

24-Month Carcinogenicity Study of in CD-1 Mice  
 Incidence of Each Type of Neoplastic Lesion by Sex and Test Group  
 All Mice (Groups I, II, and V)

Study #006-007

	Group			MALES			FEMALES		
	I	II	V	I	II	V	I	II	V
<u>HEART</u> # Examined	100	100	100	95	100	100			
Malignant lymphoma	1	2	2	2	4	6			
Malignant histiocytoma, fibrous	0	0	0	1	0	0			
Rhabdomyosarcoma of auricle	0	0	1	0	0	0			
<u>AORTA</u> # Examined	100	99	100	93	98	98			
Malignant lymphoma	1	2	0	2	0	2			
Tumor embolus	0	0	0	1	0	0			
<u>LUNGS WITH BRONCHI</u> # Examined	100	100	100	95	100	100			
Adenoma	20	16	19	10	10	14			
Adenocarcinoma	5	10	5	3	4	4			
Malignant lymphoma	5	8	10	11	18	14			
Malignant myeloma	0	0	2	0	0	0			
Malignant histiocytoma, fibrous	0	0	0	1	0	0			
Reticulum cell sarcoma	0	0	0	1	0	0			
Adenocarcinoma of mammary gland									
- metastatic	0	0	0	1	0	1			
Fibrosarcoma - metastatic	0	0	0	0	0	1			
Osteosarcoma - extraskeletal	0	0	0	0	0	1			
<u>TRACHEA</u> # Examined	100	100	100	95	100	100			
Malignant lymphoma	0	2	2	0	1	1			
<u>ESOPHAGUS</u> # Examined	100	100	100	95	100	100			
Malignant lymphoma	0	0	0	0	1	0			
<u>STOMACH - Cardiac</u> # Examined	100	100	100	95	100	100			
Adenoma	6	3	3	1	0	0			
Adenocarcinoma	6	3	2	1	1	0			
Malignant lymphoma	2	5	4	5	6	4			
Malignant lymphoma of esophageal part	0	0	0	0	0	1			
Fibrosarcoma - metastatic	0	0	0	0	0	1			

000404

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	MALES			FEMALES		
	I	II	V	I	II	V
<u>STOMACH - Fundic</u> # Examined	100	100	100	95	100	100
Adenoma	2	5	1	2	4	0
Adenocarcinoma	5	6	4	6	1	0
Malignant lymphoma	1	2	2	5	5	1
Fibrosarcoma - metastatic	0	0	0	0	0	1
Osteosarcoma - extraskeletal	0	0	0	0	0	1
<u>STOMACH - Pyloric</u> # Examined	100	100	100	95	100	100
Adenoma	3	0	1	0	0	1
Adenocarcinoma	3	2	3	2	0	0
Malignant lymphoma	2	2	2	4	5	1
Adenocarcinoma of uterus - metastatic	—	—	—	0	0	1
Fibrosarcoma - metastatic	0	0	0	0	0	1
Leiomyosarcoma of uterus - metastatic	—	—	—	0	1	0
<u>MANDIBULAR LYMPH NODES</u> # Examined	99	100	100	94	100	99
Malignant lymphoma	9	9	10	12	16	14
Malignant myeloma	0	0	1	0	0	0
Malignant histiocytoma, fibrous	1	1	0	1	0	1
Reticulum cell sarcoma	0	0	0	1	0	0
Adenocarcinoma of lungs - metastatic	1	0	0	0	0	0
<u>SALIVARY GLAND - Mandibular</u> # Examined	100	100	100	95	100	100
Malignant lymphoma	6	8	9	10	11	6
Malignant myeloma	0	0	1	0	0	0
Malignant histiocytoma, fibrous	1	0	0	1	0	0
Reticulum cell sarcoma	0	0	0	1	0	0
<u>SALIVARY GLAND - Sublingual</u> # Examined	99	100	100	95	100	99
Malignant lymphoma	1	2	4	6	4	2
<u>SALIVARY GLAND - Parotid</u> # Examined	100	100	100	95	100	100
Malignant lymphoma	2	7	6	10	6	3
Malignant histiocytoma, fibrous	1	0	0	0	0	0
<u>DUODENUM</u> # Examined	100	100	100	95	100	100
Adenocarcinoma	0	1	0	0	0	0
Malignant lymphoma	2	3	2	0	1	2

000405

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	MALES			FEMALES		
	I	II	V	I	II	V
<b>JEJUNUM # Examined</b>	100	100	100	95	100	100
Hemangioma	0	0	0	0	0	1
Malignant lymphoma	2	1	1	1	2	2
<b>ILEUM # Examined</b>	100	100	100	95	100	100
Adenocarcinoma	1	0	0	0	0	0
Malignant lymphoma	1	2	2	1	3	2
Reticulum cell sarcoma	0	0	0	1	0	0
Osteoma	0	0	0	1	0	0
<b>COLON # Examined</b>	100	100	100	95	100	100
Malignant lymphoma	1	4	2	2	3	2
Reticulum cell sarcoma	0	0	0	1	0	0
<b>THYMUS # Examined</b>	81	85	83	87	91	93
Malignant lymphoma	13	11	18	24	39	22
Malignant myeloma	0	0	1	0	0	0
Malignant histiocytoma, fibrous	0	0	0	2	0	1
Reticulum cell sarcoma	0	0	0	1	0	0
Fibrosarcoma	1	0	0	0	0	0
Thymoma	1	0	0	0	0	0
Adenocarcinoma of lungs - metastatic	0	0	0	0	1	0
<b>SPLEEN # Examined</b>	100	100	100	95	100	100
Hemangioma	1	3	0	2	0	1
Hemangiosarcoma	0	0	2	0	0	1
Malignant lymphoma	11	9	11	18	18	14
Malignant myeloma	0	0	2	0	0	0
Reticulum cell sarcoma	0	0	0	2	0	0
Hemangiosarcoma - metastatic	0	0	1	1	0	0
Malignant histiocytoma	0	0	0	1	0	1
<b>PANCREAS # Examined</b>	100	100	100	95	100	99
Malignant lymphoma	3	5	5	7	13	3
Malignant histiocytoma, fibrous	0	0	0	1	0	1
Adenocarcinoma of stomach - metastatic	1	0	0	0	0	0
Endometrial stromal sarcoma - metastatic	—	—	—	1	0	0
Fibrosarcoma - metastatic	0	0	0	1	0	1

000406

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	MALES			FEMALES		
	I	II	V	I	II	V
<b>LIVER # Examined</b>	100	100	100	95	100	100
Adenoma of hepatocytes	15	12	17	1	4	2
Adenocarcinoma of hepatocytes	13	13	11	0	0	0
Hemangioma	1	0	2	0	0	0
Malignant lymphoma	7	8	11	10	18	10
Malignant myeloma	1	0	2	0	0	0
Malignant histiocytoma, fibrous	0	0	0	3	0	2
Reticulum cell sarcoma	0	0	0	1	0	0
Endometrial stromal sarcoma - metastatic	—	—	—	0	2	0
Hemangiosarcoma - metastatic	0	0	1	0	0	0
Leiomyosarcoma of uterus - metastatic	—	—	—	1	1	0
<b>GALL BLADDER # Examined</b>	98	96	100	94	99	99
Malignant lymphoma	4	3	2	1	5	4
Malignant myeloma	0	0	1	0	0	0
Malignant histiocytoma, fibrous	0	0	0	1	0	0
<b>KIDNEYS # Examined</b>	100	100	100	95	100	100
Adenoma	1	1	1	0	0	0
Adenocarcinoma	1	0	1	0	0	0
Malignant lymphoma	8	9	14	12	20	14
Malignant myeloma	0	0	2	0	0	0
Malignant histiocytoma, fibrous	0	0	0	1	0	0
Endometrial stromal sarcoma, unilateral - metastatic	—	—	—	1	0	0
<b>ADRENALS # Examined</b>	100	100	95	95	100	100
Adenoma of cortex	0	1	0	0	0	0
Adenoma of cortical spindle cells	0	0	0	0	1	0
Adenocarcinoma of cortical spindle cells	0	0	0	1	0	1
Pheochromocytoma	0	0	0	3	0	0
Malignant lymphoma	0	1	2	3	6	5
Malignant myeloma	0	0	1	0	0	0
Malignant histiocytoma, fibrous	0	0	0	1	0	0
Reticulum cell sarcoma	0	0	3	1	0	0
Fibrosarcoma - metastatic	0	0	0	1	0	0

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	MALES			FEMALES		
	I	II	V	I	II	V
<b>PITUITARY # Examined</b>	100	98	95	94	97	95
Adenoma	0	1	1	6	2	0
Malignant lymphoma	2	0	4	1	2	1
Malignant histiocytoma, fibrous	0	1	0	0	0	0
<b>TESTES # Examined</b>	100	100	100	--	--	--
Interstitial cell adenoma	1	0	1	--	--	--
Papillary cyst adenoma	0	1	0	--	--	--
Hemangioma	0	1	0	--	--	--
Malignant lymphoma	0	1	2	--	--	--
<b>EPIDIDYMIDES # Examined</b>	100	100	100	--	--	--
Malignant lymphoma	0	2	1	--	--	--
<b>PROSTATE # Examined</b>	100	100	100	--	--	--
Malignant lymphoma	5	6	3	--	--	--
Malignant myeloma	0	0	1	--	--	--
<b>OVARIES # Examined</b>	--	--	--	95	100	100
Adenoma	--	--	--	1	2	1
Granulosa cell tumor	--	--	--	1	3	0
Luteoma	--	--	--	1	0	0
Thecoma	--	--	--	1	1	0
Hemangioma	--	--	--	1	0	0
Malignant lymphoma	--	--	--	9	14	9
Malignant histiocytoma, fibrous	--	--	--	1	0	1
Reticulum cell sarcoma	--	--	--	1	0	0
Endometrial stromal sarcoma - metastatic	--	--	--	1	1	0
Leiomyosarcoma of uterus - metastatic	--	--	--	1	0	0
<b>UTERINE HORNS # Examined</b>	--	--	--	95	100	100
Adenocarcinoma	--	--	--	1	0	1
Endometrial stromal polyp	--	--	--	0	2	1
Endometrial stromal sarcoma	--	--	--	3	5	2
Leiomyoma	--	--	--	2	2	1
Leiomyosarcoma	--	--	--	3	1	0
Uterine endometrial polyp	--	--	--	0	1	0
Hemangioma	--	--	--	1	0	0
Hemangiosarcoma	--	--	--	0	1	0
Malignant lymphoma	--	--	--	6	7	3
Malignant histiocytoma, fibrous	--	--	--	1	0	2

000408

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	MALES			FEMALES		
	I	II	V	I	II	V
<b>URINARY BLADDER # Examined</b>	100	100	100	95	99	100
Carcinoma - <u>in situ</u>	1	0	0	0	0	0
Leiomyoma	0	0	0	0	1	0
Malignant lymphoma	4	5	3	12	12	6
Malignant histiocytoma, fibrous	0	0	0	0	0	1
<b>BRAIN - Cerebrum # Examined</b>	100	100	100	95	100	100
Glioma	0	0	1	0	0	0
Meningioma	1	0	0	0	0	0
Malignant lymphoma	1	1	2	1	2	0
<b>BRAIN - Midbrain # Examined</b>	100	100	100	95	100	100
Glioma	0	0	1	0	0	0
Malignant lymphoma	0	0	1	4	1	0
<b>BRAIN - Cerebellum # Examined</b>	100	100	100	95	99	99
No neoplasm seen						
<b>BRAIN - Pons # Examined</b>	100	100	100	95	100	100
Malignant lymphoma	0	0	0	0	1	0
<b>THYROIDS # Examined</b>	98	100	100	95	100	100
Adenoma	1	1	1	0	1	1
Adenocarcinoma	0	0	0	1	0	0
Malignant lymphoma	0	4	1	6	4	2
<b>PARATHYROIDS # Examined</b>	97	93	97	89	94	94
Malignant lymphoma	0	2	1	2	3	0
<b>STERNUM # Examined</b>	100	100	100	95	100	100
Malignant lymphoma	3	7	2	7	8	8
Malignant myeloma	0	0	2	0	0	0
Malignant histiocytoma, fibrous	0	0	0	0	0	1
Fibrosarcoma - metastatic	0	0	0	0	0	1
Hemangiosarcoma - metastatic	0	0	0	1	0	0

000409

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 All Mice (Groups I, II, and V)

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	Group			MALES			FEMALES		
	I	II	V	I	II	V	I	II	V
<u>SKIN</u> # Examined	100	100	100	95	100	100			
Fibrosarcoma of skin and subcutis	0	0	0	0	0	1			
Squamous cell carcinoma	0	0	0	0	0	1			
Malignant lymphoma	0	3	1	3	3	5			
Fibrosarcoma - metastatic	0	0	0	1	0	0			
<u>MAMMARY GLAND</u> # Examined	26	28	28	94	98	97			
Adenocarcinoma	0	1	0	4	4	4			
Malignant lymphoma	0	2	1	3	7	5			
<u>BONE MARROW SMEAR</u> # Examined	99	100	100	95	100	99			
Myelogenous leukemia	1	0	0	0	0	0			
Malignant lymphoma	2	4	3	3	4	6			
Malignant myeloma	0	0	1	0	0	0			
<u>BLOOD SMEAR</u> # Examined	65	63	52	47	50	49			
Monocytic leukemia	0	0	0	1	0	0			
Myelogenous leukemia	0	0	1	0	0	0			
<u>LYMPH NODES</u>									
Malignant lymphoma	6	5	7	8	16	12			
Malignant myeloma	0	0	1	0	0	0			
Malignant histiocytoma, fibrous	1	1	0	2	0	1			
Adenocarcinoma of infraorbital lacrimal gland - metastatic	1	0	0	0	0	0			
Adenocarcinoma of lungs - metastatic	1	0	0	0	0	0			
Endometrial stromal sarcoma - metastatic	—	—	—	1	0	0			
<u>Mesenteric Lymph Nodes</u>									
Malignant lymphoma	3	3	4	7	9	5			
Malignant histiocytoma, fibrous	0	0	0	0	0	1			
Fibrosarcoma - metastatic	0	0	0	1	0	1			
Hemangiosarcoma	0	0	0	1	0	0			
Adenocarcinoma of uterus - metastatic	—	—	—	0	0	1			

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	MALES			FEMALES		
	I	II	V	I	II	V
<u>MASSES/LESIONS<sup>a</sup></u>						
Group						
Adenocarcinoma	0	0	0	0	2	0
Carcinoma	0	0	1	1	0	0
Fibrosarcoma	1	0	0	2	1	0
Hemangioma	0	2	0	2	0	0
Hemangiosarcoma	0	0	1	1	0	0
Leiomyosarcoma	0	0	0	0	1	0
Malignant lymphoma	3	2	5	4	6	5
Malignant histiocytoma, fibrous	1	0	0	1	0	0
Reticulum cell sarcoma	0	0	0	1	0	1
Osteoma	0	0	0	1	0	0
Adenocarcinoma of lungs - metastatic	0	0	0	0	1	0
Fibrosarcoma - metastatic	0	0	0	1	0	0
Leiomyosarcoma of uterus - metastatic	--	--	--	0	1	0
<u>Cervix</u>						
Adenoma	--	--	--	0	0	1
Endometrial stromal sarcoma	--	--	--	0	1	1
Leiomyoma	--	--	--	0	1	2
Leiomyosarcoma	--	--	--	0	1	1
Malignant lymphoma	--	--	--	0	2	0
Malignant histiocytoma, fibrous	--	--	--	0	0	1
<u>Femur</u>						
Osteoma	0	0	1	2	6	0
Hemangiosarcoma	0	1	0	0	0	0
Malignant lymphoma	0	0	0	0	1	0
<u>Humerus</u>						
Osteoma	0	0	0	1	0	0
<u>Infraorbital Lacrimal Gland</u>						
Adenoma	2	1	1	0	0	0
Adenocarcinoma	1	0	0	0	0	0

<sup>a</sup> This category lists histologic findings from tissues which, in accordance with the protocol, were to be examined only if a gross lesion was found.



