

**TDMS No.** 20008 - 03  
**Test Type:** CHRONIC  
**Route:** DOSED FEED  
**Species/Strain:** RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

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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DAY ON TEST	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6	7	7	7	7	7	7	4	7	7	6	6	7	7	7	7	6	5	7	6	7	7	7	6	
	8	1	2	2	2	2	3	3	7	3	3	7	0	3	3	0	3	6	9	2	1	3	1	3	1
	7	0	9	9	9	9	1	1	7	0	0	2	0	0	0	2	0	0	9	9	3	0	1	0	9

  

FISCHER 344 RATS MALE	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANIMAL ID	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0 PPM	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5

males  
(cont...)

**ALIMENTARY SYSTEM**

Esophagus Inflammation, Acute	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Intestine Large, Cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Intestine Large, Colon Edema Ulcer	+	A	+	+	+	+	+	+	+	+	+	3	+	+	+	+	+	+	+	+	+	+	+	2	
Intestine Large, Rectum Necrosis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+
Intestine Small, Duodenum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Intestine Small, Ileum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Intestine Small, Jejunum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Angiectasis																							3		
Atrophy																								2	
Basophilic Focus				X	X		X	X	X		X	X		X	X	X		X	X	X	X	X	X	X	
Clear Cell Focus				X	X	X	X	X	X		X	X		X	X	X		X						X	
Eosinophilic Focus					X				X												X				
Hematopoietic Cell Proliferation									1																

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
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 I .. Insufficient tissue

M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

Page 2

	DAY ON TEST																									males (cont...)
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	6	7	7	7	7	7	7	4	7	7	6	6	7	7	7	7	6	5	7	6	7	7	7	6	0	
	8	1	2	2	2	2	3	3	7	3	3	7	0	3	3	0	3	6	9	2	1	3	1	3	1	
	7	0	9	9	9	9	1	1	7	0	0	2	0	0	0	2	0	0	9	9	3	0	1	0	9	
FISCHER 344 RATS MALE	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ANIMAL ID	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
0 PPM	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	
Hepatodiaphragmatic Nodule																X	X									
Infiltration Cellular, Mixed Cell				1	1		1	1	2		1	1		1	1		1	1		1	1		1	1	1	
Mixed Cell Focus			X				X										X		X							
Necrosis, Focal																										
Pigmentation, Focal																										
Bile Duct, Hyperplasia	3	2	2	2	4	2	2	2	3	2	2	2	2	2	4	2	2	3	2	2	4	3	2	2	2	3
Hepatocyte, Vacuolization Cytoplasmic	3											2	4			2									3	
Mesentery					+											+	+									
Fat, Necrosis					2											2	2									
Pancreas																										
Atrophy	3		1		2	1	1	1	1	1	2	3	1	1	2		3	2	2	3	2	2	2	2	2	
Acinus, Hyperplasia, Focal							1			1																
Duct, Ectasia	2		2			1			4			1		2	1	2	2			2					2	
Salivary Glands	M																									
Atrophy		3										1	2													
Inflammation, Acute																										
Stomach, Forestomach																										
Edema	3																								3	
Ulcer	4	4																							4	
Epithelium, Hyperplasia	2	2											3													
Stomach, Glandular																										
Cyst																										
Edema																										
Erosion																									2	

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DAY ON TEST		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
FISCHER 344 RATS MALE		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
0 PPM		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
ANIMAL ID		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
		1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5

males (cont...)

Ulcer	2											4											3			
Tongue																										

CARDIOVASCULAR SYSTEM

Blood Vessel																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiomyopathy	1	2	2	1	2	1	1	1	2	2	2	1	3	1	1	1	1		1	2	2	2	2	1	2	
Thrombosis											2											4				
Myocardium, Necrosis											3															
Valve, Hyperplasia																						2				

ENDOCRINE SYSTEM

Adrenal Cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Accessory Adrenal Cortical Nodule				1				2			2			1	2	1												
Degeneration, Cystic																												
Degeneration, Fatty	2				2	2	1			1	1			3	1			1	2			1	1	2	1			
Hyperplasia, Focal	2											2											2					
Adrenal Medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Angiectasis																												
Hyperplasia	2												1	1			4											2
Islets, Pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		

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DAY ON TEST	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	6	7	7	7	7	7	7	7	4	7	7	6	6	7	7	7	7	6	5	7	6	7	7	6	
	8	1	2	2	2	2	3	3	7	3	3	7	0	3	3	0	3	6	9	2	1	3	1	3	1
	7	0	9	9	9	9	1	1	7	0	0	2	0	0	0	2	0	0	9	9	3	0	1	0	9

  

FISCHER 344 RATS MALE 0 PPM	ANIMAL ID																									males (cont...)
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	

Hyperplasia

Parathyroid Gland

.....  
 +  
 .....

Pituitary Gland

Infiltration Cellular, Histiocyte

Pigmentation

Pars Distalis, Angiectasis

Pars Distalis, Cyst

Pars Distalis, Hyperplasia

Pars Distalis, Hyperplasia, Focal

Pars Intermedia, Cyst

Rathke's Cleft, Hemorrhage

.....  
 +  
 .....  
 2  
 3  
 .....  
 3  
 2  
 .....  
 2  
 .....  
 2  
 .....  
 2  
 .....  
 2  
 .....  
 2  
 .....  
 2  
 .....  
 2

Thyroid Gland

Degeneration, Cystic

Ultimobranchial Cyst

C-cell, Hyperplasia

.....  
 + A +  
 .....  
 1  
 .....  
 1  
 .....  
 1  
 .....  
 1

GENERAL BODY SYSTEM

Tissue NOS

.....  
 +  
 .....

GENITAL SYSTEM

Epididymis

Inflammation

.....  
 +  
 .....

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| DAY ON TEST                        | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                    | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 6 | 7 | 7 | 7 | 6 |
| FISCHER 344 RATS MALE<br>ANIMAL ID | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|                                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 PPM                              | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|                                    | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

males (cont...)

|                                |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|--------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Inflammation, Chronic          |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Preputial Gland                | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cyst                           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia                    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic          | 2 3 2 3 2 1 2 3 2 2 2 2 2 2 2 2 2 1               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prostate                       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic          | 2 1 2 2 2 2 2 2 2 1 1 2                           |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Epithelium, Hyperplasia        | 2 2 1 1 1 1                                       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Seminal Vesicle                | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation                   | 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Testes                         | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Germinal Epithelium, Atrophy   | 4 3 4 4 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Interstitial Cell, Hyperplasia | 1 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**HEMATOPOIETIC SYSTEM**

|                                   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Bone Marrow                       | + A + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Amyloid Deposition                |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia                       | 4 4 2 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infiltration Cellular, Histiocyte |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Myelofibrosis                     | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lymph Node                        | + + + + +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mediastinal, Ectasia              |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

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| DAY ON TEST | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|             | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 6 | 7 | 7 | 7 | 6 |   |
|             | 8 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 7 | 3 | 3 | 7 | 0 | 3 | 3 | 0 | 3 | 6 | 9 | 2 | 1 | 3 | 1 | 3 | 1 |
|             | 7 | 0 | 9 | 9 | 9 | 9 | 1 | 1 | 7 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 9 | 9 | 3 | 0 | 1 | 0 | 9 |

  

| FISCHER 344 RATS MALE | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ANIMAL ID             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0 PPM                 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                       | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

males (cont...)

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mediastinal, Hemorrhage            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |
| Mediastinal, Hyperplasia, Lymphoid |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 | 1 |   |
| Mediastinal, Pigmentation          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pancreatic, Ectasia                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |
| Pancreatic, Hemorrhage             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |
| Lymph Node, Mandibular             | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |   |   |
| Lymph Node, Mesenteric             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |
| Ectasia                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Hemorrhage                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |
| Hyperplasia, Lymphoid              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Pigmentation                       | 1 | 2 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 |   |   |
| Spleen                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |
| Accessory Spleen                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Fibrosis                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Hematopoietic Cell Proliferation   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   | 2 |
| Hyperplasia, Lymphoid, Focal       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |
| Necrosis                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |
| Pigmentation                       |   | 1 | 3 | 3 |   | 2 | 2 | 3 | 1 | 1 | 3 |   | 2 | 1 | 2 |   | 3 | 1 |   | 3 | 1 | 3 | 2 | 1 | 2 |   |
| Lymphoid Follicle, Hyperplasia     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Thymus                             | + | + | + | M | + | I | + | + | + | + | + | I | + | + | + | I | + | + | I | + | + | + | + | + |   |   |
| Cyst                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |

**INTEGUMENTARY SYSTEM**

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                              | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                            |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------------|
|  | 6 7 7 7 7 7 7 7 4 7 7 6 6 7 7 7 7 6 5 7 6 7 7 7 6 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                            |
| FISCHER 344 RATS MALE<br>0 PPM ANIMAL ID | 8 1 2 2 2 2 3 3 7 3 3 7 0 3 3 0 3 6 9 2 1 3 1 3 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                            |
|  | 7 0 9 9 9 9 1 1 7 0 0 2 0 0 0 2 0 0 9 9 3 0 1 0 9 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                            |
|  | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | <b>males<br/>(cont...)</b> |
|  | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                            |
|  | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                            |
|  | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |                            |
|  | 1   | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |                            |

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Fibrosis                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia               |   | 1 |   |   |   |   |   | 1 |   |   |   | 1 |   |   | 3 |   |   |   |   |   |   |   |   |   | 2 |
| Duct, Ectasia             |   |   |   |   | 3 |   |   |   |   |   |   | 2 |   |   | 3 |   |   |   |   |   |   |   |   |   |   |
| Skin                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst Epithelial Inclusion |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperkeratosis            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic     |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Epidermis, Hyperplasia    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**MUSCULOSKELETAL SYSTEM**

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Femur, Osteopetrosis |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Skeletal Muscle      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**NERVOUS SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Compression                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Degeneration                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infiltration Cellular, Lymphocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Necrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

| DAY ON TEST | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | males<br>(cont...) |
|-------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------------|
|             | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                    |
| 6           | 7         | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 6 | 7 | 7 | 7 | 6 | 0 |                    |
| 8           | 1         | 2 | 2 | 2 | 2 | 3 | 3 | 7 | 3 | 3 | 7 | 0 | 3 | 3 | 0 | 3 | 6 | 9 | 2 | 1 | 3 | 1 | 3 | 1 | 0 |                    |
| 7           | 0         | 9 | 9 | 9 | 9 | 1 | 1 | 7 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 9 | 9 | 3 | 0 | 1 | 0 | 9 | 0 |                    |

**FISCHER 344 RATS MALE**

**0 PPM**

Peripheral Nerve

Spinal Cord

**RESPIRATORY SYSTEM**

Lung

- Congestion
- Hemorrhage
- Infiltration Cellular, Histiocyte
- Inflammation, Chronic
- Metaplasia, Osseous
- Thrombosis
- Alveolar Epithelium, Hyperplasia

Nose

- Foreign Body
- Inflammation, Chronic
- Necrosis
- Thrombosis
- Respiratory Epithelium, Hyperplasia
- Respiratory Epithelium, Metaplasia, Squamous

Trachea

**SPECIAL SENSES SYSTEM**

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              |  | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 6 | 7 | 7 | 7 | 6 |   |
|                              |  | 8 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 7 | 3 | 3 | 7 | 0 | 3 | 3 | 0 | 3 | 6 | 9 | 2 | 1 | 3 | 1 | 3 | 1 |
|                              |  | 7 | 0 | 9 | 9 | 9 | 9 | 1 | 1 | 7 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 9 | 9 | 3 | 0 | 1 | 0 | 9 |
| <b>FISCHER 344 RATS MALE</b> |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                    |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>0 PPM</b>                 |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                              |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                              |  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                              |  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |   |

males (cont...)

