mineral                                 | 13 (26%)   | 11 (22%)     | 2 (4%)       | 4 (8%)        |
| Nephropathy, Chronic Progressive        | 50 (100%)  | 50 (100%)    | 50 (100%)    | 49 (98%)      |
| Thrombus                                | 1 (2%)     |              |              |               |
| Capsule, Fibrosis                       |            |              | 1 (2%)       |               |
| Epithelium, Renal Tubule, Hyperplasia   |            | 1 (2%)       |              |               |
| Pelvis, Dilation                        | 31 (62%)   | 24 (48%)     | 16 (32%)     | 17 (34%)      |
| Renal Tubule, Atypical Hyperplasia      | 1 (2%)     |              |              |               |
| Renal Tubule, Dilation                  |            | 1 (2%)       |              |               |
| Renal Tubule, Inflammation, Suppurative | 25 (50%)   | 33 (66%)     | 35 (70%)     | 41 (82%)      |
| Renal Tubule, Regeneration              |            | 1 (2%)       |              |               |
| Urothelium, Hyperplasia                 | 1 (2%)     |              |              |               |
| Urinary Bladder                         | (50)       | (50)         | (50)         | (50)          |
| Calculus Gross Observation              |            |              | 1 (2%)       |               |
| Hemorrhage                              |            | 1 (2%)       |              |               |
| Inflammation, Acute                     |            |              |              | 1 (2%)        |
| Inflammation, Chronic                   | 1 (2%)     | 1 (2%)       | 1 (2%)       | 1 (2%)        |
| Inflammation, Chronic Active            |            | 1 (2%)       |              |               |
| Serosa, Inflammation, Chronic Active    | 1 (2%)     |              |              |               |
| Urothelium, Hyperplasia                 |            | 1 (2%)       |              |               |
| Urothelium, Hyperplasia, Atypical       |            |              | 1 (2%)       |               |

