TDMS No. 20008 - 03
Test Type: CHRONIC
Route: DOSED FEED

Species/Strain: RATS/F 344/N

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

Milk thistle extract

CAS Number: 84604-20-6

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

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

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Route: DOSED FEED

TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Disposition Summary				
Animals Initially in Study Early Deaths	50	50	50	50
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
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(49)
Inflammation, Acute Intestine Large, Cecum	1 (2%) (49)	(49)	(49)	(47)
Ulcer	(49)	(49)	1 (2%)	(47)
Intestine Large, Colon	(46)	(48)	(47)	(47)
Edema	1 (2%)	,		1 (2%)
Necrosis			1 (2%)	
Ulcer	1 (2%)	()	>	1 (2%)
Intestine Large, Rectum	(47)	(50)	(47)	(46)
Edema		1 (2%)		1 (2%)
Fibrosis		1 (2%)		1 (2%) 1 (2%)
Hemorrhage Hemorrhage, Chronic				1 (2%)
Inflammation, Chronic				1 (2%)
Necrosis	1 (2%)			· (= /0)
Intestine Small, Duodenum	(48)	(48)	(48)	(49)
Intestine Small, Ileum	(47)	(47)	(48)	(48)
Intestine Small, Jejunum	(46)	(48)	(47)	(47)
Perforation				1 (2%)
Ulcer	(==)	1 (2%)	(50)	(50)
Liver	(50)	(50)	(50)	(50)
Angiectasis	3 (6%)			1 (2%)
Atrophy Basophilic Focus	1 (2%) 33 (66%)	36 (72%)	32 (64%)	34 (68%)
Clear Cell Focus	29 (58%)	29 (58%)	32 (64%)	34 (66%)
Degeneration, Cystic	25 (5070)	29 (36%)	31 (02/0)	33 (00/0)
Eosinophilic Focus	12 (24%)	7 (14%)	10 (20%)	19 (38%)
Hematopoietic Cell Proliferation	1 (2%)	. ()	- (=0,0)	(55/5)
Hepatodiaphragmatic Nodule	4 (8%)	4 (8%)	6 (12%)	3 (6%)
Infarct			, ,	2 (4%)
Infiltration Cellular, Mixed Cell	31 (62%)	32 (64%)	27 (54%)	15 (30%)

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

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Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Malformation			1 (2%)		
Mixed Cell Focus	9 (18%)	5 (10%)	7 (14%)	5 (10%)	
Necrosis, Focal	1 (2%)	3 (1373)	. (/ 5)	1 (2%)	
Pigmentation, Focal	1 (2%)			. (= /0)	
Bile Duct, Hyperplasia	50 (100%)	48 (96%)	44 (88%)	17 (34%)	
Hepatocyte, Vacuolization Cytoplasmic	8 (16%)	9 (18%)	9 (18%)	4 (8%)	
Serosa, Fibrosis	0 (1070)	3 (1070)	3 (1070)	1 (2%)	
Mesentery	(3)	(2)	(6)	(6)	
Accessory Spleen	(3)	(2)	1 (17%)	2 (33%)	
Fat. Necrosis	3 (100%)	1 (50%)	3 (50%)	4 (67%)	
Oral Mucosa	(0)	(0)	(1)	(0)	
Pharyngeal, Hyperplasia	(0)	(0)	1 (100%)	(0)	
Pancreas	(50)	(50)	(50)	(50)	
Atrophy	42 (84%)	36 (72%)	35 (70%)	30 (60%)	
Metaplasia, Hepatocyte	42 (0470)	30 (72%)	1 (2%)	1 (2%)	
Acinus, Hyperplasia, Focal	5 (10%)	4 (8%)	8 (16%)	9 (18%)	
Duct, Ectasia					
Salivary Glands	24 (48%)	27 (54%)	19 (38%)	27 (54%)	
	(48)	(50)	(50)	(50)	
Atrophy	7 (15%)	7 (14%)	4 (8%)	9 (18%)	
Hyperplasia, Lymphoid	4 (00()			1 (2%)	
Inflammation, Acute	1 (2%)	(50)	(50)	(50)	
Stomach, Forestomach	(50)	(50)	(50)	(50)	
Edema	2 (4%)	4 (8%)	5 (10%)	3 (6%)	
Inflammation, Chronic Active	- 4	1 (2%)		- /	
Ulcer	3 (6%)	4 (8%)	4 (8%)	3 (6%)	
Epithelium, Hyperplasia	3 (6%)	6 (12%)	7 (14%)	5 (10%)	
Stomach, Glandular	(50)	(50)	(49)	(50)	
Cyst	1 (2%)	1 (2%)			
Edema	1 (2%)	2 (4%)	2 (4%)	1 (2%)	
Erosion	3 (6%)	3 (6%)	3 (6%)	2 (4%)	
Ulcer	4 (8%)	1 (2%)	4 (8%)	3 (6%)	
Glands, Hyperplasia		1 (2%)		1 (2%)	
Tongue	(1)	(1)	(0)	(0)	
Hyperplasia		1 (100%)			
RDIOVASCULAR SYSTEM					
	(50)	(50)	(50)	(50)	
Heart	(50) 48 (96%)	(50)	(50) 45 (90%)	(50) 42 (84%)	
Cardiomyopathy Thrombosis		45 (90%)			
	3 (6%)	4 (8%)	7 (14%)	2 (4%)	
Myocardium, Necrosis	1 (2%)	1 (2%)	1 (2%)	2 (69/)	
Valve, Hyperplasia	1 (2%)	1 (2%)	3 (6%)	3 (6%)	

ENDOCRINE SYSTEM

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Species/Strain: RATS/F 344/N