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cataract              | 1 | 2 | 1 |   | 1 |   | 2 |   |   | 1 | 3 |   | 1 | 1 |   |   | 1 |   |   |   |   |   |   | 4 |   |
| Bilateral, Cataract   |   |   |   | 2 |   | 1 |   | 4 |   |   |   |   | 1 |   |   |   |   | 4 |   |   |   | 2 |   |   |   |
| Retina, Degeneration  |   |   |   |   |   |   |   | 4 |   |   | 1 |   |   |   |   |   |   | 4 |   |   |   |   | 4 |   |   |
| Harderian Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Focal    |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic |   |   |   | 3 |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |

URINARY SYSTEM

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney                               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |
| Mineralization                       | 1 | 1 |   |   |   |   |   | 1 |   |   |   |   |   |   | 2 |   |   | 1 |   | 1 |   |   |   |   | 1 |
| Nephropathy                          | 1 |   | 1 | 2 | 2 | 2 | 1 | 1 | 3 | 1 | 1 |   | 3 | 1 | 1 | 3 |   | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 4 |
| Renal Tubule, Hyperplasia            |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal Tubule, Necrosis               |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia | 1 |   | 1 |   | 1 |   |   |   |   | 1 | 1 |   | 1 |   | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 |   | 2 | 1 |
| Urinary Bladder                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Transitional Epithelium, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |

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 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | * TOTALS |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|                              | 7 | 7 | 7 | 6 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 0 |          |
|                              | 3 | 3 | 3 | 0 | 3 | 9 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 9 | 2 | 3 | 3 | 3 | 3 | 0 |          |
|                              | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 9 | 9 | 9 | 0 |          |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| <b>0 PPM</b>                 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
|                              | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |          |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 0 |   |          |

ALIMENTARY SYSTEM

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |     |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|
| Esophagus<br>Inflammation, Acute  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1   | 1.0 |
| Intestine Large, Cecum  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | 49 |     |     |
| Intestine Large, Colon<br>Edema<br>Ulcer  | + | + | + | A | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | 46 | 1   | 3.0 |
| Intestine Large, Rectum<br>Necrosis   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | A | + | + | + | + | 47 | 1   | 1.0 |
| Intestine Small, Duodenum   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | 48 |     |     |
| Intestine Small, Ileum  | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | 47 |     |     |
| Intestine Small, Jejunum  | + | + | + | A | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | 46 |     |     |
| Liver<br>Angiectasis<br>Atrophy<br>Basophilic Focus<br>Clear Cell Focus<br>Eosinophilic Focus<br>Hematopoietic Cell Proliferation | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 3   | 2.0 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   | 1  | 3.0 |     |
|   |   | X | X |   | X | X | X | X | X |   | X |   |   | X | X |   | X | X | X | X | X |   | X | X |   |   | 33 |     |     |
|   |   | X |   |   | X | X | X | X | X |   | X |   |   | X | X | X | X | X | X | X |   |   | X |   |   |   | 29 |     |     |
|   | X | X | X |   | X |   | X | X |   | X |   |   |   | X |   | X |   |   |   |   |   |   |   |   |   |   | 12 |     |     |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 1.0 |     |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
Page 11

1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked



TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 10/09/2008

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

Lab: SRI

|                              |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |
|------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|---|
| DAY ON TEST                  | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>6<br>0<br>1 | 0<br>7<br>3<br>0 | 0<br>5<br>9<br>1 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>2 | 0<br>7<br>3<br>2 | 0<br>7<br>3<br>2 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>1 | 0<br>7<br>3<br>1 | 0<br>7<br>3<br>1 | 0<br>6<br>2<br>9 | 0<br>7<br>2<br>9 | 0<br>7<br>3<br>9 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 |   |
| <b>FISCHER 344 RATS MALE</b> | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0 |
| <b>0 PPM</b>                 | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0 |
| ANIMAL ID                    | 2                | 2                | 2                | 2                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 5 |
|                              | 6                | 7                | 8                | 9                | 0                | 1                | 2                | 3                | 4                | 5                | 6                | 7                | 8                | 9                | 0                | 1                | 2                | 3                | 4                | 5                | 6                | 7                | 8                | 9                | 0                |                  |   |
|                              | <b>* TOTALS</b>  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |

|        |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |              |
|--------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--------------|
| Ulcer  | 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | <b>4 2.8</b> |
| Tongue | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | <b>1</b>     |

CARDIOVASCULAR SYSTEM

|                      |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |  |  |  |  |              |               |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|--|---|---|---|---|---|---|---|---|--|--|--|--|--------------|---------------|
| Blood Vessel         | + |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |  |  |  |  | <b>1</b>     |               |
| Heart                | + |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |  |  |  |  | <b>50</b>    |               |
| Cardiomyopathy       | 2 | 2 | 1 | 2 | 2 | 1 | 1 | 1 | 3 | 2 | 1 | 1 |  | 2 | 2 | 2 | 1 | 1 | 2 | 1 | 2 |  |  |  |  |              | <b>48 1.5</b> |
| Thrombosis           |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |  |  |  |  | <b>3 2.7</b> |               |
| Myocardium, Necrosis |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |  |  |  |  | <b>1 3.0</b> |               |
| Valve, Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |  |  |  |  | <b>1 2.0</b> |               |

ENDOCRINE SYSTEM

|                                   |   |   |   |  |   |  |  |   |  |  |  |   |  |   |   |   |  |   |   |   |  |   |   |   |  |               |               |              |
|-----------------------------------|---|---|---|--|---|--|--|---|--|--|--|---|--|---|---|---|--|---|---|---|--|---|---|---|--|---------------|---------------|--------------|
| Adrenal Cortex                    | + |   |   |  |   |  |  |   |  |  |  |   |  |   |   |   |  |   |   |   |  |   |   |   |  | <b>50</b>     |               |              |
| Accessory Adrenal Cortical Nodule | 1 | 2 | 1 |  | 2 |  |  | 1 |  |  |  |   |  | 2 | 2 |   |  | 2 | 1 | 1 |  | 1 | 1 | 1 |  | 1             | <b>26 1.4</b> |              |
| Degeneration, Cystic              | 4 |   |   |  |   |  |  |   |  |  |  |   |  |   |   |   |  |   |   |   |  |   |   |   |  | <b>1 4.0</b>  |               |              |
| Degeneration, Fatty               |   |   |   |  |   |  |  |   |  |  |  |   |  |   |   |   |  |   |   |   |  |   |   |   |  | <b>17 1.5</b> |               |              |
| Hyperplasia, Focal                | 1 |   |   |  |   |  |  |   |  |  |  |   |  |   |   | 2 |  |   |   |   |  |   |   |   |  |               | 2             | <b>7 1.9</b> |
| Adrenal Medulla                   | + |   |   |  |   |  |  |   |  |  |  |   |  |   |   |   |  |   |   |   |  |   |   |   |  | <b>50</b>     |               |              |
| Angiectasis                       |   |   |   |  |   |  |  |   |  |  |  |   |  |   |   |   |  |   |   |   |  |   |   |   |  | <b>1 3.0</b>  |               |              |
| Hyperplasia                       | 1 | 1 | 1 |  | 4 |  |  |   |  |  |  | 2 |  | 1 | 3 |   |  |   |   |   |  |   | 4 |   |  | 1             | <b>14 2.0</b> |              |
| Islets, Pancreatic                | + |   |   |  |   |  |  |   |  |  |  |   |  |   |   |   |  |   |   |   |  |   |   |   |  | <b>50</b>     |               |              |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

|                                   | DAY ON TEST                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   |    |     |   |   |     |     |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|---|---|----|-----|-----|---|---|-----|---|----|-----|---|---|-----|-----|
|                                   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0   | 0 | 0 | 0  | 0   | 0   | 0 | 0 | 0   | 0 |    |     |   |   |     |     |
|                                   | 7   | 7 | 7 | 6 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7   | 7 | 7 | 7  | 7   | 7   | 6 | 7 | 7   | 7 |    |     |   |   |     |     |
|                                   | 3   | 3 | 3 | 0 | 3 | 9 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3   | 3 | 3 | 3  | 3   | 2   | 9 | 2 | 3   | 3 |    |     |   |   |     |     |
|                                   | 0   | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 2 | 2 | 2 | 0 | 0 | 0 | 0   | 0 | 0 | 0  | 1   | 1   | 1 | 9 | 9   | 0 | 0  |     |   |   |     |     |
| <b>FISCHER 344 RATS MALE</b>      | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0   | 0 | 0 | 0  | 0   | 0   | 0 | 0 | 0   | 0 |    |     |   |   |     |     |
| ANIMAL ID                         | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0   | 0 | 0 | 0  | 0   | 0   | 0 | 0 | 0   | 0 |    |     |   |   |     |     |
| 0 PPM                             | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0   | 0 | 0 | 0  | 0   | 0   | 0 | 0 | 0   | 0 |    |     |   |   |     |     |
|                                   | 2   | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3   | 4 | 4 | 4  | 4   | 4   | 4 | 4 | 4   | 5 |    |     |   |   |     |     |
|                                   | 6   | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0   | 1 | 2 | 3  | 4   | 5   | 6 | 7 | 8   | 9 | 0  |     |   |   |     |     |
|                                   | <b>* TOTALS</b>                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   |    |     |   |   |     |     |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     | 4   | 1 | 2 | 2.5 |   |    |     |   |   |     |     |
| Parathyroid Gland                 | + |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   | 50 |     |   |   |     |     |
| Pituitary Gland                   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   | 50 |     |   |   |     |     |
| Infiltration Cellular, Histiocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   | 1  | 2.0 |   |   |     |     |
| Pigmentation                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   | 1  | 3.0 |   |   |     |     |
| Pars Distalis, Angiectasis        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   | 1  | 2.0 |   |   |     |     |
| Pars Distalis, Cyst               |   |   |   |   |   |   |   |   |   |   |   | 1 | 2 | 2 | 2.0 |   |   |    |     |     |   |   |     |   |    |     |   |   |     |     |
| Pars Distalis, Hyperplasia        |   |   |   |   |   |   |   |   |   |   |   | 2 | 3 | 1 | 3.0 |   |   |    |     |     |   |   |     |   |    |     |   |   |     |     |
| Pars Distalis, Hyperplasia, Focal | 3   |   |   |   |   |   |   |   |   |   |   |   | 1 | 2 | 3   | 3 | 1 | 11 | 1.7 |     |   |   |     |   |    |     |   |   |     |     |
| Pars Intermedia, Cyst             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   | 2  | 2.0 |   |   |     |     |
| Rathke's Cleft, Hemorrhage        | 3   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   |    |     |   | 2 | 2.5 |     |
| Thyroid Gland                     | + |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   | 48 |     |   |   |     |     |
| Degeneration, Cystic              | 1   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |    |     |     |   |   |     |   |    | 1   | 3 | 1 | 6   | 1.3 |
| Ultimobranchial Cyst              |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 | 1 | 1.0 |   |   |    |     |     |   |   |     |   |    |     |   |   |     |     |
| C-cell, Hyperplasia               | 4   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1   | 1 | 1 | 1  | 9   | 1.3 |   |   |     |   |    |     |   |   |     |     |