<sup>\*\*\*</sup> END OF MALE \*\*\*

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

# P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS FEMALE | 0mg/L female | 250mg/L female | 500mg/L female | 1000mg/L female |
|-----------------------------------|--------------|----------------|----------------|-----------------|
| Disposition Summary               |              |                |                |                 |
| Animals Initially In Study        | 50           | 50             | 50             | 50              |
| Early Deaths                      |              |                |                |                 |
| Moribund Sacrifice                | 13           | 10             | 13             | 9               |
| Natural Death                     | 7            | 7              | 6              | 10              |
| Survivors                         |              |                |                |                 |
| Moribund Sacrifice                |              |                |                | 1               |
| Terminal Sacrifice                | 30           | 33             | 31             | 30              |
| Animals Examined Microscopically  | 50           | 50             | 50             | 50              |
| ALIMENTARY SYSTEM                 |              |                |                |                 |
| Esophagus                         | (50)         | (50)           | (49)           | (50)            |
| Intestine Large, Cecum            | (50)         | (50)           | (50)           | (49)            |
| Edema                             | 1 (2%)       | 1 (2%)         | . ,            |                 |
| Epithelium, Hyperplasia           |              |                | 1 (2%)         | 2 (4%)          |
| Intestine Large, Colon            | (50)         | (50)           | (50)           | (50)            |
| Parasite Metazoan                 |              | 1 (2%)         | 3 (6%)         | 2 (4%)          |
| Polyarteritis Nodosa              |              |                | 1 (2%)         | . ,             |
| Lymphoid Tissue, Hyperplasia      | 3 (6%)       | 1 (2%)         | 1 (2%)         | 2 (4%)          |
| Intestine Large, Rectum           | (50)         | (50)           | (50)           | (50)            |
| Parasite Metazoan                 | 5 (10%)      | 6 (12%)        | 2 (4%)         | 8 (16%)         |
| Lymphoid Tissue, Hyperplasia      |              |                | 1 (2%)         |                 |
| Intestine Small                   | (1)          | (0)            | (0)            | (0)             |
| Intestine Small, Duodenum         | (50)         | (50)           | (50)           | (50)            |
| Peyer's Patch, Hyperplasia        |              |                |                | 1 (2%)          |
| Intestine Small, Ileum            | (50)         | (50)           | (50)           | (49)            |
| Peyer's Patch, Hyperplasia        |              |                |                | 1 (2%)          |
| Intestine Small, Jejunum          | (50)         | (50)           | (50)           | (50)            |
| Peyer's Patch, Hyperplasia        | 1 (2%)       | 2 (4%)         | 2 (4%)         | 2 (4%)          |
| Liver                             | (50)         | (50)           | (50)           | (50)            |
| Angiectasis                       | 2 (4%)       |                |                |                 |
| Clear Cell Focus                  | 8 (16%)      | 12 (24%)       | 3 (6%)         | 7 (14%)         |
| Congestion                        | 1 (2%)       |                |                |                 |
| Eosinophilic Focus                | 2 (4%)       |                |                | 2 (4%)          |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS FEMALE       | 0mg/L female | 250mg/L female | 500mg/L female | 1000mg/L female |  |
|---|--------------|----------------|----------------|-----------------|--|
| Extramedullary Hematopoiesis            | 1 (2%)       | 2 (4%)         |                | 1 (2%)          |  |
| Fatty Change, Diffuse                   | 2 (4%)       | 1 (2%)         |                | , ,             |  |
| Fibrosis                                |              |                | 1 (2%)         |                 |  |
| Mixed Cell Focus                        | 2 (4%)       | 8 (16%)        | 2 (4%)         | 1 (2%)          |  |
| Pigment                                 |              |                |                | 1 (2%)          |  |
| Bile Duct, Cholangiofibrosis            |              |                | 1 (2%)         | , ,             |  |
| Bile Duct, Cyst                         | 2 (4%)       |                | 1 (2%)         | 3 (6%)          |  |
| Bile Duct, Hyperplasia                  | 1 (2%)       | 5 (10%)        | 2 (4%)         | 4 (8%)          |  |
| Centrilobular, Hepatocyte, Degeneration | ,            | ,              | ,              | 1 (2%)          |  |
| Centrilobular, Hepatocyte, Fatty Change |              | 1 (2%)         |                |                 |  |
| Centrilobular, Hepatocyte, Hypertrophy  |              | ,              |                | 1 (2%)          |  |
| Hepatocyte, Fatty Change, Focal         | 3 (6%)       | 1 (2%)         |                | 1 (2%)          |  |
| Hepatocyte, Necrosis                    | 1 (2%)       | 1 (2%)         | 1 (2%)         |                 |  |
| Hepatocyte, Vacuolation, Cytoplasmic    | 1 (2%)       | ,              | ,              |                 |  |
| Serosa, Fibrosis                        | 1 (2%)       |                |                |                 |  |
| Mesentery                               | (1)          | (0)            | (1)            | (2)             |  |
| Polyarteritis Nodosa                    | ( )          | ( )            | ( )            | 1 (50%)         |  |