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MASSES/LESIONS (cont'd.)	Group	MALES			FEMALES		
		I	II	V	I	II	V
<u>Limbs</u>							
Osteosarcoma		0	0	0	0	0	2
<u>Pubis</u>							
Osteoma		0	0	0	1	1	0
<u>Rectum</u>							
Leiomyosarcoma of uterus - metastatic		—	—	—	0	1	0
<u>Ribs</u>							
Fibroma		0	1	0	0	0	0
Fibrosarcoma		2	0	0	0	0	0
Osteoma		0	0	0	1	0	0
<u>Sebaceous Gland</u>							
Adenoma		0	0	0	1	0	0
<u>Seminal Vesicles</u>							
Malignant lymphoma		1	0	0	—	—	—
<u>Skull</u>							
Osteoma		1	0	1	0	4	1
<u>Tongue</u>							
Papilloma		0	0	0	0	1	0
Squamous cell carcinoma		0	0	1	0	0	0
<u>Ureters</u>							
Malignant lymphoma		0	0	1	1	0	0
<u>Vertebrae</u>							
Malignant lymphoma		1	0	1	0	0	1

000412

24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund

Study #006-007

HEART # Examined	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
Myocarditis, acute, focal	1	1	1	0	3	1	0	1	2	0
Myocarditis, subacute, focal	2	0	0	0	0	2	0	1	1	0
Myocarditis, chronic, focal	0	1	2	2	2	0	0	0	1	3
Myocarditis, chronic, diffuse	0	0	0	0	1	0	0	0	0	0
Pericarditis, acute, focal	1	0	0	1	1	0	4	0	0	1
Pericarditis, acute, diffuse	0	0	0	0	0	1	0	1	0	0
Pericarditis, chronic, focal	0	0	0	0	0	0	2	1	0	0
Pericarditis, chronic, diffuse	1	0	0	0	0	0	2	0	1	0
Inflammation, acute, focal	0	0	0	0	0	1	0	0	0	0
Endocarditis, bacterial	0	0	0	1	0	0	0	0	0	0
Arteritis, subacute, focal	0	0	0	0	0	0	0	1	0	1
Mineralization, focal	0	0	1	0	0	1	0	0	1	0
Hemorrhage, focal	0	0	0	0	0	0	0	0	2	0
Necrosis, focal	0	1	0	0	0	1	0	0	0	0
Bacteria	0	0	1	0	1	2	1	3	2	1
Bacterial embolus	0	0	1	0	0	0	0	0	0	0
Thrombus	1	0	1	1	0	2	1	1	2	0
Thrombus in auricle	0	1	0	0	0	0	1	0	1	0
Thrombus of pulmonary artery	0	0	0	1	0	0	0	0	0	0
<b>AORTA # Examined</b>	<b>38</b>	<b>39</b>	<b>37</b>	<b>37</b>	<b>49</b>	<b>49</b>	<b>50</b>	<b>43</b>	<b>49</b>	<b>54</b>
Arteritis, subacute, focal	2	0	0	2	1	0	2	2	0	1
Arteritis, chronic, focal	0	0	0	0	1	0	0	0	0	1
Atrophy, medial	0	0	0	0	1	0	0	0	0	0
Thrombus	0	0	0	0	0	0	0	0	1	0
Bacteria	0	0	0	0	0	0	0	0	0	0

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**Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
<b>LUNGS-WITH BRONCHI # Examined</b>										
Pneumonia, acute, focal	1	0	1	0	0	1	0	0	0	0
Pneumonia, focal, interstitial	1	0	1	0	0	0	0	2	0	0
Pneumonia, chronic, focal	2	0	0	1	0	0	0	0	0	0
Pneumonia, chronic, diffuse	0	0	0	1	0	2	0	0	0	2
Bronchitis, acute, focal	0	0	0	1	1	0	1	0	0	0
Bronchitis, acute, diffuse	0	0	1	0	0	0	0	0	0	0
Pleuritis, acute, focal	0	0	0	0	0	1	1	1	0	0
Pleuritis, acute, diffuse	0	0	0	0	0	1	0	0	0	0
Pleuritis, chronic, focal	1	0	0	1	1	1	1	2	2	1
Pleuritis, chronic, diffuse	1	0	0	0	0	0	0	0	1	0
Focus or foci of pigmented macrophages	0	0	0	0	0	0	0	0	0	2
Thrombosis	0	0	2	0	1	0	1	0	2	0
Hemorrhage	0	0	0	0	0	0	1	1	0	0
Hemorrhage, focal	0	0	0	0	1	2	1	0	1	1
Necrosis	0	0	1	1	0	0	0	0	0	0
Bacteria	0	0	1	0	0	0	1	0	1	0
Food particle in bronchiole	1	0	0	0	0	0	1	0	0	1
Congestion	0	0	0	0	0	0	1	1	0	0
Edema	0	0	1	0	0	0	0	0	0	0
Perforation	0	1	0	0	0	0	0	0	0	0
<b>TRACHEA # Examined</b>	38	39	37	37	49	50	51	43	50	55
Tracheitis, acute, focal	0	0	0	2	0	0	0	0	0	0
Tracheitis, acute, diffuse	1	0	1	0	0	0	0	0	0	0
Tracheitis, chronic, focal	0	2	0	0	0	0	2	0	0	0
Arteritis, acute, diffuse	0	0	0	0	0	0	1	0	0	0

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**Found Dead or Killed Moribund**

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Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
<u>ESOPHAGUS</u> # Examined	1	0	0	0	0	0	1	0	0	0
Inflammation, acute, diffuse	0	0	0	0	0	1	1	0	1	1
Inflammation, chronic, focal	1	0	0	0	0	0	0	0	0	0
Inflammation, chronic, diffuse	1	0	0	0	0	1	1	0	0	0
Perforation	0	0	0	0	0	0	0	0	0	0
<u>STOMACH - Cardiac</u> # Examined	38	39	37	37	49	50	51	43	50	55
Inflammation, subacute, focal	0	0	0	0	0	1	0	0	0	0
Inflammation, subacute, diffuse	0	0	0	0	0	0	0	0	0	1
Inflammation, chronic, diffuse	0	0	0	0	0	0	1	0	0	0
Arteritis, subacute, focal	0	0	0	0	0	0	0	1	0	0
Serositis, chronic, focal	0	0	0	0	1	0	0	0	0	0
Ectopic mucosa	0	1	0	0	0	0	0	0	0	0
Hypertrophic gastritis	0	1	0	0	0	0	0	0	0	0
Autolysis	0	1	0	0	0	0	0	0	0	0
<u>STOMACH - Fundic</u> # Examined	38	39	37	37	49	50	51	43	50	55
Inflammation, acute, focal	0	1	1	0	0	0	1	0	0	0
Inflammation, subacute, focal	0	0	0	0	1	0	0	0	0	0
Inflammation, subacute, diffuse	0	0	0	0	0	0	0	0	0	1
Inflammation, chronic, diffuse	0	0	0	0	0	0	1	0	0	0
Ulcer, acute	0	0	0	0	1	0	0	0	0	0
Serositis, chronic, focal	0	0	0	0	0	0	1	1	0	0
Necrosis, focal	1	1	0	0	0	1	0	0	0	0
Erosion	1	0	0	0	0	0	1	0	0	0
Hypertrophic gastritis	0	2	0	0	0	0	0	0	0	0
Autolysis	0	1	0	0	0	0	0	0	0	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	42	50	55
<u>STOMACH - Pyloric # Examined</u>	1	0	0	1	1	3	0	0	3	1
Serositis, chronic, focal	0	0	0	0	0	0	1	0	0	0
Serositis, chronic, diffuse	0	0	0	0	0	1	0	1	0	0
Arteritis, subacute, focal	0	0	0	0	1	0	0	0	0	0
Ulcer, chronic	0	0	1	0	0	0	0	0	0	0
Necrosis, focal	0	1	0	0	0	0	0	0	0	0
Autolysis	0	1	0	0	0	1	0	0	0	0
<u>MANDIBULAR LYMPH NODES # Examined</u>	37	39	36	36	49	49	51	41	50	54
Lymphadenitis, acute, focal	0	0	0	0	0	3	0	1	0	0
Lymphadenitis, acute, diffuse	1	0	2	0	0	0	0	0	1	0
Lymphadenitis, subacute, diffuse	0	0	1	1	0	0	2	0	1	1
Lymphadenitis, chronic, diffuse	2	0	2	1	1	2	3	4	4	2
Plasma cells prominent	1	1	0	1	1	3	2	0	2	0
Arteritis, chronic, focal	0	0	0	0	0	1	0	0	0	1
Hemstoptosis - slight	0	1	0	0	0	0	0	0	0	0
Marked erythrophagocytosis	0	1	0	0	0	0	0	0	0	0
Bacteria	0	0	0	0	0	1	0	2	0	0
<u>SALIVARY GLANDS - Mandibular # Examined</u>	38	39	37	37	49	50	51	43	50	55
Inflammation, subacute, focal	4	7	6	3	5	4	9	6	4	8
Inflammation, chronic, focal	0	1	0	0	0	0	1	0	1	0
<u>SALIVARY GLANDS - Sublingual # Examined</u>	37	39	37	37	49	50	51	43	50	54
Inflammation, subacute, focal	0	0	0	0	0	1	0	0	0	0

**24-Month Carcinogenicity Study of**  
**Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group**  
**Found Dead or Killed Moribund**

Study #006-007

	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
<b>SALIVARY GLANDS - Parotid # Examined</b>										
Inflammation, subacute, focal	1	0	0	0	1	1	0	1	0	1
Inflammation, chronic, diffuse	0	0	0	0	0	0	1	0	0	0
Megalocytosis, focal	0	0	0	0	0	0	0	0	2	0
Amyloid	0	1	0	0	0	0	1	0	1	0
Cytoplasmic vacuolization, diffuse	0	0	1	0	0	0	1	0	0	0
Thrombus	0	0	1	0	0	0	0	0	0	0
<b>DUODENUM # Examined</b>	38	39	37	37	49	50	51	43	50	55
Amyloid	1	3	0	0	0	1	1	0	0	0
Edema	0	0	0	1	0	0	0	0	0	0
Serositis, chronic, focal	0	0	0	1	0	0	0	0	0	0
Necrosis of anterior part	0	1	0	0	0	0	0	0	0	0
Black pigment in tip of villus	0	0	0	0	1	0	0	0	0	0
Autolysis	8	12	10	5	13	16	20	15	9	18
<b>JEJUNUM # Examined</b>	38	39	37	37	49	50	51	43	50	55
Inflammation, acute, focal	0	0	0	0	0	0	0	0	1	0
Inflammation, acute, diffuse	0	0	0	0	0	0	1	0	0	1
Amyloid	0	1	0	0	1	2	1	0	0	0
Edema	0	0	0	1	0	0	0	0	0	0
Autolysis	5	6	4	2	6	9	8	6	1	10

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
<u>ILEUM # Examined</u>	0	0	0	0	0	0	0	0	1	0
Inflammation, acute, focal	0	1	0	0	0	0	1	0	0	2
Inflammation, acute, diffuse	0	0	0	0	0	1	0	0	0	0
Inflammation, chronic, focal	0	0	0	0	0	0	0	1	0	0
Necrosis, diffuse	0	0	0	0	0	0	0	1	0	0
Hemorrhage, focal	0	0	0	0	0	0	0	1	0	0
Amyloid	0	1	1	0	0	0	1	0	0	0
Autolysis	3	2	3	2	2	6	4	4	1	6
<u>COLON # Examined</u>	38	39	37	37	49	50	51	43	50	55
Inflammation, acute, diffuse	0	0	0	0	2	0	0	0	0	0
Autolysis	1	0	0	1	0	1	2	1	1	0
<u>THYMUS # Examined</u>	26	34	30	28	35	43	43	36	43	51
Inflammation, acute, diffuse	0	0	0	1	0	2	1	1	1	0
Inflammation, subacute, focal	0	0	0	0	1	0	0	0	0	0
Inflammation, subacute, diffuse	0	0	0	0	0	0	1	0	1	1
Inflammation, chronic, diffuse	1	0	0	0	1	2	1	0	2	0
Lymphoid hyperplasia	1	1	1	1	1	0	3	1	2	0
Lymphocytolysis	2	1	0	2	2	1	2	2	2	6
Hemorrhage, focal	0	0	0	0	1	0	0	0	0	0
Necrosis, focal	0	0	0	0	0	1	0	0	0	0
Arteritis, subacute, focal	0	0	0	0	0	0	0	0	1	0
Plasma cells prominent	0	0	0	0	0	1	0	0	0	1
Hematopoiesis	0	0	1	0	0	0	0	0	0	0
Bacteria	0	0	0	0	0	0	0	1	0	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
<u>SPLEEN # Examined</u>	2	0	2	0	3	2	3	1	0	4
Hematopoiesis - slight	9	6	4	10	9	14	9	11	12	4
Hematopoiesis - moderate	1	0	5	4	4	7	10	4	13	4
Hematopoiesis - severe	1	0	0	0	0	2	0	1	0	1
Hematopoiesis - extreme	0	1	0	0	0	0	0	0	0	0
Inflammation, acute, focal	0	0	0	0	0	0	0	0	0	0
Inflammation, subacute, focal	0	0	0	0	0	0	0	0	0	0
Inflammation, subacute, diffuse	0	0	0	0	1	0	0	0	0	0
Inflammation, subacute, diffuse	0	0	0	0	0	0	1	0	0	0
Inflammation, chronic, focal	0	0	0	0	0	0	0	0	0	0
Inflammation, chronic, diffuse	0	0	0	0	0	0	0	0	1	0
Hemorrhage	0	1	0	0	1	0	0	0	0	1
Serositis, acute, diffuse	0	0	0	0	1	0	0	0	0	0
Serositis, subacute, focal	0	0	0	0	0	0	1	0	0	0
Serositis, chronic, focal	0	0	0	0	0	0	1	0	0	0
Erythrophagocytosis	0	1	1	0	0	0	1	0	0	0
Lymphocytolysis	0	0	0	2	0	0	2	0	1	6
Arteritis, acute, focal	0	0	0	0	0	0	0	0	0	1
Macrophages prominent	1	1	0	0	1	0	0	0	0	0
Amyloid	0	0	0	0	0	0	0	0	0	0
Bacteria	0	0	0	0	0	0	0	0	1	0
<u>PANCREAS # Examined</u>	38	39	37	37	49	50	51	43	50	54
Inflammation, subacute, focal	1	0	1	0	1	1	0	0	2	0
Inflammation, chronic, focal	0	1	1	1	0	0	1	0	1	0
Inflammation, chronic, diffuse	0	0	0	1	0	0	0	0	0	0
Serositis, chronic, focal	0	1	0	0	0	0	1	0	0	0
Karyomegaly	0	0	0	0	0	0	0	0	0	1
Hyparplasia, focal	0	0	0	0	0	1	0	0	0	0
Atrophy of acinar part	0	0	0	0	0	1	0	0	0	0



**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

LIVER # Examined	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
Group										
Hepatitis, acute, focal	2	2	2	2	0	3	0	0	0	0
Hepatitis, acute, diffuse	0	0	0	0	0	0	0	2	0	0
Hepatitis, subacute, focal	2	0	0	0	0	1	1	2	1	1
Hepatitis, chronic, focal	0	0	0	0	0	0	2	0	1	0
Hepatitis, chronic, diffuse	0	1	0	0	0	0	1	0	1	1
Necrosis, focal	0	0	0	0	0	0	1	0	0	0
Necrosis, focal, random distribution	1	1	0	2	0	1	1	2	0	1
Necrosis, diffuse	2	1	1	0	2	3	1	2	0	1
Necrosis, diffuse centrilobular distribution	0	0	0	0	0	1	2	0	0	0
Hematopoiesis - minimal	1	0	0	0	0	0	0	1	1	0
Hematopoiesis - slight	0	0	2	0	0	2	3	0	4	1
Hematopoiesis - moderate	0	0	1	2	0	2	2	0	0	3
Hematopoiesis - severe	0	0	0	1	0	0	0	1	1	0
Cytoplasmic vacuolation, fat, diffuse	0	0	0	0	0	0	1	0	0	0
Cytoplasmic vacuolation, fat, portal distribution, diffuse	0	0	0	0	0	0	1	0	1	0
Cytoplasmic vacuolation, fat, centrilobular distribution, focal	0	0	0	0	0	0	0	0	1	0
Serositis, chronic, focal	0	0	0	0	1	0	0	0	0	0
Congestion, chronic, passive	0	0	0	0	0	0	0	0	1	0
Arteritis, chronic, focal	0	1	0	0	0	0	0	0	0	0
Erythrophagocytosis, marked	0	1	0	0	0	0	0	0	0	0
Focus of cellular atypia	0	0	1	0	0	0	0	0	0	0
Area of cellular basophilia	1	0	0	0	0	0	0	0	0	0
Karyomegaly	2	2	2	3	0	0	0	0	1	0
Amyloid	1	1	0	0	0	0	0	0	1	0
Bile duct proliferation	1	0	0	0	0	0	0	0	0	0