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FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Adrenal Cortex	(50)	(50)	(50)	(50)	
Accessory Adrenal Cortical Nodule	26 (52%)	24 (48%)	18 (36%)	16 (32%)	
Degeneration, Cystic	1 (2%)				
Degeneration, Fatty	17 (34%)	17 (34%)	24 (48%)	15 (30%)	
Hyperplasia, Focal	7 (14%)	12 (24%)	14 (28%)	6 (12%)	
Hypertrophy, Focal	(,	4 (8%)	1 (2%)	1 (2%)	
Necrosis		(() ()	1 (2%)	1 (2%)	
Adrenal Medulla	(50)	(49)	(50)	(50)	
Angiectasis	1 (2%)	(10)	(88)	(00)	
Hyperplasia	14 (28%)	16 (33%)	10 (20%)	15 (30%)	
Islets. Pancreatic	(50)	(50)	(50)	(50)	
	(50)	1 (2%)	(30)	(50)	
Amyloid Deposition, Focal	2 (40/)	I (∠%)	2 (60()		
Hyperplasia	2 (4%)	2 (4%)	3 (6%)	(47)	
Parathyroid Gland	(50)	(49)	(49)	(47)	
Cyst			1 (2%)		
Hyperplasia, Focal		1 (2%)			
Pituitary Gland	(50)	(50)	(50)	(50)	
Hemorrhage		1 (2%)			
Infiltration Cellular, Histiocyte	1 (2%)				
Pigmentation	1 (2%)		1 (2%)		
Pars Distalis, Angiectasis	2 (4%)	4 (8%)	1 (2%)		
Pars Distalis, Cyst	6 (Ì2%)	2 (4%)	5 (10%)	5 (10%)	
Pars Distalis, Hyperplasia	1 (2%)	1 (2%)	2 (4%)	5 (10%)	
Pars Distalis, Hyperplasia, Focal	11 (22%)	14 (28%)	19 (38%)	15 (30%)	
Pars Distalis, Hypertrophy	11 (2270)	1 (2%)	1 (2%)	10 (0070)	
Pars Intermedia, Cyst	2 (4%)	4 (8%)	1 (2%)	2 (4%)	
Rathke's Cleft, Hemorrhage	2 (4%)	4 (078)	2 (4%)	2 (470)	
Thyroid Gland	(48)	(49)	(50)	(49)	
Pagagaratian Custia		(- /	5 (10%)		
Degeneration, Cystic	6 (13%)	7 (14%)	5 (10%)	4 (8%)	
Pigmentation	4 (50)	0 ((())	1 (2%)	4 (00.1)	
Ultimobranchial Cyst	1 (2%)	2 (4%)	2 (4%)	4 (8%)	
C-cell, Hyperplasia	9 (19%)	25 (51%)	15 (30%)	16 (33%)	
Follicular Cell, Hyperplasia, Focal		4 (8%)	2 (4%)		
NERAL BODY SYSTEM					
Tissue NOS	(1)	(1)	(1)	(2)	
Inflammation, Chronic	(1)	(1)	(1)	(2) 1 (50%)	
		1 (100%)		1 (50%)	
Necrosis		1 (100%)			
NITAL SYSTEM					
Epididymis	(50)	(50)	(50)	(50)	
Granuloma Sperm	(30)	1 (2%)	(30)	1 (2%)	
CHARLOUG CUEITI		1.12.701		1 12 /01	

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FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Inflammation	1 (2%)	1 (2%)			
Inflammation, Chronic	1 (2%)	. (270)			
Preputial Gland	(50)	(49)	(50)	(50)	
Cyst	1 (2%)	1 (2%)	1 (2%)	1 (2%)	
Hyperplasia	3 (6%)	6 (12%)	1 (270)	2 (4%)	
Inflammation, Chronic	39 (78%)	37 (76%)	40 (80%)	40 (80%)	
Duct, Ectasia	39 (7678)	37 (70%)	1 (2%)	40 (80 %)	
Prostate	(50)	(50)	(50)	(50)	
Fibrosis	(50)	(50)	(50)	(50) 1 (2%)	
	40 (200()	47 (240/)	42 (200)	1 (2%)	
Inflammation, Chronic	19 (38%)	17 (34%)	13 (26%)	16 (32%)	
Epithelium, Hyperplasia	9 (18%)	8 (16%)	8 (16%)	7 (14%)	
Seminal Vesicle	(50)	(50)	(50)	(50)	
Inflammation	1 (2%)	(==)	(==)	(=0)	
Testes	(50)	(50)	(50)	(50)	
Atrophy				1 (2%)	
Inflammation			1 (2%)		
Germinal Epithelium, Atrophy	6 (12%)	8 (16%)	11 (22%)	7 (14%)	
Interstitial Cell, Hyperplasia	3 (6%)	4 (8%)	5 (10%)	5 (10%)	
MATOPOIETIC SYSTEM					
Bone Marrow	(48) 1 (2%)	(50)	(50)	(49)	
Bone Marrow Amyloid Deposition	1 (2%)		, ,		
Bone Marrow Amyloid Deposition Hyperplasia	1 (2%) 5 (10%)	7 (14%)	(50) 9 (18%)	(49) 6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte	1 (2%) 5 (10%) 1 (2%)	7 (14%) 1 (2%)	9 (18%)		
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis	1 (2%) 5 (10%) 1 (2%) 1 (2%)	7 (14%) 1 (2%) 1 (2%)	9 (18%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node	1 (2%) 5 (10%) 1 (2%)	7 (14%) 1 (2%)	9 (18%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10)	7 (14%) 1 (2%) 1 (2%) (11)	9 (18%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%)	9 (18%) 2 (4%) (18)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%)	9 (18%) 2 (4%) (18) 3 (17%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%)	9 (18%) 2 (4%) (18) 3 (17%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%)	6 (12%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%)	6 (12%) (6) 1 (17%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%)	6 (12%) (6) 1 (17%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1)	6 (12%) (6) 1 (17%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia Hyperplasia, Lymphoid	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%) 1 (10%) (1)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1) 1 (100%)	6 (12%) (6) 1 (17%) (3) 1 (33%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia Hyperplasia, Lymphoid Lymph Node, Mesenteric	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1)	6 (12%) (6) 1 (17%) (3) 1 (33%) (50)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia Hyperplasia, Lymphoid Lymph Node, Mesenteric Atrophy	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%) 1 (10%) (1) (50)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1) 1 (100%) (50)	6 (12%) (6) 1 (17%) (3) 1 (33%) (50) 1 (2%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia Hyperplasia, Lymphoid Lymph Node, Mesenteric Atrophy Ectasia	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%) (1) (50) 1 (2%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%) (1) (1)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1) 1 (100%) (50) 1 (2%)	6 (12%) (6) 1 (17%) (3) 1 (33%) (50) 1 (2%) 1 (2%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia Hyperplasia, Lymphoid Lymph Node, Mesenteric Atrophy Ectasia Hemorrhage	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%) (1) (50) 1 (2%) 3 (6%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%) (1) (50)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1) 1 (100%) (50) 1 (2%) 1 (2%)	6 (12%) (6) 1 (17%) (3) 1 (33%) (50) 1 (2%) 1 (2%) 3 (6%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Ectasia Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia Hyperplasia, Lymphoid Lymph Node, Mesenteric Atrophy Ectasia Hemorrhage Hyperplasia, Lymphoid	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%) (1) (50) 1 (2%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%) (1) (1)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1) 1 (100%) (50) 1 (2%)	6 (12%) (6) 1 (17%) (3) 1 (33%) (50) 1 (2%) 1 (2%) 3 (6%) 20 (40%)	
Bone Marrow Amyloid Deposition Hyperplasia Infiltration Cellular, Histiocyte Myelofibrosis Lymph Node Mediastinal, Abscess Mediastinal, Ectasia Mediastinal, Hemorrhage Mediastinal, Hyperplasia, Lymphoid Mediastinal, Pigmentation Pancreatic, Ectasia Pancreatic, Hemorrhage Pancreatic, Hyperplasia, Lymphoid Lymph Node, Mandibular Ectasia Hyperplasia, Lymphoid Lymph Node, Mesenteric Atrophy Ectasia Hemorrhage	1 (2%) 5 (10%) 1 (2%) 1 (2%) (10) 1 (10%) 2 (20%) 2 (20%) 1 (10%) 1 (10%) (1) (50) 1 (2%) 3 (6%)	7 (14%) 1 (2%) 1 (2%) (11) 1 (9%) 1 (9%) 2 (18%) 1 (9%) (1) (50)	9 (18%) 2 (4%) (18) 3 (17%) 4 (22%) 2 (11%) 1 (6%) (1) 1 (100%) (50) 1 (2%) 1 (2%)	6 (12%) (6) 1 (17%) (3) 1 (33%) (50) 1 (2%) 1 (2%) 3 (6%)	