| Fat, Necrosis                           |              |                |                | 1 (50%)         |  |
| Pancreas                                | (50)         | (50)           | (50)           | (50)            |  |
| Basophilic Focus                        | ( )          | 1 (2%)         | ,              |                 |  |
| Polyarteritis Nodosa                    | 1 (2%)       | ,              | 1 (2%)         | 2 (4%)          |  |
| Acinus, Atrophy                         | 1 (2%)       | 4 (8%)         | ,              | 1 (2%)          |  |
| Acinus, Hyperplasia                     | 5 (10%)      | 5 (10%)        |                | 5 (10%)         |  |
| Acinus, Inflammation, Acute             | ,            | 1 (2%)         |                | ,               |  |
| Salivary Glands                         | (50)         | (50)           | (49)           | (50)            |  |
| Stomach, Forestomach                    | (50)         | (50)           | (50)           | (50)            |  |
| Inflammation, Acute                     | ()           | 1 (2%)         | 2 (4%)         | ()              |  |
| Inflammation, Chronic                   | 1 (2%)       | ( /            | ( /            |                 |  |
| Inflammation, Chronic Active            | 1 (2%)       |                |                |                 |  |
| Mineral                                 | 1 (2%)       |                | 1 (2%)         |                 |  |
| Ulcer                                   | 1 (2%)       | 2 (4%)         | (/             |                 |  |
| Epithelium, Hyperplasia                 | 3 (6%)       | 1 (2%)         | 2 (4%)         |                 |  |
| Stomach, Glandular                      | (50)         | (50)           | (50)           | (50)            |  |
| Erosion                                 | ()           | (/             | (/             | 1 (2%)          |  |
| Mineral                                 | 3 (6%)       | 4 (8%)         |                | 2 (4%)          |  |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS FEMALE       | 0mg/L female | 250mg/L female | 500mg/L female | 1000mg/L female |  |
|---|--------------|----------------|----------------|-----------------|--|
|   |              |                |                |                 |  |
| CARDIOVASCULAR SYSTEM                   |              |                |                |                 |  |
| Blood Vessel                            | (50)         | (50)           | (50)           | (49)            |  |
| Mineral                                 | 1 (2%)       |                |                |                 |  |
| Heart                                   | (50)         | (50)           | (49)           | (50)            |  |
| Cardiomyopathy                          | 29 (58%)     | 25 (50%)       | 23 (47%)       | 23 (46%)        |  |
| Mineral                                 | 1 (2%)       |                | 1 (2%)         |                 |  |
| ENDOCRINE SYSTEM                        |              |                |                |                 |  |
| Adrenal Cortex                          | (50)         | (50)           | (50)           | (50)            |  |
| Angiectasis                             | 7 (14%)      | 3 (6%)         | 2 (4%)         | , ,             |  |
| Atrophy                                 | ,            | 1 (2%)         | ,              |                 |  |
| Degeneration, Cystic                    | 2 (4%)       | 3 (6%)         | 2 (4%)         | 2 (4%)          |  |
| Extramedullary Hematopoiesis            | , ,          | 1 (2%)         | 2 (4%)         | ,               |  |
| Hemorrhage                              |              | ,              | 1 (2%)         |                 |  |
| Hyperplasia, Focal                      | 7 (14%)      | 11 (22%)       | 15 (30%)       | 9 (18%)         |  |
| Hypertrophy, Focal                      | 15 (30%)     | 19 (38%)       | 14 (28%)       | 17 (34%)        |  |
| Infiltration Cellular, Mononuclear Cell | 1 (2%)       | ,              | ,              | ,               |  |
| Necrosis                                | 1 (2%)       |                | 1 (2%)         |                 |  |
| Pigment                                 | 1 (2%)       |                | ,              |                 |  |
| Thrombus                                | 1 (2%)       |                | 1 (2%)         | 1 (2%)          |  |
| Bilateral, Hyperplasia, Focal           | 4 (8%)       | 6 (12%)        | 3 (6%)         | 4 (8%)          |  |
| Bilateral, Hypertrophy, Focal           | 3 (6%)       | 4 (8%)         | 2 (4%)         | 4 (8%)          |  |
| Adrenal Medulla                         | (50)         | (50)           | (50)           | (50)            |  |
| Hyperplasia, Focal                      | 12 (24%)     | 11 (22%)       | 9 (18%)        | 9 (18%)         |  |
| Pigment                                 | ,            | 1 (2%)         | ,              | ,               |  |
| Thrombus                                | 2 (4%)       | ,              |                |                 |  |
| Bilateral, Hyperplasia, Focal           | 1 (2%)       | 3 (6%)         |                | 2 (4%)          |  |
| Islets, Pancreatic                      | (50)         | (50)           | (50)           | (50)            |  |
| Parathyroid Gland                       | (46)         | (47)           | (44)           | (44)            |  |
| Angiectasis                             | 1 (2%)       | ,              | , ,            | ,               |  |
| Hyperplasia, Focal                      | 2 (4%)       | 1 (2%)         | 4 (9%)         | 3 (7%)          |  |
| Hyperplasia, Diffuse                    | 3 (7%)       | 7 (15%)        | 8 (18%)        | 8 (18%)         |  |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