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**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
<u>LIVER (cont'd.)</u>										
Bacteria	0	0	0	0	1	1	0	1	0	1
Abscess	0	0	1	0	1	0	0	0	2	0
Cyst	0	1	0	0	1	0	0	0	0	0
Hemorrhage	0	0	0	0	1	0	0	0	0	0
<u>GALL BLADDER # Examined</u>	38	37	35	37	49	49	50	43	50	55
Inflammation, acute, diffuse	0	0	0	0	0	0	0	0	0	1
Inflammation, subacute, focal	0	1	0	0	0	0	0	1	0	0
Inflammation, subacute, diffuse	0	0	0	0	2	0	0	0	0	0
Inflammation, chronic, focal	0	1	0	0	0	0	0	0	1	0
Edema	0	0	0	0	0	0	2	0	0	0
Abscess	0	0	0	0	1	0	0	0	0	0
Autolysis	11	15	12	14	14	21	17	16	22	18
Section inadequate for diagnosis	1	0	0	0	0	0	0	0	0	0
<u>KIDNEYS # Examined</u>	38	39	37	37	49	50	51	43	50	55
Nephritis, acute, focal, unilateral	1	0	0	0	1	1	0	0	0	0
Nephritis, acute, focal, bilateral	0	0	0	0	0	3	1	2	0	0
Nephritis, acute, diffuse, unilateral	1	0	0	0	0	0	0	0	0	0
Nephritis, acute, diffuse, bilateral	1	0	0	0	0	0	0	0	0	0
Nephritis, acute, diffuse, unilateral, bacterial	0	0	0	1	0	0	0	0	0	0
Nephritis, subacute, focal, unilateral	1	1	0	0	0	0	0	0	0	0
Nephritis, subacute, focal, bilateral	0	2	5	4	5	2	6	5	5	2

24-Month Carcinogenicity Study of  
 Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
 Found Dead or Killed Moribund

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
<u>KIDNEYS</u> (cont'd.)										
Nephritis, chronic, focal, unilateral - minimal	2	1	0	0	0	0	0	0	1	0
Nephritis, chronic, focal, unilateral - slight	1	0	1	1	0	0	1	0	1	0
Nephritis, chronic, focal, bilateral - minimal	0	0	1	1	1	0	1	1	0	2
Nephritis, chronic, focal, bilateral - slight	2	4	1	0	4	3	2	1	3	6
Nephritis, chronic, focal, bilateral - moderate	1	0	0	1	1	2	0	1	1	14
Nephritis, chronic, focal, bilateral - severe	1	1	0	0	1	2	0	1	0	3
Nephritis, chronic, diffuse, unilateral	1	1	0	0	0	0	0	0	0	0
Nephritis, chronic, diffuse, bilateral	1	3	1	1	1	3	3	0	4	7
Pyelonephritis, focal, bilateral	1	0	0	1	0	0	0	0	0	0
Pyelonephritis, diffuse, unilateral	0	1	1	1	2	0	0	0	1	0
Pyelonephritis, diffuse, bilateral	0	0	1	2	3	0	0	0	0	0
Pyelitis, acute, unilateral	1	0	0	0	1	0	0	0	0	0
Pyelitis, chronic, bilateral	0	0	0	0	1	0	0	0	1	0
Bacteria, unilateral	2	0	1	0	1	2	0	1	0	0
Bacteria, bilateral	0	0	0	0	1	1	1	1	1	0
Arteritis, subacute, focal	0	0	0	0	0	0	0	0	0	1
Mineralization, renal pelvis, focal, unilateral	0	0	0	0	0	1	0	0	0	0
Mineralization, renal cortex, focal, bilateral	0	1	0	0	0	0	0	0	1	0
Glomerulonephritis, diffuse, bilateral	1	0	1	0	0	2	1	2	0	1
Necrosis, focal, bilateral	0	0	0	0	0	0	1	0	0	0
Necrosis, diffuse, bilateral of inner cortex	0	0	0	0	0	0	0	1	0	0
Necrosis, papillae	0	1	0	0	0	0	0	0	0	0
Dilated pelvis, unilateral	0	1	0	0	1	0	0	0	0	0
Dilated pelvis, bilateral	2	1	2	0	1	1	0	0	0	1
Amyloid	1	3	1	0	2	0	2	0	2	1
Hyaline droplets	0	1	0	1	0	3	2	2	2	2
Pigment in tubular epithelium, bilateral	0	0	0	0	0	0	1	1	0	0
Hematoma, perirenal, unilateral	0	0	0	0	0	1	0	0	0	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

ADRENALS # Examined	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	48	50	51	43	49	55
Foci of dark cells - medulla	0	0	0	0	0	0	0	1	0	0
Focus of cellular atypia - cortex	2	1	0	1	1	0	0	0	0	0
Blood-filled spaces	0	0	0	1	1	1	0	0	0	0
Inflammation, subacute, focal	0	0	0	0	0	1	0	0	0	0
Hematopoiesis - minimal	0	0	0	0	0	0	1	0	0	0
Hematopoiesis - moderate	0	0	0	0	0	0	0	0	0	1
Arteritis, subacute, focal	0	0	0	0	0	0	1	0	0	0
Amyloid	0	3	0	0	0	0	0	0	0	0
Serositis, chronic, focal	0	0	0	0	1	0	0	0	0	0
Cytoplasmic vacuolization, fat, focal - cortex	0	0	1	0	0	0	0	0	0	0
Focal hyperplasia - type A cells	0	0	0	0	0	0	0	1	0	0
Focal fibrosis - cortex	0	0	0	0	0	0	0	1	0	0
Cyst	0	0	1	0	0	0	0	0	0	0
<b>PITUITARY # Examined</b>	<b>38</b>	<b>39</b>	<b>36</b>	<b>37</b>	<b>45</b>	<b>49</b>	<b>48</b>	<b>43</b>	<b>50</b>	<b>50</b>
Cyst	0	0	0	0	0	1	0	0	1	1
Congestion	0	0	1	0	0	0	0	0	0	0
Bacteria	0	0	0	0	0	0	0	1	0	0
Hemorrhage, focal	0	0	0	0	0	1	0	0	0	0
Section inadequate for diagnosis	0	0	0	1	0	0	1	0	0	1

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
in CD-1 Mice  
Found Dead or Killed Moribund**

Study #006-007

Group

TESTES # Examined

Hypospermatogenesis, focal, unilateral  
Hypospermatogenesis, focal, bilateral  
Hypospermatogenesis, diffuse, unilateral  
Hypospermatogenesis, diffuse, bilateral  
Inflammation, acute, diffuse  
Arteritis, subacute, focal  
Mineralization, focal  
Bacteria  
Cyst

EPIDIDYMIDES # Examined

Inflammation, acute, diffuse  
Inflammation, subacute, focal

PROSTATE # Examined

Prostatitis, acute, focal  
Prostatitis, acute, diffuse  
Prostatitis, subacute, focal  
Prostatitis, subacute, diffuse  
Prostatitis, chronic, focal  
Prostatitis, chronic, diffuse  
Serositis, acute, focal  
Hemorrhage, focal  
Hemorrhage, diffuse  
Bacteria

	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49					
Hypospermatogenesis, focal, unilateral	1	2	0	0	1					
Hypospermatogenesis, focal, bilateral	0	2	0	1	0					
Hypospermatogenesis, diffuse, unilateral	1	2	1	0	1					
Hypospermatogenesis, diffuse, bilateral	0	2	3	1	3					
Inflammation, acute, diffuse	1	0	0	0	0					
Arteritis, subacute, focal	0	1	0	0	0					
Mineralization, focal	0	1	0	0	0					
Bacteria	1	0	0	0	0					
Cyst	0	1	0	0	0					
<u>EPIDIDYMIDES</u>	38	39	37	37	49					
Inflammation, acute, diffuse	1	0	0	0	0					
Inflammation, subacute, focal	0	0	0	0	1					
<u>PROSTATE</u>	38	39	37	37	49					
Prostatitis, acute, focal	0	0	2	0	0					
Prostatitis, acute, diffuse	6	3	2	3	7					
Prostatitis, subacute, focal	0	1	0	2	1					
Prostatitis, subacute, diffuse	1	0	0	1	1					
Prostatitis, chronic, focal	0	3	3	1	1					
Prostatitis, chronic, diffuse	2	0	0	3	2					
Serositis, acute, focal	1	0	0	0	0					
Hemorrhage, focal	0	0	1	0	0					
Hemorrhage, diffuse	1	0	0	0	0					
Bacteria	1	0	0	0	0					

**24-Month Carcinogenicity Study of**  
**Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group**  
**Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	50					55				
<b>OVARIES # Examined</b>										
Arteritis, acute, focal						0	0	0	0	2
Arteritis, subacute, focal						0	1	1	0	1
Arteritis, chronic, focal						1	0	0	0	0
Hemorrhage						9	7	3	7	6
Cyst						29	31	25	30	33
Bacteria						0	1	1	1	0
Abscess						0	1	0	0	0
<b>UTERINE HORNS # Examined</b>						50	51	43	50	55
Cystic endometrial hyperplasia, diffuse, unilateral)						2	2	0	0	0
Cystic endometrial hyperplasia, diffuse, bilateral)						19	23	17	23	27
Inflammation, acute, focal						0	0	0	0	1
Inflammation, acute, diffuse						0	0	0	2	0
Inflammation, chronic, focal						1	0	0	0	0
Hydrometra, unilateral)						0	1	1	1	0
Hydrometra, bilateral)						1	1	0	1	0
Endometritis, acute, unilateral)						2	0	0	0	0
Endometritis, acute, bilateral)						0	0	0	0	1
Endometritis, chronic, unilateral)						0	0	1	0	0
Arteritis, subacute, focal						1	0	0	1	0
Arteritis, chronic, focal						2	0	0	0	0
Hemorrhage						6	3	2	3	1
Necrosis, diffuse						0	1	2	2	2
Necrosis, focal						0	0	1	0	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	42	49	55
<u>UTERINE HORNS (cont'd.)</u>										
Thrombus	--	--	--	--	--	0	1	0	0	0
Cysts	--	--	--	--	--	0	0	0	1	0
Bacteria	--	--	--	--	--	1	0	1	1	1
Abscess	--	--	--	--	--	0	0	1	0	0
<u>URINARY BLADDER # Examined</u>										
Cystitis, acute, focal	1	0	0	1	1	1	1	0	0	0
Cystitis, acute, diffuse	3	1	1	1	2	0	0	1	0	1
Cystitis, subacute, focal	6	6	4	8	8	7	9	6	5	9
Cystitis, subacute, diffuse	1	0	0	1	1	1	0	0	0	0
Cystitis, chronic, focal	0	1	1	0	0	0	0	0	0	0
Cystitis, chronic, diffuse	0	0	1	2	1	0	0	0	1	0
Serositis, acute, focal	0	0	0	0	0	0	0	0	1	0
Serositis, chronic, focal	0	0	0	0	0	1	0	0	0	0
Serositis, chronic, diffuse	0	0	0	0	1	0	1	0	0	0
Calculi	0	0	1	0	0	0	0	0	0	0
Calculi, minute	0	0	0	0	0	0	0	0	0	1
Arteritis, subacute, focal	0	0	0	0	0	0	0	0	0	1
Autolysis	0	1	0	0	0	0	0	0	0	0
<u>BRAIN - Cerebrum # Examined</u>										
Meningitis, chronic	0	0	0	1	0	0	0	0	0	0
Meningitis, lymphocytic, focal	0	0	0	1	0	0	0	0	0	0
Encephalitis, acute, focal	0	0	1	0	0	1	0	1	0	0
Mineralization, focal	0	0	0	0	0	1	0	0	0	0
Old hemorrhage	0	0	0	0	0	1	0	0	0	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55
<u>BRAIN - Midbrain</u> # Examined	0	0	0	1	0	0	0	0	0	0
Meningitis, chronic	0	0	0	0	0	0	0	1	0	1
Mineralization, focal	0	0	0	0	0	0	0	0	1	0
Inflammation, subacute, focal of choroid	0	0	0	0	0	1	0	0	0	0
Hemorrhage, focal	0	0	1	0	0	0	0	0	0	0
Encephalitis, acute, focal	0	0	0	0	0	0	0	0	0	0
Arteritis, chronic, focal	0	0	0	0	0	0	0	1	0	0
<u>BRAIN - Cerebellum</u> # Examined	38	39	37	36	49	50	50	43	50	54
No lesion seen										
<u>BRAIN - Pons</u> # Examined	38	39	37	37	49	50	51	43	50	55
Encephalitis, acute, focal	0	0	1	0	0	0	0	0	0	0
<u>THYROID</u> # Examined	36	39	37	37	49	50	51	43	50	54
Inflammation, subacute, focal	0	0	0	1	0	1	1	0	0	3
Inflammation, subacute, diffuse	0	0	0	0	0	0	1	0	0	0
Inflammation, chronic, focal	0	0	0	0	0	1	0	0	0	0
Arteritis, subacute, focal	0	0	0	0	0	0	0	1	0	1
Amyloid	0	2	0	0	0	0	0	0	0	0
Cyst	0	0	1	0	0	1	0	1	1	1
<u>PARATHYROID</u> # Examined	35	36	37	37	48	48	48	42	44	52
Inflammation, subacute, focal	0	1	0	0	0	0	0	0	0	2
Amyloid	0	0	0	0	0	0	0	0	1	0
Hyperplasia	0	0	0	0	0	0	0	0	0	1



**24-Month Carcinogenicity Study of CD-1 Mice  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES										FEMALES				
	I	II	III	IV	V	I	II	III	IV	V	I	II	III	IV	V
	38	39	37	37	49	50	51	43	50	55					
<b>STERNUM # Examined</b>	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Macrophages in marrow	2	0	3	2	2	3	0	5	6	3	0	0	0	0	0
Myeloid hyperplasia of marrow	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0
Marrow hyperplasia	0	0	0	0	0	1	0	1	0	3	0	0	0	0	0
Fibro-osseous lesion	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Erythrophagocytosis	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Necrosis, focal of marrow	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inflammation, chronic, focal	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Myositis, chronic, focal	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Arteritis, subacute, focal	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Osteoporosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hematopoiesis, extramedullary	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Increased bone formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Depletion of marrow	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
<b>SKIN # Examined</b>	0	0	2	1	2	0	0	0	0	0	0	0	0	0	0
Inflammation, acute, focal	1	0	2	0	2	1	1	0	0	0	0	0	0	0	0
Inflammation, acute, diffuse	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0
Inflammation, acute, diffuse, subcutaneous	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Inflammation, subacute, diffuse	0	0	1	0	2	1	0	0	1	0	0	0	1	0	0
Inflammation, chronic, diffuse	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0
Inflammation, chronic, focal	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0
Ulcer, acute	1	1	5	0	2	1	1	1	3	0	0	0	0	0	0
Ulcer, chronic	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0
Necrosis, diffuse	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Folliculitis, acute	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Intracytoplasmic inclusion bodies	1	4	2	2	1	5	5	6	7	5	0	0	0	0	0
Edema	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Autolysis	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group

MAMMARY GLAND # Examined

Cyst  
Necrosis, diffuse  
Inflammation, acute, diffuse  
Inflammation, subacute, focal