**GENERAL BODY SYSTEM**

|            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|
| Tissue NOS |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|

**GENITAL SYSTEM**

|              |   |  |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |    |   |     |
|--------------|---|--|--|--|--|--|--|--|--|--|--|---|--|--|--|--|--|--|--|--|--|--|--|--|----|---|-----|
| Epididymis   | + |  |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  | 50 |   |     |
| Inflammation |   |  |  |  |  |  |  |  |  |  |  | 2 |  |  |  |  |  |  |  |  |  |  |  |  |    | 1 | 2.0 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

Page 14

TDMS No. 20008 - 03

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                    |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|--------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
| DAY ON TEST                    |           | 7 | 7 | 7 | 6 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7               |
| DAY ON TEST                    |           | 3 | 3 | 3 | 0 | 3 | 9 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 9 | 2 | 3 | 3 | 0 | 0 | 0               |
| DAY ON TEST                    |           | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 2 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 9 | 9 | 9 | 0 | 0 | 0               |
| <b>FISCHER 344 RATS MALE</b>   | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| <b>0 PPM</b>                   | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                                |           | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5               |
|                                |           | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | <b>* TOTALS</b> |
| Inflammation, Chronic          |           | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>    |
| Preputial Gland                |           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>       |
| Cyst                           |           | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 3.0</b>    |
| Hyperplasia                    |           |   |   |   | 2 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>3 2.3</b>    |
| Inflammation, Chronic          |           | 2 | 2 | 2 | 2 | 1 |   | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 1 |   | <b>39 1.8</b>   |
| Prostate                       |           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>       |
| Inflammation, Chronic          |           |   |   |   |   |   | 3 | 2 | 2 |   |   |   |   |   | 2 | 2 |   |   | 1 | 2 |   |   |   |   |   |   | <b>19 1.8</b>   |
| Epithelium, Hyperplasia        |           |   |   |   |   |   | 2 | 1 | 1 |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | <b>9 1.2</b>    |
| Seminal Vesicle                |           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>       |
| Inflammation                   |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 4.0</b>    |
| Testes                         |           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>       |
| Germinal Epithelium, Atrophy   |           |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   | <b>6 3.7</b>    |
| Interstitial Cell, Hyperplasia |           |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | <b>3 1.0</b>    |

HEMATOPOIETIC SYSTEM

|                                   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |           |              |
|-----------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|-----------|--------------|
| Bone Marrow                       |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + |  | <b>48</b> |              |
| Amyloid Deposition                |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |           | <b>1 3.0</b> |
| Hyperplasia                       |  |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |           | <b>5 3.2</b> |
| Infiltration Cellular, Histiocyte |  |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |  |           | <b>1 3.0</b> |
| Myelofibrosis                     |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |           | <b>1 1.0</b> |
| Lymph Node                        |  |   |   |   |   |   | + |   |   |   |   | + | + |   |   |   |   |   |   |   |   | + |   |   |  | <b>10</b> |              |
| Mediastinal, Ectasia              |  |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |           | <b>1 4.0</b> |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 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

| DAY ON TEST                  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ANIMAL ID                    |  | 7 | 7 | 7 | 6 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 |   |   |
| <b>FISCHER 344 RATS MALE</b> |  | 3 | 3 | 3 | 0 | 3 | 9 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 9 | 2 | 3 | 3 |   |
| <b>0 PPM</b>                 |  | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 9 | 9 | 9 | 0 | 0 |
| <b>* TOTALS</b>              |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                                    |   |          |            |
|------------------------------------|---|----------|------------|
| Mediastinal, Hemorrhage            | 2 | <b>2</b> | <b>2.5</b> |
| Mediastinal, Hyperplasia, Lymphoid |   | <b>2</b> | <b>2.0</b> |
| Mediastinal, Pigmentation          | 2 | <b>1</b> | <b>2.0</b> |
| Pancreatic, Ectasia                |   | <b>1</b> | <b>3.0</b> |
| Pancreatic, Hemorrhage             |   | <b>1</b> | <b>2.0</b> |

|                                  |  |           |            |
|----------------------------------|--|-----------|------------|
| Lymph Node, Mandibular           | M M M M M M M M M M M M + M M M M M M M M M M M M M 1  |           |            |
| Lymph Node, Mesenteric           | + 50     |           |            |
| Ectasia                          |  | <b>1</b>  | <b>2.0</b> |
| Hemorrhage                       |  | 1         | <b>3</b>   |
| Hyperplasia, Lymphoid            |  |           | <b>1.0</b> |
| Pigmentation                     | 1 3 2 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2            | <b>15</b> | <b>1.8</b> |
|                                  |  | <b>45</b> | <b>1.2</b> |
| Spleen                           | + 50     |           |            |
| Accessory Spleen                 |  | X         | <b>1</b>   |
| Fibrosis                         | 3  |           | <b>4</b>   |
| Hematopoietic Cell Proliferation |  |           | <b>2.8</b> |
| Hyperplasia, Lymphoid, Focal     |  |           | <b>4</b>   |
| Necrosis                         |  |           | <b>1</b>   |
| Pigmentation                     | 1 2 1 1 3 2 3 2 2 1 2 1 1 2 2 2 1 1 3 3 2 3 1 3 1      | <b>44</b> | <b>1.9</b> |
| Lymphoid Follicle, Hyperplasia   |  | 2 2       | <b>5</b>   |
|                                  |  |           | <b>2.2</b> |
| Thymus                           | + + + + + + + + + + + + + + + + + + + I M I + + M + 41 |           |            |
| Cyst                             |  |           | <b>1</b>   |
|                                  |  |           | <b>2.0</b> |

**INTEGUMENTARY SYSTEM**

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 Page 16  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked





| DAY ON TEST           |  | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | * TOTALS |  |
|-----------------------|--|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------|--|
|                       |  | 7 7 7 6 7 5 7 7 7 7 7 7 7 7 7 7 7 7 7 7 6 7 7 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |  |
| FISCHER 344 RATS MALE |  | 3 3 3 0 3 9 3 3 3 3 3 3 3 3 3 3 3 3 3 3 2 9 2 3 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |  |
| 0 PPM                 |  | 0 0 0 1 0 1 0 0 2 2 2 0 0 0 0 0 0 0 0 0 9 9 9 0 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |  |
| ANIMAL ID             |  | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |  |
|                       |  | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |  |
|                       |  | 2 2 2 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 4 4 4 4 5 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |  |
|                       |  | 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |  |

|                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |        |  |
|-----------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--------|--|
| Eye                   | + A + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 48     |  |
| Cataract              |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 18 1.4 |  |
| Bilateral, Cataract   | 2 1 1 3 1 2 1 4 1 1 4 4 4 4 4 4 4 4 4 4 4 4 4 5     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 19 1.9 |  |
| Retina, Degeneration  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 7 3.0  |  |
| Harderian Gland       | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50     |  |
| Hyperplasia, Focal    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 1.0  |  |
| Inflammation, Chronic |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 3 2.0  |  |

### URINARY SYSTEM

|                                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |        |  |
|--------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--------|--|
| Kidney                               | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50     |  |
| Cyst                                 |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 1.0  |  |
| Mineralization                       | 1 1 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 13 1.1 |  |
| Nephropathy                          | 2 1 1 1 1 2 2 2 2 1 1 1 1 1 1 1 2 1 1 1 1 1 1     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 46 1.4 |  |
| Renal Tubule, Hyperplasia            |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 2.0  |  |
| Renal Tubule, Necrosis               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 2.0  |  |
| Transitional Epithelium, Hyperplasia | 1 1 1 1 1 2 1 2 1 1                               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 25 1.2 |  |
| Urinary Bladder                      | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50     |  |
| Transitional Epithelium, Hyperplasia |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 2.0  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue

M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

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| DAY ON TEST                        | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|                                    | 7 7 6 7 7 7 6 6 7 7 7 6 7 7 7 7 5 7 6 5 5 7 7 7 7 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS MALE<br>12500 PPM | 3 3 2 3 3 3 4 7 2 3 3 4 2 2 2 2 9 3 4 8 0 3 3 3 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 0 0 3 0 0 0 7 2 9 1 1 7 9 9 9 1 1 0 7 7 1 1 1 1 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 5 5 5 5 5 5 5 5 5 6 6 6 6 6 6 6 6 6 6 7 7 7 7 7 7 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

males  
(cont...)