Lab: BAT

| Harlan Sprague Dawley RATS FEMALE       | 0mg/L female | 250mg/L female | 500mg/L female | 1000mg/L female |
|---|--------------|----------------|----------------|-----------------|
| Pituitary Gland                         | (50)         | (50)           | (50)           | (50)            |
| Pigment                                 | 1 (2%)       |                |                |                 |
| Pars Distalis, Atrophy                  |              |                | 1 (2%)         |                 |
| Pars Distalis, Hyperplasia              | 19 (38%)     | 18 (36%)       | 17 (34%)       | 21 (42%)        |
| Pars Distalis, Pigment                  |              |                | 1 (2%)         |                 |
| Pars Distalis, Vacuolation, Cytoplasmic | 1 (2%)       |                |                |                 |
| Pars Intermedia, Angiectasis            |              |                |                | 1 (2%)          |
| Pars Intermedia, Hyperplasia            |              |                |                | 1 (2%)          |
| Pars Intermedia, Pigment                |              | 1 (2%)         |                | 1 (2%)          |
| Thyroid Gland                           | (50)         | (50)           | (49)           | (50)            |
| C-cell, Hyperplasia                     | 14 (28%)     | 13 (26%)       | 9 (18%)        | 12 (24%)        |

## **GENERAL BODY SYSTEM**

None

| Clitoral Gland               | (50)    | (50)    | (50)     | (49)    |
|------------------------------|---------|---------|----------|---------|
| Inflammation, Chronic Active |         | 1 (2%)  |          |         |
| Duct, Cyst                   |         | 1 (2%)  |          |         |
| Ovary                        | (50)    | (50)    | (50)     | (50)    |
| Cyst                         | 2 (4%)  |         |          | 3 (6%)  |
| Inflammation, Chronic Active |         |         |          | 1 (2%)  |
| Bursa, Cyst                  | 1 (2%)  | 1 (2%)  | 1 (2%)   | 3 (6%)  |
| Follicle, Cyst               | 5 (10%) | 8 (16%) | 4 (8%)   | 7 (14%) |
| Paraovarian Tissue, Cyst     | 1 (2%)  |         | 1 (2%)   | 1 (2%)  |
| Uterus                       | (50)    | (50)    | (50)     | (50)    |
| Adenomyosis                  |         | 2 (4%)  |          |         |
| Atrophy                      |         |         |          | 1 (2%)  |
| Cyst                         |         |         |          | 2 (4%)  |
| Cyst, Squamous               |         |         |          | 1 (2%)  |
| Dilation                     | 1 (2%)  |         | 2 (4%)   | 2 (4%)  |
| Hemorrhage                   |         |         | 2 (4%)   |         |
| Hyperplasia, Atypical        | 4 (8%)  | 7 (14%) | 19 (38%) | 8 (16%) |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

