Rats Final 1

NTP Study Number:	C00058B
Lock Date:	10/02/2018
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

Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Disposition Summary				
Animals Initially In Study	**50**	**50**	**50**	**50**
Early Deaths				
Moribund Sacrifice	**16**	**14**	**11**	**8**
Natural Death	**19**	**20**	**18**	**26**
Survivors				
Natural Death		**1**		
Terminal Sacrifice	**15**	**15**	**21**	**16**
Animals Examined Microscopically	**50**	**50**	**50**	**50**
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Intestine Large, Cecum	(50)	(49)	(50)	(49)
Erosion	3 (6%)	4 (8%)		2 (4%)
Infiltration Cellular, Lymphoid		1 (2%)		
Inflammation, Acute	1 (2%)			1 (2%)
Inflammation, Chronic	2 (4%)	2 (4%)		1 (2%)
Inflammation, Chronic Active	1 (2%)	1 (2%)		3 (6%)
Mineral	3 (6%)	4 (8%)	1 (2%)	5 (10%)
Polyarteritis Nodosa	3 (6%)	8 (16%)	1 (2%)	4 (8%)
Ulcer	2 (4%)	1 (2%)		1 (2%)
Intestine Large, Colon	(50)	(50)	(50)	(50)
Infiltration Cellular, Lymphoid		1 (2%)		
Inflammation, Chronic	1 (2%)			
Inflammation, Chronic Active				1 (2%)
Mineral		1 (2%)	1 (2%)	
Parasite Metazoan	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Polyarteritis Nodosa	1 (2%)	2 (4%)	2 (4%)	3 (6%)
Ulcer			1 (2%)	
Lymphoid Tissue, Hyperplasia	1 (2%)	4 (8%)	2 (4%)	
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Parasite Metazoan		3 (6%)	1 (2%)	2 (4%)
Polyarteritis Nodosa	2 (4%)	2 (4%)	1 (2%)	
Intestine Small, Duodenum	(50)	(50)	(49)	(49)

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

Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Polyarteritis Nodosa	2 (4%)		3 (6%)	1 (2%)
Intestine Small, Ileum	(49)	(50)	(50)	(50)
Polyarteritis Nodosa	1 (2%)	1 (2%)		1 (2%)
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Polyarteritis Nodosa	2 (4%)	1 (2%)		1 (2%)
Peyer's Patch, Hyperplasia		1 (2%)	1 (2%)	1 (2%)
Liver	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)			
Basophilic Focus		2 (4%)	1 (2%)	4 (8%)
Clear Cell Focus	19 (38%)	13 (26%)	24 (48%)	17 (34%)
Degeneration, Cystic			2 (4%)	1 (2%)
Eosinophilic Focus	5 (10%)	7 (14%)	2 (4%)	1 (2%)
Extramedullary Hematopoiesis		3 (6%)	1 (2%)	3 (6%)
Fatty Change, Focal		1 (2%)		1 (2%)
Hepatodiaphragmatic Nodule		1 (2%)	2 (4%)	3 (6%)
Inflammation, Granulomatous		1 (2%)		
Mixed Cell Focus	2 (4%)	1 (2%)		2 (4%)
Necrosis	8 (16%)	3 (6%)	4 (8%)	2 (4%)
Polyarteritis Nodosa	2 (4%)			1 (2%)
Artery, Inflammation, Chronic Active	1 (2%)			
Bile Duct, Cyst	4 (8%)	4 (8%)	1 (2%)	1 (2%)
Bile Duct, Dilation	3 (6%)	1 (2%)	1 (2%)	
Bile Duct, Hyperplasia	27 (54%)	19 (38%)	25 (50%)	18 (36%)
Bile Duct, Inflammation, Chronic Active				1 (2%)
Centrilobular, Degeneration				1 (2%)
Centrilobular, Necrosis		1 (2%)		
Mesentery	(0)	(3)	(1)	(0)
Hemorrhage		1 (33%)		
Pigment		1 (33%)		
Polyarteritis Nodosa		1 (33%)		
Fat, Necrosis			1 (100%)	
Oral Mucosa	(0)	(0)	(1)	(0)
Pancreas	(50)	(50)	(50)	(50)
Polyarteritis Nodosa	6 (12%)	6 (12%)	7 (14%)	10 (20%)
Acinus, Atrophy	5 (10%)	4 (8%)	1 (2%)	4 (8%)
Acinus, Hyperplasia	9 (18%)	9 (18%)	8 (16%)	6 (12%)