ALIMENTARY SYSTEM

|                                   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Esophagus                         | +             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Cecum            | + A + + + + +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Colon            | + + A + A + + + + +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Rectum           | +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Edema                             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fibrosis                          | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Duodenum         | + + A + A + + + + +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Ileum            | + + A + M + A + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Jejunum          | + + A + A + + + + +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ulcer                             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Liver                             | +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Basophilic Focus                  | X             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Clear Cell Focus                  | X             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Degeneration, Cystic              |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Eosinophilic Focus                | X             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hepatodiaphragmatic Nodule        |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infiltration Cellular, Mixed Cell | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 1 1 1 1 1 1 1 1             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mixed Cell Focus                  | X             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

|                                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DAY ON TEST                           | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 6 | 5 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
|                                       | 3 | 3 | 2 | 3 | 3 | 3 | 4 | 7 | 2 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 9 | 3 | 4 | 8 | 0 | 3 | 3 | 3 | 3 | 3 | 3 |
|                                       | 0 | 0 | 3 | 0 | 0 | 0 | 7 | 2 | 9 | 1 | 1 | 7 | 9 | 9 | 9 | 1 | 1 | 0 | 7 | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| FISCHER 344 RATS MALE<br>12500 PPM    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                                       | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
|                                       | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 5 | 5 |
|                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bile Duct, Hyperplasia                | 2 | 3 |   |   |   | 2 | 2 | 1 | 3 | 3 | 2 | 2 | 4 | 2 | 3 | 3 | 3 | 2 | 2 | 3 | 3 | 2 | 2 | 3 | 3 | 3 | 3 |
| Hepatocyte, Vacuolization Cytoplasmic |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   | 4 | 2 |   | 2 |   |   |   |   |   |   |   |
| Mesentery                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Fat, Necrosis                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pancreas                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Atrophy                               | 1 | 2 | 2 |   | 1 | 1 | 2 |   | 1 | 1 | 2 | 1 | 2 | 1 | 2 | 2 | 3 | 1 | 2 |   |   |   | 2 | 2 | 2 | 1 | 1 |
| Acinus, Hyperplasia, Focal            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Duct, Ectasia                         |   |   | 1 | 1 | 1 |   | 3 | 1 |   | 1 |   | 1 |   | 1 |   | 1 | 1 | 1 |   | 2 |   |   | 3 | 2 | 2 |   |   |
| Salivary Glands                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Atrophy                               |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 1 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |
| Stomach, Forestomach                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Edema                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   | 2 |   |   |   |   |
| Inflammation, Chronic Active          |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   | 4 |   |   |   |   |
| Epithelium, Hyperplasia               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   | 2 |   |   |   |   |
| Stomach, Glandular                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Edema                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |
| Erosion                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |
| Glands, Hyperplasia                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Tongue                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

males (cont...)

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------------------------|
|                              | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 6 | 5 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7                      |
|                              | 3 | 3 | 2 | 3 | 3 | 3 | 4 | 7 | 2 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 9 | 3 | 4 | 8 | 0 | 3 | 3 | 3 | 3 | 3 | 3                      |
|                              | 0 | 0 | 3 | 0 | 0 | 0 | 7 | 2 | 9 | 1 | 1 | 7 | 9 | 9 | 9 | 1 | 1 | 0 | 7 | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 2                      |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |
| <b>ANIMAL ID</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |
| <b>12500 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |
|                              | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7                      |
|                              | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   | <b>males (cont...)</b> |

CARDIOVASCULAR SYSTEM

Blood Vessel

+

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Heart                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cardiomyopathy       | 2 | 1 | 1 | 1 | 1 | 2 | 1 |   | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 2 |   | 1 | 1 | 1 | 1 | 1 |   |   |   | 1 |   |
| Thrombosis           |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   | 4 |   |   | 1 |   |   |   |   |   |   |   |   |
| Myocardium, Necrosis |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Valve, Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |

ENDOCRINE SYSTEM

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Accessory Adrenal Cortical Nodule |   | 2 |   |   | 1 | 1 |   | 1 | 2 | 1 | 2 | 2 | 1 |   |   | 2 | 1 | 1 | 2 |   |   | 1 |   |   |   | 1 | 1 |
| Degeneration, Fatty               |   |   | 1 |   |   |   | 1 |   |   |   |   |   |   |   |   | 2 | 1 | 1 | 1 | 1 |   |   |   |   |   | 1 |   |
| Hyperplasia, Focal                |   |   |   | 2 | 1 |   |   |   |   |   |   |   | 2 |   |   | 1 |   |   |   |   | 1 | 1 |   |   |   |   |   |
| Hypertrophy, Focal                |   |   |   | 1 |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                       |   |   | 2 |   |   |   |   | 2 | 2 |   | 1 | 1 |   |   |   |   |   | 2 | 2 |   |   | 2 |   |   | 2 | 2 |   |
| Islets, Pancreatic                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Amyloid Deposition, Focal         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   | 1 |   |   |   |   |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

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1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

TDMS No. 20008 - 03  
Test Type: CHRONIC  
Route: DOSED FEED  
Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                        |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|------------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FISCHER 344 RATS MALE<br>12500 PPM | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                                    |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

|                                     |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hyperplasia, Focal                  |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Pituitary Gland                     |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage                          |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Angiectasis          |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Pars Distalis, Cyst                 |  |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Hyperplasia          |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Hyperplasia, Focal   |  |   | 1 |   |   |   |   | 1 | 2 |   |   |   |   | 2 | 1 |   |   |   |   |   | 1 |   |   |   |   |   |
| Pars Distalis, Hypertrophy          |  |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Intermedia, Cyst               |  |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 2 |   |   |   |   |   |   |   |   |   |
| Thyroid Gland                       |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + |   |
| Degeneration, Cystic                |  |   |   |   | 1 |   |   | 1 | 1 |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |
| Ultimobranchial Cyst                |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| C-cell, Hyperplasia                 |  |   |   | 3 |   | 1 | 1 |   | 1 | 1 |   | 1 |   | 3 | 3 |   |   |   |   | 1 |   |   |   |   | 1 | 1 |
| Follicular Cell, Hyperplasia, Focal |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |

GENERAL BODY SYSTEM

|            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Tissue NOS |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Necrosis   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

GENITAL SYSTEM

|                 |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Epididymis      |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Granuloma Sperm |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |
| Inflammation    |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked  
Page 23

| DAY ON TEST                        | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|                                    | 7 7 6 7 7 7 6 6 7 7 7 6 7 7 7 7 5 7 6 5 5 7 7 7 7 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS MALE<br>12500 PPM | 3 3 2 3 3 3 4 7 2 3 3 4 2 2 2 2 9 3 4 8 0 3 3 3 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 0 0 3 0 0 0 7 2 9 1 1 7 9 9 9 1 1 0 7 7 1 1 1 1 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 5 5 5 5 5 5 5 5 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

males (cont...)

|                                |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|--------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Preputial Gland                | + M + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cyst                           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia                    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic          | 2 3 2 3 2 2 2 1 2 2 3 2 2 2 2 1 3 2 1               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prostate                       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic          | 3 2 3 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Epithelium, Hyperplasia        | 1 1 2 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Seminal Vesicle                | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Testes                         | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Germinal Epithelium, Atrophy   | 4 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Interstitial Cell, Hyperplasia | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

HEMATOPOIETIC SYSTEM

|                                    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Bone Marrow                        | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia                        | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infiltration Cellular, Histiocyte  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Myelofibrosis                      | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lymph Node                         | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mediastinal, Ectasia               | 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mediastinal, Hemorrhage            |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mediastinal, Hyperplasia, Lymphoid | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mediastinal, Pigmentation          |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 5 | 7 | 6 | 5 | 5 | 7 | 7 | 7 | 7 |
|                              | 3 | 3 | 2 | 3 | 3 | 3 | 4 | 7 | 2 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 9 | 3 | 4 | 8 | 0 | 3 | 3 | 3 | 3 |
|                              | 0 | 0 | 3 | 0 | 0 | 0 | 7 | 2 | 9 | 1 | 1 | 7 | 9 | 9 | 9 | 1 | 1 | 0 | 7 | 7 | 1 | 1 | 1 | 1 | 2 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>12500 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>ANIMAL ID</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                              | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |   |
|                              | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

males  
(cont...)

|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lymph Node, Mandibular         | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M |
| Lymph Node, Mesenteric         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage                     | 1 |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 1 |   |
| Hyperplasia, Lymphoid          | 2 |   | 3 | 1 | 2 | 3 | 2 |   |   | 2 | 2 |   | 1 | 2 | 3 |   | 2 |   |   |   | 2 | 2 |   |   | 2 |
| Pigmentation                   | 1 | 1 | 1 |   | 1 |   | 1 |   | 1 | 1 | 1 |   |   | 1 |   |   | 1 |   |   |   |   | 1 |   | 1 | 1 |
| Spleen                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Fibrosis                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Necrosis                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pigmentation                   | 3 | 2 | 3 | 3 | 2 | 1 | 3 | 1 | 2 | 2 | 1 |   | 2 | 3 | 2 | 1 | 4 | 1 | 1 | 3 | 3 | 3 |   | 1 | 3 |
| Lymphoid Follicle, Hyperplasia |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thymus                         | + | + |   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**INTEGUMENTARY SYSTEM**

|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                    |   |   | 1 |   |   |   |   | 1 | 1 |   |   | 1 |   |   |   | 2 | 2 |   | 2 | 2 | 1 | 1 | 1 | 3 |   |
| Duct, Ectasia                  |   |   | 1 | 2 |   |   |   |   | 3 |   |   |   |   |   |   | 2 |   |   | 3 |   |   |   | 1 |   |   |
| Skin                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst Epithelial Inclusion      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Fibrosis                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperkeratosis                 |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   | 3 |   |   |   |   |   |   |   |   |   |   |
| Epidermis, Hyperplasia         |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 1 |   |   |   |   |   |   |   |   |   |   |
| Prepuce, Inflammation, Chronic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
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 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
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|                              |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
|------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
| DAY ON TEST                  |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                              |  | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 6 | 5 | 5 | 7 | 7 | 7 | 7 | 7 | 7               |
|                              |  | 3 | 3 | 2 | 3 | 3 | 3 | 4 | 7 | 2 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 9 | 3 | 4 | 8 | 0 | 3 | 3 | 3 | 3 | 3               |
|                              |  | 0 | 0 | 3 | 0 | 0 | 0 | 7 | 2 | 9 | 1 | 1 | 7 | 9 | 9 | 9 | 1 | 1 | 0 | 7 | 7 | 1 | 1 | 1 | 1 | 1 | 2               |
| <b>FISCHER 344 RATS MALE</b> |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| ANIMAL ID                    |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| <b>12500 PPM</b>             |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                              |  | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               |
|                              |  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | males (cont...) |

**MUSCULOSKELETAL SYSTEM**

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skeletal Muscle | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + |

**NERVOUS SYSTEM**

|                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Compression      |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   | 2 |   |   |   |   |   |   |   |
| Hemorrhage       | 1 |   | 2 |   |   | 1 |   |   |   |   | 1 |   |   | 1 |   |   |   |   | 1 |   | 1 |   |   |   |   |   |
| Hyperplasia      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Peripheral Nerve |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   | + |
| Spinal Cord      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   | + |