# P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS FEMALE   | 0mg/L female                                | 250mg/L female                                  | 500mg/L female            | 1000mg/L female           |
|---|---|---|---------------------------|---------------------------|
| Hyperplasia, Stromal  | 1 (2%)                                      |   |                           |                           |
| Inflammation, Suppurative   |   |   |                           | 2 (4%)                    |
| Inflammation, Acute   |   |   |                           | 1 (2%)                    |
| Inflammation, Chronic   |   |   | 1 (2%)                    |                           |
| Inflammation, Chronic Active  |   |   | 3 (6%)                    | 3 (6%)                    |
| Pigment   | 1 (2%)                                      |   |                           |                           |
| Squamous Metaplasia   | 29 (58%)                                    | 23 (46%)  | 32 (64%)                  | 26 (52%)                  |
| Thrombus  | 1 (2%)                                      |   |                           | 1 (2%)                    |
| Cervix, Squamous Metaplasia   | 1 (2%)                                      |   |                           |                           |
| Cervix, Epithelium, Hyperplasia   | 2 (4%)                                      |   |                           |                           |
| Endometrium, Hyperplasia, Cystic  | 32 (64%)                                    | 25 (50%)  | 34 (68%)                  | 27 (54%)                  |
| Myometrium, Malformation  | ` '   | • •   | 1 (2%)                    | • •                       |
| Vagina  | (49)  | (50)  | (50)                      | (50)                      |
| Inflammation, Acute   | , ,   | 1 (2%)  | , ,                       | ,                         |
| Inflammation, Chronic Active  | 1 (2%)                                      |   |                           |                           |
| HEMATOPOIETIC SYSTEM  Bone Marrow   | (50)  | (50)  | (50)                      | (50)                      |
| Lymph Node  | (0)   | (2)   | (1)                       | (2)                       |
| Lymphitode  | (3)   | (3)   | (1)                       | ( <del>-</del> )          |
| Lumbar, Hemorrhage  | (3)   | 1 (33%)   | (1)                       | (2)                       |
| • •   | (3)<br>1 (33%)                              |   | (1)                       | (2)                       |
| Lumbar, Hemorrhage  |   |   | (1)                       | 1 (50%)                   |
| Lumbar, Hemorrhage<br>Lumbar, Hyperplasia, Lymphocyte   |   |   | (1)                       |                           |
| Lumbar, Hemorrhage<br>Lumbar, Hyperplasia, Lymphocyte<br>Lumbar, Hyperplasia, Plasma Cell   | 1 (33%)                                     |   | (1)                       |                           |
| Lumbar, Hemorrhage<br>Lumbar, Hyperplasia, Lymphocyte<br>Lumbar, Hyperplasia, Plasma Cell<br>Lumbar, Infiltration Cellular, Neutrophil  | 1 (33%)<br>1 (33%)                          |   | (1)                       |                           |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment   | 1 (33%)<br>1 (33%)                          | 1 (33%)   | (1)                       |                           |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment Lumbar, Lymphatic Sinus, Dilation   | 1 (33%)<br>1 (33%)                          | 1 (33%)<br>1 (33%)                              | (49)                      |                           |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment Lumbar, Lymphatic Sinus, Dilation Renal, Hyperplasia, Lymphocyte  | 1 (33%)<br>1 (33%)<br>1 (33%)               | 1 (33%)<br>1 (33%)<br>1 (33%)                   |                           | 1 (50%)                   |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment Lumbar, Lymphatic Sinus, Dilation Renal, Hyperplasia, Lymphocyte Lymph Node, Mandibular   | 1 (33%)<br>1 (33%)<br>1 (33%)               | 1 (33%)<br>1 (33%)<br>1 (33%)                   | (49)                      | 1 (50%)                   |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment Lumbar, Lymphatic Sinus, Dilation Renal, Hyperplasia, Lymphocyte Lymph Node, Mandibular Hemorrhage  | 1 (33%)<br>1 (33%)<br>1 (33%)<br>(50)       | 1 (33%)<br>1 (33%)<br>1 (33%)<br>(50)           | (49)                      | 1 (50%)                   |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment Lumbar, Lymphatic Sinus, Dilation Renal, Hyperplasia, Lymphocyte Lymph Node, Mandibular Hemorrhage Hyperplasia, Lymphocyte  | 1 (33%) 1 (33%) 1 (33%) (50) 3 (6%)         | 1 (33%)<br>1 (33%)<br>1 (33%)<br>(50)<br>1 (2%) | (49)<br>1 (2%)            | 1 (50%)                   |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment Lumbar, Lymphatic Sinus, Dilation Renal, Hyperplasia, Lymphocyte Lymph Node, Mandibular Hemorrhage Hyperplasia, Lymphocyte Hyperplasia, Plasma Cell                                   | 1 (33%) 1 (33%) 1 (33%) (50) 3 (6%) 7 (14%) | 1 (33%)<br>1 (33%)<br>1 (33%)<br>(50)<br>1 (2%) | (49)<br>1 (2%)            | 1 (50%)<br>(50)<br>2 (4%) |
| Lumbar, Hemorrhage Lumbar, Hyperplasia, Lymphocyte Lumbar, Hyperplasia, Plasma Cell Lumbar, Infiltration Cellular, Neutrophil Lumbar, Pigment Lumbar, Lymphatic Sinus, Dilation Renal, Hyperplasia, Lymphocyte Lymph Node, Mandibular Hemorrhage Hyperplasia, Lymphocyte Hyperplasia, Plasma Cell Infiltration Cellular, Histiocyte | 1 (33%) 1 (33%) 1 (33%) (50) 3 (6%) 7 (14%) | 1 (33%)<br>1 (33%)<br>1 (33%)<br>(50)<br>1 (2%) | (49)<br>1 (2%)<br>5 (10%) | 1 (50%)<br>(50)<br>2 (4%) |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS FEMALE | 0mg/L female | 250mg/L female | 500mg/L female | 1000mg/L female |  |
|-----------------------------------|--------------|----------------|----------------|-----------------|--|
| Atrophy                           |              | 2 (4%)         |                |                 |  |
| Hemorrhage                        |              |                | 1 (2%)         |                 |  |
| Infiltration Cellular, Histiocyte | 8 (16%)      | 3 (6%)         | 1 (2%)         | 1 (2%)          |  |
| Lymphatic Sinus, Dilation         |              | 1 (2%)         |                | 1 (2%)          |  |