BONE MARROW SMEAR # Examined

Autolysis  
Smear inadequate for diagnosis

BLOOD SMEAR # Examined

Smear inadequate for diagnosis

LYMPH NODES

Lymphadenitis, acute, diffuse  
Lymphadenitis, acute, focal  
Lymphadenitis, subacute, focal  
Lymphadenitis, subacute, diffuse  
Lymphadenitis, chronic, diffuse  
Necrosis, focal  
Necrosis, diffuse  
Arteritis, subacute, focal  
Plasma cells prominent  
Marked erythrophagocytosis  
Abscess  
Bacteria

	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
	13	14	13	12	13	49	49	37	47	52
	1	1	4	4	3	2	1	0	4	1
	0	0	0	0	0	0	0	1	0	0
	0	0	0	0	0	0	1	0	0	0
	0	0	0	0	0	0	0	0	1	0
	37	39	37	36	49	50	51	43	50	55
	0	0	0	0	1	0	0	0	0	0
	3	2	2	2	3	3	7	2	1	5
	3	2	3	3	2	2	1	5	5	5
	0	0	0	0	0	0	0	0	1	0
	0	0	1	0	0	0	0	0	0	1
	0	0	0	0	0	0	0	0	0	1
	1	0	0	0	0	0	0	0	0	0
	1	0	0	1	0	0	0	0	0	2
	2	2	1	2	2	1	2	3	3	0
	0	0	0	0	0	0	0	1	0	0
	0	0	0	0	0	0	0	0	0	1
	0	0	0	0	0	0	0	1	0	0
	0	0	0	1	0	0	0	0	1	0
	0	1	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	1	0	0	0
	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	1	0	0	0
	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	1

**24-Month Carcinogenicity Study of**  
**Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group**  
**Found Dead or Killed Moribund**  
**in CD-1 Mice**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
<u>Mesenteric Lymph Node</u>										
Lymphadenitis, acute, diffuse	0	1	0	0	0	0	0	0	0	1
Lymphadenitis, subacute, diffuse	0	0	0	1	0	0	1	0	0	0
Congestion	0	0	1	0	0	0	0	1	0	0
Edema	1	0	0	0	0	0	0	0	0	0
Lymphoid hyperplasia	0	0	0	0	0	1	0	0	0	0
<u>MASSES/LESIONS:<sup>a</sup></u>										
Inflammation, acute, diffuse	2	0	0	0	0	0	0	0	0	0
Epidermal inclusion cyst	0	0	1	0	0	0	0	0	0	0
Abscess	0	0	0	0	0	0	0	0	1	1
Necrosis, diffuse	1	0	0	0	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0	0	1	0	0
Bacteria	1	0	0	0	0	0	0	0	0	0
<u>Bulbourethral Gland</u>										
Inflammation, chronic, diffuse	0	0	0	0	1	--	--	--	--	--
<u>Cecum</u>										
Necrosis, diffuse	0	0	0	0	0	0	0	1	0	0
Hemorrhage, focal	0	0	0	0	0	0	0	1	0	0

<sup>a</sup> This category lists histologic findings from tissues which in accordance with the protocol, were to be examined only if a gross lesion was found.

**24-Month Carcinogenicity Study of**  
**Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group**  
**Found Dead or Killed Moribund**

Study #006-007

	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
<u>MASSES/LESIONS:</u> (cont'd.)										
<u>Cervix</u>										
Inflammation, chronic, focal	--	--	--	--	--	1	0	0	0	0
Cystic endometrial hyperplasia, diffuse	--	--	--	--	--	0	0	1	0	0
Necrosis, diffuse	--	--	--	--	--	0	0	1	0	0
Hemorrhage	--	--	--	--	--	0	0	2	0	1
<u>Eyes</u>										
Keratitis, chronic	0	1	0	0	0	0	0	0	0	0
<u>Limbs</u>										
Inflammation, acute, diffuse	1	0	0	0	0	0	0	0	0	0
Inflammation, chronic, focal	0	0	0	0	0	1	0	0	0	0
Inflammation, chronic, diffuse	0	0	1	0	1	0	0	0	1	0
Ulcer, chronic	0	0	0	0	1	0	0	0	0	0
Chronic arthritis	0	0	0	0	0	0	0	0	0	1
Healed fracture	0	0	0	0	0	1	0	1	0	0
<u>Middle Ears</u>										
Inflammation, subacute, diffuse, unilateral	0	0	0	0	1	0	0	0	0	0
<u>Nasal Cavity</u>										
Inflammation, acute, diffuse	0	0	1	0	0	0	0	0	0	0
Foreign bodies	0	0	1	0	0	0	0	0	0	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
Found Dead or Killed Moribund**

Study #006-007

Group	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
<u>MASSES/LESIONS: (cont'd.)</u>										
<u>Penis</u>										
Inflammation, acute, focal	0	1	0	1	1	--	--	--	--	--
Inflammation, acute, diffuse	0	1	2	0	2	--	--	--	--	--
Inflammation, chronic, diffuse	0	0	0	1	0	--	--	--	--	--
<u>Prepuce</u>										
Impacted	1	0	0	0	0	--	--	--	--	--
Inflammation, acute, diffuse	1	0	0	0	0	--	--	--	--	--
<u>Preputial Gland</u>										
Inflammation, acute, diffuse	0	0	0	0	1	--	--	--	--	--
<u>Rectum</u>										
Epithelial hyperplasia	1	0	0	0	0	0	0	0	0	0
<u>Rib</u>										
Fracture	0	0	0	0	0	0	0	0	1	0

24-Month Carcinogenicity Study of in CD-1 Mice  
 Incidence of Each Type of Non-neoplastic Lesion by Sex and Test Group  
 Found Dead or Killed Moribund

Study #006-007

	MALES					FEMALES				
	I	II	III	IV	V	I	II	III	IV	V
<u>Group</u>										
<u>MASSES/LESIONS: (cont'd.)</u>										
<u>Seminal Vesicles</u>										
Inflammation, acute, diffuse	3	1	0	0	1	--	--	--	--	--
Inflammation, chronic, focal	0	1	0	0	0	--	--	--	--	--
Inflammation, chronic, diffuse	0	0	0	1	0	--	--	--	--	--
Serositis, acute, focal	1	0	0	0	0	--	--	--	--	--
Abscess	0	0	0	1	0	--	--	--	--	--
<u>Ureters</u>										
Inflammation, chronic, diffuse	0	1	0	0	0	0	0	0	0	0
<u>Vagina</u>										
Necrosis, diffuse	--	--	--	--	--	0	0	1	0	0

**24-Month Carcinogenicity Study of : In CD-1 Mice**  
**Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	51	45	49	45
<b>HEART # Examined</b>						
Myocarditis, acute, focal	0	0	0	0	1	0
Myocarditis, subacute, focal	2	1	0	0	0	1
Myocarditis, chronic, focal	1	1	2	0	1	1
Arteritis, subacute, focal	1	1	0	0	0	0
Arteritis, chronic, focal	2	0	0	0	1	0
Thrombus	0	0	0	0	0	1
Valvular endocarditis	2	0	1	3	1	0
<b>AORTA # Examined</b>	62	60	51	44	48	44
Arteritis, subacute, focal	3	3	3	3	1	0
Arteritis, chronic, focal	0	0	0	0	0	2
Thrombus	0	0	1	0	0	0
<b>LUNGS WITH IRONCHI # Examined</b>	62	61	51	45	49	45
Pneumonia, subacute, focal	2	0	0	0	1	0
Pneumonia, subacute, diffuse	0	1	0	0	0	0
Pneumonia, chronic, focal	2	2	3	1	1	1
Pneumonia, chronic, diffuse	0	0	0	1	0	0
Pleuritis, subacute, focal	0	0	0	0	2	0
Pleuritis, chronic, focal	0	1	0	0	0	0
Pleuritis, chronic, diffuse	1	0	0	0	0	0
Focus or foci of macrophages	0	1	0	0	0	0
Arteritis, subacute, focal	1	4	0	1	2	0

**24-Month Carcinogenicity Study of In CD-1 Mice  
Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	51	45	49	45
<u>TRACHEA</u> # Examined	4	1	1	1	0	1
Tracheitis, chronic, focal						
<u>ESOPHAGUS</u> # Examined	62	61	51	45	49	45
Inflammation, subacute, focal	0	1	0	0	0	0
<u>STOMACH - Cardiac</u> # Examined	62	61	51	45	49	45
Inflammation, subacute, focal	4	4	2	6	2	6
Inflammation, chronic, focal	0	0	0	1	0	0
Inflammation, chronic, focal of esophageal part	0	0	0	0	1	0
Hypertrophic gastritis	0	2	0	2	0	0
<u>STOMACH - Pundic</u> # Examined	62	61	51	45	49	45
Inflammation, subacute, focal	0	2	2	3	2	5
Arteritis, subacute, focal	1	0	0	0	0	0
Necrosis, focal	0	0	1	0	0	0
<u>STOMACH - Pyloric</u> # Examined	62	61	51	45	49	45
Inflammation, subacute, focal	0	0	0	0	1	0
Serositis, chronic, focal	0	0	1	0	0	1



24-Month Carcinogenicity Study of In CD-1 Mice  
 Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	51	45	49	45
<u>MANDIBULAR LYMPH NODES</u> # Examined						
Lymphadenitis, acute, focal	0	0	0	1	0	0
Lymphadenitis, subacute, focal	0	0	1	0	0	0
Lymphadenitis, subacute, diffuse	2	2	3	1	2	2
Lymphadenitis, chronic, focal	2	0	1	0	0	0
Lymphadenitis, chronic, diffuse	1	1	1	2	0	2
Plasma cells prominent	3	1	0	3	5	3
Lymphoid hyperplasia	2	0	0	1	1	0
	62	61	51	45	49	45
<u>SALIVARY GLANDS - Mandibular</u> # Examined						
Inflammation, subacute, focal	40	32	21	11	16	19
Inflammation, chronic, diffuse	1	0	0	1	0	0
Arteritis, subacute, focal	0	0	1	1	0	0
Arteritis, chronic, focal	1	0	0	0	0	0
	62	61	51	45	49	45
<u>SALIVARY GLANDS - Sublingual</u> # Examined						
Inflammation, subacute, focal	1	0	0	1	2	2
	62	61	51	45	49	45
<u>SALIVARY GLANDS - Parotid</u> # Examined						
Inflammation, subacute, focal	10	5	5	2	5	2
Cytomegaly	0	0	0	0	1	0
Amyloid	0	0	0	0	3	0
	62	61	51	45	49	45
<u>DUODENUM</u> # Examined						
Ulcer, chronic	0	0	0	0	0	1

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**  
in CD-1 Mice

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	51	45	49	45
<u>JEJUNUM</u> # Examined	0	5	1	4	11	0
Amyloid	0	0	0	1	0	0
Inflammation, chronic, focal						
<u>ILEUM</u> # Examined	62	61	51	45	49	45
Amyloid	0	0	0	1	2	0
<u>COLON</u> # Examined	62	61	51	45	49	45
No lesion seen						
<u>THYMUS</u> # Examined	55	51	47	44	48	41
Lymphoid hyperplasia	8	4	8	13	9	14
Inflammation, acute, focal	0	0	0	0	0	1
Inflammation, chronic, diffuse	1	0	0	0	0	0
Arteritis, subacute, focal	1	0	0	0	0	0
Mineralization, diffuse	1	0	0	0	0	0
Thrombus	0	0	0	0	0	1
<u>SPLEEN</u> # Examined	62	61	51	45	49	45
Hematopoiesis - moderate	4	4	5	6	12	9
Hematopoiesis - severe	2	0	0	0	2	2
Inflammation, chronic, focal	0	0	0	1	0	0
Inflammation, chronic, diffuse	1	0	0	0	0	0
Lymphocytolysis	0	0	1	0	0	0
Lymphoid hyperplasia	0	0	0	1	1	0
Amyloid	0	0	0	0	2	0
Mineralization, focal	1	0	0	0	0	0

000437

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**  
in CD-1 Mice

TRL Study #006-007

	MALES				FEMALES			
	I	II	V		I	II	V	
	62	61	51		45	49	45	
<b>PANCREAS # Examined</b>								
Inflammation, subacute, focal	3	0	1		1	9	2	
Inflammation, chronic, focal	1	1	2		0	0	1	
Serositis, chronic, focal	0	0	0		0	1	0	
Arteritis, chronic, focal	1	1	0		0	0	0	
Atrophy of acinar part	0	0	0		1	0	0	
	62	61	51		45	49	45	
<b>LIVER # Examined</b>								
Hepatitis, acute, focal	3	5	0		4	0	0	
Hepatitis, subacute, focal	6	8	0		9	13	3	
Hepatitis, chronic, focal	1	0	4		1	1	4	
Necrosis, diffuse	0	0	0		0	1	0	
Necrosis, focal, random distribution	0	0	0		0	0	1	
Hematopoiesis - slight	0	0	0		0	0	3	
Hematopoiesis - moderate	0	0	0		0	1	0	
Infarct	0	2	0		0	0	0	
Karyomegaly	1	0	0		0	0	0	
Acidophilic focus of hepatocytes	0	1	0		0	0	0	
Area of dark hepatocytes	0	0	0		1	0	0	
Area of pale hepatocytes	1	0	0		0	0	0	
Cyst	3	0	2		1	0	1	
Dilated bile ducts	0	0	0		0	1	0	
Hyaline droplets	0	1	0		0	0	0	
	60	59	51		45	49	44	
<b>GALL BLADDER # Examined</b>								
Inflammation, subacute, focal	3	1	3		0	1	1	
Inflammation, chronic, focal	0	0	0		0	0	1	
Cystitis, subacute, focal	1	0	0		0	0	0	

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**  
in CD-1 Mice

Study #006-007

KIDNEYS # Examined	MALES				FEMALES			
	I	II	V		I	II	V	
	62	61	51		45	49	45	
Nephritis, subacute, focal, unilateral	0	1	2		1	0	0	
Nephritis, subacute, focal, bilateral	8	6	4		8	13	1	
Nephritis, chronic, focal, unilateral, minimal	7	8	3		3	1	1	
Nephritis, chronic, focal, unilateral, slight	2	4	2		2	2	0	
Nephritis, chronic, focal, bilateral, minimal	13	8	7		5	4	0	
Nephritis, chronic, focal, bilateral, slight	16	21	14		7	8	8	
Nephritis, chronic, focal, bilateral, moderate	4	0	9		1	4	26	
Nephritis, chronic, focal, bilateral, severe	1	1	0		0	0	9	
Pyelonephritis, focal, bilateral	1	0	0		0	1	0	
Pyelitis, subacute, focal	0	2	0		0	0	0	
Amyloid	0	0	0		1	3	0	
Arteritis, chronic, focal	1	1	0		0	0	0	
Dilated pelvis, unilateral	3	0	2		0	1	0	
Dilated pelvis, bilateral	1	0	0		0	0	0	
Glomerulonephritis, focal, bilateral	0	0	1		0	0	0	
Pigment in tubular epithelium, bilateral	0	0	0		2	1	0	
Ectopic bone formation	0	0	0		1	0	0	

000439

**24-Month Carcinogenicity Study of                      in CD-1 Mice**  
**Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	51	45	49	45
<b>ADRENALS            # Examined</b>						
Focus or foci of cellular atypia - cortex	8	3	3	0	0	0
Focus or foci of cellular atypia - medulla	0	1	1	2	1	0
Foci of macrophages - medulla	1	0	0	0	0	0
Atrophy - cortex	2	0	0	0	0	0
Atrophy - unilateral	0	0	1	0	0	0
Amyloid	0	0	0	0	2	0
Nodular hyperplasia	0	2	0	0	0	0
Arteritis, subacute, focal	0	0	0	0	1	0
Blood-filled spaces - cortex	1	0	0	0	0	0
Cytoplasmic vacuolization, fat, focal - cortex	1	0	0	0	0	0
Hemorrhage, focal	1	0	0	0	0	0
Cyst - cortex	1	0	0	0	0	0
<b>PITUITARY            # Examined</b>	62	59	50	45	49	45
Inflammation, subacute, focal	0	0	0	1	0	0
Congestion	0	0	0	0	1	0
<b>TESTES                # Examined</b>	62	61	51	--	--	--
Hyospermatogenesis, focal, unilateral	5	1	2	--	--	--
Hyospermatogenesis, focal, bilateral	2	0	2	--	--	--
Hyospermatogenesis, diffuse, unilateral	4	4	2	--	--	--
Hyospermatogenesis, diffuse, bilateral	3	2	0	--	--	--
<b>EPIDIDYMIDES        # Examined</b>	62	61	51	--	--	--
Inflammation, acute, focal	1	0	0	--	--	--
Inflammation, subacute, focal	0	1	0	--	--	--
Sperm granuloma	1	0	1	--	--	--