**RESPIRATORY SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lung                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Congestion                        |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage                        |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infiltration Cellular, Histiocyte | 1 | 1 |   | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Inflammation, Chronic             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Metaplasia, Osseous               |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

|   |  |                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|--|------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DAY ON TEST                                     |  | 0                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |   |
|   |  | 7                      | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 5 | 7 | 6 | 5 | 5 | 7 | 7 | 7 | 7 |
| FISCHER 344 RATS MALE<br>12500 PPM<br>ANIMAL ID |  | 3                      | 3 | 2 | 3 | 3 | 3 | 4 | 7 | 2 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 9 | 3 | 4 | 8 | 0 | 3 | 3 | 3 | 3 |
|   |  | 0                      | 0 | 3 | 0 | 0 | 0 | 7 | 2 | 9 | 1 | 1 | 7 | 9 | 9 | 9 | 1 | 1 | 0 | 7 | 7 | 1 | 1 | 1 | 1 | 1 |
|   |  | 0                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   |  | 0                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   |  | 0                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   |  | 5                      | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |   |
|   |  | 1                      | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |
|   |  | <b>males (cont...)</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|  |   |  |  |  |  |   |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  |   |   |   |  |   |   |
|--|---|--|--|--|--|---|---|---|--|--|--|--|---|---|---|---|--|---|---|---|---|---|--|---|---|---|--|---|---|
| Alveolar Epithelium, Hyperplasia             |   |  |  |  |  | 2 | 2 | 1 |  |  |  |  |   | 1 | 2 | 1 |  | 2 | 1 |   | 1 | 2 |  | 1 | 3 |   |  | 1 |   |
| Nose   | + |  |  |  |  |   |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  |   |   |   |  |   |   |
| Foreign Body                                 |   |  |  |  |  |   |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  |   | 1 |   |  |   |   |
| Hemorrhage                                   |   |  |  |  |  | 4 |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  |   |   |   |  |   |   |
| Inflammation, Chronic                        |   |  |  |  |  | 4 | 3 |   |  |  |  |  | 2 |   |   |   |  |   | 1 | 1 |   |   |  |   |   | 1 |  |   |   |
| Necrosis                                     |   |  |  |  |  | 1 |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  |   |   |   |  |   |   |
| Thrombosis                                   |   |  |  |  |  |   |   |   |  |  |  |  |   |   |   |   |  | 3 |   |   |   |   |  |   |   |   |  |   |   |
| Goblet Cell, Hyperplasia                     |   |  |  |  |  |   |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  |   |   |   |  |   |   |
| Respiratory Epithelium, Hyperplasia          |   |  |  |  |  | 2 |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  | 1 |   |   |  |   | 1 |
| Respiratory Epithelium, Metaplasia, Squamous |   |  |  |  |  |   |   |   |  |  |  |  |   |   |   |   |  | 2 |   |   |   |   |  |   |   |   |  |   |   |
| Trachea                                      | + |  |  |  |  |   |   |   |  |  |  |  |   |   |   |   |  |   |   |   |   |   |  |   |   |   |  |   |   |

SPECIAL SENSES SYSTEM

|                       |   |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  |   |   |   |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |
|-----------------------|---|--|---|--|--|---|---|--|---|---|---|--|--|--|--|--|---|---|--|--|--|--|--|--|---|---|---|---|--|---|--|--|--|--|--|---|---|--|--|--|--|--|
| Eye                   | + + + + + + + + + + + + + + + +   + + + + + + + +       |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  |   |   |   |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |
| Cataract              |   |  |   |  |  | 2 | 1 |  | 1 | 1 | 1 |  |  |  |  |  | 4 |   |  |  |  |  |  |  |   |   |   |   |  | 2 |  |  |  |  |  |   |   |  |  |  |  |  |
| Edema                 |   |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   | 3 |  |  |  |  |  |  |   |   |   |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |
| Retinal Detachment    |   |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  |   |   |   |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |
| Bilateral, Cataract   | 2   |  | 1 |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  | 2 | 1 |   | 2 |  |   |  |  |  |  |  | 1 | 1 |  |  |  |  |  |
| Retina, Degeneration  | 3   |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  |   |   | 4 |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |
| Harderian Gland       | + |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  |   |   |   |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |
| Hyperplasia, Focal    |   |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  |   |   |   |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |
| Inflammation, Chronic |   |  |   |  |  |   |   |  |   |   |   |  |  |  |  |  |   |   |  |  |  |  |  |  | 2 |   |   |   |  |   |  |  |  |  |  |   |   |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
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BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
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Page 27

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                        |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------------------------|---|
| DAY ON TEST                                     | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |   |
|   | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 6 | 5 | 5 | 7 | 7 | 7 | 7                      |   |
|   | 3 | 3 | 2 | 3 | 3 | 3 | 4 | 7 | 2 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 9 | 3 | 4 | 8 | 0 | 3 | 3 | 3                      |   |
|   | 0 | 0 | 3 | 0 | 0 | 0 | 7 | 2 | 9 | 1 | 1 | 7 | 9 | 9 | 9 | 1 | 1 | 0 | 7 | 7 | 1 | 1 | 1 | 2                      |   |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                        |   |
| FISCHER 344 RATS MALE<br>ANIMAL ID<br>12500 PPM | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |   |
|   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |   |
|   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                      |   |
|   | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7                      |   |
|   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4                      | 5 |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                        |   |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>males (cont...)</b> |   |

Zymbal's Gland +  
 Cyst X

**URINARY SYSTEM**

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney                               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Cyst                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |
| Mineralization                       |   |   | 1 |   |   | 1 |   |   |   |   | 1 |   | 1 |   | 1 |   | 1 | 1 | 1 |   |   |   |   |   |   |
| Nephropathy                          |   | 1 | 2 | 1 | 1 | 2 | 1 | 2 | 2 | 1 | 2 |   | 1 | 1 | 1 | 2 | 2 | 2 |   | 1 | 2 | 2 | 1 | 1 | 2 |
| Renal Tubule, Hyperplasia            | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |
| Renal Tubule, Pigmentation           |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia |   |   |   |   | 1 |   |   |   |   |   |   |   | 2 |   | 2 | 1 | 1 |   |   |   |   |   | 1 |   |   |
| .....                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Urinary Bladder                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Transitional Epithelium, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                  |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                              |           | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               |
|                              |           | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3 | 3 | 3 | 3               |
|                              |           | 2 | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1 | 1 | 1 | 1               |
| <b>FISCHER 344 RATS MALE</b> | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| <b>12500 PPM</b>             |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                              |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                              |           | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9               |
|                              |           | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 0 | <b>* TOTALS</b> |

ALIMENTARY SYSTEM

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |              |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|--------------|
| Esophagus                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 50           |
| Intestine Large, Cecum            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 49           |
| Intestine Large, Colon            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 48           |
| Intestine Large, Rectum           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 50           |
| Edema                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 3.0</b> |
| Fibrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |               | <b>1 2.0</b> |
| Intestine Small, Duodenum         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 48           |
| Intestine Small, Ileum            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 47           |
| Intestine Small, Jejunum          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 48           |
| Ulcer                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3             | <b>1 3.0</b> |
| Liver                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | 50           |
| Basophilic Focus                  | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X             | <b>36</b>    |
| Clear Cell Focus                  | X | X | X | X | X | X |   | X | X |   | X | X | X | X | X | X | X |   |   |   |   | X | X | X | X |   |               | <b>29</b>    |
| Degeneration, Cystic              |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>2 1.0</b> |
| Eosinophilic Focus                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>7</b>     |
| Hepatodiaphragmatic Nodule        |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |               | <b>4</b>     |
| Infiltration Cellular, Mixed Cell | 1 | 1 | 1 | 1 | 1 |   |   | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   | 1 |   |   | 1 | 1 | 1 | 1 |   | <b>32 1.0</b> |              |
| Mixed Cell Focus                  |   |   |   |   |   |   | X |   |   |   |   |   | X |   | X |   |   |   |   |   |   |   |   |   |   |   |               | <b>5</b>     |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

|   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0         | 0          |            |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|------------|------------|--|
| DAY ON TEST                                     | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7         | 7          |            |  |
|   | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3 | 3 | 3         |            |            |  |
|   | 2 | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1 | 1 | 1         |            |            |  |
| FISCHER 344 RATS MALE<br>12500 PPM<br>ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0         | * TOTALS   |            |  |
| Bile Duct, Hyperplasia                          | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 3 | 1 | 2 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 2 | 4 | 4 | 3 | 2 | 1 | 2 | 2 | <b>48</b> | <b>2.4</b> |            |  |
| Hepatocyte, Vacuolization Cytoplasmic           | 1 |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   | 3 |   | 2 |   |   |   |   | <b>9</b>  | <b>2.0</b> |            |  |
| Mesentery                                       |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2</b>  |            |            |  |
| Fat, Necrosis                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 | <b>1</b>  | <b>4.0</b> |            |  |
| Pancreas  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b> |            |            |  |
| Atrophy   | 2 | 1 | 1 |   | 1 |   |   |   |   | 1 | 2 | 1 |   | 2 |   |   | 1 |   | 1 | 2 |   |   | 1 | 2 | 1 | 4         | <b>36</b>  | <b>1.6</b> |  |
| Acinus, Hyperplasia, Focal                      |   |   |   |   | 4 |   |   |   |   | 4 |   |   |   |   | 2 |   |   |   |   |   |   |   |   | 1 |   |           | <b>4</b>   | <b>2.8</b> |  |
| Duct, Ectasia                                   |   |   | 2 | 1 | 1 |   |   |   |   | 2 | 1 | 1 | 4 | 1 |   | 1 |   | 1 |   | 2 |   |   |   |   | 2 |           | <b>27</b>  | <b>1.5</b> |  |
| Salivary Glands                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b> |            |            |  |
| Atrophy   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   | 1 |           | <b>7</b>   | <b>1.0</b> |  |
| Stomach, Forestomach                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b> |            |            |  |
| Edema   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   | 2 |   |           | <b>4</b>   | <b>2.8</b> |  |
| Inflammation, Chronic Active                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1</b>   | <b>1.0</b> |  |
| Ulcer   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   | 4 |   |           | <b>4</b>   | <b>4.0</b> |  |
| Epithelium, Hyperplasia                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   | 3 |   | 3 |   | 2 |           | <b>6</b>   | <b>2.3</b> |  |
| Stomach, Glandular                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b> |            |            |  |
| Cyst  |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |           | <b>1</b>   | <b>3.0</b> |  |
| Edema   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |           | <b>2</b>   | <b>2.5</b> |  |
| Erosion   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 2 |   |           | <b>3</b>   | <b>1.3</b> |  |
| Ulcer   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1</b>   | <b>4.0</b> |  |
| Glands, Hyperplasia                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1</b>   | <b>2.0</b> |  |
| Tongue  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1</b>   |            |  |
| Hyperplasia                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>3</b>   | <b>3.0</b> |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
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TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                  | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|------------------------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 7               | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 7 | 7 |
|                              | 3               | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3 |
|                              | 2               | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1 |
| <b>FISCHER 344 RATS MALE</b> | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>ANIMAL ID</b>             | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>12500 PPM</b>             | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
|                              | 7               | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |
|                              | 6               | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|                              | <b>* TOTALS</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**CARDIOVASCULAR SYSTEM**