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

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TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Spleen	(50)	(50)	(50)	(50)	
Accessory Spleen	1 (2%)	2 (22)	2 (12()	2 (12)	
Fibrosis Hematopoietic Cell Proliferation	4 (8%) 4 (8%)	3 (6%)	2 (4%) 3 (6%)	2 (4%) 2 (4%)	
Hyperplasia, Lymphoid, Focal	1 (2%)		1 (2%)	2 (4%)	
Necrosis	1 (2%)	1 (2%)	1 (270)	1 (2%)	
Pigmentation	44 (88%)	45 (90%)	42 (84%)	45 (90%)	
Lymphoid Follicle, Atrophy	5 (400()	0 (400()	1 (2%)	7 (4.40()	
Lymphoid Follicle, Hyperplasia Thymus	5 (10%) (41)	6 (12%) (42)	6 (12%) (46)	7 (14%) (42)	
Cyst	1 (2%)	1 (2%)	(40)	(42)	
NTEGUMENTARY SYSTEM					
Mammary Gland	(49)	(49)	(48)	(49)	
Fibrosis	1 (2%)			1 (2%)	
Hyperplasia	17 (35%)	18 (37%)	13 (27%)	13 (27%)	
Duct, Ectasia Skin	8 (16%) (50)	12 (24%) (50)	4 (8%) (50)	14 (29%) (50)	
Cyst Epithelial Inclusion	1 (2%)	2 (4%)	2 (4%)	2 (4%)	
Fibrosis	. (=/3)	1 (2%)	1 (2%)	= (170)	
Hyperkeratosis	4 (8%)	3 (6%)	1 (2%)		
Inflammation, Chronic	4 (8%)		((00()		
Ulcer Epidermis, Hyperplasia	3 (6%)	2 (4%)	1 (2%) 1 (2%)		
Prepuce, Inflammation, Chronic	3 (0%)	1 (2%)	1 (276)		
MUSCULOSKELETAL SYSTEM					
Bone	(50)	(50)	(50)	(50)	
Femur, Osteopetrosis	2 (4%)	(4)	(0)	(0)	
Skeletal Muscle	(1)	(4)	(0)	(0)	
IERVOUS SYSTEM					
Brain	(50)	(50)	(50)	(50)	
Compression	3 (6%)	4 (8%)	1 (2%)	6 (12%)	
Degeneration Developmental Malformation	1 (2%)			1 (2%)	
Gliosis, Focal				1 (2%)	
Hemorrhage	5 (10%)	18 (36%)	6 (12%)	13 (26%)	
Hyperplasia	1 (2%)	1 (2%)	` ,	,	
Infiltration Cellular, Lymphocyte	1 (2%)				

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

Test Type: CHRONIC
Route: DOSED FEED

TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Necrosis Spinal Cord	1 (2%) (8)	(5)	1 (2%) (2)	(5)	
RESPIRATORY SYSTEM					
Lung Congestion Hemorrhage	(50) 1 (2%) 1 (2%)	(50) 2 (4%) 2 (4%)	(50) 4 (8%)	(50)	
Infiltration Cellular, Histiocyte Inflammation, Chronic Metaplasia, Osseous Thrombosis	34 (68%) 3 (6%) 1 (2%) 1 (2%)	48 (96%) 1 (2%) 2 (4%)	43 (86%) 2 (4%)	39 (78%) 6 (12%) 4 (8%)	
Alveolar Epithelium, Hyperplasia Nose Foreign Body	17 (34%) (50) 10 (20%)	18 (36%) (50) 8 (16%)	17 (34%) (50) 7 (14%)	13 (26%) (50) 5 (10%)	
Hemorrhage Inflammation, Chronic Necrosis Thrombosis	16 (32%) 1 (2%) 3 (6%)	1 (2%) 15 (30%) 1 (2%) 1 (2%)	6 (12%)	9 (18%)	
Goblet Cell, Hyperplasia Respiratory Epithelium, Hyperplasia Respiratory Epithelium, Metaplasia, Squamous	6 (12%) 1 (2%)	2 (4%) 6 (12%) 1 (2%)	1 (2%) 1 (2%)	1 (2%) 1 (2%)	
PECIAL SENSES SYSTEM					
Eye Cataract Edema Inflammation, Chronic	(48) 18 (38%)	(48) 16 (33%) 2 (4%)	(48) 18 (38%) 1 (2%) 1 (2%)	(49) 20 (41%) 3 (6%)	
Retinal Detachment Bilateral, Cataract Retina, Degeneration Harderian Gland Hyperplasia, Focal	19 (40%) 7 (15%) (50) 1 (2%)	1 (2%) 10 (21%) 4 (8%) (50) 2 (4%)	1 (2%) 6 (13%) 3 (6%) (50) 1 (2%)	6 (12%) 5 (10%) (50) 3 (6%)	
Inflammation, Chronic Zymbal's Gland Cyst	3 (6%) (0)	2 (4%) (1) 1 (100%)	2 (4%) (0)	4 (8%)	
JRINARY SYSTEM					
Kidney Cyst	(50) 1 (2%)	(50) 1 (2%)	(48) 1 (2%)	(50)	