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

Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Duct, Cyst				1 (2%)
Salivary Glands	(50)	(50)	(50)	(50)
Atrophy	1 (2%)	1 (2%)		
Inflammation, Chronic Active		1 (2%)		
Stomach, Forestomach	(50)	(50)	(50)	(50)
Cyst, Squamous		1 (2%)		
Edema				1 (2%)
Erosion			1 (2%)	
Foreign Body		1 (2%)		
Infiltration Cellular, Lipocyte		1 (2%)		
Inflammation, Granulomatous	1 (2%)			
Inflammation, Acute		1 (2%)	2 (4%)	
Inflammation, Chronic	2 (4%)		1 (2%)	1 (2%)
Inflammation, Chronic Active		2 (4%)	3 (6%)	2 (4%)
Mineral	1 (2%)	2 (4%)	1 (2%)	
Necrosis			1 (2%)	
Polyarteritis Nodosa	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Ulcer		1 (2%)	3 (6%)	
Epithelium, Hyperplasia	1 (2%)	6 (12%)	5 (10%)	7 (14%)
Epithelium, Hyperplasia, Basal Cell	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Infiltration Cellular, Lipocyte		1 (2%)		
Infiltration Cellular, Lymphocyte	1 (2%)			
Inflammation, Acute		1 (2%)		
Inflammation, Chronic	1 (2%)			
Mineral	15 (30%)	16 (32%)	10 (20%)	10 (20%)
Polyarteritis Nodosa			1 (2%)	
Tongue	(0)	(1)	(0)	(0)
Edema		1 (100%)		
Inflammation, Chronic Active		1 (100%)		
Tooth	(0)	(3)	(0)	(0)
Metaplasia, Osseous		1 (33%)		
Dentine, Degeneration		2 (67%)		
Pulp, Inflammation, Chronic		1 (33%)		

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

Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
CARDIOVASCULAR SYSTEM				
Blood Vessel	(32)	(33)	(32)	(33)
Aneurysm		1 (3%)		
Mineral	14 (44%)	15 (45%)	13 (41%)	11 (33%)
Aorta, Dilation		2 (6%)	1 (3%)	1 (3%)
Carotid Artery, Polyarteritis Nodosa				1 (3%)
Intima, Hyperplasia	1 (3%)			
Pulmonary Artery, Thrombus				1 (3%)
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	37 (74%)	40 (80%)	40 (80%)	37 (74%)
Inflammation, Acute		1 (2%)		
Inflammation, Chronic Active				1 (2%)
Mineral	4 (8%)	8 (16%)	1 (2%)	3 (6%)
Polyarteritis Nodosa	2 (4%)	1 (2%)		
Thrombus		1 (2%)		
Atrium, Thrombus	2 (4%)	1 (2%)	4 (8%)	3 (6%)
Perivascular, Infiltration Cellular, Lymphocyte		1 (2%)	2 (4%)	
Valve, Inflammation, Chronic			1 (2%)	
Valve, Thrombus				1 (2%)
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Amyloid Deposition, Focal			1 (2%)	
Angiectasis				1 (2%)
Degeneration, Cystic	5 (10%)	4 (8%)	5 (10%)	4 (8%)
Hyperplasia, Focal	6 (12%)	10 (20%)	8 (16%)	9 (18%)
Hypertrophy, Focal	1 (2%)			
Necrosis	2 (4%)	3 (6%)	4 (8%)	3 (6%)
Thrombus		2 (4%)		4 (8%)
Vacuolization Cytoplasmic	1 (2%)			1 (2%)
Bilateral, Hyperplasia, Focal	1 (2%)		1 (2%)	5 (10%)
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia, Focal	9 (18%)	9 (18%)	13 (26%)	15 (30%)

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

Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Bilateral, Hyperplasia, Focal	5 (10%)	2 (4%)	3 (6%)	4 (8%)
Islets, Pancreatic	(50)	(50)	(50)	(50)
Atrophy	1 (2%)			
Hyperplasia	2 (4%)	3 (6%)	1 (2%)	3 (6%)
Parathyroid Gland	(49)	(47)	(44)	(39)
Hyperplasia, Diffuse	13 (27%)	24 (51%)	16 (36%)	14 (36%)
Pituitary Gland	(50)	(50)	(50)	(50)
Inflammation, Chronic Active	1 (2%)			
Pars Distalis, Hyperplasia	20 (40%)	15 (30%)	15 (30%)	15 (30%)
Pars Nervosa, Thrombus				1 (2%)
Thyroid Gland	(50)	(50)	(50)	(50)
Ectopic Thymus	1 (2%)			
Polyarteritis Nodosa		1 (2%)		1 (2%)
C-cell, Hyperplasia	9 (18%)	10 (20%)	9 (18%)	6 (12%)
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Atrophy	1 (2%)	2 (4%)		1 (2%)
Granuloma Sperm		1 (2%)		
Inflammation, Chronic Active			1 (2%)	
Polyarteritis Nodosa			2 (4%)	
Bilateral, Atrophy	1 (2%)			
Preputial Gland	(50)	(50)	(50)	(50)
Duct, Hyperplasia, Squamous	1 (2%)		1 (2%)	1 (2%)
Prostate	(50)	(50)	(50)	(50)
Hyperplasia	2 (4%)	3 (6%)	2 (4%)	3 (6%)
Inflammation, Chronic		1 (2%)	5 (10%)	2 (4%)
Inflammation, Chronic Active	9 (18%)	6 (12%)	4 (8%)	4 (8%)
Polyarteritis Nodosa			2 (4%)	
Seminal Vesicle	(50)	(50)	(50)	(50)