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	51	--	--	--
<b>PROSTATE # Examined</b>	1	1	0	--	--	--
Prostatitis, acute, focal	1	3	1	--	--	--
Prostatitis, subacute, focal	0	1	0	--	--	--
Prostatitis, subacute, diffuse	0	2	1	--	--	--
Prostatitis, chronic, focal	2	0	0	--	--	--
Prostatitis, chronic, diffuse	--	--	--	45	49	45
<b>OVARIES # Examined</b>	--	--	--	37	38	32
Cyst(s)	--	--	--	5	1	6
Hemorrhage	--	--	--	0	1	0
Amyloid	--	--	--	0	1	0
Abscess	--	--	--	1	0	0
Inflammation, acute, diffuse	--	--	--	0	1	0
Section inadequate for diagnosis	--	--	--	45	.49	45
<b>UTERINE HORNS # Examined</b>	--	--	--	0	0	2
Cystic endometrial hyperplasia, diffuse, unilateral	--	--	--	44	45	40
Cystic endometrial hyperplasia, diffuse, bilateral	--	--	--	0	0	1
Hydrometra, unilateral	--	--	--	0	1	0
Hydrometra, bilateral	--	--	--	3	1	0
Hemorrhage	--	--	--	1	0	0
Abscess	--	--	--	1	0	0
Inflammation, chronic, focal	--	--	--	1	0	0
Necrosis, diffuse	--	--	--	0	0	1

24-Month Carcinogenicity Study of in CD-1 Mice  
 Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	51	45	48	45
<u>URINARY BLADDER</u> # Examined	7	8	10	15	22	17
Cystitis, subacute, focal	0	0	0	1	0	0
Cystitis, chronic, focal	1	0	0	0	0	0
Cystitis, chronic, diffuse	1	0	0	0	0	0
Serositis, chronic, focal	0	0	0	0	0	1
Epithelial nest						
<u>BRAIN - Cerebrum</u> # Examined	62	61	51	45	49	45
No lesion seen						
<u>BRAIN - Midbrain</u> # Examined	62	61	51	45	49	45
Mineralization, focal	1	1	0	0	0	0
Choroiditis, subacute, focal	0	0	0	1	3	0
Inflammation, subacute, focal	0	0	1	0	0	0
<u>BRAIN - Cerebellum</u> # Examined	62	61	51	45	49	45
No lesion seen						
<u>BRAIN - Pons</u> # Examined	62	61	51	45	49	45
No lesion seen						
<u>THYROIDES</u> # Examined	62	61	51	45	49	45
Inflammation, subacute, focal	2	1	2	2	5	2
Inflammation, chronic, focal	1	0	0	0	1	0
Follicular hyperplasia	0	0	0	1	0	1
Cyst	6	5	6	4	1	2
Arteritis, subacute, focal	0	0	1	1	0	0
Amyloid	0	0	0	0	3	0

**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	57	49	41	46	43
<u>PARATHYROID</u> # Examined	1	0	0	0	0	0
Cyst	0	0	0	0	1	1
Inflammation, subacute, focal	0	0	0	0	1	0
Amyloid	62	61	51	45	49	45
<u>STERNUM</u> # Examined	0	0	0	4	7	12
Fibro-osseous lesion	0	0	0	0	0	1
Myeloid hyperplasia of marrow	62	61	51	45	49	45
<u>SKIN</u> # Examined	2	0	0	0	0	0
Inflammation, subacute, focal	0	1	0	0	0	0
Inflammation, chronic, focal	1	3	0	0	0	0
Inflammation, chronic, diffuse	1	0	0	0	0	0
Ulcer, chronic	0	1	0	0	0	0
Ulcer	1	0	0	0	0	0
Epidermal inclusion cyst	0	1	0	0	0	1
Edema	13	14	13	45	49	45
<u>MAMMARY GLAND</u> # Examined	0	0	0	1	1	3
Cyst	0	0	0	0	1	0
Inflammation, chronic, focal	0	0	0	0	1	0
Inflammation, chronic, diffuse	62	61	51	45	49	44
<u>BONE MARROW SHEAR</u> # Examined	No lesion seen					



**24-Month Carcinogenicity Study of  
Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally**

Study #006-007

	MALES			FEMALES		
	I	II	V	I	II	V
	62	61	50	45	49	45
No lesion seen	0	0	0	0	1	1
OTHER:	0	1	0	1	2	0
<u>LYMPH NODES</u>	2	0	0	0	0	2
Lymphadenitis, acute, diffuse	1	0	0	0	0	0
Lymphadenitis, subacute, diffuse	1	1	0	1	0	0
Lymphadenitis, chronic, diffuse	1	0	0	0	0	0
Abscess	1	1	0	1	0	0
Congestion	1	0	0	0	0	0
Plasma cells prominent	1	0	0	0	1	0
<u>Mesenteric Lymph Node</u>						
Lymphadenitis, acute, focal	0	0	0	1	0	0
Lymphadenitis, acute, diffuse	4	0	0	0	0	0
Lymphadenitis, chronic, focal	0	1	1	0	0	0
Lymphadenitis, chronic, diffuse	2	0	0	2	3	0
Congestion	1	0	1	0	0	0
Hematopoiesis	0	0	0	0	1	0
Lymphoid hyperplasia	0	0	0	0	1	0
<u>MASSES/LESIONS<sup>a</sup></u>						
Abscess	0	1	0	0	0	0
Inflammation, chronic, focal	1	0	0	0	0	0

<sup>a</sup> This category lists histologic findings from tissues which, in accordance with the protocol, were to be examined only if a gross lesion was found.

24-Month Carcinogenicity Study of in CD-1 Mice  
 Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally

Study #006-007

**MASSES/LESIONS (cont'd.)**

Cervix

Hemorrhage  
 Inflammation, chronic, diffuse  
 Squamous metaplasia  
 Edema  
 Cystic endometrial hyperplasia

Eyes

Keratitis, unilateral  
 Bulbus phthisis, unilateral  
 Hemorrhage  
 Inflammation, acute, diffuse of  
 anterior chamber, unilateral

Infraorbital Lacrimal Gland

Inflammation, subacute, focal

Limbs

Inflammation, chronic, diffuse  
 Myositis, chronic, focal  
 Fracture  
 Healed fracture

	MALES			FEMALES		
	I	II	V	I	II	V
Hemorrhage	--	--	--	0	1	0
Inflammation, chronic, diffuse	--	--	--	0	4	0
Squamous metaplasia	--	--	--	0	0	2
Edema	--	--	--	1	0	0
Cystic endometrial hyperplasia	--	--	--	1	0	0
Keratitis, unilateral	1	0	0	0	0	0
Bulbus phthisis, unilateral	0	0	1	0	0	0
Hemorrhage	1	0	0	0	0	0
Inflammation, acute, diffuse of anterior chamber, unilateral	0	1	0	0	0	0
Inflammation, subacute, focal	0	0	1	0	0	0
Inflammation, chronic, diffuse	0	0	0	0	0	1
Myositis, chronic, focal	0	0	0	0	0	1
Fracture	0	1	0	0	0	1
Healed fracture	0	0	0	0	1	0

24-Month Carcinogenicity Study of in CD-1 Mice  
 Incidence of Each Type of Non-Neoplastic Lesion by Sex and Test Group - Killed Terminally

Study #006-007

MASSES/LESIONS (cont'd.)	MALES			FEMALES		
	I	II	V	I	II	V
	<u>Middle Ear</u>					
Arteritis, acute, focal of trigeminal nerve	0	0	0	1	0	0
<u>Penis</u>						
Inflammation, acute, diffuse	0	1	0			
Inflammation, chronic, focal	0	0	1	--	--	--
Ulcer, chronic	0	0	1	--	--	--
<u>Preputial Gland</u>						
Squamous metaplasia	0	0	1	--	--	--
<u>Seminal Vesicles</u>						
Inflammation, chronic, focal	1	1	0	--	--	--
Inflammation, chronic, diffuse	0	0	1	--	--	--

A Brief Coversheet for Carcinogenesis Study Review

1. Species & Strain Rat (Charles River-SD, CD)

2. Name of Laboratory

3. No./sex/group 100

4. Doses (O.L.M.H)\*  
 Control I Control II LD HD  
 0 (distilled water) 0 10-15 20-25  
 (raised to (raised to  
 15 mg/kg on 25 mg/kg on  
 day 352 of day 352 of  
 study) study)  
 mg/kg/day

5. Basis for dose selection stated yes X  
 no     

6. Interim Sacrifice yes       
 no X

7. Total Duration (months) 24

8. No. Alive at termination (O.L.M.H)  
 Control I Control II LD MD HD  
 Males 33 34 31 36 24  
 Females 28 26 32 27 23

9. Statistical Methods Used  
 Survival curves analyzed by using Kaplan-Meier estimates.  
 Survival differences analyzed by using the Wilcoxon Rank test.  
 Neoplastic lesions data analyzed by using Fisher's Exact test.

10. Tumor and non-tumor data for each tissue attached.

\*Fenoldopam base

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## STATISTICAL METHODS:

The following analyses were performed for male and female rats separately:

1) Survival Analysis: Survival curves for the five groups were analyzed using Kaplan-Meier estimates. Survival differences were tested using the Wilcoxon Rank test (also referred to as the Gehan-Breslow test-Gehan (1965) and Breslow (1970)). This is an extension of the Kruskal-Wallis test for nonparametric analysis of censored data. Further details on the Kaplan-Meier survival function and the Gehan-Breslow test can be found in Kalbfleisch and Prentice (1980).

The Kaplan-Meier survival functions and results of the Wilcoxon Rank tests were obtained using PROC LIFETEST in SAS (SAS/Statistics, 1985).

1) Analysis of data on neoplastic lesions: Since there were no significant survival differences among the treatment groups for either sex (see Figures 1 and 2 and the results of the Wilcoxon rank tests in the RESULTS section), the data on neoplastic lesions was analysed on the basis of incidences of these lesions for different treatment groups.

For the rats found dead and for the set of all animals, the two control groups were compared to the high dose group separately. Fisher's exact test (programmed in SAS/Basics, 1985) was used to test for differences between control and high dose groups.

Fisher's exact test yields the probability of observing a table that gives at least as much evidence of association between tumor occurrence and treatment as the table observed, given that the null hypothesis of no association is true.

In a 2x2 table, if the row and column margins are considered fixed, then the hypergeometric probability  $p$  can be computed for every possible table. The one sided  $p$ -value presented in this analysis is the sum of the  $p$ 's which arise from tables with the same and greater treatment association than the table being analysed.

## RESULTS:

1. Survival Analysis: Figures 1 and 2 provide the Kaplan-Meier survival curves for male and female rats respectively. Results of the Wilcoxon Rank Test are as follows:

### Wilcoxon Rank Test Results

Sex	Chi-square	d.f.	approx p-value
Females	1.1687	4	0.8832
Males	0.8575	4	0.9306

There were no statistically significant ( $p > 0.05$ ) survival differences.

2. Analysis of neoplastic lesions: Tables 2 through 9 contain the results of all the Fisher exact tests. Of these the following were significant:

All Females-				
Control I vs. High Dose	Pituitary	Adenoma, pars anterior	$p=0.03$	
Control II vs. High Dose	Mammary	Fibroadenoma	$p=0.04$	

Found Dead Females-				
Control I vs. High Dose	Pituitary	Adenoma, pars anterior	$p=0.03$	

All other exact tests gave non-significant results.

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**2-Year Carcinogenicity Study in Rats**  
**Incidence of Neoplastic Lesions**  
**Animals Found Dead/Moribund Killed and Terminal Killed**

**GASTROINTESTINAL SYSTEM**

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u><b>SALIVARY GLAND</b></u>						
Number Examined	99	98	100	99	100	99
Not Remarkable	96	98	90	96	98	98
Autolysis	1	0	0	0	0	0
Lymphosarcoma	1	0	0	0	0	0
Granulocytic leukemia	0	0	1	0	0	0
<u><b>ESOPHAGUS</b></u>						
Number Examined	100	100	100	100	99	99
Not Remarkable	97	100	98	100	98	99
Autolysis	1	0	0	0	0	0
Histiocytic sarcoma	0	0	1	0	0	0
<u><b>STOMACH</b></u>						
Number Examined	100	100	100	100	100	99
Not Remarkable	45	44	54	43	25	48
Autolysis	6	0	2	0	5	0
Papilloma	1	0	1	0	1	1
Carcinoma, gastric mucosa	0	0	0	0	1	0
Lymphosarcoma	1	0	0	0	0	0
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	1	0	2	0	0	0
<u><b>DUODENUM</b></u>						
Number Examined	100	100	99	99	99	98
Not Remarkable	79	97	71	93	58	93
Autolysis	18	3	16	6	23	0
Histiocytic sarcoma	0	0	1	0	0	0
<u><b>BILE DUCT</b></u>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0



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## 2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

### GASTROINTESTINAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>ILEUM</u></b>						
Number Examined	99	100	100	100	100	98
Not Remarkable	75	93	74	92	64	94
Autolysis	20	6	21	7	28	1
Carcinoma	0	1	0	1	0	0
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	1	0	0	0	0	0
<b><u>JEJUNUM</u></b>						
Number Examined	100	100	99	100	100	98
Not Remarkable	78	94	74	89	66	95
Autolysis	19	6	21	8	28	1
Adenocarcinoma	0	0	0	1	0	0
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	1	0	1	0	0	0
<b><u>COLON</u></b>						
Number Examined	100	100	99	100	99	99
Not Remarkable	68	90	73	88	58	91
Autolysis	17	3	13	2	24	1
Lymphosarcoma	2	0	0	0	1	0
Histiocytic sarcoma	0	0	1	0	0	0
<b><u>MESOCOLON</u></b>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0
<b><u>PANCREAS</u></b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	47	58	43	60	27	65
Autolysis	3	0	0	0	3	0
Adenoma, islet cell	7	4	9	3	10	3
Adenoma, acinar cell	1	1	2	0	3	0
Carcinoma, islet cell	1	0	1	0	0	0
Carcinoma, acinar cell	0	0	0	0	1	0
Lymphosarcoma	1	0	0	1	0	0
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	1	0	1	0	0	0
Carcinoma follicular	0	0	0	0	0	1

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## 2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

### GASTROINTESTINAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>LIVER</b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	34	32	29	25	32	18
Autolysis	1	0	0	0	0	0
Adenoma, hepatocellular	0	0	1	0	0	0
Carcinoma, hepatocellular	0	1	0	0	2	0
Cystadenoma, biliary	0	0	0	2	0	0
Hemangiosarcoma	0	0	0	1	0	0
Lymphosarcoma	2	0	0	3	0	1
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	2	0	3	2	1	0
<b>CECUM</b>						
Number Examined	3	2	5	1	6	3
Not Remarkable	3	2	2	0	1	3
Autolysis	0	0	3	0	3	0
<b>RECTUM</b>						
Number Examined	0	0	1	0	1	0
Not Remarkable	0	0	0	0	1	0
<b>TONGUE</b>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0
Papilloma	0	0	0	0	1	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

### GENITAL SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>TESTES</u></b>						
Number Examined	100	0	100	0	100	0
Not Remarkable	62	0	61	0	47	0
Autolysis	1	0	1	0	0	0
Interstitial cell tumor	10	0	9	0	13	0
Histiocytic sarcoma	0	0	1	0	0	0
<b><u>PROSTATE</u></b>						
Number Examined	100	0	100	0	100	0
Not Remarkable	49	0	53	0	56	0
Autolysis	1	0	0	0	0	0
Adenoma	0	0	2	0	0	0
Adenocarcinoma, sclerosing	0	0	1	0	0	0
Leiomyosarcoma	0	0	0	0	1	0
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	0	0	2	0	0	0
<b><u>EPIDIDYMES</u></b>						
Number Examined	12	0	8	0	11	0
Not Remarkable	0	0	0	0	0	0
<b><u>SEMINAL VESICLES</u></b>						
Number Examined	9	0	3	0	8	0
Not Remarkable	0	0	1	0	0	0
<b><u>PREPUTIAL GLANDS</u></b>						
Number Examined	0	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
Histiocytic sarcoma	0	0	1	0	0	0
<b><u>PENIS</u></b>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0
Papilloma, squamous	0	0	0	0	1	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