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

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

Lab: SRI

FISCHER 344 RATS MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Inflammation, Suppurative				2 (4%)	
Metaplasia, Osseous				1 (2%)	
Mineralization	13 (26%)	11 (22%)	7 (15%)	20 (40%)	
Nephropathy	46 (92%)	47 (94%)	42 (88%)	46 (92%)	
Renal Tubule, Dilatation				1 (2%)	
Renal Tubule, Hyperplasia	1 (2%)	2 (4%)			
Renal Tubule, Necrosis	1 (2%)				
Renal Tubule, Pigmentation		1 (2%)	2 (4%)		
Transitional Epithelium, Hyperplasia	25 (50%)	10 (20%)	6 (13%)	18 (36%)	
Urinary Bladder	(50)	(50)	(50)	(50)	
Transitional Epithelium, Hyperplasia	1 (2%)	2 (4%)	, ,	, ,	

*** END OF MALE ***

TDMS No. 20008 - 03 Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

Test Type: CHRONIC
Route: DOSED FEED

TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
isposition Summary					
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	
IMENTARY SYSTEM					
Intestine Large, Cecum	(43)	(48)	(49)	(49)	
Edema				1 (2%)	
Intestine Large, Colon	(44)	(45)	(48)	(46)	
Ulcer				1 (2%)	
Liver	(50)	(50)	(49)	(50)	
Angiectasis	1 (2%)	2 (4%)	1 (2%)		
Basophilic Focus	44 (88%)	44 (88%)	44 (90%)	43 (86%)	
Clear Cell Focus	9 (18%)	10 (20%)	17 (35%)	21 (42%)	
Eosinophilic Focus	5 (10%)	13 (26%)	11 (22%)	11 (22%)	
Hematopoietic Cell Proliferation	, ,	2 (4%)	1 (2%)	, ,	
Hepatodiaphragmatic Nodule	6 (12%)	5 (Ì0%́)	4 (8%)	5 (10%)	
Infiltration Cellular, Mixed Cell	37 (74%)	34 (68%)	36 (73%)	39 (78%)	
Mixed Cell Focus	3 (6%)	6 (Ì2%) [′]	11 (22%)	10 (20%)	
Necrosis, Focal	3 (6%)	2 (4%)	/	1 (2%)	
Bile Duct, Hyperplasia	37 (74%)	10 (20%)	10 (20%)	8 (16%)	
Hepatocyte, Vacuolization Cytoplasmic	8 (16%)	9 (18%)	8 (16%)	6 (12%)	
Hepatocyte, Vacuolization Cytoplasmic, Focal	- (- / - /	2 (4%)	1 (2%)	1 (2%)	
Serosa, Fibrosis	1 (2%)	(/	(/	(/	
Mesentery	(10)	(10)	(4)	(8)	
Accessory Spleen	1 (10%)	1 (10%)	(- /	2 (25%)	
Fat. Necrosis	8 (80%)	8 (80%)	4 (100%)	6 (75%)	
Oral Mucosa	(0)	(0)	(1)	(0)	
Pharyngeal, Hyperplasia	(~)	(0)	1 (100%)	(=)	
Pancreas	(48)	(48)	(49)	(49)	
Atrophy	23 (48%)	19 (40%)	25 (51%)	26 (53%)	
Metaplasia, Hepatocyte	1 (2%)	13 (4070)	20 (3170)	20 (00/0)	
Acinus, Hyperplasia, Focal	2 (4%)	1 (2%)	2 (4%)	1 (2%)	
Duct, Ectasia	14 (29%)	14 (29%)	16 (33%)	17 (35%)	
Salivary Glands	(50)	(50)	(50)	(50)	
Jantary Jiana	1 (2%)	(00)	(00)	(00)	

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

Test Type: CHRONIC
Route: DOSED FEED

TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Atrophy	12 (24%)	10 (20%)	13 (26%)	16 (32%)	
Hyperplasia, Lymphoid		1 (2%)			
Infiltration Cellular	1 (2%)	, ,			
Stomach, Forestomach	(49)	(48)	(49)	(50)	
Edema	2 (4%)	1 (2%)	1 (2%)	1 (2%)	
Erosion	1 (2%)	, ,	, ,	1 (2%)	
Inflammation, Chronic Active	, ,	1 (2%)		` '	
Ulcer	1 (2%)	1 (2%)		1 (2%)	
Epithelium, Hyperplasia	3 (6%)	5 (10%)	2 (4%)	1 (2%)	
Stomach, Glandular	(49)	(47)	(49)	(49)	
Edema	(10)	2 (4%)	(10)	(10)	
Erosion	7 (14%)	2 (4%)	2 (4%)	1 (2%)	
Infiltration Cellular, Mononuclear Cell	1 (2%)	2 (470)	2 (470)	· (2/0)	
Inflammation	1 (2/0)		1 (2%)		
Ulcer	2 (4%)	1 (2%)	1 (2%)	3 (6%)	
	2 (4%)	1 (2%)	1 (270)	3 (0%)	
Epithelium, Hyperplasia	(0)	(4)	1 (2%)	(0)	
Tongue	(0)	(1)	(1)	(0)	
Hyperplasia		1 (100%)			
Heart Cardiomyopathy Thrombosis Valve, Hyperplasia	(50) 32 (64%) 1 (2%)	(50) 33 (66%) 1 (2%) 1 (2%)	(50) 28 (56%) 2 (4%)	(50) 34 (68%) 1 (2%)	
ENDOCRINE SYSTEM					
Adrenal Cortex	(48)	(48)	(49)	(50)	
Accessory Adrenal Cortical Nodule	7 (15%)	15 (31%)	11 (22%)	7 (14%)	
Degeneration, Fatty	16 (33%)	17 (35%)	24 (49%)	22 (44%)	
Fibrosis	1 (2%)	(====,	(/	(33)	
Hyperplasia, Focal	21 (44%)	21 (44%)	21 (43%)	29 (58%)	
Hypertrophy, Focal	2 (4%)	3 (6%)	1 (2%)	1 (2%)	
Necrosis	1 (2%)	1 (2%)	1 (2%)	. (270)	
Capsule, Hyperplasia	. (270)	. (270)	1 (2%)	1 (2%)	
Adrenal Medulla	(48)	(48)	(48)	(50)	
Hyperplasia	3 (6%)	10 (21%)	3 (6%)	6 (12%)	
Infiltration Cellular, Lipocyte	3 (0 /0)	10 (21 /0)	3 (0 /0)	0 (12/0)	
	4 (20/)	1 (2%)			
Bilateral, Hyperplasia	1 (2%)	(40)	(40)	(40)	
Islets, Pancreatic	(48)	(48)	(49)	(49)	
Hyperplasia	1 (2%)	(45)	(4-)	(12)	
Parathyroid Gland	(49)	(48)	(47)	(49)	
Pituitary Gland	(50)	(50)	(50)	(50)	