| Spleen                            | (50)         | (50)           | (50)           | (50)            |  |
| Extramedullary Hematopoiesis      | 18 (36%)     | 11 (22%)       | 14 (28%)       | 14 (28%)        |  |
| Fibrosis                          | 1 (2%)       |                |                |                 |  |
| Hemorrhage                        | , ,          |                |                | 1 (2%)          |  |
| Hyperplasia, Lymphocyte           |              | 1 (2%)         |                | , ,             |  |
| Infarct                           | 1 (2%)       | , ,            | 1 (2%)         |                 |  |
| Lymphocyte, Hyperplasia           | 7 (14%)      | 1 (2%)         | ,              | 1 (2%)          |  |
| Red Pulp, Atrophy                 | 1 (2%)       | ,              |                | ,               |  |
| White Pulp, Atrophy               | 1 (2%)       | 2 (4%)         | 3 (6%)         |                 |  |
| Thymus                            | (47)         | (49)           | (49)           | (50)            |  |
| Cyst                              | ,            | , ,            | 1 (2%)         | 1 (2%)          |  |
| INTEGUMENTARY SYSTEM              |              |                |                |                 |  |
| Mammary Gland                     | (50)         | (50)           | (50)           | (50)            |  |
| Hyperplasia                       | 2 (4%)       | 2 (4%)         | 1 (2%)         | 3 (6%)          |  |
| Inflammation, Chronic             | ,            | 1 (2%)         | 1 (2%)         | 1 (2%)          |  |
| Duct, Cyst                        | 1 (2%)       | ( /            | ()             | ( /             |  |
| Duct, Dilation                    | 4 (8%)       | 9 (18%)        | 2 (4%)         | 5 (10%)         |  |
| Duct, Inflammation, Chronic       | ( ( ) )      | ((,-)          | _ ( . , , ,    | 1 (2%)          |  |
| Skin                              | (50)         | (50)           | (50)           | (50)            |  |
| Cyst Epithelial Inclusion         | 1 (2%)       | (00)           | (00)           | (00)            |  |
| Inflammation, Chronic             | 1 (270)      | 1 (2%)         |                |                 |  |
| mammaton, emonie                  |              | (270)          |                |                 |  |
| MUSCULOSKELETAL SYSTEM            |              |                |                |                 |  |
| Bone                              | (50)         | (50)           | (50)           | (50)            |  |
| Joint, Inflammation, Chronic      | (00)         | (30)           | 1 (2%)         | ()              |  |
| Skeletal Muscle                   | (0)          | (0)            | (1)            | (0)             |  |
| 22.2                              | (=)          | (*)            | ( · /          | (5)             |  |
|                                   |              |                |                |                 |  |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS FEMALE                      | 0mg/L female | 250mg/L female | 500mg/L female | 1000mg/L female |
|--|--------------|----------------|----------------|-----------------|
| NERVOUS SYSTEM   |              |                |                |                 |
| Brain  | (50)         | (50)           | (50)           | (50)            |
| Hemorrhage   | 1 (2%)       | 1 (2%)         | ()             | 1 (2%)          |
| Peripheral Nerve                                       | (0)          | (1)            | (0)            | (0)             |
|  |              |                |                |                 |
| RESPIRATORY SYSTEM                                     |              |                |                |                 |
| Lung   | (50)         | (50)           | (49)           | (50)            |
| Infiltration Cellular, Histiocyte                      | 38 (76%)     | 36 (72%)       | 34 (69%)       | 30 (60%)        |
| Inflammation, Chronic                                  | 9 (18%)      | 9 (18%)        | 5 (10%)        | 5 (10%)         |
| Inflammation, Chronic Active                           |              |                |                | 1 (2%)          |
| Metaplasia, Squamous                                   | 1 (2%)       | 1 (2%)         |                |                 |
| Mineral  | 1 (2%)       |                |                |                 |
| Thrombus   |              | 1 (2%)         |                |                 |
| Alveolar Epithelium, Hyperplasia                       | 1 (2%)       | 1 (2%)         | 2 (4%)         |                 |
| Alveolus, Infiltration Cellular, Histiocyte            |              | 1 (2%)         |                |                 |
| Nose   | (50)         | (50)           | (50)           | (50)            |
| Inflammation, Acute                                    |              | 1 (2%)         |                |                 |
| Thrombus   | 1 (2%)       |                |                |                 |
| Glands, Respiratory Epithelium, Dilation               | 2 (4%)       |                | 1 (2%)         |                 |
| Glands, Respiratory Epithelium, Hyperplasia            | 1 (2%)       |                |                |                 |
| Goblet Cell, Nasopharyngeal Duct, Hyperplasia          | 3 (6%)       | 3 (6%)         | 1 (2%)         | 1 (2%)          |
| Goblet Cell, Respiratory Epithelium, Hyperplasia       | 3 (6%)       | 6 (12%)        | 2 (4%)         | 1 (2%)          |
| Olfactory Epithelium, Accumulation, Hyaline<br>Droplet | 50 (100%)    | 50 (100%)      | 50 (100%)      | 50 (100%)       |
| Olfactory Epithelium, Inflammation, Acute              |              |                |                | 1 (2%)          |
| Respiratory Epithelium, Accumulation, Hyaline Droplet  | 1 (2%)       | 12 (24%)       | 10 (20%)       | 8 (16%)         |
| Respiratory Epithelium, Hyperplasia                    |              | 1 (2%)         |                |                 |
| Respiratory Epithelium, Inflammation, Chronic Active   |              | 2 (4%)         |                |                 |
| Trachea  | (50)         | (50)           | (49)           | (50)            |

