

**TDMS No.** 20008 - 03

**P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS  
ABRIDGED) (a)**

**Date Report Requested:** 10/09/2008

**Test Type:** CHRONIC

Milk thistle extract

**Time Report Requested:** 11:00:55

**Route:** DOSED FEED

**CAS Number:** 84604-20-6

**First Dose M/F:** 03/04/03 / 03/04/03

**Species/Strain:** RATS/F 344/N

**Lab:** SRI

F1\_R2

**C Number:** C20008

**Lock Date:** 06/29/2006

**Cage Range:** ALL

**Date Range:** ALL

**Reasons For Removal:** ALL

**Removal Date Range:** ALL

**Treatment Groups:** Include ALL

**Study Gender:** Both

**TDMSE Version:** 2.0.0

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Disposition Summary</b>				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	10	12	12	9
Natural Death	4	2	3	3
Survivors				
Terminal Sacrifice	36	36	35	38
Animals Examined Microscopically	50	50	50	50
<b>ALIMENTARY SYSTEM</b>				
Esophagus	(50)	(50)	(50)	(49)
Intestine Large, Cecum	(49)	(49)	(49)	(47)
Intestine Large, Colon	(46)	(48)	(47)	(47)
Hemangioma	1 (2%)			
Intestine Large, Rectum	(47)	(50)	(47)	(46)
Sarcoma, Metastatic, Pancreas			1 (2%)	
Intestine Small, Duodenum	(48)	(48)	(48)	(49)
Intestine Small, Ileum	(47)	(47)	(48)	(48)
Intestine Small, Jejunum	(46)	(48)	(47)	(47)
Sarcoma Stromal		1 (2%)		
Liver	(50)	(50)	(50)	(50)
Cholangioma	1 (2%)			
Hepatocellular Adenoma	3 (6%)	5 (10%)	3 (6%)	2 (4%)
Hepatocellular Adenoma, Multiple		1 (2%)	2 (4%)	1 (2%)
Mesentery	(3)	(2)	(6)	(6)
Oral Mucosa	(0)	(0)	(1)	(0)
Pancreas	(50)	(50)	(50)	(50)
Sarcoma			1 (2%)	
Acinus, Adenoma	2 (4%)	1 (2%)		
Salivary Glands	(48)	(50)	(50)	(50)
Myoepithelioma		1 (2%)		
Stomach, Forestomach	(50)	(50)	(50)	(50)
Stomach, Glandular	(50)	(50)	(49)	(50)
Tongue	(1)	(1)	(0)	(0)
Squamous Cell Papilloma	1 (100%)			

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

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Schwannoma Malignant	1 (2%)	2 (4%)		
Schwannoma Nos				1 (2%)
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Adenoma	2 (4%)			
Adrenal Medulla	(50)	(49)	(50)	(50)
Pheochromocytoma Benign	5 (10%)	10 (20%)	5 (10%)	4 (8%)
Pheochromocytoma Complex	1 (2%)			
Pheochromocytoma Malignant			1 (2%)	1 (2%)
Bilateral, Pheochromocytoma Benign				2 (4%)
Islets, Pancreatic	(50)	(50)	(50)	(50)
Adenoma	3 (6%)	3 (6%)	1 (2%)	3 (6%)
Carcinoma	1 (2%)			
Parathyroid Gland	(50)	(49)	(49)	(47)
Pituitary Gland	(50)	(50)	(50)	(50)
Pars Distalis, Adenoma	13 (26%)	15 (30%)	8 (16%)	11 (22%)
Pars Distalis, Carcinoma			1 (2%)	
Thyroid Gland	(48)	(49)	(50)	(49)
C-cell, Adenoma	5 (10%)	6 (12%)	2 (4%)	7 (14%)
C-cell, Carcinoma	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Follicular Cell, Adenoma		2 (4%)		
GENERAL BODY SYSTEM				
Tissue NOS	(1)	(1)	(1)	(2)
Fibrosarcoma			1 (100%)	
Thoracic, Paraganglioma	1 (100%)			
GENITAL SYSTEM				
Epididymis	(50)	(50)	(50)	(50)
Preputial Gland	(50)	(49)	(50)	(50)
Adenoma	1 (2%)	6 (12%)	2 (4%)	3 (6%)
Carcinoma	2 (4%)	3 (6%)		1 (2%)