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

Test Type: CHRONIC
Route: DOSED FEED

Species/Strain: RATS/F 344/N

TDMS No. 20008 - 03

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

Pars Distalis, Angiectasis 10 (20%) 6 (12%) 5 (10%) 7 (14%) Pars Distalis, Cyst Multiple Pars Distalis, Cyst, Multiple Pars Distalis, Cyst, Multiple Pars Distalis, Cyst, Multiple Pars Distalis, Hyperplasia Pars Distalis, Hyperplasia, Focal 12 (24%) 2 (4%) 1 (2%) 2 (4%) Pars Distalis, Hyperplasia, Focal 12 (24%) 9 (18%) 5 (10%) 8 (16%) Pars Distalis, Hyperplasia, Focal 12 (24%) 4 (8%) 5 (10%) 8 (16%) Pars Distalis, Hyperplasia, Focal 12 (24%) 4 (8%) 5 (10%) 8 (16%) Pars Intermedia, Angiectasis 1 (2%) 1 (2%) 2 (4%) 2 (4%) 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Angiectasis 1 (2%) 2 (4%) 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Angiectasis 1 (2%) 2 (4%) 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 3 (6%) 4 (6%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 3 (6%) 2 (4%) 4 (6%) 1 (2%) Pars Intermedia, Cyst 3 (24%) 4 (6%) 1 (2%) 1	FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Pars Distalis, Cyst, Multiple Pars Distalis, Hyperplasia 1 (2%) 2 (4%) 1 (2%) 2 (4%) Pars Distalis, Hyperplasia 1 (2%) 9 (18%) 5 (10%) 8 (16%) Pars Distalis, Hyperplasia, Focal 1 (2%) 9 (18%) 5 (10%) 8 (16%) Pars Intermedia, Anglectasis 1 (2%) 1 (2%) 2 (4%) Pars Intermedia, Anglectasis 1 (2%) 2 (4%) 2 (4%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cysti 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cysti 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cysti 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cysti 2 (4%) 3 (6%) Pars Intermedia, Cysti 2 (4%) 4 (8%) Pars Intermedia, Cysti 2 (4%) 3 (6%) Pars Intermedia, Cysti 2 (4%) 4 (8%) Pars Intermedia, Cysti 3 (4%) 5 (10%) Pars Intermedia, Cysti 3 (6%) 6 (12%) Pars Intermedia, Cysti 3 (6%) 8 (16%) Pars Intermedia, Cysti 3 (6%) Pars Intermedia, Cysti 3 (6%) 8 (16%) Pars Intermedia, Cysti 3 (6%) Pars Intermedia, Cysti 4 (6%) Pars Intermedia, Cysti 5 (6%) Pars Intermedia, Cysti 5 (6%) Pars Intermedia, Cysti 6 (6%) Pars Intermedia, Cysti 7 (6%) Pars Intermedia, Cysti 7 (6%) Pars Intermedia, Cysti 7 (6%) Pars Intermedia,			6 (12%)		7 (14%)	
Pars Distalis, Hyperplasia Pars Distalis, Hyperplasia, Focal Pars Intermedia, Anglectasis 1 (2%) Pars Intermedia, Anglectasis 1 (2%) Pars Intermedia, Anglectasis 1 (2%) Pars Intermedia, Cyst 2 (4%) Pars Intermedia, Cyst Pars Intermedia,	Pars Distalis, Cyst	12 (24%)	18 (36%)	20 (40%)	14 (28%)	
Pars Distalls, Hyperplasia, Focal 12 (24%) 9 (18%) 5 (10%) 8 (16%) Pars Intermedia, Anglectasis 1 (2%) 1 (2%) 2 (4%) Pars Intermedia, Anglectasis 1 (2%) 2 (4%) 2 (4%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 3 (47) (49) (50) Degeneration, Cystic 2 (4%) 8 (16%) 5 (10%) 4 (6%) Ultimobranchial Cyst 1 (2%) 1 (2%) 3 (6%) ENERAL BODY SYSTEM Tissue NOS Fat, Mediastinum, Necrosis 1 (33%) ENITAL SYSTEM Clitical Gland (50) (49) (50) (50) Abscess 1 (2%) 1 (2%) Cyst 2 (4%) 4 (6%) Hyperplasia, Squamous 1 (2%) Hyperplasia, Squamous 1 (2%) Hyperplasia, Squamous 1 (2%) Hyperplasia, Squamous 1 (2%) Inflammation, Acute 1 (2%) Inflammation, Acute 1 (2%) Inflammation, Chronic 5 (10%) 6 (12%) 6 (12%) Cyst 9 (10%) 1 (2%) Inflammation, Chronic 1 (2%) 1 (2%) Inflammation, Chronic 1 (2%) 1 (2%) Ovary (50) (49) (50) (50) Cyst 9 (10%) 8 (16%) 6 (12%) Ulterus (50) (40%) 9 (50) (50) Cyst 9 (10%) 9 (10%) 9 (50) (50) Cyst 9 (10%) 9 (10%) 9 (10%) Hiffarmation, Acute 1 (2%) Inflammation, Chronic 1 (2%) Inflammation, Chronic 1 (2%) Inflammation, Chronic 1 (2%) Horizon (50) (4%) 9 (50) (50) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (10%) Cyst 9 (10%) 9 (10%) 9 (10%) 9 (Pars Distalis, Cyst, Multiple	4 (20()	1 (2%)	4 (20/)	2 (40/)	
Pars Distalis, Hypertrophy 2 (4%) 4 (8%) Pars Intermedia, Anglectasis 1 (2%) 2 (4%) 2 (4%) 2 (4%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 1 (2%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 8 (16%) 5 (10%) 4 (9%) Pars Intermedia, Cyst 2 (4%) 1 (2%) 1 (2%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) Pars Intermedia, Cyst 2 (4%) 1 (2%) Pars Intermedia, Chronic 1 (2%) Pars Intermedia, Chronic 1 (2%) Pars Intermedia, Cyst 2 (4%) Pars Inte	Pars Distalls, Hyperplasia Pars Distalls, Hyperplasia Focal	1 (2%)	2 (4%) 9 (18%)			
Pars Intermedia, Anglectasis 1 (2%) 1 (2%) 2 (4%) 2 (4%) Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) 1 (2%)	Pars Distalis Hyperplasia, 1 ocal	2 (4%)	9 (1070)		0 (10%)	
Pars Intermedia, Cyst 2 (4%) 2 (4%) 2 (4%) 2 (4%) 1 (2%) 1	Pars Intermedia, Angiectasis	1 (2%)	1 (2%)	. (670)	2 (4%)	
Thyroid Gland (47) (49) (49) (50) Degeneration, Cystic 2 (4%) 8 (16%) 5 (10%) 4 (8%) Ultimobranchial Cyst 1 (2%) 1 (2%) 3 (6%) C-cell, Hyperplasia, Focal 18 (38%) 17 (35%) 20 (41%) 21 (42%) Follicular Cell, Hyperplasia, Focal 3 (6%) EENERAL BODY SYSTEM Tissue NOS (0) (0) (3) (3) (0) Fat, Necrosis 1 (33%) Fat, Mediastinum, Necrosis 1 (33%) Fat, Mediastinum, Necrosis 1 (33%) EENITAL SYSTEM Clitral Gland (50) (49) (50) (50) Abscess 1 (2%) 2 (4%) 4 (8%) 1 (2%) Cyst 4 (49%) 3 (6%) 7 (14%) Hyperplasia, Squamous 1 (2%) Hyperplasia, Squamous 1 (2%) Inframmation, Acute 1 (2%) Inframmation, Chronic 5 (10%) 6 (12%) 6 (12%) Ovary (50) (49) (50) (50) Cyst 9 (18%) 8 (16%) 1 (2%) Toyst 9 (18%) 8 (16%) 1 (2%) Toyst 9 (18%) 8 (16%) 19 (38%) 10 (20%) Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) Ulterus (50) (49) (50) (50) Ulterus (50) (50) (50) (50) Ulterus (50) (50) (50) Ulterus (50) (50) (50) (50) (50) Ulterus (Pars Intermedia, Cyst	2 (4%)	2 (4%)	2 (4%)	(/	