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Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Inflammation, Chronic Active	3 (6%)	2 (4%)	1 (2%)	1 (2%)
Metaplasia, Squamous			1 (2%)	
Mineral		1 (2%)		
Polyarteritis Nodosa			2 (4%)	
Testis	(50)	(50)	(50)	(50)
Edema				1 (2%)
Granuloma Sperm	1 (2%)			1 (2%)
Mineral	1 (2%)			
Polyarteritis Nodosa	24 (48%)	25 (50%)	24 (48%)	23 (46%)
Bilateral, Germinal Epithelium, Degeneration	14 (28%)	21 (42%)	19 (38%)	10 (20%)
Germinal Epithelium, Degeneration	12 (24%)	5 (10%)	6 (12%)	16 (32%)
Interstitial Cell, Hyperplasia	1 (2%)	2 (4%)	2 (4%)	1 (2%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Hemorrhage	10 (20%)	19 (38%)	15 (30%)	21 (42%)
Hypercellularity	28 (56%)	27 (54%)	30 (60%)	29 (58%)
Myelofibrosis		2 (4%)		
Necrosis				1 (2%)
Lymph Node	(5)	(4)	(3)	(4)
Lumbar, Hemorrhage			1 (33%)	
Lumbar, Hyperplasia, Lymphoid	1 (20%)			
Lumbar, Hyperplasia, Plasma Cell				1 (25%)
Lumbar, Infiltration Cellular, Histiocyte			1 (33%)	
Lumbar, Pigment			1 (33%)	
Lumbar, Lymphatic Sinus, Ectasia				1 (25%)
Mediastinal, Hemorrhage		1 (25%)		1 (25%)
Mediastinal, Infiltration Cellular, Histiocyte	1 (20%)			
Mediastinal, Pigment				1 (25%)
Mediastinal, Thrombus	1 (20%)			
Pancreatic, Infiltration Cellular, Plasma Cell			1 (33%)	
Renal, Ectasia				2 (50%)
Renal, Hemorrhage	1 (20%)	1 (25%)	1 (33%)	
Renal, Pigment		1 (25%)	1 (33%)	

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

Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Lymph Node, Mandibular	(50)	(50)	(50)	(50)
Atrophy			1 (2%)	
Ectasia			2 (4%)	
Hyperplasia, Lymphoid	1 (2%)			1 (2%)
Infiltration Cellular, Plasma Cell	2 (4%)	2 (4%)		2 (4%)
Inflammation		2 (4%)		
Lymph Node, Mesenteric	(50)	(50)	(49)	(48)
Atrophy	1 (2%)			1 (2%)
Hyperplasia, Lymphoid	1 (2%)	1 (2%)		
Infiltration Cellular, Histiocyte	1 (2%)			
Necrosis	1 (2%)			
Spleen	(50)	(50)	(49)	(50)
Extramedullary Hematopoiesis	41 (82%)	41 (82%)	42 (86%)	39 (78%)
Hemorrhage		1 (2%)		
Necrosis				1 (2%)
Pigment	38 (76%)	39 (78%)	43 (88%)	40 (80%)
Polyarteritis Nodosa	1 (2%)			
White Pulp, Atrophy	17 (34%)	19 (38%)	13 (27%)	17 (34%)
Thymus	(46)	(48)	(46)	(49)
Atrophy	43 (93%)	41 (85%)	44 (96%)	40 (82%)
Cyst			1 (2%)	
Ectopic Parathyroid Gland	2 (4%)	1 (2%)	2 (4%)	
Hyperplasia, Lymphoid				1 (2%)
Polyarteritis Nodosa	2 (4%)	1 (2%)	1 (2%)	
INTEGUMENTARY SYSTEM				
Mammary Gland	(48)	(48)	(49)	(48)
Galactocele	1 (2%)			
Hyperplasia	1 (2%)	1 (2%)	1 (2%)	
Mineral		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Cyst Epithelial Inclusion	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Edema				1 (2%)
Foreign Body				1 (2%)