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

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Prostate	(50)	(50)	(50)	(50)
Seminal Vesicle	(50)	(50)	(50)	(50)
Testes	(50)	(50)	(50)	(50)
Bilateral, Interstitial Cell, Adenoma	43 (86%)	36 (72%)	31 (62%)	32 (64%)
Interstitial Cell, Adenoma	3 (6%)	8 (16%)	10 (20%)	12 (24%)
HEMATOPOIETIC SYSTEM				
Bone Marrow	(48)	(50)	(50)	(49)
Lymph Node	(10)	(11)	(18)	(6)
Lymph Node, Mandibular	(1)	(1)	(1)	(3)
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Spleen	(50)	(50)	(50)	(50)
Thymus	(41)	(42)	(46)	(42)
Thymoma Benign			1 (2%)	
INTEGUMENTARY SYSTEM				
Mammary Gland	(49)	(49)	(48)	(49)
Fibroadenoma		1 (2%)	1 (2%)	2 (4%)
Skin	(50)	(50)	(50)	(50)
Basal Cell Adenoma		1 (2%)	1 (2%)	
Basal Cell Carcinoma	1 (2%)			
Keratoacanthoma	3 (6%)	1 (2%)	2 (4%)	3 (6%)
Keratoacanthoma, Multiple	1 (2%)			
Neural Crest Tumor		1 (2%)		
Sarcoma			1 (2%)	
Schwannoma Malignant		1 (2%)		
Squamous Cell Carcinoma	1 (2%)			
Squamous Cell Papilloma	1 (2%)			
Prepuce, Squamous Cell Carcinoma			1 (2%)	
Subcutaneous Tissue, Fibroma	3 (6%)	7 (14%)	2 (4%)	1 (2%)
Subcutaneous Tissue, Fibrosarcoma		1 (2%)		
Subcutaneous Tissue, Lipoma	1 (2%)			
Subcutaneous Tissue, Neural Crest	1 (2%)			
Tumor, Malignant				
Subcutaneous Tissue, Sarcoma	1 (2%)			

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

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Osteoma	1 (2%)			
Skeletal Muscle	(1)	(4)	(0)	(0)
Lipoma		1 (25%)		
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Astrocytoma Malignant			1 (2%)	
Granular Cell Tumor Benign		1 (2%)		
Spinal Cord	(8)	(5)	(2)	(5)
Oligodendroglioma Malignant		1 (20%)		
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Alveolar/Bronchiolar Adenoma	1 (2%)	2 (4%)	2 (4%)	2 (4%)
Alveolar/Bronchiolar Carcinoma		1 (2%)		1 (2%)
Nose	(50)	(50)	(50)	(50)
Leiomyosarcoma		1 (2%)		
SPECIAL SENSES SYSTEM				
Eye	(48)	(48)	(48)	(49)
Harderian Gland	(50)	(50)	(50)	(50)
Zymbal's Gland	(0)	(1)	(0)	(1)
Adenoma				1 (100%)
URINARY SYSTEM				
Kidney	(50)	(50)	(48)	(50)
Renal Tubule, Carcinoma				1 (2%)
Urinary Bladder	(50)	(50)	(50)	(50)
SYSTEMIC LESIONS				

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Histiocytic Sarcoma	3 (6%)	1 (2%)		
Leukemia Mononuclear	17 (34%)	17 (34%)	17 (34%)	16 (32%)
Mesothelioma Malignant		1 (2%)	1 (2%)	

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

\* Number of animals with any tissue examined microscopically

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Tumor Summary for Males</b>				
Total Animals with Primary Neoplasms (b)	50	49	49	50
Total Primary Neoplasms	125	140	100	108
Total Animals with Benign Neoplasms	50	49	45	48
Total Benign Neoplasms	95	108	73	86
Total Animals with Malignant Neoplasms	26	26	25	20
Total Malignant Neoplasms	30	31	27	21
Total Animals with Metastatic Neoplasms	1	1	1	
Total Metastatic Neoplasms	2	1	1	
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant		1		1
Total Uncertain Neoplasms		1		1