Degeneration, Cystic 2 (4%) 8 (16%) 5 (10%) 4 (8%)						
Ultimobranchial Cyst		(47)				
Cecell, Hyperplasia Follicular Cell, Hyperplasia, Focal 18 (38%) Follicular Cell, Hyperplasia, Focal 19 (0) (0) (3) (0) (3) (0) Fal, Necrosis Fal, Necrosis Fal, Mediastinum, Necrosis 10 (3) (0) Follicular Cell, Hyperplasia		2 (4%)		5 (10%)	4 (8%)	
Follicular Cell, Hyperplasia, Focal SENERAL BODY SYSTEM Tissue NOS (0) (0) (3) (0) Fat, Necrosis 1 (33%) Fat, Mediastinum, Necrosis 1 (33%) SENITAL SYSTEM Cilitoral Gland (50) (49) (50) (50) Abscess 1 (2%) 1 (2%) Cyst 2 (4%) 4 (8%) 7 (14%) Hyperplasia Squamous 1 (2%) Hyperplasia, Squamous 1 (2%) Inflammation, Acute 1 (2%) 1 (2%) Inflammation, Chronic 5 (10%) 6 (12%) 6 (12%) 6 (12%) Inflammation, Chronic 5 (10%) 8 (16%) 19 (38%) 10 (20%) Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) Userus (50) (49) (50) (50) Decidual Reaction (50) (50) (50) (50) (50) Decidual Reaction (50) (50) (50) (50) (50) (50) (50) (50)					04 (400()	
Tissue NOS Fat, Necrosis Fat, Mediastinum, Necrosis Clitoral Gland Abscess 1 (2%) Cyst Hyperplasia Hyperplasia, Squamous Inflammation, Chronic Start Clyst Squamous Inflammation, Chronic Cyst Squamous Inflammation, Chronic Cyst Squamous Inflammation, Chronic Inflammation, Ch	C-ceil, Hyperplasia Follicular Cell, Hyperplasia, Focal	18 (38%)	3 (6%)	20 (41%)	21 (42%)	
Fat, Necrosis Fat, Mediastinum, Necrosis Ciltoral Gland Clitoral Gland Abscess 1 (2%) Cyst Hyperplasia Hyperplasia, Granulosa Cell, Hyperplasia Coary Granulosa Cell, Hyperplasia Telemorthage Hyperplasia, Cystic Selemorthage Hyperplasia Telemorthage Hyperplasia Telemorthage Hyperplasia Telemorthage Hyperplasia Telemorthage Hyperplasia Telemorthage Hyperplasia Telemorthage Telemor	GENERAL BODY SYSTEM					
ENITAL SYSTEM Clitoral Gland (50) (49) (50) (50) Abscess 1 (2%) 2 (4%) 4 (8%) Hyperplasia, Squamous Inflammation, Acute 1 (2%) Inflammation, Chronic 5 (10%) 6 (12%) 6 (12%) Cyst 9 (80) (49) (50) (50) Cyst 1 (2%) Inflammation, Chronic 5 (10%) 6 (12%) 6 (12%) Inflammation, Chronic 5 (10%) 8 (16%) 19 (38%) 10 (20%) Cyst 9 (18%) 8 (16%) 19 (38%) 10 (20%) Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) Uterus (50) (49) (50) (50) Decidual Reaction 1 (2%) Hyperplasia, Cystic 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5)		(0)	(0)	(3)	(0)	
Clitoral Gland				1 (33%)		
Clitoral Gland (50) (49) (50) (50) (50) Abscess 1 (2%)	Fat, Mediastinum, Necrosis			1 (33%)		
Abscess 1 (2%) 2 (4%) 4 (8%) 1 (2%) 7 (14%) 1 (2%)	GENITAL SYSTEM					
Cyst Hyperplasia Hyperplasia, Squamous Inflammation, Acute Inflammation, Chronic Ovary Cyst Granulosa Cell, Hyperplasia Decidual Reaction Hyperplasia, Cystic Vagina Cyst (2 (4%) 4 (8%) 4 (8%) 7 (14%) 4 (8%) 7 (14%) 8 (16%) 7 (14%) 8 (16%) 7 (14%) 8 (16%) 6 (12%) 6 (1			(49)	(50)	(50)	
Hyperplasia 7 (14%) 3 (6%) 8 (16%) 7 (14%) Hyperplasia, Squamous 1 (2%) 1 (2%) Inflammation, Acute 1 (2%) 1 (2%) Inflammation, Chronic 5 (10%) 6 (12%) 6 (12%) Ovary (50) (49) (50) (50) Cyst 9 (18%) 8 (16%) 19 (38%) 10 (20%) Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) (50) (50) (50) Uterus (50) (49) (50) (50) (50) Decidual Reaction 1 (2%) (2%) (50) (50) (50) Hyperplasia, Cystic 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5)		1 (2%)	2 (40/)	4 (00()	1 (2%)	
Hyperplasia, Squamous Inflammation, Acute I (2%) Inflammation, Chronic I (2%) I (2%) I (2%) I (2%) I (2%) I (2%) I (38%) I (2%) I		7 (1/1%)			7 (1/19/4)	
Inflammation, Acute 1 (2%) 1 (2%) 6 (12%) 6 (12%) 6 (12%) Inflammation, Chronic 5 (10%) 6 (12%) 6 (12%) 6 (12%) Ovary (50) (49) (50) (50) Cyst 9 (18%) 8 (16%) 19 (38%) 10 (20%) Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) Uterus (50) (49) (50) (50) Decidual Reaction 1 (2%) Hemorrhage 1 (2%) Hyperplasia, Cystic 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5)		7 (1470)	3 (078)		7 (1470)	
Inflammation, Chronic 5 (10%) 6 (12%) 6 (12%) 6 (12%) Ovary (50) (49) (50) (50) Cyst 9 (18%) 8 (16%) 19 (38%) 10 (20%) Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) Uterus (50) (49) (50) (50) Decidual Reaction 1 (2%) Hemorrhage 1 (2%) Hyperplasia, Cystic 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5)		1 (2%)		1 (2%)		
Ovary (50) (49) (50) (50) Cyst 9 (18%) 8 (16%) 19 (38%) 10 (20%) Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) Uterus (50) (49) (50) (50) Decidual Reaction 1 (2%) 1 (2%) 1 (2%) Hemorrhage 1 (2%) 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5)	Inflammation, Chronic	5 (10%)	6 (12%)		6 (12%)	
Granulosa Cell, Hyperplasia 1 (2%) 2 (4%) Uterus (50) (49) (50) Decidual Reaction 1 (2%) Hemorrhage 1 (2%) Hyperplasia, Cystic 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5)	Ovary	(50)		(50)		
Uterus (50) (49) (50) (50) Decidual Reaction 1 (2%) Hemorrhage 1 (2%) Hyperplasia, Cystic 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5)	Cyst	9 (18%)		19 (38%)	10 (20%)	
Decidual Reaction				(50)	(50)	
Hemorrhage Hyperplasia, Cystic Vagina 1 (2%) 30 (61%) 33 (66%) 31 (62%) (2) (2) (3) STEMATOPOIETIC SYSTEM		(50)		(50)	(50)	
Hyperplasia, Cystic 32 (64%) 30 (61%) 33 (66%) 31 (62%) Vagina (2) (2) (3) (5) IEMATOPOIETIC SYSTEM			1 (2%)			
Vagina (2) (2) (3) (5) (5) HEMATOPOIETIC SYSTEM		32 (64%)		33 (66%)	31 (62%)	
Bone Marrow (49) (50) (50) (50)						
Depletion Cellular (49) (30) (30)	Bone Marrow	(49)	(50)	(50)	(50)	