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC
Route: DOSED WATER
Species/Strain: RATS/HSD

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Sodium Tungstate Dihydrate CAS Number: 10213-10-2

Date Report Requested: 02/28/2019 Time Report Requested: 13:33:08 First Dose M/F: 01/30/12 / 01/31/12

| Harlan Sprague Dawley RATS FEMALE           | 0mg/L female | 250mg/L female | 500mg/L female | 1000mg/L female |  |
|---|--------------|----------------|----------------|-----------------|--|
| SPECIAL SENSES SYSTEM                       |              |                |                |                 |  |
| Eye<br>Cornea, Inflammation, Chronic Active | (50)         | (50)           | (50)<br>1 (2%) | (50)            |  |
| Harderian Gland                             | (50)         | (50)           | (50)           | (50)            |  |
| Hyperplasia                                 |              | 1 (2%)         | 2 (4%)         | 1 (2%)          |  |
| Inflammation, Acute                         | (0)          | 1 (2%)         | (4)            | (0)             |  |
| Zymbal's Gland                              | (0)          | (0)            | (1)            | (0)             |  |
| URINARY SYSTEM                              |              |                |                |                 |  |
| Kidney                                      | (50)         | (50)           | (50)           | (50)            |  |
| Calculus Micro Observation Only             |              |                | 1 (2%)         |                 |  |
| Infarct                                     |              |                |                | 3 (6%)          |  |
| Metaplasia, Osseous                         |              |                |                | 1 (2%)          |  |
| Mineral                                     | 4 (8%)       | 4 (8%)         | 10 (20%)       | 2 (4%)          |  |
| Nephropathy, Chronic Progressive            | 49 (98%)     | 49 (98%)       | 48 (96%)       | 47 (94%)        |  |
| Cortex, Cyst                                | 1 (2%)       | 1 (2%)         |                |                 |  |
| Pelvis, Dilation                            | 3 (6%)       | 1 (2%)         | 9 (18%)        | 7 (14%)         |  |
| Renal Tubule, Dilation                      |              |                | 2 (4%)         | 1 (2%)          |  |
| Renal Tubule, Hyperplasia, Oncocytic        |              |                |                | 1 (2%)          |  |
| Renal Tubule, Inflammation, Suppurative     | 8 (16%)      | 9 (18%)        | 6 (12%)        | 19 (38%)        |  |
| Renal Tubule, Regeneration                  |              |                |                | 18 (36%)        |  |
| Urinary Bladder                             | (50)         | (50)           | (50)           | (50)            |  |

<sup>\*\*\*</sup> END OF REPORT \*\*\*

a - Number of animals examined microscopically at site and number of animals with lesion