\*\*\* END OF MALE \*\*\*

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

b - Primary tumors: all tumors except metastatic tumors

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
<b>Disposition Summary</b>				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	6	9	14	8
Natural Death	6	5	2	5
Survivors				
Natural Death		1		
Terminal Sacrifice	38	35	34	37
Animals Examined Microscopically	50	50	50	50
<b>ALIMENTARY SYSTEM</b>				
Intestine Large, Cecum	(43)	(48)	(49)	(49)
Intestine Large, Colon	(44)	(45)	(48)	(46)
Liver	(50)	(50)	(49)	(50)
Hepatocellular Adenoma	2 (4%)	1 (2%)	3 (6%)	
Mesentery	(10)	(10)	(4)	(8)
Osteosarcoma, Metastatic, Bone		1 (10%)		
Oral Mucosa	(0)	(0)	(1)	(0)
Pancreas	(48)	(48)	(49)	(49)
Salivary Glands	(50)	(50)	(50)	(50)
Stomach, Forestomach	(49)	(48)	(49)	(50)
Stomach, Glandular	(49)	(47)	(49)	(49)
Tongue	(0)	(1)	(1)	(0)
<b>CARDIOVASCULAR SYSTEM</b>				
Heart	(50)	(50)	(50)	(50)
Schwannoma Malignant			1 (2%)	
<b>ENDOCRINE SYSTEM</b>				
Adrenal Cortex	(48)	(48)	(49)	(50)
Adenoma		1 (2%)		
Adrenal Medulla	(48)	(48)	(48)	(50)
Pheochromocytoma Benign	1 (2%)	1 (2%)	4 (8%)	1 (2%)

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Pheochromocytoma Complex	1 (2%)			
Islets, Pancreatic	(48)	(48)	(49)	(49)
Adenoma			3 (6%)	
Parathyroid Gland	(49)	(48)	(47)	(49)
Pituitary Gland	(50)	(50)	(50)	(50)
Pars Distalis, Adenoma	20 (40%)	20 (40%)	18 (36%)	28 (56%)
Pars Distalis, Carcinoma	1 (2%)			
Thyroid Gland	(47)	(49)	(49)	(50)
C-cell, Adenoma	2 (4%)	3 (6%)	6 (12%)	2 (4%)
C-cell, Carcinoma		3 (6%)	1 (2%)	2 (4%)
Follicular Cell, Carcinoma	1 (2%)			
GENERAL BODY SYSTEM				
Tissue NOS	(0)	(0)	(3)	(0)
Alveolar/Bronchiolar Carcinoma,			1 (33%)	
Metastatic, Lung				
Fat, Mediastinum, Rhabdomyosarcoma,			1 (33%)	
Metastatic, Skeletal Muscle				
GENITAL SYSTEM				
Clitoral Gland	(50)	(49)	(50)	(50)
Adenoma	11 (22%)	8 (16%)	4 (8%)	5 (10%)
Carcinoma	3 (6%)	5 (10%)	1 (2%)	1 (2%)
Bilateral, Adenoma				1 (2%)
Ovary	(50)	(49)	(50)	(50)
Granulosa Cell Tumor Benign		1 (2%)		
Granulosa Cell Tumor Malignant	2 (4%)			
Tubulostromal Adenoma				1 (2%)
Uterus	(50)	(49)	(50)	(50)
Adenoma	1 (2%)			
Polyp Stromal	9 (18%)	12 (24%)	15 (30%)	16 (32%)
Polyp Stromal, Multiple			1 (2%)	
Bilateral, Polyp Stromal	1 (2%)			
Vagina	(2)	(2)	(3)	(5)
HEMATOPOIETIC SYSTEM				