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

Test Type: CHRONIC
Route: DOSED FEED

TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Hyperplasia	5 (10%)	5 (10%)	8 (16%)	1 (2%)	
Infiltration Cellular, Histiocyte	3 (1070)	0 (1070)	2 (4%)	1 (270)	
Myelofibrosis			1 (2%)		
Lymph Node	(9)	(8)	(5)	(8)	
Deep Cervical, Ectasia	(3)	(0)	(0)	1 (13%)	
Deep Cervical, Hemorrhage		1 (13%)		1 (1070)	
Deep Cervical, Pigmentation		1 (13%)			
Mediastinal, Ectasia		1 (13%)			
Mediastinal, Hemorrhage	2 (22%)	2 (25%)	2 (40%)	1 (13%)	
Mediastinal, Hyperplasia, Lymphoid	3 (33%)	3 (38%)	2 (4070)	1 (1370)	
Mediastinal, Hyperplasia, Plasma Cell	3 (3378)	3 (30 %)	1 (20%)		
Mediastinal, Tryperplasia, Flasina Cell Mediastinal, Infiltration Cellular, Histiocyte	1 (11%)		1 (20%)		
Mediastinal, Illinitiation Celidial, Histocyte Mediastinal, Pigmentation	4 (44%)			1 (13%)	
Pancreatic, Ectasia	4 (44%) 1 (11%)			1 (13/0)	
Pancreatic, Ectasia Pancreatic, Hemorrhage	1 (11%)	1 (13%)		1 (13%)	
Pancreatic, Hemormage Pancreatic, Hyperplasia, Lymphoid	1 (1170)	1 (13%)		1 (13%)	
Pancreatic, Hyperplasia, Lymphold Pancreatic, Pigmentation	1 (110/)	1 (13%)		1 (120/)	
Lymph Node, Mandibular	1 (11%)	(2)	(2)	1 (13%)	
	(1)	(3)	(2)	(2)	
Ectasia		1 (33%)	4 (500/)		
Hemorrhage		4 (220/)	1 (50%)		
Hyperplasia, Lymphoid		1 (33%)	1 (50%)		
Infiltration Cellular, Histiocyte		1 (33%)			
Pigmentation	(40)	1 (33%)	(50)	(50)	
Lymph Node, Mesenteric	(49)	(48)	(50)	(50)	
Ectasia	1 (2%)	1 (2%)	1 (2%)		
Fibrosis	1 (2%)	4 (22()	0 (00()	E (400()	
Hemorrhage	3 (6%)	4 (8%)	3 (6%)	5 (10%)	
Hyperplasia, Lymphoid	1 (2%)	9 (19%)	5 (10%)	2 (4%)	
Hyperplasia, Reticulum Cell	47 (000()	00 (040()	00 (500()	1 (2%)	
Pigmentation	47 (96%)	39 (81%)	29 (58%)	18 (36%)	
Spleen	(49)	(50)	(50)	(49)	
Fibrosis	- //	_ //	_ ,,	1 (2%)	
Hematopoietic Cell Proliferation	5 (10%)	5 (10%)	7 (14%)	2 (4%)	
Hyperplasia, Focal	1 (2%)				
Necrosis	1 (2%)			1 (2%)	
Pigmentation	43 (88%)	42 (84%)	37 (74%)	42 (86%)	
Lymphoid Follicle, Atrophy	1 (2%)	1 (2%)		1 (2%)	
Lymphoid Follicle, Hyperplasia	2 (4%)	5 (10%)	7 (14%)	1 (2%)	
Thymus	(50)	(49)	(48)	(49)	
Čyst			2 (4%)	1 (2%)	
Hemorrhage	17 (34%)	15 (31%)	13 (27%)	14 (29%)	
FEGUMENTARY SYSTEM					
Mammary Gland	(50)	(50)	(50)	(50)	