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Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Hemorrhage				1 (2%)
Inflammation, Granulomatous	1 (2%)		1 (2%)	1 (2%)
Inflammation, Chronic Active	1 (2%)	1 (2%)	1 (2%)	6 (12%)
Ulcer	1 (2%)	1 (2%)	1 (2%)	5 (10%)
Epidermis, Hyperplasia				3 (6%)
Subcutaneous Tissue, Polyarteritis Nodosa			1 (2%)	
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Cyst		1 (2%)		
Fibrous Osteodystrophy			1 (2%)	
Osteopetrosis			2 (4%)	1 (2%)
Cartilage, Joint, Degeneration			1 (2%)	
Skeletal Muscle	(0)	(0)	(1)	(3)
Degeneration				1 (33%)
Polyarteritis Nodosa				1 (33%)
NERVOUS SYSTEM				
Brain	(50)	(50)	(49)	(50)
Edema			1 (2%)	
Gliosis			2 (4%)	1 (2%)
Hemorrhage	1 (2%)	2 (4%)		
Inflammation, Chronic Active				1 (2%)
Necrosis		1 (2%)	2 (4%)	2 (4%)
Thrombus			1 (2%)	
Nerve Trigeminal	(0)	(1)	(0)	(0)
Peripheral Nerve	(0)	(1)	(1)	(2)
Degeneration				1 (50%)
Axon, Sciatic, Degeneration			1 (100%)	1 (50%)
Axon, Tibial, Degeneration			1 (100%)	1 (50%)
Axon, Trigeminal, Degeneration			1 (100%)	2 (100%)
Trigeminal, Fibrosis				1 (50%)
Spinal Cord	(0)	(1)	(1)	(2)

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Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Gliosis			1 (100%)	
Hemorrhage		1 (100%)		
Axon, Degeneration		1 (100%)	1 (100%)	1 (50%)
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Hemorrhage		2 (4%)		
Infiltration Cellular, Histiocyte	21 (42%)	19 (38%)	29 (58%)	26 (52%)
Inflammation, Granulomatous	10 (20%)	9 (18%)	13 (26%)	9 (18%)
Inflammation, Acute	3 (6%)	4 (8%)	1 (2%)	1 (2%)
Inflammation, Chronic Active			1 (2%)	4 (8%)
Mineral	6 (12%)	11 (22%)	1 (2%)	5 (10%)
Polyarteritis Nodosa				1 (2%)
Squamous Metaplasia		1 (2%)		
Thrombus				2 (4%)
Alveolar Epithelium, Hyperplasia	2 (4%)	1 (2%)	2 (4%)	2 (4%)
Alveolar Epithelium, Hypertrophy				1 (2%)
Alveolus, Fibrosis		1 (2%)		
Alveolus, Foreign Body	1 (2%)			
Bronchiole, Fibrosis		1 (2%)	1 (2%)	1 (2%)
Bronchiole, Foreign Body		1 (2%)		
Interstitium, Fibrosis	1 (2%)	1 (2%)		1 (2%)
Peribronchiolar, Fibrosis			1 (2%)	
Perivascular, Infiltration Cellular, Lymphoid	1 (2%)			
Perivascular, Inflammation, Chronic		1 (2%)		
Pleura, Fibrosis				1 (2%)
Nose	(50)	(50)	(50)	(50)
Foreign Body	6 (12%)	1 (2%)	1 (2%)	
Inflammation, Suppurative	5 (10%)	6 (12%)		3 (6%)
Inflammation, Acute	2 (4%)		2 (4%)	
Inflammation, Chronic	3 (6%)		2 (4%)	
Inflammation, Chronic Active	3 (6%)	4 (8%)	3 (6%)	4 (8%)
Nasolacrimal Duct, Inflammation, Suppurative	1 (2%)	1 (2%)		
Nasolacrimal Duct, Inflammation, Chronic	8 (16%)	4 (8%)	2 (4%)	5 (10%)

