

Experiment Number: 88122-03
Test Type: 90-DAY
Route: GAVAGE
Species/Strain: Rat/F 344/N

**P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH
AVERAGE SEVERITY GRADES[b]**

Test Compound: Elmiron (sodium pentosanpolysulfate)
CAS Number: 37319-17-8

Date Report Requested: 10/19/2014
Time Report Requested: 16:05:37
First Dose M/F: NA / NA
Lab: BAT

| | |
|-----------------------------|------------|
| C Number: | C88122 |
| Lock Date: | 11/13/1996 |
| Cage Range: | All |
| Date Range: | All |
| Reasons For Removal: | All |
| Removal Date Range: | All |
| Treatment Groups: | All |
| Study Gender: | Both |
| PWG Approval Date | NONE |

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CAS Number: 37319-17-8

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First Dose M/F: NA / NA

Lab: BAT

| F 344/N Rat MALE | 0 MG/KG | 63 MG/KG | 125 MG/KG | 250 MG/KG | 500 MG/KG | 1000 MG/KG |
|---|---------|----------|-----------|-----------|-----------|------------|
| Disposition Summary | | | | | | |
| Animals Initially In Study | 10 | 10 | 10 | 10 | 10 | 10 |
| Early Deaths | | | | | | |
| Dosing Accident | | 1 | | | 1 | 2 |
| Survivors | | | | | | |
| Terminal Sacrifice | 10 | 9 | 10 | 10 | 9 | 8 |
| Animals Examined Microscopically | 10 | 10 | 10 | 10 | 10 | 10 |
| ALIMENTARY SYSTEM | | | | | | |
| Esophagus | (10) | (1) | (0) | (0) | (2) | (10) |
| Muscularis, Inflammation, Chronic Ulcer | 4 [1.5] | | | | 1 [1.0] | 7 [1.0] |
| Ulcer | | | | | 1 [1.0] | |
| Intestine Large, Cecum | (10) | (1) | (0) | (0) | (1) | (10) |
| Intestine Large, Colon | (10) | (1) | (0) | (0) | (1) | (10) |
| Intestine Large, Rectum | (10) | (10) | (10) | (10) | (10) | (9) |
| Infiltration Cellular, Histiocyte Inflammation, Chronic Active Ulcer, Chronic | | | 3 [1.0] | 7 [1.1] | 9 [1.6] | 8 [2.0] |
| Inflammation, Chronic Active Ulcer, Chronic | | | 2 [1.0] | 7 [1.0] | 8 [1.1] | 8 [1.8] |
| Ulcer, Chronic | | | 1 [1.0] | 3 [1.0] | 7 [1.0] | 7 [1.4] |
| Intestine Small, Duodenum | (10) | (1) | (0) | (0) | (1) | (10) |
| Intestine Small, Ileum | (10) | (1) | (0) | (0) | (1) | (10) |
| Intestine Small, Jejunum | (10) | (1) | (0) | (0) | (1) | (10) |
| Liver | (10) | (2) | (2) | (10) | (10) | (10) |
| Hepatodiaphragmatic Nodule Inflammation | 2 [1.0] | | 2 | | 1 | 4 |
| Inflammation, Granulomatous Midzonal, Vacuolization Cytoplasmic | | 1 [1.0] | | 1 [1.0] | 4 [1.0] | 6 [1.2] |
| Midzonal, Vacuolization Cytoplasmic | | | | | 4 [1.0] | 8 [1.6] |
| Pancreas | (10) | (1) | (0) | (0) | (1) | (10) |
| Acinus, Atrophy | | | | | | 2 [1.0] |
| Atrophy, Acute | 1 [1.0] | | | | | |

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

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P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]

Test Compound: Elmiron (sodium pentosanpolysulfate)