Blood Vessel

1

Heart

50

Cardiomyopathy

45 1.2

Thrombosis

4 2.8

Myocardium, Necrosis

1 3.0

Valve, Hyperplasia

1 2.0

**ENDOCRINE SYSTEM**

Adrenal Cortex

50

Accessory Adrenal Cortical Nodule

24 1.5

Degeneration, Fatty

17 1.3

Hyperplasia, Focal

12 1.5

Hypertrophy, Focal

4 1.5

Adrenal Medulla

49

Hyperplasia

16 1.7

Islets, Pancreatic

50

Amyloid Deposition, Focal

1 2.0

Hyperplasia

2 2.0

Parathyroid Gland

49

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                  | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|                              | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 7 | 7 |          |
|                              | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3 | 3        |
|                              | 2 | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1 | 1        |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |
| <b>12500 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1        |
|                              | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0        |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0        |

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |              |  |              |               |   |               |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|--------------|--|--------------|---------------|---|---------------|
| Hyperplasia, Focal                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 2.0</b> |  |              |               |   |               |
| Pituitary Gland                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +            | <b>50</b>    |  |              |               |   |               |
| Hemorrhage                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | <b>1 1.0</b> |              |  |              |               |   |               |
| Pars Distalis, Angiectasis          |   |   |   |   |   |   |   |   |   | 4 |   |   |   | 3 | 2 |   |   |   |   |   |   |   |   | <b>4 3.0</b> |              |  |              |               |   |               |
| Pars Distalis, Cyst                 |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>2 2.0</b> |  |              |               |   |               |
| Pars Distalis, Hyperplasia          |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 2.0</b> |  |              |               |   |               |
| Pars Distalis, Hyperplasia, Focal   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 2 | 2 |   |   |   | 1 | 3 |   |              | 1            |  |              | 2             | 1 | <b>14 1.5</b> |
| Pars Distalis, Hypertrophy          |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 3.0</b> |  |              |               |   |               |
| Pars Intermedia, Cyst               |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>4 2.3</b> |  |              |               |   |               |
| Thyroid Gland                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>49</b>    |              |  |              |               |   |               |
| Degeneration, Cystic                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   |   |   |              |              |  | <b>7 1.0</b> |               |   |               |
| Ultimobranchial Cyst                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   |   |   |              |              |  | <b>2 1.0</b> |               |   |               |
| C-cell, Hyperplasia                 |   |   |   | 1 | 1 | 3 | 2 | 2 |   |   |   |   | 1 | 2 | 1 | 2 | 1 | 2 |   |   | 1 |   |   | 1            | 2            |  |              | <b>25 1.6</b> |   |               |
| Follicular Cell, Hyperplasia, Focal |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |              |              |  |              |               |   | <b>4 1.8</b>  |

**GENERAL BODY SYSTEM**

|            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |              |          |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|--|--|--|--|--|--|--------------|----------|
| Tissue NOS |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |              | <b>1</b> |
| Necrosis   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 |  |  |  |  |  |  | <b>1 1.0</b> |          |

**GENITAL SYSTEM**

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |              |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|--------------|
| Epididymis      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b> |              |
| Granuloma Sperm |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1 4.0</b> |
| Inflammation    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1 2.0</b> |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
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TDMS No. 20008 - 03  
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 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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |    |          |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----------|
|                              | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 7 | 7  | * TOTALS |
|                              | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3 | 49 |          |
|                              | 2 | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1 |    |          |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |    |          |
| <b>12500 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |    |          |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |    |          |
|                              | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 |    |          |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |    |          |

**HEMATOPOIETIC SYSTEM**

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Bone Marrow                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |
| Hyperplasia                        |   | 3 | 1 |   | 1 |   |   |   | 1 |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   | 7  | 1.9 |
| Infiltration Cellular, Histiocyte  |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 1.0 |
| Myelofibrosis                      |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |
| Lymph Node                         |   |   |   |   |   | + |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 11 |     |
| Mediastinal, Ectasia               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 4.0 |
| Mediastinal, Hemorrhage            |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 4.0 |
| Mediastinal, Hyperplasia, Lymphoid |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2.0 |
| Mediastinal, Pigmentation          |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3.0 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
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 Time Report Requested: 11:00:55  
 First Dose M/F: 03/04/03 / 03/04/03  
 Lab: SRI

| DAY ON TEST                                      | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|  | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 7 |          |
|  | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3 | 3        |
|  | 2 | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1 | 1        |
| <b>FISCHER 344 RATS MALE</b><br><b>12500 PPM</b> | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |
|  | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |
|  | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |
|  | 7 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |
|  | 6 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |

|                                | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 1      |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Lymph Node, Mandibular         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
| Lymph Node, Mesenteric         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Hemorrhage                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 1.3  |
| Hyperplasia, Lymphoid          | 3 | 1 | 1 |   | 1 | 3 |   | 2 | 2 |   | 1 | 1 | 2 | 2 |   | 1 |   | 2 |   |   |   | 2 | 1 |   | 2 | 31 1.9 |
| Pigmentation                   | 1 | 1 | 1 | 1 | 1 | 1 |   |   |   | 1 |   | 1 | 1 |   |   |   | 1 | 1 |   |   | 1 |   | 1 |   |   | 27 1.0 |
| Spleen                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Fibrosis                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 2.0  |
| Necrosis                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |
| Pigmentation                   | 2 | 1 | 1 | 2 | 2 | 1 | 2 | 3 | 3 |   | 2 | 3 | 2 | 3 | 3 | 2 | 1 |   |   | 1 | 1 | 2 | 2 | 1 | 3 | 45 2.1 |
| Lymphoid Follicle, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 6 1.5  |
| Thymus                         | + | + | + | + |   | + | + | + | + | + | + | + |   | + | M | + | + | + | + | + | + | M | + | + | + | 42     |
| Cyst                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |

**INTEGUMENTARY SYSTEM**

|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Mammary Gland                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | 49     |
| Hyperplasia                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 18 1.5 |
| Duct, Ectasia                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 12 1.9 |
| Skin                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Cyst Epithelial Inclusion      | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2      |
| Fibrosis                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |
| Hyperkeratosis                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 3.0  |
| Epidermis, Hyperplasia         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 1.5  |
| Prepuce, Inflammation, Chronic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked



|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|
|                              | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
| DAY ON TEST                  | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 7 | 7               | 7 |
|                              | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3               | 3 |
|                              | 2 | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1               | 1 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
| 0                            | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
| <b>12500 PPM</b>             | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9               | 0 |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9               | 0 |
|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |   |

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|---|
| Alveolar Epithelium, Hyperplasia             | 1 |   |   |   | 3 | 1 | 2 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |           |   |
| Nose   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +         | + |
| Foreign Body                                 |   | 2 |   | 1 |   |   | 2 |   |   |   |   | 2 |   |   |   |   |   | 2 |   | 2 | 2 |   |   |           |   |
| Hemorrhage                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |   |
| Inflammation, Chronic                        | 1 | 2 |   | 1 |   |   | 3 |   |   |   |   | 1 | 2 |   | 1 |   |   |   | 1 |   | 3 | 3 |   |           |   |
| Necrosis                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |   |
| Thrombosis                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |   |
| Goblet Cell, Hyperplasia                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 2 |   |   |           |   |
| Respiratory Epithelium, Hyperplasia          |   | 2 |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |           |   |
| Respiratory Epithelium, Metaplasia, Squamous |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |   |
| Trachea                                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +         | + |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b> |   |

**SPECIAL SENSES SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|---|
| Eye                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +            | + |
| Cataract              |   | 1 |   |   |   | 1 |   | 2 | 1 |   |   |   |   | 1 | 1 |   |   | 1 |   |   |   |   | 2 | 1            |   |
| Edema                 |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |              |   |
| Retinal Detachment    |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |              |   |
| Bilateral, Cataract   |   |   |   | 4 |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 2 |   |              |   |
| Retina, Degeneration  |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |              |   |
| Harderian Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +            | + |
| Hyperplasia, Focal    |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   |              |   |
| Inflammation, Chronic |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |              |   |
|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b>    |   |
|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 1.0</b> |   |
|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 2.0</b> |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

|                              |                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DAY ON TEST                  | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                              | 7               | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 7 | 7 |
|                              | 3               | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 4 | 0 | 6 | 3 | 3 | 3 |
|                              | 2               | 2 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 8 | 9 | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 3 | 2 | 7 | 1 | 1 | 1 |
| <b>FISCHER 344 RATS MALE</b> | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                    | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0                            | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| <b>12500 PPM</b>             | 7               | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |
| 6                            | 7               | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |
|                              | <b>* TOTALS</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                |   |
|----------------|---|
| Zymbal's Gland | 1 |
| Cyst           | 1 |

URINARY SYSTEM

|                                      |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |
|--------------------------------------|-------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|--|--|
| Kidney                               | +     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |  |  |
| Cyst                                 |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |
| Mineralization                       |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |
| Nephropathy                          | 2     | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 3 | 1 | 1 | 1 | 1 | 1 | 1 | 1  |  |  |  |
| Renal Tubule, Hyperplasia            |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |
| Renal Tubule, Pigmentation           |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |
| Transitional Epithelium, Hyperplasia | 2     |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   | 1  |  |  |  |
| Urinary Bladder                      | +     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |  |  |
| Transitional Epithelium, Hyperplasia |       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |
|                                      | 1     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |
|                                      | 2 1.0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

Page 37

| DAY ON TEST                                     | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|   | 5 3 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS MALE<br>25000 PPM<br>ANIMAL ID | 4 1 3 3 3 3 3 3 3 3 2 2 2 3 3 3 3 2 3 2 8 2 3 0 2 8 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 9 0 0 0 0 0 1 1 1 9 1 9 0 0 0 0 8 0 9 6 9 8 2 9 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| 25000 PPM<br>ANIMAL ID                          | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 2 3 4 5 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

males  
(cont...)