### CARDIOVASCULAR SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>HEART</u></b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	22	25	29	24	16	37
Autolysis	1	0	0	0	0	0
Hemangioma	0	0	0	0	0	1
Hemangiosarcoma	0	0	0	0	1	0
Lymphosarcoma	2	0	0	2	0	1
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	0	1	1	1	0	0
Adenocarcinoma, unknown origin	1	0	0	0	0	0
<b><u>AORTA</u></b>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0
<b><u>VENA CAVA</u></b>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0

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## 2-Year Carcinogenicity Study in Rats

### Incidence of Neoplastic Lesions Animals Found Dead/Moribund Killed and Terminal Killed

#### ENDOCRINE SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>THYROID</u>						
Number Examined	99	100	99	98	100	99
Not Remarkable	83	90	77	86	77	94
Autolysis	1	1	0	0	1	0
Adenoma, follicular	3	0	4	1	3	0
Adenoma, C cell	4	2	3	3	4	1
Carcinoma, follicular	0	2	1	1	0	1
Carcinoma, medullary	0	2	0	1	0	3
Granulocytic leukemia	0	0	1	0	0	0
<u>PARATHYROIDS</u>						
Number Examined	97	86	93	88	92	83
Not Remarkable	86	80	89	78	77	80
Autolysis	1	0	0	0	0	0
Adenoma	1	2	0	3	4	2
<u>ADRENALS</u>						
Number Examined	100	100	100	100	100	99
Not Remarkable	28	17	28	14	29	6
Autolysis	1	0	0	0	0	0
Adenoma, cortical	0	9	0	8	1	4
Carcinoma, adrenal cortex	1	3	1	1	0	0
Pheochromocytoma	9	1	12	1	10	4
Lymphosarcoma	1	0	0	1	0	1
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	1	1	2	0	0	0
Carcinoma, follicular thyroid	0	0	0	0	0	1
<u>PITUITARY</u>						
Number Examined	98	100	98	99	97	99
Not Remarkable	33	28	32	18	24	14
Autolysis	1	0	0	0	0	0
Adenoma, pars anterior	53	71	51	78	63	82
Adenoma, pars intermedia	0	0	0	0	1	0
Carcinoma, pars anterior	1	0	3	0	1	0
Lymphosarcoma	0	0	0	1	0	0
Granulocytic leukemia	0	0	1	0	0	0
Sarcoma, unclassified	0	1	0	0	0	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

### HEMOLYMPHATIC SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>SPLEEN</u></b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	67	25	61	14	60	8
Autolysis	1	0	0	0	0	0
Fibrosarcoma	0	0	1	1	0	0
Leiomyoma	0	0	0	0	1	0
Liposarcoma	0	0	1	0	0	0
Sarcoma	0	0	1	0	0	0
Lymphosarcoma	3	0	0	2	0	1
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	1	0	2	0	0	0
<b><u>THYMUS</u></b>						
Number Examined	82	65	90	72	99	75
Not Remarkable	71	49	84	64	82	53
Autolysis	1	0	0	0	0	0
Lymphosarcoma	1	0	0	2	0	1
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	0	1	1	0	1	0
<b><u>SUBMANDIBULAR LYMPH NODE</u></b>						
Number Examined	98	93	98	85	90	85
Not Remarkable	83	41	87	23	75	16
Autolysis	1	0	0	0	0	0
Carcinoma, follicular, thyroid	0	0	0	0	0	1
Lymphosarcoma	0	0	0	1	0	0
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	0	0	0	1	0	0
<b><u>MESENTERIC LYMPH NODE</u></b>						
Number Examined	99	100	100	100	99	96
Not Remarkable	76	66	80	62	78	77
Autolysis	1	0	0	0	0	0
Hemangioma	2	2	3	0	1	0
Lymphosarcoma	3	1	0	1	0	0
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	2	1	2	1	1	0

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2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

HEMOLYMPHATIC SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>AXILLARY LYMPH NODE</u>						
Number Examined	1	0	1	0	0	1
Not Remarkable	0	0	0	0	0	0
Granulocytic leukemia	0	0	1	0	0	0
<u>CARDIAC LYMPH NODE</u>						
Number Examined	0	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
Liposarcoma	0	0	1	0	0	0
<u>ILIAC LYMPH NODE</u>						
Number Examined	2	1	3	2	5	3
Not Remarkable	0	0	0	0	0	0
Lymphosarcoma	1	0	0	0	0	0
Granulocytic leukemia	0	0	1	0	0	0
<u>INGUINAL LYMPH NODE</u>						
Number Examined	2	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
<u>LUMBAR LYMPH NODE</u>						
Number Examined	1	0	3	1	0	0
Not Remarkable	0	0	0	0	0	0
Histiocytic sarcoma	1	0	1	1	0	0
<u>MEDIASTINAL LYMPH NODE</u>						
Number Examined	1	0	1	1	0	0
Not Remarkable	1	0	0	0	0	0
Lymphosarcoma	0	0	0	1	0	0
<u>PANCREATIC LYMPH NODE</u>						
Number Examined	0	0	1	0	2	0
Not Remarkable	0	0	0	0	0	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

### HEMOLYMPHATIC SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>PARARENAL LYMPH NODE</u>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0
<u>RENAL LYMPH NODE</u>						
Number Examined	4	1	5	1	9	0
Not Remarkable	0	0	0	0	1	0
Pheochromocytoma	1	0	0	0	0	0
Lymphosarcoma	1	0	0	0	0	0
Histiocytic sarcoma	0	0	0	0	1	0
<u>STERNAL LYMPH NODE</u>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0
Histiocytic sarcoma	1	0	0	0	0	0
<u>BONE MARROW</u>						
Number Examined	99	100	100	100	100	99
Not Remarkable	89	90	92	93	94	95
Carcinoma, adrenal cortex	1	0	0	0	0	0
Lymphosarcoma	3	0	0	1	0	2
Granulocytic leukemia	0	0	1	0	0	0
Histiocytic sarcoma	0	0	1	2	1	0
<u>FEMORAL BONE MARROW</u>						
Number Examined	1	0	0	0	0	0
Not Remarkable	1	0	0	0	0	0



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## 2-Year Carcinogenicity Study in Rats

### Incidence of Neoplastic Lesions Animals Found Dead/Moribund Killed and Terminal Killed

#### CENTRAL NERVOUS SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>BRAIN</u></b>						
Number Examined	100	100	99	98	99	99
Not Remarkable	93	96	93	92	92	94
Autolysis	1	0	0	0	0	0
Adenoma, pars anterior, local extension	0	2	0	0	0	1
Adenocarcinoma, pars anterior	1	0	2	1	1	0
Astrocytoma	1	0	0	2	0	1
Oligodendroglioma	0	1	0	1	0	0
Granular cell tumor	0	0	1	0	1	0
Lymphosarcoma	0	0	0	2	0	0
Granulocytic leukemia	0	0	1	0	0	0
Carcinoma, auditory canal	0	0	0	0	1	0
Carcinoma follicular	0	0	0	0	0	1
<b><u>SPINAL CORD</u></b>						
Number Examined	1	0	1	0	0	0
Not Remarkable	0	0	1	0	0	0
<b><u>EYES</u></b>						
Number Examined	13	6	15	15	15	7
Not Remarkable	8	3	6	8	11	4
Leiomyosarcoma	0	0	0	1	0	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Neoplastic Lesions  
Animals Found Dead/Moribund Killed and Terminal Killed

### SEROSAL SURFACES

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>THORACIC CAVITY</u>						
Number Examined	1	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
Lipoma	1	0	0	0	0	0
<u>ABDOMEN</u>						
Number Examined	5	0	3	3	3	6
Not Remarkable	1	0	1	0	0	0
Adenocarcinoma, intestinal	1	0	0	0	0	0
Carcinoma, unclassified	0	0	0	0	0	2
Lipoma	0	0	0	1	0	1
Fibroma	0	0	1	0	0	0
Fibrosarcoma	0	0	0	0	1	0
Leiomyosarcoma	0	0	0	1	1	0
Histiocytic sarcoma	0	0	0	1	0	0
Sarcoma, unclassified	0	0	0	1	0	1
<u>DIAPHRAGM</u>						
Number Examined	1	0	1	0	1	0
Not Remarkable	0	0	0	0	0	0
Adenocarcinoma, bile duct	0	0	0	0	1	0
Fibroma	1	0	0	0	0	0
<u>MESENTERY</u>						
Number Examined	5	0	3	3	16	2
Not Remarkable	0	0	0	0	0	0
Carcinoma, gastric mucosa	0	0	0	0	1	0
Lipoma	0	0	0	0	1	0
Hemangioma	0	0	0	1	0	0
Leiomyosarcoma	0	0	0	0	1	0
<u>ADIPOSE TISSUE</u>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0

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2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

URINARY SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>KIDNEYS</b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	4	7	7	4	1	1
Autolysis	1	0	0	0	3	0
Glomerulonephropathy, bilateral	83	27	79	37	94	65
Glomerulonephropathy, unilateral	1	4	5	13	1	10
Mineralization, pelvic, bilateral	4	59	0	55	0	29
Mineralization, pelvic, unilateral	4	23	10	24	1	38
Hyperplasia/hypertrophy, epithelial, pelvic, papillary base, bilateral	9	20	12	16	22	39
Hyperplasia/hypertrophy, epithelial, pelvic, papillary base, unilateral	17	29	18	40	22	36
Inflammatory debris, intratubular accumulation, collecting ducts, bilateral	0	0	0	0	37	27
Inflammatory debris, intratubular accumulation, collecting ducts, unilateral	0	0	0	0	12	15
Hyperplasia/hypertrophy, epithelial collecting ducts, bilateral	2	0	2	0	0	13
Hyperplasia/hypertrophy, epithelial collecting ducts, unilateral	0	0	0	0	1	23
Hyperplasia/hypertrophy, epithelial, pelvic, papillary tip, bilateral	8	6	2	10	17	45
Hyperplasia/hypertrophy, epithelial, pelvic, papillary tip, unilateral	8	20	5	27	18	19
Cyst, cortical, bilateral	0	0	1	0	5	1
Cyst, cortical, unilateral	3	3	1	5	12	2
Degeneration, hyalin droplet, proximal tubular, bilateral	1	0	1	0	0	0
Hydronephrosis, bilateral	0	2	1	0	2	1
Hydronephrosis, unilateral	2	1	2	1	5	2
Infarction, cortical, unilateral	1	2	0	1	0	1

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## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### URINARY SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>KIDNEYS (Continued)</b>						
Infiltrate, lymphocytic, interstitial, bilateral	0	0	0	1	0	0
Infiltrate, lymphocytic, interstitial, unilateral	1	0	1	0	0	0
Mineralization, tubular, cortical, bilateral	5	0	4	0	3	1
Mineralization, tubular, cortical, unilateral	0	0	2	1	0	0
Mineralization, tubular, medullary, bilateral	2	0	0	0	0	0
Mineralization, tubular, medullary, unilateral	0	2	2	1	0	1
Nephrosis, tubular, bilateral	1	0	1	0	2	0
Pigmentation, epithelial, tubular, bilateral	2	0	2	0	4	1
Pigmentation, epithelial, tubular, unilateral	1	0	1	0	1	0
Pyelitis, bilateral	2	2	2	2	0	0
Pyelitis, unilateral	3	7	6	6	0	0
Pyelonephritis, suppurative, bilateral	2	0	1	0	1	0
Pyelonephritis, suppurative, unilateral	0	0	1	0	0	0
Fibrosis, lamina propria, ureter, bilateral	1	0	1	0	0	0
Fibrosis, lamina propria, ureter, unilateral	1	0	0	0	0	0
Nephritis, embolic, bilateral	0	0	0	1	0	0
Crystalline material, intratubular, bilateral	0	0	0	0	12	13
Crystalline material, intratubular, unilateral	0	2	0	6	7	14
Hyperplasia, parietal epithelium, pelvic, bilateral	1	0	0	0	1	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### URINARY SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>KIDNEYS (Continued)</u></b>						
Hyperplasia, parietal epithelium, pelvic, unilateral	0	0	1	0	1	1
Polyarteritis nodosa, bilateral	2	0	2	0	3	0
Polyarteritis nodosa, unilateral	0	0	1	0	7	0
Calculi, pelvic, multiple, unilateral	1	0	0	0	0	0
Mineralization, arterial, bilateral	0	0	3	0	3	0
Mineralization, arterial, unilateral	5	0	6	0	7	0
Infiltrate, globular leukocytes, pelvic, unilateral	1	0	0	0	0	0
Arteritis, mononuclear, unilateral	0	0	1	0	0	0
Mineralization, interstitial, bilateral	0	0	0	0	5	0
Mineralization, interstitial, unilateral	0	1	0	0	0	0
Arterial degeneration, fibrinoid, unilateral	0	0	0	0	1	0
Polyps, edematous, papillary tip, bilateral	0	0	1	0	1	1
Polyps, edematous, papillary tip, unilateral	0	0	0	0	0	5
Embolism, bilateral	0	0	0	0	0	1
Fibrosis, capsular, unilateral	0	0	1	0	0	0
<b><u>URINARY BLADDER</u></b>						
Number Examined	100	100	100	100	99	99
Not Remarkable	91	68	86	81	91	70
Autolysis	1	1	1	0	0	0
Cystitis	5	3	9	1	7	1
Hyperplasia, epithelial	6	27	5	17	1	28
Calculi, multiple	0	1	1	0	0	0
Calculi, microgranular	1	0	0	0	0	0
Hemorrhage	1	0	0	0	0	0
Peritonitis	0	0	0	1	0	0
Crystalline material	0	0	0	0	1	0
Edema	0	1	0	0	1	0
<b><u>URETERS</u></b>						
Number Examined	0	0	0	1	1	1
Not Remarkable	0	0	0	0	0	1
Dilatation	0	0	0	0	1	0
Hydroureter	0	0	0	1	0	0

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2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

GASTROINTESTINAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>STOMACH</u>						
Number Examined	100	100	100	100	100	99
Not Remarkable	45	44	54	43	25	48
Hyperkeratosis, nonglandular epithelium	12	27	19	47	9	22
Hyperplasia, nonglandular epithelium	20	30	15	43	17	28
Polyarteritis nodosa	6	0	5	0	47	7
Autolysis	6	0	2	0	5	0
Gastritis, ulcerative, nonglandular	8	8	6	9	1	3
Gastritis, ulcerative, glandular	6	10	1	5	8	2
Gastritis, eosinophilic	4	1	9	0	4	0
Gastritis, uremic	5	0	4	0	9	1
Gastritis, lymphocytic	0	0	2	0	3	0
Gastritis, hypertrophic	0	0	1	0	0	1
Necrosis	0	0	1	2	3	0
Dilation, mucosal glands	5	15	10	11	13	16
Granuloma, serosal surface	1	0	0	0	0	0
Mineralization, glandular mucosa	2	0	0	0	16	0
Mineralization, arterial	1	0	0	0	8	1
Adhesion	1	0	0	0	0	0
Nematode, solitary	1	0	0	0	0	0
Infarction, secondary to polyarteritis	0	0	1	0	0	0
Peritonitis	0	0	0	1	0	0
Fibrosis, lamina propria	0	0	0	0	1	0
Edema, submucosal	0	0	0	0	1	0
Ectopic squamous mucosa	0	0	0	0	1	0
<u>DUODENUM</u>						
Number Examined	100	100	99	99	99	98
Not Remarkable	79	97	71	93	58	93
Autolysis	18	3	16	6	23	0
Enteritis	0	0	3	0	5	0
Polyarteritis nodosa	5	0	8	0	15	5
Mineralization, arterial	1	0	0	0	3	0
Infarction, secondary to polyarteritis	0	0	1	0	0	0
Necrosis	0	0	0	0	1	0
<u>BILE DUCT</u>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0
Bile stasis	0	0	0	0	1	0