CAS Number: 37319-17-8

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First Dose M/F: NA / NA

Lab: BAT

| F 344/N Rat MALE | 0 MG/KG | 63 MG/KG | 125 MG/KG | 250 MG/KG | 500 MG/KG | 1000 MG/KG |
|-----------------------------------|---------|----------|-----------|-----------|-----------|------------|
| Hemorrhage | | | | | 1 [2.0] | |
| Salivary Glands | (10) | (1) | (0) | (0) | (1) | (10) |
| Stomach, Forestomach | (10) | (1) | (0) | (0) | (1) | (10) |
| Hemorrhage | | | | | 1 [2.0] | |
| Stomach, Glandular | (10) | (1) | (0) | (0) | (1) | (9) |
| CARDIOVASCULAR SYSTEM | | | | | | |
| Blood Vessel | (10) | (1) | (0) | (0) | (1) | (10) |
| Heart | (10) | (1) | (0) | (0) | (1) | (10) |
| Myocardium, Degeneration | 8 [1.0] | | | | | 7 [1.0] |
| ENDOCRINE SYSTEM | | | | | | |
| Adrenal Cortex | (10) | (1) | (0) | (0) | (1) | (10) |
| Adrenal Medulla | (10) | (1) | (0) | (0) | (1) | (10) |
| Islets, Pancreatic | (10) | (1) | (0) | (0) | (1) | (10) |
| Parathyroid Gland | (9) | (1) | (0) | (0) | (1) | (8) |
| Pituitary Gland | (9) | (1) | (0) | (0) | (0) | (10) |
| Pars Distalis, Hyperplasia, Focal | | | | | | 1 [1.0] |
| Thyroid Gland | (10) | (1) | (0) | (0) | (1) | (10) |
| GENERAL BODY SYSTEM | | | | | | |
| None | | | | | | |
| GENITAL SYSTEM | | | | | | |
| Epididymis | (10) | (1) | (0) | (0) | (1) | (10) |
| Inflammation, Chronic | | | | | | 1 [2.0] |
| Preputial Gland | (10) | (1) | (0) | (0) | (1) | (10) |
| Prostate | (10) | (1) | (0) | (0) | (1) | (10) |
| Inflammation, Chronic | | | | | | 1 [2.0] |
| Seminal Vesicle | (10) | (1) | (0) | (0) | (1) | (10) |
| Inflammation, Chronic | | | | | | 1 [3.0] |

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

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Experiment Number: 88122-03

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Species/Strain: Rat/F 344/N

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Test Compound: Elmiron (sodium pentosanpolysulfate)

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Time Report Requested: 16:05:37

First Dose M/F: NA / NA

Lab: BAT

| F 344/N Rat MALE | 0 MG/KG | 63 MG/KG | 125 MG/KG | 250 MG/KG | 500 MG/KG | 1000 MG/KG |
|---|---------|----------|-----------|-----------|-----------|------------|
| Testes | (10) | (1) | (0) | (0) | (1) | (10) |
| HEMATOPOIETIC SYSTEM | | | | | | |
| Bone Marrow | (10) | (1) | (0) | (0) | (1) | (10) |
| Lymph Node, Mandibular | (10) | (1) | (10) | (10) | (10) | (10) |
| Infiltration Cellular, Histiocyte | | | | 3 [1.0] | 8 [1.1] | 7 [1.3] |
| Lymph Node, Mesenteric | (10) | (1) | (10) | (10) | (10) | (9) |
| Infiltration Cellular, Histiocyte | | | | 6 [1.0] | 8 [1.4] | 8 [1.8] |
| Spleen | (10) | (1) | (0) | (10) | (10) | (10) |
| Lymph Follic, Depletion Cellular | | | | | 1 [3.0] | 1 [3.0] |
| Thymus | (10) | (1) | (0) | (0) | (1) | (10) |
| Atrophy | | | | | 1 [2.0] | |
| INTEGUMENTARY SYSTEM | | | | | | |
| Mammary Gland | (6) | (1) | (0) | (0) | (1) | (7) |
| Skin | (10) | (1) | (0) | (0) | (1) | (10) |
| MUSCULOSKELETAL SYSTEM | | | | | | |
| Bone | (10) | (1) | (0) | (0) | (1) | (10) |
| NERVOUS SYSTEM | | | | | | |
| Brain | (10) | (1) | (0) | (0) | (1) | (10) |
| Peripheral Nerve | (0) | (1) | (0) | (0) | (0) | (0) |
| Spinal Cord | (0) | (1) | (0) | (0) | (0) | (0) |
| RESPIRATORY SYSTEM | | | | | | |
| Lung | (10) | (10) | (10) | (10) | (10) | (10) |
| Alveolus, Infiltration Cellular, Histiocyte | | 2 [1.0] | 5 [1.0] | 6 [1.2] | 10 [1.1] | 8 [1.3] |
| Congestion | | | | | | 1 [2.0] |
| Hemorrhage | | | | | | 1 [3.0] |
| Inflammation, Acute | | | | | 1 [3.0] | |
| Interstitial, Edema | | 1 [3.0] | | | | 2 [2.0] |

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b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

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AVERAGE SEVERITY GRADES[b]**

Test Compound: Elmiron (sodium pentosanpolysulfate)