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Bone Marrow	(49)	(50)	(50)	(50)
Lymph Node	(9)	(8)	(5)	(8)
Deep Cervical, Carcinoma, Metastatic, Thyroid Gland				1 (13%)
Mediastinal, Rhabdomyosarcoma, Metastatic, Skeletal Muscle			1 (20%)	
Lymph Node, Mandibular	(1)	(3)	(2)	(2)
Lymph Node, Mesenteric	(49)	(48)	(50)	(50)
Spleen	(49)	(50)	(50)	(49)
Capsule, Granulosa Cell Tumor	1 (2%)			
Malignant, Metastatic, Ovary				
Thymus	(50)	(49)	(48)	(49)
Carcinoma, Metastatic, Thyroid Gland				1 (2%)
INTEGUMENTARY SYSTEM				
Mammary Gland	(50)	(50)	(50)	(50)
Adenoma				1 (2%)
Adenoma, Multiple				1 (2%)
Carcinoma	3 (6%)	1 (2%)	2 (4%)	3 (6%)
Carcinoma, Multiple	1 (2%)			
Fibroadenoma	24 (48%)	20 (40%)	14 (28%)	15 (30%)
Fibroadenoma, Multiple	4 (8%)	7 (14%)	3 (6%)	3 (6%)
Skin	(50)	(50)	(50)	(50)
Basal Cell Adenoma		1 (2%)	1 (2%)	
Keratoacanthoma		1 (2%)	1 (2%)	
Epidermis, Squamous Cell Carcinoma	1 (2%)			
Subcutaneous Tissue, Fibroma	1 (2%)			2 (4%)
Subcutaneous Tissue, Fibrosarcoma	1 (2%)	2 (4%)	1 (2%)	
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Hemangioma			1 (2%)	
Osteosarcoma		2 (4%)		
Skeletal Muscle	(1)	(0)	(1)	(0)
Head, Rhabdomyosarcoma			1 (100%)	

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Astrocytoma Malignant			2 (4%)	
Oligodendroglioma Malignant	1 (2%)			
Rhabdomyosarcoma, Metastatic, Skeletal Muscle			1 (2%)	
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(49)	(50)
Alveolar/Bronchiolar Adenoma			2 (4%)	1 (2%)
Alveolar/Bronchiolar Carcinoma	1 (2%)			
Alveolar/Bronchiolar Carcinoma, Multiple			1 (2%)	
Carcinoma, Metastatic, Thyroid Gland				1 (2%)
Granular Cell Tumor Malignant, Metastatic, Ovary	1 (2%)			
Osteosarcoma, Metastatic, Bone		1 (2%)		
Rhabdomyosarcoma, Metastatic, Skeletal Muscle			1 (2%)	
Nose	(50)	(50)	(49)	(50)
Trachea	(50)	(50)	(50)	(50)
Carcinoma, Metastatic, Thyroid Gland				1 (2%)
SPECIAL SENSES SYSTEM				
Eye	(48)	(48)	(49)	(50)
Harderian Gland	(50)	(49)	(50)	(50)
Zymbal's Gland	(0)	(1)	(2)	(0)
Carcinoma		1 (100%)	1 (50%)	
Rhabdomyosarcoma, Metastatic, Skeletal Muscle			1 (50%)	
URINARY SYSTEM				
Kidney	(48)	(49)	(49)	(48)
Renal Tubule, Adenoma			1 (2%)	
Urinary Bladder	(50)	(49)	(50)	(50)

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Species/Strain: RATS/F 344/N

Lab: SRI

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
SYSTEMIC LESIONS				
Multiple Organs	*(50)	*(50)	*(50)	*(50)
Adenolipoma			1 (2%)	
Histiocytic Sarcoma				1 (2%)
Leukemia Erythrocytic	1 (2%)			
Leukemia Mononuclear	6 (12%)	9 (18%)	13 (26%)	9 (18%)

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

\* Number of animals with any tissue examined microscopically

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Lab: SRI

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
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### Tumor Summary for Females

Total Animals with Primary Neoplasms (b)	46	48	46	44
Total Primary Neoplasms	99	99	102	93
Total Animals with Benign Neoplasms	39	42	41	43
Total Benign Neoplasms	76	76	77	77
Total Animals with Malignant Neoplasms	18	20	23	16
Total Malignant Neoplasms	23	23	24	16
Total Animals with Metastatic Neoplasms	1	2	2	1
Total Metastatic Neoplasms	2	4	6	4
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

\*\*\* END OF REPORT \*\*\*

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

b - Primary tumors: all tumors except metastatic tumors