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2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

GASTROINTESTINAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>MESOCOLON</b>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0
Polyarteritis nodosa	0	0	0	0	1	0
Dilation, cystic, sinusoidal, lymph nodes	0	0	0	0	1	0
<b>PANCREAS</b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	47	58	43	60	27	65
Autolysis	3	0	0	0	3	0
Hyperplasia, islet cell	13	27	17	20	3	8
Hyperplasia, acinar cell	3	0	9	0	2	3
Polyarteritis nodosa	6	2	4	1	53	9
Fibrosis, periductular	4	9	14	7	13	11
Pancreatitis, mononuclear	2	3	3	2	1	0
Mineralization, arterial	4	0	1	0	10	2
Pigmentation, peri-islet tissue	6	0	6	0	3	0
Hemosiderosis	2	0	0	0	0	0
Atrophy, acinar cell	11	1	11	2	4	0
Fibrosis, islet of Langerhans	2	1	2	1	1	0
Necrosis, coagulative	2	0	0	0	2	0
Pancreatitis, suppurative	0	0	0	1	0	1
Vasculitis, uremic, with mineralization	1	0	0	0	0	0
Pancreatitis, fibrosing	0	0	0	1	0	0
Steatitis, nodular	0	0	0	1	0	0
Peritonitis	0	0	0	1	0	0
Hypertrophy, smooth muscle, arterial	0	0	0	1	0	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### GASTROINTESTINAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>LIVER (Number Examined)</b>	100	100	100	100	100	99
Not Remarkable	34	32	29	25	32	18
Autolysis	1	0	0	0	0	0
Congestion	3	0	5	0	5	1
Necrosis, coagulative, subcapsular	5	12	5	10	1	3
Necrosis, coagulative, hepatocellular, centrilobular	5	2	3	1	8	6
Cholangitis, proliferative	15	18	17	17	11	16
Cholangitis, mononuclear	11	1	11	3	12	4
Cholangitis, suppurative	0	0	0	3	1	0
Degeneration, vacuolar, hepatocellular, cytoplasmic, centrilobular	12	0	5	2	11	4
Degeneration, vacuolar, hepatocellular, cytoplasmic	13	7	15	19	15	12
Degeneration, vacuolar, hepatocellular, cytoplasmic, periportal	0	13	1	6	1	12
Hepatopathy, fibrosing, subcapsular	0	1	1	0	0	0
Hepatopathy	0	0	0	0	1	0
Focus of altered hepatocytes	4	3	9	3	8	10
Bile accumulation, Kupffer cells	0	0	0	0	0	1
Dilation, sinusoidal	9	0	7	0	11	0
Hyperplasia, bile duct	5	3	5	3	1	1
Atrophy, hepatocellular	1	0	0	0	1	0
Cholangiofibrosis	2	0	8	1	8	0
Fibrosis, perivascular	2	1	1	0	0	0
Hemosiderosis, Kupffer cells	2	0	0	0	0	0
Karyomegaly	1	1	1	0	1	19
Abscess	0	2	2	0	2	0
Thrombosis, hepatic vein	1	0	1	0	0	0
Infiltrate, mononuclear, random	4	18	0	23	2	26
Hyperplastic nodule	0	0	4	0	2	0
Hematopoiesis, extramedullary	0	3	1	3	2	3
Mineralization, arterial	1	0	0	0	0	0
Hypertrophy, hepatocellular, periportal	0	1	0	3	0	0
Fracture	0	0	0	0	1	0

009216

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## 2-Year Carcinogenicity Study in Rats

### Incidence of Non-Neoplastic Lesions

All Animals Found Dead/Moribund Killed and Terminal Killed

#### GASTROINTESTINAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>CECUM</u></b>						
Number Examined	3	2	5	1	6	3
Not Remarkable	3	2	2	0	1	3
Autolysis	0	0	3	0	3	0
Typhlitis, ulcerative	0	0	0	1	1	0
Hemorrhage	0	0	0	0	3	0
Congestion	0	0	0	0	3	0
<b><u>RECTUM</u></b>						
Number Examined	0	0	1	0	1	0
Not Remarkable	0	0	0	0	1	0
Edema, submucosal	0	0	1	0	0	0
Peritonitis, suppurative	0	0	1	0	0	0
<b><u>TONGUE</u></b>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0

009217

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## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### GENITAL SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>TESTES</b>						
Number Examined	100	0	100	0	100	0
Not Remarkable	62	0	61	0	47	0
Autolysis	1	0	1	0	0	0
Polyarteritis nodosa, bilateral	16	0	16	0	36	0
Polyarteritis nodosa, unilateral	1	0	1	0	3	0
Atrophy, seminiferous tubules, bilateral	8	0	9	0	15	0
Atrophy, seminiferous tubules, unilateral	9	0	7	0	3	0
Infiltrate, lymphocytic, perivascular, epididymis	2	0	0	0	0	0
Mineralization, arterial, bilateral	0	0	1	0	1	0
Mineralization, arterial, unilateral	0	0	1	0	3	0
Edema, bilateral	1	0	3	0	2	0
Edema, unilateral	1	0	2	0	4	0
Aspermia, bilateral	4	0	2	0	0	0
Aspermia, unilateral	1	0	0	0	0	0
Granuloma, sperm, unilateral	2	0	1	0	0	0
Arteritis, necrotizing, bilateral	1	0	0	0	0	0
Mineralization, seminiferous tubules, unilateral	0	0	1	0	0	0
Infarction, unilateral	0	0	0	0	1	0
Hemorrhage, unilateral	0	0	0	0	1	0
<b>PROSTATE</b>						
Number Examined	100	0	100	0	100	0
Not Remarkable	49	0	53	0	56	0
Autolysis	1	0	0	0	0	0
Prostatitis	38	0	41	0	41	0
Polyarteritis nodosa	1	0	1	0	2	0
Hypertrophy, epithelial	5	0	0	0	0	0
Hyperplasia, epithelial	2	0	0	0	0	0
Atrophy, epithelial	6	0	1	0	2	0
Mineralization, arterial	1	0	0	0	0	0
Hemorrhage	1	0	0	0	0	0

009218

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## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Horibund Killed and Terminal Killed

### GENITAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>EPIDIDYMES</u></b>						
Number Examined	12	0	8	0	11	0
Not Remarkable	0	0	0	0	0	0
Degeneration, vacuolar, epithelial, bilateral	7	0	5	0	6	0
Degeneration, vacuolar, epithelial, unilateral	0	0	3	0	4	0
Hyperplasia, epithelial, bilateral	2	0	0	0	0	0
Hyperplasia, epithelial, unilateral	1	0	0	0	0	0
Epididymitis, suppurative, bilateral	1	0	0	0	0	0
Atrophy, bilateral	1	0	0	0	0	0
Granuloma, sperm, bilateral	0	0	0	0	1	0
<b><u>SEMINAL VESICLES</u></b>						
Number Examined	9	0	3	0	8	0
Not Remarkable	0	0	1	0	0	0
Hemorrhage	1	0	1	0	0	0
Atrophy	5	0	1	0	7	0
Hypertrophy	1	0	0	0	1	0
Inflammation, suppurative	1	0	0	0	0	0
Cystic dilatation	1	0	0	0	0	0
<b><u>PREPUTIAL GLANDS</u></b>						
Number Examined	0	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
<b><u>PENIS</u></b>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0

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## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### GENITAL SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>MAMMARY GLAND</u>						
Number Examined	98	99	99	99	96	96
Not Remarkable	67	72	80	69	64	77
Autolysis	1	0	0	0	0	0
Duct ectasia	1	16	3	20	2	4
Dermatitis	2	0	0	2	0	0
Hyperplasia, glandular	4	0	1	1	1	0
Pigmentation, brown, intralobular	22	0	14	0	29	0
Granuloma, lipid	2	0	0	4	0	1
Mastitis, suppurative	1	1	0	0	0	0
Mineralization, arterial	1	0	0	0	1	0
Polyarteritis nodosa	0	0	0	0	4	0
<u>OVARIES</u>						
Number Examined	0	99	0	100	0	99
Not Remarkable	0	81	0	85	0	82
Atrophy, bilateral	0	8	0	4	0	4
Atrophy, unilateral	0	0	0	1	0	5
Cyst, bilateral	0	3	0	1	0	1
Cyst, unilateral	0	8	0	6	0	7
Peritonitis, unilateral	0	0	0	0	0	1
<u>MESOVARIIUM</u>						
Number Examined	0	0	0	2	0	1
Not Remarkable	0	0	0	0	0	0
Steatitis	0	0	0	1	0	1

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2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

CARDIOVASCULAR SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>HEART</u></b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	22	25	29	24	16	37
Autolysis	1	0	0	0	0	0
Cardiomyopathy	68	70	64	73	75	58
Mineralization	12	1	10	2	20	4
Necrosis, Zenker's	3	1	0	0	0	0
Endocarditis	1	0	0	0	1	0
Myocarditis	0	1	0	3	0	0
Thrombosis, right ventricle	1	0	0	0	1	0
Arteritis	0	0	0	0	2	1
Thrombosis, right auricle	2	0	2	1	0	0
Thrombosis, left auricle	6	0	1	1	8	0
Thrombosis, left ventricle	1	0	0	0	1	0
Embolism, mural	1	0	0	0	0	0
Mastocytosis, pericardial space	2	0	0	0	3	0
Degeneration, fibrinoid, arterial	0	0	1	0	4	5
Fibrosis, intimal, arterial	0	0	1	0	1	0
Hypertrophy, arterial smooth muscle, myocardium	0	0	1	0	0	0
Vasculitis, uremic, with mineralization	1	0	0	0	0	0
Pericarditis, suppurative	0	0	0	1	0	0
Polyarteritis nodosa	0	0	0	0	2	0
Pleuritis	0	1	0	0	0	1
<b><u>AORTA</u></b>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0
Mineralization, medial	1	0	0	0	0	0
<b><u>VENA CAVA</u></b>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0
Hematoma	1	0	0	0	0	0

BEST POSSIBLE

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

RESPIRATORY SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>LUNG</u>						
Number Examined	100	100	100	100	100	99
Not Remarkable	21	26	13	21	3	11
Autolysis	2	0	0	0	0	0
Congestion and/or edema	15	5	25	9	26	15
Hyperplasia, lymphoid	25	50	21	52	22	54
Hyperplasia, lymphoid, perivascular	2	2	1	2	0	1
Hyperplasia, smooth muscle, arteriolar	1	0	1	0	0	0
Mineralization	42	9	47	23	51	37
Mineralization, interstitial	6	1	5	0	13	0
Pneumonia, granulomatous	0	2	1	2	2	2
Pneumonia, granulocytic, histiocytic	12	6	20	7	26	19
Bronchopneumonia	1	1	0	2	1	3
Pneumonia, interstitial	10	0	9	0	14	1
Hypertrophy, smooth muscle, medial	10	7	5	8	14	19
Atelectasis	1	7	3	7	2	6
Bronchitis	0	0	3	0	0	1
Arteritis, mononuclear	0	0	0	0	3	0
Arteritis, suppurative	2	0	0	0	0	0
Thrombus	0	0	0	0	0	1
Intravascular coagulation, pulmonary arteries	1	0	0	0	0	0
Foreign material, intrabronchiolar	1	2	1	0	0	0
Embolism, pulmonary	2	0	2	0	2	1
Bronchiolitis, suppurative	1	0	0	0	0	0
Hemosiderosis	2	0	0	0	0	0
Hyperplasia, type II epithelium	1	0	0	0	0	0
Infiltrate, globular leukocytes, perivascular	0	0	1	0	0	0
Abscess	1	0	0	0	0	1
Vasculitis, uremic, with mineralization	1	0	0	0	0	0
Pleuritis, fibrotic	0	1	0	0	0	0
Polyarteritis nodosa	0	0	0	0	2	0
Fibrosis, intimal, mural, arterial	0	0	0	0	1	0
Degeneration, fibrinoid, arterial	0	0	0	0	1	0
Hemorrhage	0	0	0	0	0	1
Necrosis, alveolar	0	0	0	0	0	1

009223

# BEST POSSIBLE

## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### RESPIRATORY SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>TRACHEA</u>						
Number Examined	100	100	100	100	100	99
Not Remarkable	88	84	86	76	85	82
Autolysis	2	0	0	0	1	0
Tracheitis	10	16	13	24	12	17
Mineralization, lamina propria	2	0	0	0	4	0
Vasculitis, uremic, with mineralization	1	0	0	0	0	0

000224



BEST POSSIBLE

**2-Year Carcinogenicity Study in Rats**  
**Incidence of Non-Neoplastic Lesions**  
**All Animals Found Dead/Moribund Killed and Terminal Killed**

**ENDOCRINE SYSTEM**

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u><b>THYROID</b></u>						
Number Examined	99	100	99	98	100	99
Not Remarkable	83	90	77	86	77	94
Autolysis	1	1	0	0	1	0
Atrophy, follicular epithelium	2	1	0	0	0	0
Cyst	3	0	5	0	3	0
Hyperplasia, follicular epithelium	0	0	1	0	1	0
Metaplasia, squamous, thyroglossal duct	1	0	1	0	2	0
Pigmentation, follicular epithelium	4	0	0	0	0	0
Hyperplasia, C cell	1	2	4	5	7	0
Mineralization, colloid	1	0	0	0	4	0
Polyarteritis nodosa	0	0	2	0	0	0
Vasculitis	0	0	0	0	1	0
Thyroiditis, suppurative	0	0	0	1	0	0
<u><b>PARATHYROIDS</b></u>						
Number Examined	97	86	93	88	92	83
Not Remarkable	86	80	89	78	77	80
Autolysis	1	0	0	0	0	0
Hyperplasia, bilateral	5	0	1	0	6	0
Hyperplasia, unilateral	3	0	2	0	5	0
Fibrosis, bilateral	0	2	0	0	0	0
Fibrosis, unilateral	0	2	0	7	0	1
Hypertrophy, unilateral	2	0	0	0	0	0

NOT POSSIBLE

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

ENDOCRINE SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>ADRENALS</b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	28	17	28	14	29	6
Autolysis	1	0	0	0	0	0
Dilation, sinusoidal, bilateral	8	50	10	59	12	48
Dilation, sinusoidal, unilateral	5	13	12	13	5	20
Degeneration, vacuolar, zona fasciculata, bilateral	37	3	24	6	36	9
Degeneration, vacuolar, zona fasciculata, unilateral	20	11	18	9	19	25
Hyperplasia, zona fasciculata, bilateral	0	1	4	5	1	0
Hyperplasia, zona fasciculata, unilateral	5	4	3	6	2	5
Hypertrophy, cortical, bilateral	1	0	0	0	2	0
Hypertrophy, cortical, unilateral	3	0	1	3	1	1
Hyperplasia, cortical, bilateral	2	0	1	0	1	0
Hyperplasia, cortical, unilateral	0	0	1	1	0	0
Hyperplasia, medullary, bilateral	7	0	5	0	5	0
Hyperplasia, medullary, unilateral	5	0	8	0	5	1
Hyperplasia, zona glomerulosa, bilateral	3	19	4	19	0	28
Hyperplasia, zona glomerulosa, unilateral	0	7	5	6	1	26
Atrophy, cortical, bilateral	0	3	0	2	1	0
Atrophy, cortical, unilateral	0	2	0	0	0	2
Mineralization, arterial, bilateral	1	0	0	0	1	0
Mineralization, arterial, unilateral	0	0	0	0	1	0
Necrosis, cortical, bilateral	0	0	1	0	1	1
Necrosis, cortical, unilateral	1	0	1	1	2	1
Hematopoiesis, extramedullary, bilateral	1	7	1	9	3	8
Hematopoiesis, extramedullary, unilateral	1	0	0	0	0	4
Mineralization, cortical	0	1	0	0	0	0
Mineralization, cortical, unilateral	0	0	0	0	0	2
Hemorrhage, cortical, bilateral	0	0	0	0	2	0
Polyarteritis nodosa, bilateral	0	0	0	0	1	0
Hematoma, organizing, unilateral	0	0	0	0	1	0
Nodule, accessory, cortical, unilateral	0	0	0	0	0	0
Infarct, bilateral	0	0	0	0	0	1