ALIMENTARY SYSTEM

|                                    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Esophagus                          | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Cecum<br>Ulcer    | A + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Colon<br>Necrosis | A + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Rectum            | A + + + + + + + + + + + M + + + + + + + + + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Duodenum          | A + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Ileum             | A + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Jejunum           | A + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Liver                              | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Basophilic Focus                   | X       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Clear Cell Focus                   | X       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Eosinophilic Focus                 | X       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hepatodiaphragmatic Nodule         | X       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infiltration Cellular, Mixed Cell  | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 1 1 1 1 1 1       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Malformation                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mixed Cell Focus                   | X       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Bile Duct, Hyperplasia             | 2 2 3 3 2 3 2 1 2 3 3 2 2 2 3 2 2 1 3               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                           | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|--|--|
|                                       | 5 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 0 | 7 | 6 | 7 | 7 | 6 |   |  |  |  |
| FISCHER 344 RATS MALE<br>25000 PPM    | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
|                                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |  |  |  |
| ANIMAL ID                             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |  |  |  |
|                                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |  |  |  |
|                                       | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   |   |  |  |  |
| Hepatocyte, Vacuolization Cytoplasmic |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   | 3 |   |  |  |  |
| Mesentery                             | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Accessory Spleen                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Fat, Necrosis                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Oral Mucosa                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Pharyngeal, Hyperplasia               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Pancreas                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |  |  |  |
| Atrophy                               |   | 1 | 2 | 4 | 3 | 1 | 1 | 1 | 2 | 2 |   |   | 1 | 1 |   |   |   |   | 2 | 2 |   | 1 | 1 | 3 | 1 | 1 |   |  |  |  |
| Metaplasia, Hepatocyte                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Acinus, Hyperplasia, Focal            |   |   | 4 | 2 | 3 |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |  |  |  |
| Duct, Ectasia                         |   |   | 1 |   | 2 | 2 |   |   | 1 |   |   |   | 2 | 2 |   |   |   |   |   | 2 |   |   |   |   | 2 | 2 |   |  |  |  |
| Salivary Glands                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |  |  |  |
| Atrophy                               |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 1 |   |   |   |   | 1 |   |   |   |   |   |   |  |  |  |
| Stomach, Forestomach                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |  |  |  |
| Edema                                 |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |  |  |  |
| Ulcer                                 |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Epithelium, Hyperplasia               |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   | 2 |   |  |  |  |
| Stomach, Glandular                    | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |  |  |  |
| Edema                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Erosion                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 2 |   |   |   |   | 2 |   |  |  |  |
| Ulcer                                 |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |  |  |  |

males (cont...)

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST           |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|-----------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                       |  | 5 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 0 | 7 | 6 | 7 | 7 | 6 |   |   |   |                 |
|                       |  | 4 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 8 | 2 | 3 | 0 | 2 | 8 |   |                 |
|                       |  | 9 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 9 | 1 | 9 | 0 | 0 | 0 | 0 | 8 | 0 | 9 | 6 | 9 | 8 | 2 | 9 | 7 |   |                 |
| FISCHER 344 RATS MALE |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| ANIMAL ID             |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| 25000 PPM             |  | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               |
|                       |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                       |  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   | males (cont...) |

### CARDIOVASCULAR SYSTEM

Blood Vessel

+ +

Heart

+ +

Cardiomyopathy

1 1 1 1 2 2 2 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 2 1 2

Thrombosis

1 4

Myocardium, Necrosis

Valve, Hyperplasia

2

### ENDOCRINE SYSTEM

Adrenal Cortex

+ +

Accessory Adrenal Cortical Nodule

1 1 1 2 2 2 1 3 1 1 2 1

Degeneration, Fatty

1 1 1 1 2 1 2 1 2 1 1 1 2 2

Hyperplasia, Focal

2 1 1 3 1 1 2

Hypertrophy, Focal

Necrosis

1

Adrenal Medulla

+ +

Hyperplasia

1 3 1 2

Islets, Pancreatic

+ +

Hyperplasia

1 2

Parathyroid Gland

+ +

Cyst

2

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

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TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 5 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 0 | 7 | 6 | 7 | 7 | 6 |   |
|                              | 4 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 8 | 2 | 3 | 0 | 2 | 8 |
|                              | 9 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 9 | 1 | 9 | 0 | 0 | 0 | 0 | 8 | 0 | 9 | 6 | 9 | 8 | 2 | 9 | 7 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>25000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                    | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
|                              | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                              | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |
|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

males (cont...)

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pituitary Gland                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pigmentation                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |
| Pars Distalis, Angiectasis          |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Cyst                 |   |   |   | 2 |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   | 4 |   |   |
| Pars Distalis, Hyperplasia          |   |   |   | 3 |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Hyperplasia, Focal   |   | 1 | 4 |   | 1 |   | 4 |   |   |   | 2 | 2 | 1 | 2 | 1 |   | 2 |   |   |   |   | 1 |   |   |
| Pars Distalis, Hypertrophy          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |
| Pars Intermedia, Cyst               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Rathke's Cleft, Hemorrhage          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thyroid Gland                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Degeneration, Cystic                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |
| Pigmentation                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ultimobranchial Cyst                |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |
| C-cell, Hyperplasia                 |   |   |   | 2 | 2 |   | 1 | 2 | 1 | 2 |   |   | 1 |   |   |   |   | 4 |   |   |   | 1 |   |   |
| Follicular Cell, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |

GENERAL BODY SYSTEM

|            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|
| Tissue NOS |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | + |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|

GENITAL SYSTEM

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Epididymis      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
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 A .. Autolysis precludes evaluation  
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 1-4 .. Lesion qualified as:  
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TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                        | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|                                    | 5 3 7 7 7 7 7 7 7 7 7 7 7 7 7 7 4 7 7 0 7 6 7 7 6   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS MALE<br>25000 PPM | 4 1 3 3 3 3 3 3 3 3 2 2 2 3 3 3 3 2 3 2 8 2 3 0 2 8 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 9 0 0 0 0 0 1 1 1 9 1 9 0 0 0 0 8 0 9 6 9 8 2 9 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

males (cont...)

|  |   |   |   |  |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |  |   |   |  |
|--|---|---|---|--|---|---|---|---|---|---|--|---|---|---|---|---|---|---|---|---|---|--|---|---|--|
| Cyst   | 2 |   |   |  |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |  |   |   |  |
| Inflammation, Chronic Duct, Ectasia                                      | 2 | 2 | 2 |  | 3 | 2 |   | 2 | 2 | 2 |  | 2 | 2 | 1 | 2 | 2 | 2 |   | 2 | 2 | 2 |  | 2 | 2 |  |
| Prostate   | + |   |   |  |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |  |   |   |  |
| Inflammation, Chronic Epithelium, Hyperplasia                            |   |   |   |  |   |   | 3 | 1 |   |   |  |   |   |   |   | 3 |   |   |   |   | 2 |  |   |   |  |
| Seminal Vesicle  | + |   |   |  |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |  |   |   |  |
| Testes   | + |   |   |  |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |  |   |   |  |
| Inflammation Germinal Epithelium, Atrophy Interstitial Cell, Hyperplasia |   |   |   |  |   | 4 |   |   |   |   |  |   |   |   |   | 1 |   | 1 |   | 4 |   |  |   |   |  |

HEMATOPOIETIC SYSTEM

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
| Bone Marrow                        | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Hyperplasia                        |   | 2 |   |   |   |   |   |   | 2 |   |   |   |   |   | 4 | 2 |   |   |   | 1 |   |   |   |   |  |
| Myelofibrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Lymph Node                         | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Mediastinal, Hemorrhage            | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |  |
| Mediastinal, Hyperplasia, Lymphoid | 3 |   |   |   |   | 2 |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   | 2 |   |   |  |
| Mediastinal, Pigmentation          | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |  |
| Pancreatic, Hyperplasia, Lymphoid  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Lymph Node, Mandibular             | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |  |

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x .. Lesion present  
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Page 42

TDMS No. 20008 - 03

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Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                                     | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|---|---|
|   | 5 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               | 6 | 7 | 7 |
| 4   | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 8 | 2 | 3 | 0 | 2 | 8 |                 |   |   |   |
| 9   | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 9 | 1 | 9 | 0 | 0 | 0 | 0 | 8 | 0 | 9 | 6 | 9 | 8 | 2 | 9 | 7 |                 |   |   |   |
| FISCHER 344 RATS MALE<br>25000 PPM<br>ANIMAL ID | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |   |   |
|   | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |   |   |
|   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |   |   |
|   | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |   |   |
|   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |   |   |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | males (cont...) |   |   |   |

|                                  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Hyperplasia, Lymphoid            |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lymph Node, Mesenteric           | +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ectasia                          |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhage                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia, Lymphoid            | 3 2 2 1 3 2 2 2 2 2 2 3 1 2                               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pigmentation                     | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Spleen                           | +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fibrosis                         |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hematopoietic Cell Proliferation | 4 1 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia, Lymphoid, Focal     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pigmentation                     | 2 1 3 3 2 2 1 2 2 3 1 3 3 2 3 1 1 2 2 3                   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lymphoid Follicle, Atrophy       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lymphoid Follicle, Hyperplasia   | 2 2 3 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Thymus                           | + + + + + M + + + + + + + + + + + + + + + + + + +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

INTEGUMENTARY SYSTEM

|                           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Mammary Gland             | + + + + + M + + + + + + + + + + + + + + + + + + +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia               | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Duct, Ectasia             | 2 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Skin                      | +         |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cyst Epithelial Inclusion |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fibrosis                  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperkeratosis            | 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked  
Page 43

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |   |
| DAY ON TEST                  | 5 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 0 | 7 | 6 | 7 | 7 | 6 |   |
|                              | 4 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 3 | 3 | 3 | 2 | 3 | 2 | 8 | 2 | 3 | 0 | 2 | 8 |   |
|                              | 9 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 9 | 1 | 9 | 0 | 0 | 0 | 0 | 8 | 0 | 9 | 6 | 9 | 8 | 2 | 9 | 7 |
| .....                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>25000 PPM</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |
|                              | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |   |   |
|                              | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

males (cont...)

Ulcer  
Epidermis, Hyperplasia 2

MUSCULOSKELETAL SYSTEM

Bone +

NERVOUS SYSTEM

Brain +  
 Compression  
Hemorrhage 1  
Necrosis

Peripheral Nerve +

Spinal Cord +

RESPIRATORY SYSTEM

Lung +  
 Hemorrhage 2 1 1 1  
 Infiltration Cellular, Histiocyte 1  
 Inflammation, Chronic 1  
 Alveolar Epithelium, Hyperplasia 3 4 1 2 1 3 1 1 1

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
Test Type: CHRONIC  
Route: DOSED FEED  
Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST           |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                    |
|-----------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------------|
| FISCHER 344 RATS MALE |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                    |
| 25000 PPM             |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                    |
| ANIMAL ID             |  | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |                    |
|                       |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                    |
|                       |  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | males<br>(cont...) |

Nose +  
Foreign Body 2  
Inflammation, Chronic  
Goblet Cell, Hyperplasia 2  
Respiratory Epithelium, Metaplasia,  
Squamous

Trachea +

SPECIAL SENSES SYSTEM

Eye A +  
Cataract 1 1 1 3 3 1 1  
Edema  
Inflammation, Chronic  
Retinal Detachment 3  
Bilateral, Cataract 1 2 1 2 1  
Retina, Degeneration 4 1 1

Harderian Gland +  
Hyperplasia, Focal  
Inflammation, Chronic 2

URINARY SYSTEM

Kidney +  
Cyst  
Mineralization 1 1 1

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                                      |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|--|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DAY ON TEST                                      |           | 5 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 0 | 7 | 6 | 7 | 7 | 6 | 6 |   |
| DAY ON TEST                                      |           | 4 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 8 | 2 | 3 | 0 | 2 | 8 |
| DAY ON TEST                                      |           | 9 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 9 | 1 | 9 | 0 | 0 | 0 | 0 | 8 | 0 | 9 | 6 | 9 | 8 | 2 | 9 | 7 |
| <b>FISCHER 344 RATS MALE</b><br><b>25000 PPM</b> | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|  | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|  | ANIMAL ID | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |
|  | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|  | ANIMAL ID | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |
| Nephropathy                                      |           | 1 |   | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 2 |   | 2 | 1 | 2 | 2 | 1 | 1 | 2 | 1 |   | 2 | 1 |   | 1 | 2 |
| Renal Tubule, Pigmentation                       |           |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia             |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Urinary Bladder                                  |           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

males  
(cont...)