CAS Number: 37319-17-8

Date Report Requested: 10/19/2014

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First Dose M/F: NA / NA

Lab: BAT

| F 344/N Rat MALE | 0 MG/KG | 63 MG/KG | 125 MG/KG | 250 MG/KG | 500 MG/KG | 1000 MG/KG |
|---|---------|----------|-----------|-----------|-----------|------------|
| Interstitial, Inflammation, Chronic | | | | | 1 [1.0] | 3 [1.0] |
| Nose | (10) | (1) | (0) | (0) | (1) | (10) |
| Trachea | (10) | (1) | (0) | (0) | (1) | (10) |
| Hemorrhage | | | | | 1 [1.0] | |
| SPECIAL SENSES SYSTEM | | | | | | |
| None | | | | | | |
| URINARY SYSTEM | | | | | | |
| Kidney | (10) | (1) | (0) | (0) | (10) | (9) |
| Hemorrhage | | | | | | 1 [2.0] |
| Infarct | 1 [2.0] | | | | | |
| Inflammation | | | | | 1 [1.0] | 1 [1.0] |
| Renal Tubule, Cyst | 2 [2.0] | | | | | |
| Renal Tubule, Necrosis | | | | | 1 [3.0] | |
| Renal Tubule, Vacuolization Cytoplasmic | | | | | | 8 [1.0] |
| Urinary Bladder | (10) | (1) | (0) | (0) | (1) | (10) |

END OF MALE DATA

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Lab: BAT

| F 344/N Rat FEMALE | 0 MG/KG | 63 MG/KG | 125 MG/KG | 250 MG/KG | 500 MG/KG | 1000 MG/KG |
|-------------------------------------|---------|----------|-----------|-----------|-----------|------------|
| Disposition Summary | | | | | | |
| Animals Initially In Study | 10 | 10 | 10 | 10 | 10 | 10 |
| Early Deaths | | | | | | |
| Survivors | | | | | | |
| Terminal Sacrifice | 10 | 10 | 10 | 10 | 10 | 10 |
| Animals Examined Microscopically | 10 | 10 | 10 | 10 | 10 | 10 |
| ALIMENTARY SYSTEM | | | | | | |
| Esophagus | (10) | (0) | (0) | (0) | (0) | (10) |
| Muscularis, Inflammation, Chronic | 4 [1.3] | | | | | 7 [1.0] |
| Intestine Large, Cecum | (10) | (0) | (0) | (1) | (0) | (10) |
| Infiltration Cellular, Histiocyte | | | | 1 [1.0] | | |
| Inflammation, Chronic Active | | | | | | 1 [2.0] |
| Intestine Large, Colon | (10) | (0) | (0) | (0) | (0) | (10) |
| Intestine Large, Rectum | (10) | (10) | (10) | (10) | (10) | (10) |
| Infiltration Cellular, Histiocyte | | 2 [1.0] | 1 [1.0] | 2 [1.0] | 10 [1.5] | 10 [2.0] |
| Inflammation, Chronic Active | | | | | 9 [1.0] | 10 [1.4] |
| Ulcer, Chronic | | | | | 6 [1.0] | 8 [1.0] |
| Intestine Small, Duodenum | (10) | (0) | (0) | (0) | (0) | (10) |
| Intestine Small, Ileum | (10) | (0) | (0) | (0) | (0) | (10) |
| Intestine Small, Jejunum | (10) | (0) | (0) | (0) | (0) | (10) |
| Liver | (10) | (10) | (10) | (10) | (10) | (10) |
| Hepatodiaphragmatic Nodule | 1 | | | 1 | | 1 |
| Inflammation, Granulomatous | 9 [1.2] | 10 [1.0] | 10 [1.0] | 10 [1.0] | 9 [1.2] | 10 [1.3] |
| Midzonal, Vacuolization Cytoplasmic | | | | | | 7 [1.0] |
| Pancreas | (10) | (0) | (0) | (0) | (0) | (10) |
| Acinus, Atrophy | 2 [1.0] | | | | | |
| Salivary Glands | (10) | (0) | (0) | (0) | (0) | (10) |
| Stomach, Forestomach | (10) | (0) | (0) | (0) | (0) | (10) |

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

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Species/Strain: Rat/F 344/N

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AVERAGE SEVERITY GRADES[b]**