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Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Nasolacrimal Duct, Inflammation, Chronic Active	2 (4%)	4 (8%)	4 (8%)	5 (10%)
Nasopharyngeal Duct, Inflammation, Chronic Active		1 (2%)		
Nasopharyngeal Duct, Squamous Metaplasia		1 (2%)		
Olfactory Epithelium, Degeneration				1 (2%)
Olfactory Epithelium, Metaplasia, Respiratory	1 (2%)	1 (2%)		
Olfactory Epithelium, Squamous Metaplasia		1 (2%)		
Respiratory Epithelium, Hyperplasia	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Respiratory Epithelium, Squamous Metaplasia			1 (2%)	1 (2%)
Trachea	(50)	(50)	(50)	(50)
Mineral		1 (2%)		
SPECIAL SENSES SYSTEM				
Eye	(50)	(50)	(50)	(50)
Cataract	1 (2%)			
Inflammation, Acute			1 (2%)	
Inflammation, Chronic		1 (2%)		
Cornea, Inflammation, Acute	5 (10%)	5 (10%)	2 (4%)	4 (8%)
Cornea, Inflammation, Chronic	2 (4%)	2 (4%)		2 (4%)
Cornea, Inflammation, Chronic Active	1 (2%)	6 (12%)	11 (22%)	4 (8%)
Optic Nerve, Polyarteritis Nodosa				1 (2%)
Retina, Degeneration	3 (6%)		1 (2%)	
Retina, Dysplasia		1 (2%)		
Retina, Fibrosis	1 (2%)			
Retina, Hyperplasia		1 (2%)		
Harderian Gland	(50)	(50)	(50)	(50)
Atrophy	1 (2%)		2 (4%)	1 (2%)
Inflammation, Suppurative				1 (2%)
Metaplasia		1 (2%)	1 (2%)	
Zymbal's Gland	(2)	(1)	(1)	(0)
URINARY SYSTEM				

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Harlan Sprague Dawley RATS MALE	0 mg/kg male	75 mg/kg male	250 mg/kg male	750 mg/kg male
Kidney	(50)	(50)	(50)	(50)
Amphophilic/Vacuolar Hyperplasia			1 (2%)	1 (2%)
Calculus Micro Observation Only	1 (2%)	2 (4%)		
Cyst				1 (2%)
Hemorrhage	1 (2%)	1 (2%)		1 (2%)
Hyperplasia, Oncocytic	2 (4%)			
Infarct	1 (2%)			1 (2%)
Inflammation, Chronic				1 (2%)
Nephropathy, Chronic Progressive	50 (100%)	50 (100%)	50 (100%)	50 (100%)
Polyarteritis Nodosa	1 (2%)	2 (4%)		
Pelvis, Dilation	1 (2%)			
Pelvis, Inflammation, Acute	1 (2%)		1 (2%)	
Pelvis, Inflammation, Chronic Active	2 (4%)	2 (4%)	1 (2%)	
Renal Tubule, Accumulation, Hyaline Droplet	2 (4%)			2 (4%)
Renal Tubule, Cyst	4 (8%)	5 (10%)	4 (8%)	6 (12%)
Renal Tubule, Dilation	1 (2%)			
Urinary Bladder	(50)	(50)	(50)	(50)
Infiltration Cellular, Lymphocyte			1 (2%)	
Inflammation, Chronic	4 (8%)	1 (2%)		1 (2%)
Inflammation, Chronic Active		1 (2%)		
Polyarteritis Nodosa		1 (2%)		1 (2%)
Perivascular, Infiltration Cellular, Lymphocyte	1 (2%)			
Transitional Epithelium, Hyperplasia		1 (2%)		

*** END OF MALE ***

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

Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
Disposition Summary				
Animals Initially In Study	**50**	**50**	**50**	**50**
Early Deaths				
Moribund Sacrifice	**13**	**14**	**15**	**14**
Natural Death	**9**	**12**	**6**	**16**
Survivors				
Terminal Sacrifice	**28**	**24**	**29**	**20**
Animals Examined Microscopically	**50**	**50**	**50**	**50**
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(49)
Intestine Large, Cecum	(50)	(50)	(50)	(49)
Erosion				1 (2%)
Polyarteritis Nodosa		1 (2%)	1 (2%)	1 (2%)
Intestine Large, Colon	(50)	(50)	(50)	(50)
Parasite Metazoan	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Polyarteritis Nodosa		1 (2%)	1 (2%)	
Lymphoid Tissue, Hyperplasia			2 (4%)	
Intestine Large, Rectum	(50)	(50)	(50)	(50)
Parasite Metazoan	1 (2%)	4 (8%)	3 (6%)	3 (6%)
Polyarteritis Nodosa		2 (4%)	2 (4%)	3 (6%)
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Polyarteritis Nodosa			1 (2%)	
Intestine Small, Ileum	(50)	(50)	(50)	(50)
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Polyarteritis Nodosa				1 (2%)
Liver	(50)	(50)	(50)	(48)
Angiectasis	2 (4%)	1 (2%)	2 (4%)	3 (6%)
Basophilic Focus	4 (8%)	3 (6%)	2 (4%)	
Clear Cell Focus	15 (30%)	6 (12%)	8 (16%)	4 (8%)
Degeneration, Cystic				2 (4%)
Eosinophilic Focus	10 (20%)	5 (10%)	10 (20%)	13 (27%)
Extramedullary Hematopoiesis	3 (6%)	5 (10%)	8 (16%)	5 (10%)
Hepatodiaphragmatic Nodule		2 (4%)		1 (2%)