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Test Type: CHRONIC
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TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Hyperplasia	20 (40%)	17 (34%)	24 (48%)	23 (46%)	
Hyperplasia, Focal	20 (40%)	26 (52%)	11 (22%)	20 (40%)	
Duct, Ectasia	44 (88%)	37 (74%)	36 (72%)	40 (80%)	
Duct, Hyperplasia	1 (2%)				
Skin	(50)	(50)	(50)	(50)	
Cyst Epithelial Inclusion	1 (2%)	1 (2%)	1 (2%)	1 (2%)	
Hyperkeratosis	1 (2%)			2 (4%)	
Ulcer				1 (2%)	
Epidermis, Hyperplasia	1 (2%)			2 (4%)	
MUSCULOSKELETAL SYSTEM					
Bone	(50)	(50)	(50)	(50)	
Femur, Osteopetrosis	1 (2%)	1 (2%)	1 (2%)	2 (4%)	
Skeletal Muscle	(1)	(0)	(1)	(0)	
NERVOUS SYSTEM					
Brain	(50)	(50)	(50)	(50)	
Compression	5 (10%)	9 (18%)	12 (24%)	10 (20%)	
Developmental Malformation			1 (2%)		
Gliosis			1 (2%)		
Hemorrhage	4 (8%)	7 (14%)	8 (16%)	14 (28%)	
Mineralization				1 (2%)	
Necrosis			2 (4%)	1 (2%)	
RESPIRATORY SYSTEM					
Lung	(50)	(50)	(49)	(50)	
Congestion		2 (4%)	1 (2%)		
Hemorrhage	3 (6%)	4 (8%)	2 (4%)	6 (12%)	
Hyperplasia, Lymphoid			1 (2%)	47 (225)	
Infiltration Cellular, Histiocyte	45 (90%)	44 (88%)	45 (92%)	45 (90%)	
Inflammation, Suppurative	4 (00()		1 (2%)	40 (000)	
Inflammation, Chronic	1 (2%)	4 (00)	2 (4%)	10 (20%)	
Metaplasia, Osseous	1 (2%)	1 (2%)	00 (500()	1 (2%)	
Alveolar Epithelium, Hyperplasia	25 (50%)	25 (50%)	29 (59%)	25 (50%)	
Nose	(50)	(50)	(49)	(50)	
Foreign Body		3 (6%)	1 (2%)	4 (8%)	
Hemorrhage	7 /4 40/\	1 (2%)	7 (4 40/)	0 (460/)	
Inflammation, Chronic	7 (14%)	9 (18%)	7 (14%)	8 (16%)	
Goblet Cell, Hyperplasia	1 (2%)	1 (2%)	1 (2%)	4 (20()	
Nasolacrimal Duct, Cyst		1 (2%)		1 (2%)	

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Test Type: CHRONIC
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TDMS No. 20008 - 03

Species/Strain: RATS/F 344/N

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008 Time Report Requested: 11:00:55 First Dose M/F: 03/04/03 / 03/04/03

FISCHER 344 RATS FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Nasolacrimal Duct, Hyperplasia, Squamous Respiratory Epithelium, Hyperplasia Trachea Inflammation, Acute	2 (4%) (50) 1 (2%)	1 (2%) 5 (10%) (50)	1 (2%) 1 (2%) (50)	2 (4%) (50)	
PECIAL SENSES SYSTEM					
Eye Cataract Edema Inflammation, Chronic Cornea, Hyperplasia Retina, Degeneration Harderian Gland Atrophy	(48) 1 (2%) 1 (2%) (50)	(48) 6 (13%) 4 (8%) 1 (2%) 1 (2%) 5 (10%) (49)	(49) 3 (6%) 3 (6%) 1 (2%) 1 (2%) 3 (6%) (50) 1 (2%)	(50) 4 (8%) 4 (8%) 1 (2%) 3 (6%) (50)	
Hyperplasia, Focal Inflammation, Chronic Zymbal's Gland	1 (2%) 12 (24%) (0)	2 (4%) 7 (14%) (1)	10 (20%) (2)	1 (2%) 12 (24%) (0)	
IRINARY SYSTEM					
Kidney Casts Granular Cyst Infarct	(48) 1 (2%) 1 (2%)	(49) 3 (6%)	(49) 1 (2%) 1 (2%)	(48) 1 (2%)	
Inflammation Inflammation, Chronic Inflammation, Chronic Active	1 (2%)	1 (2%)	1 (2%)	1 (2%)	
Mineralization Necrosis Nephropathy Vacuolization Cytoplasmic	21 (44%) 1 (2%) 36 (75%) 2 (4%)	28 (57%) 45 (92%)	30 (61%) 43 (88%)	26 (54%) 42 (88%)	
Bilateral, Infarct . Renal Tubule, Accumulation, Hyaline Droplet Renal Tubule, Hyperplasia	1 (2%)	4 (8%)	1 (2%) 6 (12%)	1 (2%) 1 (2%)	
Renal Tubule, Necrosis Transitional Epithelium, Hyperplasia Urinary Bladder	3 (6%) (50)	3 (6%) (49)	2 (4%) 4 (8%) (50)	1 (2%) 4 (8%) (50)	

^{***} END OF REPORT ***

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