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First Dose M/F: NA / NA

Lab: BAT

| F 344/N Rat FEMALE | 0 MG/KG | 63 MG/KG | 125 MG/KG | 250 MG/KG | 500 MG/KG | 1000 MG/KG |
|-----------------------------------|---------|----------|-----------|-----------|-----------|------------|
| Stomach, Glandular | (10) | (0) | (0) | (0) | (0) | (10) |
| CARDIOVASCULAR SYSTEM | | | | | | |
| Blood Vessel | (10) | (0) | (0) | (0) | (0) | (10) |
| Heart | (10) | (0) | (0) | (0) | (0) | (10) |
| Myocardium, Degeneration | 2 [1.0] | | | | | 5 [1.0] |
| ENDOCRINE SYSTEM | | | | | | |
| Adrenal Cortex | (10) | (0) | (0) | (0) | (0) | (10) |
| Adrenal Medulla | (10) | (0) | (0) | (0) | (0) | (10) |
| Islets, Pancreatic | (10) | (0) | (0) | (0) | (0) | (10) |
| Parathyroid Gland | (10) | (0) | (0) | (0) | (0) | (9) |
| Pituitary Gland | (10) | (0) | (0) | (0) | (0) | (10) |
| Thyroid Gland | (10) | (0) | (0) | (0) | (0) | (10) |
| GENERAL BODY SYSTEM | | | | | | |
| None | | | | | | |
| GENITAL SYSTEM | | | | | | |
| Clitoral Gland | (9) | (0) | (0) | (0) | (0) | (10) |
| Ovary | (10) | (0) | (0) | (1) | (0) | (10) |
| Cyst | 1 [3.0] | | | 1 [3.0] | | 1 [3.0] |
| Uterus | (10) | (0) | (0) | (0) | (0) | (10) |
| Endometrium, Hyperplasia, Cystic | 1 [1.0] | | | | | |
| HEMATOPOIETIC SYSTEM | | | | | | |
| Bone Marrow | (10) | (0) | (0) | (0) | (0) | (10) |
| Lymph Node, Mandibular | (10) | (1) | (2) | (10) | (10) | (10) |
| Infiltration Cellular, Histiocyte | | 1 [1.0] | 2 [1.0] | 3 [1.0] | 3 [1.0] | 10 [1.2] |
| Lymph Node, Mesenteric | (10) | (2) | (5) | (7) | (10) | (10) |
| Infiltration Cellular, Histiocyte | | 2 [1.0] | 5 [1.2] | 7 [1.0] | 7 [1.0] | 10 [1.1] |
| Spleen | (10) | (0) | (0) | (0) | (10) | (10) |

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

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First Dose M/F: NA / NA

Lab: BAT

| F 344/N Rat FEMALE | 0 MG/KG | 63 MG/KG | 125 MG/KG | 250 MG/KG | 500 MG/KG | 1000 MG/KG |
|---|---------|----------|-----------|-----------|-----------|------------|
| Capsule, Inflammation, Focal | | | | | | 1 [1.0] |
| Thymus | (10) | (0) | (0) | (0) | (0) | (10) |
| INTEGUMENTARY SYSTEM | | | | | | |
| Mammary Gland | (9) | (0) | (0) | (0) | (0) | (10) |
| Skin | (10) | (0) | (0) | (0) | (0) | (10) |
| MUSCULOSKELETAL SYSTEM | | | | | | |
| Bone | (10) | (0) | (0) | (0) | (0) | (10) |
| NERVOUS SYSTEM | | | | | | |
| Brain | (10) | (0) | (0) | (0) | (0) | (10) |
| RESPIRATORY SYSTEM | | | | | | |
| Lung | (10) | (10) | (10) | (10) | (10) | (10) |
| Alveolus, Foreign Body | | | | | 1 | |
| Alveolus, Infiltration Cellular, Histiocyte | | 7 [1.0] | 5 [1.0] | 6 [1.0] | 7 [1.0] | 9 [1.3] |
| Bronchiole, Foreign Body | | 1 | | | | |
| Hematopoietic Cell Proliferation | | | | | | 1 [1.0] |
| Infiltration Cellular, Histiocyte | | | | 1 [1.0] | | |
| Interstitial, Inflammation, Chronic | | 1 [1.0] | | 1 [1.0] | 3 [1.0] | 6 [1.0] |
| Nose | (10) | (0) | (0) | (0) | (0) | (10) |
| Trachea | (10) | (0) | (0) | (0) | (0) | (10) |
| SPECIAL SENSES SYSTEM | | | | | | |
| None | | | | | | |
| URINARY SYSTEM | | | | | | |
| Kidney | (10) | (0) | (0) | (0) | (10) | (10) |
| Renal Tubule, Vacuolization Cytoplasmic | | | | | | 10 [1.0] |
| Urinary Bladder | (10) | (0) | (0) | (0) | (0) | (10) |

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