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

Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
Mixed Cell Focus		1 (2%)		
Necrosis	4 (8%)	10 (20%)	3 (6%)	9 (19%)
Pigment		3 (6%)		
Regeneration		1 (2%)		
Bile Duct, Cyst	4 (8%)	7 (14%)	10 (20%)	8 (17%)
Bile Duct, Dilation			3 (6%)	1 (2%)
Bile Duct, Hyperplasia	11 (22%)	14 (28%)	14 (28%)	9 (19%)
Centrilobular, Necrosis	1 (2%)	1 (2%)		
Hepatocyte, Hyperplasia	1 (2%)			
Hepatocyte, Hypertrophy		1 (2%)		
Hepatocyte, Multinucleated		1 (2%)		
Oval Cell, Hyperplasia	1 (2%)			
Serosa, Fibrosis		1 (2%)	1 (2%)	
Mesentery	(1)	(0)	(1)	(1)
Hemorrhage	1 (100%)			
Oral Mucosa	(0)	(0)	(1)	(0)
Pancreas	(50)	(50)	(50)	(49)
Basophilic Focus	1 (2%)		1 (2%)	
Inflammation, Chronic				1 (2%)
Polyarteritis Nodosa	1 (2%)	2 (4%)	1 (2%)	3 (6%)
Acinus, Atrophy	3 (6%)	2 (4%)		2 (4%)
Acinus, Hyperplasia, Focal		1 (2%)		
Salivary Glands	(50)	(50)	(50)	(48)
Atrophy		1 (2%)		
Polyarteritis Nodosa			1 (2%)	
Stomach, Forestomach	(50)	(50)	(50)	(50)
Cyst, Squamous				1 (2%)
Inflammation, Acute	1 (2%)	1 (2%)		
Inflammation, Chronic	2 (4%)		2 (4%)	1 (2%)
Inflammation, Chronic Active	1 (2%)			1 (2%)
Mineral	1 (2%)			3 (6%)
Polyarteritis Nodosa		1 (2%)	1 (2%)	2 (4%)
Ulcer	1 (2%)	1 (2%)		1 (2%)
Epithelium, Hyperplasia	3 (6%)	2 (4%)	1 (2%)	4 (8%)
Stomach, Glandular	(50)	(50)	(50)	(50)
Erosion			1 (2%)	1 (2%)

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Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
Mineral	2 (4%)	4 (8%)	5 (10%)	2 (4%)
Polyarteritis Nodosa				1 (2%)
Submucosa, Inflammation, Chronic			1 (2%)	
Tooth	(0)	(0)	(1)	(1)
Dysplasia				1 (100%)
Inflammation, Chronic				1 (100%)
Malformation			1 (100%)	
CARDIOVASCULAR SYSTEM				
Blood Vessel	(49)	(48)	(48)	(43)
Mineral			2 (4%)	1 (2%)
Carotid Artery, Polyarteritis Nodosa				1 (2%)
Media, Hypertrophy		1 (2%)		
Heart	(50)	(50)	(50)	(48)
Cardiomyopathy	4 (8%)	9 (18%)	13 (26%)	9 (19%)
Infiltration Cellular, Histiocyte		1 (2%)		
Polyarteritis Nodosa				1 (2%)
Atrium, Thrombus		1 (2%)		
Endocardium, Hyperplasia, Schwann Cell				1 (2%)
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(48)
Angiectasis	5 (10%)	2 (4%)	3 (6%)	3 (6%)
Degeneration, Cystic	6 (12%)	11 (22%)	9 (18%)	7 (15%)
Extramedullary Hematopoiesis		2 (4%)		
Hyperplasia, Focal	2 (4%)	2 (4%)	4 (8%)	4 (8%)
Hypertrophy, Focal	1 (2%)		1 (2%)	
Infiltration Cellular, Lipocyte	1 (2%)			
Metaplasia, Osseous	1 (2%)			
Necrosis		2 (4%)	1 (2%)	2 (4%)
Thrombus	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Bilateral, Degeneration, Cystic	2 (4%)	3 (6%)	1 (2%)	
Bilateral, Hyperplasia, Focal	1 (2%)			1 (2%)