BEST POSSIBLE

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

ENDOCRINE SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>PITUITARY</u>						
Number Examined	98	100	98	99	97	99
Not Remarkable	33	28	32	18	24	14
Autolysis	1	0	0	0	0	0
Angiectasis	7	1	19	18	34	20
Cyst	5	2	3	0	7	4
Cholesterol clefts	5	0	0	2	1	0
Hyperplasia, pars anterior	8	0	8	1	2	0
Hyperplasia, pars intermedia	0	0	1	0	0	0
Vacuolation	0	0	0	1	1	0
Mineralization	0	0	0	1	0	0
Abscess	0	0	0	0	0	1

000227

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## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### HEMO-LYMPHATIC SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>SPLEEN</u></b>						
Number Examined	100	100	100	100	100	99
Not Remarkable	67	25	61	14	60	8
Autolysis	1	0	0	0	0	0
Hemosiderosis	27	52	28	60	30	62
Hematopoiesis, extramedullary	3	25	4	46	2	54
Atrophy	1	1	0	0	0	0
Infarct	1	0	1	1	3	2
Mastocytosis	1	0	0	0	0	0
Mineralization, arterial	1	0	0	0	6	1
Splenitis, suppurative	0	1	0	2	0	0
Arteritis, necrotizing	0	0	1	0	0	0
Hyperplasia, lymphoid	0	0	1	0	2	1
Depletion, lymphoid	1	0	0	0	0	0
Plasmacytosis, red pulp	1	0	0	0	1	0
Polyarteritis nodosa	0	0	0	0	4	0
Necrosis	0	0	0	1	0	0
Degeneration, fibrinoid, arterial	0	0	0	0	1	0
<b><u>THYMUS</u></b>						
Number Examined	82	65	90	72	99	75
Not Remarkable	71	49	84	64	82	53
Autolysis	1	0	0	0	0	0
Hyperplasia, epithelial	1	6	0	1	0	1
Congestion and/or hemorrhage	5	1	3	2	4	0
Cyst	1	7	0	4	0	17
Mineralization, arterial	2	0	0	0	3	1
Polyarteritis nodosa	1	0	1	0	6	0
Abscess	0	0	0	0	1	0
Pleuritis	0	1	0	0	0	1
Degeneration, fibrinoid, arterial	0	0	0	0	0	1
Mastocytosis	0	0	0	0	2	0
Dilation, cystic, sinusoidal	0	0	0	0	1	0

009228

# BEST POSSIBLE

## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

### HEMOLYMPHATIC SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>SUBMANDIBULAR LYMPH NODE</u>						
Number Examined	98	93	98	85	90	85
Not Remarkable	83	41	87	23	75	16
Autolysis	1	0	0	0	0	0
Mastocytosis	2	0	1	0	1	0
Dilation, cystic, sinusoidal	4	1	1	0	5	0
Plasmacytosis, medullary	6	45	8	60	8	68
Edema, medullary	0	1	0	0	0	0
Eosinophilia	1	0	0	0	0	0
Hemorrhage	1	0	0	1	0	0
Hemosiderosis	2	0	0	0	0	0
Hyperplasia, lymphoid	0	0	2	0	0	0
Lymphadenitis, suppurative	0	5	0	0	1	0
Mineralization, arterial	0	0	0	0	1	0
<u>MESENTERIC LYMPH NODE</u>						
Number Examined	99	100	100	100	99	96
Not Remarkable	76	66	80	62	78	77
Autolysis	1	0	0	0	0	0
Fibrosis	3	0	2	0	0	0
Edema	1	15	2	7	0	6
Plasmacytosis, medullary	0	15	1	26	2	11
Lymphadenitis	1	2	0	2	1	0
Histiocytosis, medullary, sinusoidal	3	0	0	0	3	2
Mastocytosis	2	0	1	0	0	0
Dilation, cystic, sinusoidal	1	0	1	0	3	0
Hemosiderosis	4	1	6	0	0	0
Erythrophagocytosis	2	0	0	0	0	0
Eosinophilia	1	0	0	0	0	0
Granuloma, solitary	1	0	0	0	0	0
Hemorrhage	2	0	3	1	7	0
Hyperplasia, lymphoid	0	0	2	0	0	0
Depletion, lymphoid	1	0	0	0	0	0
Dilation, aneurysmal, arterial	1	0	0	0	0	0
Vasculitis, uremic, with mineralization	1	0	0	0	0	0
Polyarteritis nodosa	0	0	0	0	6	0

009229

BEST POSSIBLE

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

HEMOLYMPHATIC SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>AXILLARY LYMPH NODE</u>						
Number Examined	1	0	1	0	0	1
Not Remarkable	0	0	0	0	0	0
Plasmacytosis, medullary	1	0	0	0	0	1
Lymphadenitis	0	0	0	0	0	1
<u>CARDIAC LYMPH NODE</u>						
Number Examined	0	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
<u>CERVICAL LYMPH NODE</u>						
Number Examined	1	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
Hemorrhage	0	0	1	0	0	0
Hemosiderosis	0	0	1	0	0	0
Edema, medullary	1	0	0	0	0	0
Erythrophagocytosis	1	0	0	0	0	0
<u>ILIAC LYMPH NODE</u>						
Number Examined	2	1	3	2	5	3
Not Remarkable	0	0	0	0	0	0
Dilation, cystic, sinusoidal	1	0	0	0	4	0
Hemosiderosis	0	0	1	0	0	0
Hyperplasia, lymphoid	0	0	2	0	0	0
Plasmacytosis, medullary	0	1	0	2	1	3
Hemorrhage	0	0	0	0	2	0
Lymphadenitis	0	0	0	0	0	1
Fibrosis	0	0	0	0	1	0
<u>INGUINAL LYMPH NODE</u>						
Number Examined	2	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
Plasmacytosis, medullary	1	0	1	0	0	0
Dilation, cystic, sinusoidal	2	0	0	0	0	0

000230

BEST POSSIBLE

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

HEMOLYMPHATIC SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>LUMBAR LYMPH NODE</u>						
Number Examined	1	0	3	1	0	0
Not Remarkable	0	0	0	0	0	0
Plasmacytosis, medullary	0	0	1	0	0	0
Dilation, cystic, sinusoidal	0	0	1	0	0	0
Edema, medullary	0	0	1	0	0	0
<u>MEDIASTINAL LYMPH NODE</u>						
Number Examined	1	0	1	1	0	0
Not Remarkable	1	0	0	0	0	0
Polyarteritis nodosa	0	0	1	0	0	0
<u>PANCREATIC LYMPH NODE</u>						
Number Examined	0	0	1	0	2	0
Not Remarkable	0	0	0	0	0	0
Polyarteritis nodosa	0	0	1	0	2	0
Dilation, cystic, sinusoidal	0	0	0	0	1	0
<u>PARARENAL LYMPH NODE</u>						
Number Examined	0	0	0	0	1	0
Not Remarkable	0	0	0	0	0	0
Dilation, cystic, sinusoidal	0	0	0	0	1	0
Polyarteritis nodosa	0	0	0	0	1	0
Hyperplasia, lymphoid	0	0	0	0	1	0
<u>RENAL LYMPH NODE</u>						
Number Examined	4	1	5	1	9	0
Not Remarkable	0	0	0	0	1	0
Plasmacytosis, medullary	0	1	2	1	1	0
Edema, medullary	0	0	1	0	0	0
Hemorrhage	1	0	1	0	0	0
Hemosiderosis	1	0	1	0	0	0
Dilation, cystic, sinusoidal	1	0	2	0	6	0
Erythrophagocytosis	1	0	0	0	0	0
Hyperplasia, lymphoid	0	0	0	0	1	0

000231

**2-Year Carcinogenicity Study in Rats**

**Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed**

HEMOLYMPHATIC SYSTEM (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>STERNAL LYMPH NODE</u>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0
<u>BONE MARROW</u>						
Number Examined	99	100	100	100	100	99
Not Remarkable	89	90	92	93	94	95
Hyperplasia, granulocytic	5	10	3	4	3	2
Myelofibrosis	0	0	0	1	1	0
Hypoplasia	1	0	3	0	1	0
<u>FEMORAL BONE MARROW</u>						
Number Examined	1	0	0	0	0	0
Not Remarkable	1	0	0	0	0	0



BEST POSSIBLE

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

CENTRAL NERVOUS SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b>BRAIN</b>						
Number Examined	100	100	99	98	99	99
Not Remarkable	93	96	93	92	92	94
Autolysis	1	0	0	0	0	0
Hydrocephalus	4	1	1	0	1	0
Hemorrhage	1	0	1	0	0	0
Mineralization	1	0	0	0	3	0
Aneurysm	1	0	0	0	0	2
Gliosis, focal	0	0	1	0	0	0
Malacia	0	1	0	0	0	0
Embolism, septic	0	0	0	1	0	0
<b>SPINAL CORD</b>						
Number Examined	1	0	1	0	0	0
Not Remarkable	0	0	1	0	0	0
Hemorrhage	1	0	0	0	0	0
Degeneration, Wallerian, secondary to compression	1	0	0	0	0	0
<b>EYES</b>						
Number Examined	13	6	15	15	15	7
Not Remarkable	8	3	6	8	11	4
Degeneration, retinal, bilateral	1	2	1	4	1	1
Degeneration, retinal, unilateral	0	0	1	2	0	1
Keratitis, bilateral	1	0	1	0	0	0
Keratitis, unilateral	1	0	2	0	1	0
Cataract, bilateral	0	0	1	0	1	0
Cataract, unilateral	1	0	1	0	0	1
Dysplasia, retinal, bilateral	0	0	0	0	1	0
Dysplasia, retinal, unilateral	0	0	1	0	0	0
Aphakia, unilateral	0	0	1	0	0	0
Hemosiderosis, unilateral	0	0	1	0	0	0
Iritis, unilateral	0	0	1	0	0	1
Panophthalmitis, unilateral	1	0	0	0	0	0
Hemorrhage, retinal, unilateral	0	1	0	0	0	0
Phthisis bulbi, unilateral	0	0	0	0	1	0

000233

SECRET

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

SKELETAL SYSTEM

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>STERNUM</u>						
Number Examined	99	100	99	100	100	99
Not Remarkable	88	82	94	87	90	70
Mineralization	2	0	1	1	0	0
Myositis	0	2	1	0	0	0
Osteodystrophy, fibrous	4	0	0	0	9	0
Chondrodysplasia	0	15	0	9	0	29
Abscess, necrotizing, suppurative	1	0	0	0	0	0
Polyarteritis nodosa	0	0	2	0	3	0
Mineralization, arterial	2	0	0	0	0	0
Vasculitis, uremic, with mineralization	1	0	0	0	0	0
Myopathy, nonsuppurative	0	1	0	3	0	0
<u>VERTEBRAL COLUMN</u>						
Number Examined	1	0	1	0	0	1
Not Remarkable	1	0	0	0	0	0
Hemorrhage	0	0	0	0	0	1
<u>BONE</u>						
Number Examined	1	0	1	0	1	0
Not Remarkable	0	0	0	0	0	0
Reactive, secondary to trauma	0	0	1	0	0	0
<u>SKELETAL MUSCLE</u>						
Number Examined	0	1	0	0	1	1
Not Remarkable	0	1	0	0	1	0
Myositis, active	0	0	0	0	0	1
Thrombosis, arterial	0	0	0	0	0	1

## 2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Horibund Killed and Terminal Killed

### SKIN

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>SKIN</u></b>						
Number Examined	11	14	20	9	13	15
Not Remarkable	5	4	10	1	4	3
Alopecia	1	4	1	3	1	5
Dermatitis	1	2	1	5	3	4
Cyst, epidermal, inclusion	0	0	1	0	0	0
Abscess	0	0	1	0	0	0
Hyperkeratosis	2	0	0	0	3	1
Hypoplasia, adnexal	0	0	0	2	0	0
Acanthosis	0	0	0	0	1	0
<b><u>SUBCUTANEOUS TISSUE</u></b>						
Number Examined	33	75	27	69	23	75
Not Remarkable	11	25	10	17	5	18
Abscess	1	0	1	0	2	3
Dermatitis	2	1	0	1	0	0
Duct ectasia	0	15	0	10	1	11
Adipose tissue	1	1	0	0	0	0
Cyst	0	0	0	1	0	0
Cyst, epidermal, inclusion	1	0	1	0	4	0
Steatitis	0	2	0	1	0	0
Hyperkeratosis	1	0	0	0	0	0
Lymph node, plasmacytosis, medullary	0	0	1	0	0	0
Hyperplasia, mammary gland	1	3	0	0	1	0
Granuloma, lipid	0	3	0	3	0	6
Pigmentation, brown, intralobular	0	0	1	0	0	0
Mastitis, suppurative	0	0	0	0	0	1
<b><u>EARS</u></b>						
Number Examined	1	0	0	4	4	2
Not Remarkable	0	0	0	0	0	0
Otitis externa	1	0	0	0	2	0
Chondrodysplasia	0	0	0	3	0	2
Dermatitis	0	0	0	2	0	0
Hyperkeratosis	0	0	0	0	1	0
Chondrodystrophy	0	0	0	0	2	0
Alopecia	0	0	0	1	0	0

000235

**2-Year Carcinogenicity Study in Rats**

**Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed**

SKIN (CONT'D)

Group:	<u>I</u>		<u>II</u>		<u>V</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<b><u>EYELIDS</u></b>						
Number Examined	11	14	14	22	17	19
Not Remarkable	10	11	13	18	16	15
Dermatitis	1	2	1	4	0	4
Ulceration, suppurative	0	1	0	0	0	0
Hyperplasia, epidermal	0	1	0	0	0	0
Parakeratosis	0	0	0	1	0	0
Duct ectasia	0	0	0	0	1	0
Hyperkeratosis	1	0	0	0	0	0
<b><u>TAIL</u></b>						
Number Examined	1	1	0	0	2	0
Not Remarkable	0	0	0	0	1	0
Hyperkeratosis	1	0	0	0	0	0
Inflammation, suppurative	0	1	0	0	0	0
Necrosis	0	0	0	0	1	0

2-Year Carcinogenicity Study in Rats

Incidence of Non-Neoplastic Lesions  
All Animals Found Dead/Moribund Killed and Terminal Killed

SEROSAL SURFACES

Group:	<u>I</u>		<u>II</u>		<u>III</u>	
	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>	<u>M</u>	<u>F</u>
<u>THORACIC CAVITY</u>						
Number Examined	1	0	1	0	0	0
Not Remarkable	0	0	0	0	0	0
Mastocytosis, (fluid)	0	0	1	0	0	0
<u>ABDOMEN</u>						
Number Examined	5	0	3	3	3	3
Not Remarkable	1	0	1	0	0	0
Prostatitis, suppurative	1	0	0	0	0	0
Necrosis, coagulative, abdominal wall	1	0	0	0	0	0
Adipose tissue, colon related	1	0	0	0	0	0
Dilation, cystic, sinusoidal, lymph node	0	0	1	0	0	0
Steatitis	0	0	0	0	0	0
<u>DIAPHRAGM</u>						
Number Examined	1	0	1	0	1	0
Not Remarkable	0	0	0	0	0	0
Peritonitis, active	0	0	1	0	0	0
<u>INTESTINE</u>						
Number Examined	5	0	3	3	16	2
Not Remarkable	0	0	0	0	0	0
Polyarteritis nodosa	2	0	3	0	12	0
Hematoma, organizing	1	0	0	0	0	0
Necrosis, coagulative	1	0	0	0	0	0
Necrosis, coagulative, hepatocellular (accessory hepatic tissue)	1	0	0	0	0	0
Steatitis	0	0	0	2	0	0
Mineralization, arterial	0	0	0	0	1	0
Fat necrosis	0	0	0	0	1	0
Ectopic spleen	0	0	0	0	0	0
<u>ADIPOSE TISSUE</u>						
Number Examined	1	0	0	0	0	0
Not Remarkable	0	0	0	0	0	0
Steatitis	1	0	0	0	0	0

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