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Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
Bilateral, Hypertrophy, Focal			1 (2%)	
Adrenal Medulla	(50)	(50)	(50)	(48)
Hyperplasia, Focal	5 (10%)	7 (14%)	12 (24%)	5 (10%)
Necrosis		1 (2%)		
Bilateral, Hyperplasia, Focal				3 (6%)
Islets, Pancreatic	(50)	(50)	(50)	(49)
Hyperplasia	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Parathyroid Gland	(46)	(40)	(39)	(38)
Hyperplasia, Focal		1 (3%)		
Hyperplasia, Diffuse		1 (3%)		
Pituitary Gland	(50)	(50)	(50)	(50)
Cyst		1 (2%)		
Polyarteritis Nodosa				1 (2%)
Pars Distalis, Hyperplasia	18 (36%)	18 (36%)	19 (38%)	24 (48%)
Thyroid Gland	(50)	(49)	(50)	(49)
Polyarteritis Nodosa			1 (2%)	
C-cell, Hyperplasia	14 (28%)	6 (12%)	10 (20%)	6 (12%)
Follicle, Cyst	1 (2%)			
Follicular Cell, Hyperplasia				1 (2%)
GENERAL BODY SYSTEM				
Peritoneum	(0)	(2)	(1)	(0)
GENITAL SYSTEM				
Clitoral Gland	(49)	(48)	(49)	(49)
Squamous Metaplasia	1 (2%)			1 (2%)
Ovary	(50)	(50)	(50)	(49)
Atrophy	32 (64%)	39 (78%)	38 (76%)	47 (96%)
Cyst	1 (2%)			4 (8%)
Inflammation, Chronic Active			1 (2%)	
Polyarteritis Nodosa			1 (2%)	1 (2%)
Bursa, Cyst	1 (2%)	2 (4%)	2 (4%)	
Corpus Luteum, Cyst			1 (2%)	

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Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
Follicle, Cyst	12 (24%)	7 (14%)	9 (18%)	6 (12%)
Follicle, Cyst, Multiple	1 (2%)			
Interstitial Cell, Hyperplasia			1 (2%)	
Periovarian Tissue, Cyst	1 (2%)	3 (6%)	3 (6%)	
Rete Ovarii, Cyst	1 (2%)			
Oviduct	(0)	(0)	(2)	(0)
Cyst			1 (50%)	
Inflammation, Acute			1 (50%)	
Uterus	(50)	(50)	(50)	(49)
Adenomyosis		2 (4%)	2 (4%)	1 (2%)
Angiectasis			1 (2%)	1 (2%)
Cyst, Squamous				1 (2%)
Dilation	2 (4%)	3 (6%)	9 (18%)	22 (45%)
Hemorrhage	1 (2%)			8 (16%)
Hyperplasia, Atypical	3 (6%)	4 (8%)	5 (10%)	5 (10%)
Hyperplasia, Stromal			1 (2%)	
Inflammation, Acute	2 (4%)		2 (4%)	4 (8%)
Inflammation, Chronic		1 (2%)		
Inflammation, Chronic Active	4 (8%)	5 (10%)	7 (14%)	7 (14%)
Polyarteritis Nodosa			2 (4%)	1 (2%)
Squamous Metaplasia	21 (42%)	25 (50%)	30 (60%)	38 (78%)
Thrombus	1 (2%)		5 (10%)	5 (10%)
Ulcer		1 (2%)	3 (6%)	9 (18%)
Cervix, Cyst, Squamous		1 (2%)		
Cervix, Hyperplasia, Squamous	3 (6%)	1 (2%)	1 (2%)	3 (6%)
Cervix, Hyperplasia, Stromal	1 (2%)		1 (2%)	
Cervix, Hypertrophy, Stromal	1 (2%)			
Endometrium, Hyperplasia, Cystic	19 (38%)	26 (52%)	23 (46%)	13 (27%)
Vagina	(50)	(50)	(50)	(50)
Hyperplasia, Squamous		1 (2%)		1 (2%)
Inflammation, Acute	1 (2%)		4 (8%)	
Inflammation, Chronic				1 (2%)
Inflammation, Chronic Active		1 (2%)		

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Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Hemorrhage	10 (20%)			9 (18%)
Hypercellularity	31 (62%)	31 (62%)	34 (68%)	42 (84%)
Lymph Node	(0)	(6)	(0)	(3)
Lumbar, Hemorrhage		1 (17%)		
Lumbar, Infiltration Cellular, Plasma Cell				1 (33%)
Lumbar, Sinus, Ectasia		1 (17%)		
Mediastinal, Hemorrhage		1 (17%)		1 (33%)
Mediastinal, Infiltration Cellular, Plasma Cell		1 (17%)		
Lymph Node, Mandibular	(50)	(50)	(50)	(49)
Atrophy				1 (2%)
Infiltration Cellular, Plasma Cell			2 (4%)	
Lymph Node, Mesenteric	(50)	(50)	(50)	(49)
Spleen	(50)	(50)	(50)	(49)
Accessory Spleen			1 (2%)	
Extramedullary Hematopoiesis	47 (94%)	48 (96%)	47 (94%)	47 (96%)
Hemorrhage		1 (2%)	1 (2%)	
Pigment	35 (70%)	34 (68%)	37 (74%)	21 (43%)
White Pulp, Atrophy	9 (18%)	10 (20%)	3 (6%)	9 (18%)
Thymus	(49)	(49)	(48)	(48)
Atrophy	46 (94%)	44 (90%)	43 (90%)	45 (94%)
Ectopic Parathyroid Gland				2 (4%)
Polyarteritis Nodosa				1 (2%)
INTEGUMENTARY SYSTEM				
Mammary Gland	(50)	(50)	(50)	(49)
Galactocele	2 (4%)		4 (8%)	2 (4%)
Hyperplasia	13 (26%)	8 (16%)	4 (8%)	2 (4%)
Hyperplasia, Atypical	1 (2%)			
Skin	(50)	(50)	(50)	(50)
Inflammation, Chronic			1 (2%)	

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Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Skeletal Muscle	(0)	(0)	(0)	(1)
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Gliosis				2 (4%)
Necrosis	1 (2%)			
Glial Cell, Hyperplasia	1 (2%)			
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(48)
Infiltration Cellular, Histiocyte	39 (78%)	38 (76%)	45 (90%)	46 (96%)
Inflammation, Granulomatous	7 (14%)	6 (12%)	16 (32%)	10 (21%)
Inflammation, Acute	1 (2%)			2 (4%)
Inflammation, Chronic Active	1 (2%)	1 (2%)	4 (8%)	1 (2%)
Polyarteritis Nodosa				1 (2%)
Squamous Metaplasia		1 (2%)		4 (8%)
Thrombus				2 (4%)
Alveolar Epithelium, Hyperplasia	4 (8%)	2 (4%)	1 (2%)	1 (2%)
Alveolar Epithelium, Metaplasia, Respiratory		1 (2%)		
Bronchiole, Foreign Body				1 (2%)
Bronchiole, Foreign Body, Multiple			1 (2%)	
Bronchiole, Hyperplasia	1 (2%)			
Interstitium, Fibrosis			1 (2%)	
Peribronchiolar, Fibrosis		1 (2%)		
Nose	(50)	(50)	(50)	(50)
Foreign Body			2 (4%)	2 (4%)
Inflammation, Suppurative		2 (4%)	1 (2%)	1 (2%)
Inflammation, Acute	1 (2%)		2 (4%)	3 (6%)
Inflammation, Chronic	1 (2%)		1 (2%)	3 (6%)

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

Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
Inflammation, Chronic Active				1 (2%)
Nasolacrimal Duct, Inflammation, Chronic	4 (8%)		1 (2%)	5 (10%)
Nasolacrimal Duct, Inflammation, Chronic Active			1 (2%)	
Respiratory Epithelium, Hyperplasia		1 (2%)	2 (4%)	1 (2%)
Respiratory Epithelium, Squamous Metaplasia			1 (2%)	
Turbinate, Atrophy				1 (2%)
Trachea	(50)	(50)	(50)	(48)
SPECIAL SENSES SYSTEM				
Eye	(50)	(50)	(50)	(50)
Phthisis Bulbi		1 (2%)		
Cornea, Inflammation, Acute				1 (2%)
Harderian Gland	(50)	(50)	(50)	(50)
Fibrosis			1 (2%)	
Lacrimal Gland	(1)	(0)	(0)	(0)
Inflammation, Granulomatous	1 (100%)			
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(49)
Amphophilic/Vacuolar Hyperplasia			1 (2%)	
Edema, Focal				1 (2%)
Infarct				2 (4%)
Inflammation, Chronic				1 (2%)
Inflammation, Chronic Active				1 (2%)
Nephropathy, Chronic Progressive	43 (86%)	40 (80%)	45 (90%)	47 (96%)
Polyarteritis Nodosa				2 (4%)
Capsule, Inflammation, Chronic				1 (2%)
Pelvis, Dilation	1 (2%)	2 (4%)		1 (2%)
Pelvis, Inflammation, Acute		1 (2%)		
Pelvis, Inflammation, Chronic				1 (2%)
Renal Tubule, Accumulation, Hyaline Droplet	2 (4%)			1 (2%)
Renal Tubule, Apoptosis				4 (8%)

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Harlan Sprague Dawley RATS FEMALE	0 mg/kg female	75 mg/kg female	250 mg/kg female	750 mg/kg female
Renal Tubule, Cyst			1 (2%)	
Renal Tubule, Dilation		1 (2%)		1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
Inflammation, Acute		1 (2%)		
Inflammation, Chronic Active		2 (4%)		

*** END OF REPORT ***

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