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 46

| DAY ON TEST                  | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|------------------------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 6               | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
|                              | 6               | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 |
|                              | 7               | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 2 | 2 |
| <b>FISCHER 344 RATS MALE</b> | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>25000 PPM</b>             | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                    | 1               | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |
|                              | 2               | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |   |
|                              | 6               | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |   |
|                              | <b>* TOTALS</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

ALIMENTARY SYSTEM

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |    |     |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|----|-----|
| Esophagus                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 50 |     |
| Intestine Large, Cecum            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 49 |     |
| Ulcer                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4   | 1  | 4.0 |
| Intestine Large, Colon            | + | + | A | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 47 |     |
| Necrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4   | 1  | 4.0 |
| Intestine Large, Rectum           | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 47 |     |
| Intestine Small, Duodenum         | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 48 |     |
| Intestine Small, Ileum            | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 48 |     |
| Intestine Small, Jejunum          | + | + | A | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 47 |     |
| Liver                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 50 |     |
| Basophilic Focus                  |   | X |   | X | X | X | X |   | X | X |   | X |   |   |   | X | X | X |   | X |   | X | X | X | 32  |    |     |
| Clear Cell Focus                  |   |   |   | X | X | X |   |   | X | X |   | X |   |   | X | X | X | X |   | X |   | X | X | X | 31  |    |     |
| Eosinophilic Focus                |   |   |   | X |   |   |   |   |   |   |   | X |   |   |   | X |   |   |   |   |   | X |   |   | 10  |    |     |
| Hepatodiaphragmatic Nodule        |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 6   |    |     |
| Infiltration Cellular, Mixed Cell |   |   |   |   | 1 | 1 |   |   | 2 | 1 | 1 |   |   |   |   | 1 |   |   |   | 1 |   | 1 | 1 | 1 | 27  |    |     |
| Malformation                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1   |    |     |
| Mixed Cell Focus                  |   | X |   |   |   | X |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   | 7   |    |     |
| Bile Duct, Hyperplasia            | 2 | 2 | 4 | 3 | 3 | 1 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 2 | 2 | 2 | 1 | 2 | 2 | 2   | 44 |     |
|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2.1 |    |     |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |        |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|--------|
|                                       | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7        |        |
|                                       | 6 | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 3        |        |
|                                       | 7 | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 2        |        |
| FISCHER 344 RATS MALE<br>25000 PPM    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |        |
| ANIMAL ID                             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |        |
|                                       | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1        |        |
|                                       | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5        |        |
|                                       | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9        |        |
|                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |        |
| Hepatocyte, Vacuolization Cytoplasmic | 4 | 3 |   |   |   |   | 4 |   | 1 | 2 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |          | 9 2.4  |
| Mesentery                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 6      |
| Accessory Spleen                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 1      |
| Fat, Necrosis                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 3 1.7  |
| Oral Mucosa                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 1      |
| Pharyngeal, Hyperplasia               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 1 3.0  |
| Pancreas                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 50     |
| Atrophy                               | 2 | 1 | 1 |   | 2 |   |   |   |   |   | 2 |   | 1 | 2 | 3 | 1 | 1 | 1 |   | 1 |   | 4 | 1 | 2        | 35 1.7 |
| Metaplasia, Hepatocyte                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 1 1.0  |
| Acinus, Hyperplasia, Focal            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 8 2.8  |
| Duct, Ectasia                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 19 1.6 |
| Salivary Glands                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 50     |
| Atrophy                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 4 1.3  |
| Stomach, Forestomach                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 50     |
| Edema                                 | 2 |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 5 2.2  |
| Ulcer                                 | 2 |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 4 2.5  |
| Epithelium, Hyperplasia               | 3 |   | 2 |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 7 2.7  |
| Stomach, Glandular                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 49     |
| Edema                                 | 2 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 2 2.0  |
| Erosion                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 3 1.7  |
| Ulcer                                 |   |   | 3 |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          | 4 2.8  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 48

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
|                              | 6 | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 |   |
|                              | 7 | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 2 | 2 | 2 |   |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>25000 PPM</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |
|                              | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5 |   |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 0 |   |
| <b>* TOTALS</b>              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**CARDIOVASCULAR SYSTEM**

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|
| Blood Vessel         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2</b>      |
| Heart                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Cardiomyopathy       | 1 | 1 |   | 1 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 2 | 1 | 1 | 2 | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 2 |   | <b>45 1.3</b> |
| Thrombosis           | 2 |   | 3 |   |   |   |   | 3 |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   | <b>7 2.6</b>  |
| Myocardium, Necrosis |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |
| Valve, Hyperplasia   |   |   | 2 |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>3 2.3</b>  |

**ENDOCRINE SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|
| Adrenal Cortex                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Accessory Adrenal Cortical Nodule |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 2 | 1 | 1 |   |   |   |   |   |   |   |   | 2 | <b>18 1.4</b> |
| Degeneration, Fatty               | 1 | 1 | 2 |   | 2 |   | 3 |   |   |   |   |   | 2 | 2 | 1 | 2 | 1 | 1 |   |   |   |   |   |   |   |   | <b>24 1.5</b> |
| Hyperplasia, Focal                |   |   |   |   | 2 |   |   |   |   | 1 | 2 |   |   |   | 3 | 3 | 3 |   | 1 |   |   |   |   |   |   |   | <b>14 1.9</b> |
| Hypertrophy, Focal                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | <b>1 1.0</b>  |
| Necrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |
| Adrenal Medulla                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 | 2 | 1 |   |   | 3 |   | 2 |   |   |   | 1 |   | <b>10 2.0</b> |
| Islets, Pancreatic                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | <b>3 1.3</b>  |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | <b>49</b>     |
| Cyst                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 2.0</b>  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 49

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                              | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |                 |
|                              | 6 | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 |                 |
|                              | 7 | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 2 | 2 |                 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| 25000 PPM                    | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |                 |
|                              | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5 |                 |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | <b>* TOTALS</b> |

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |               |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|---------------|
| Pituitary Gland                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b> |               |
| Pigmentation                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1 1.0</b>  |
| Pars Distalis, Angiectasis          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1 3.0</b>  |
| Pars Distalis, Cyst                 |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |           | <b>5 2.4</b>  |
| Pars Distalis, Hyperplasia          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>2 3.5</b>  |
| Pars Distalis, Hyperplasia, Focal   | 1 | 1 |   |   | 2 |   | 2 |   |   | 2 |   |   | 1 | 1 |   |   | 2 |   |   |   |   |   |   |   |   |           | <b>19 1.7</b> |
| Pars Distalis, Hypertrophy          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1 3.0</b>  |
| Pars Intermedia, Cyst               |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1 2.0</b>  |
| Rathke's Cleft, Hemorrhage          |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |           | <b>2 2.0</b>  |
| Thyroid Gland                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b> |               |
| Degeneration, Cystic                |   |   |   | 1 |   |   |   |   |   | 1 |   | 1 | 3 |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>5 1.8</b>  |
| Pigmentation                        |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |           | <b>1 2.0</b>  |
| Ultimobranchial Cyst                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |           | <b>2 1.5</b>  |
| C-cell, Hyperplasia                 |   |   |   |   | 3 |   |   |   |   | 1 |   |   |   | 1 |   |   |   |   | 4 |   |   | 1 | 3 |   |   |           | <b>15 1.9</b> |
| Follicular Cell, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |           | <b>2 3.0</b>  |

**GENERAL BODY SYSTEM**

|            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------|
| Tissue NOS |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | <b>1</b> |
|------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------|

**GENITAL SYSTEM**

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|
| Epididymis      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b> |
| Preputial Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b> |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

l .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                              | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               |
|                              | 6 | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3               |
|                              | 7 | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 2 | 2 | 2               |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| <b>25000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| <b>ANIMAL ID</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               |
|                              | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5               |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 0 | 0               |
|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |

|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |              |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|--------------|
| Cyst                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 2.0</b> |
| Inflammation, Chronic          | 2 | 2 | 2 | 2 |   |   | 3 | 2 | 2 | 2 |   | 1 | 2 | 2 |   | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 1 | 2 | 1 |   | <b>40 1.9</b> |              |
| Duct, Ectasia                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 4.0</b> |
| Prostate                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |              |
| Inflammation, Chronic          |   |   |   | 2 |   | 2 |   |   |   |   |   | 1 | 2 | 3 |   | 1 |   | 2 |   |   |   | 1 |   | 2 |   |   | <b>13 1.9</b> |              |
| Epithelium, Hyperplasia        |   |   |   |   |   |   |   |   |   |   |   | 2 | 1 |   |   |   | 1 |   |   |   |   | 1 |   | 1 |   |   | <b>8 1.3</b>  |              |
| Seminal Vesicle                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |              |
| Testes                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |              |
| Inflammation                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 | <b>1 3.0</b>  |              |
| Germinal Epithelium, Atrophy   | 4 |   |   |   |   | 2 |   | 4 | 4 | 4 |   |   |   |   | 1 |   |   |   |   |   |   | 4 |   |   |   |   | <b>11 3.0</b> |              |
| Interstitial Cell, Hyperplasia | 2 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   | <b>5 1.6</b>  |              |

HEMATOPOIETIC SYSTEM

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|
| Bone Marrow                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>    |
| Hyperplasia                        |   |   |   |   |   |   | 2 |   | 1 |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   | 2 |   | <b>9 2.0</b> |
| Myelofibrosis                      | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   | <b>2 1.0</b> |
| Lymph Node                         | + | + | + |   |   |   |   | + |   |   |   |   |   | + | + |   |   |   |   |   |   | + |   | + |   |   | <b>18</b>    |
| Mediastinal, Hemorrhage            |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   | <b>3 3.0</b> |
| Mediastinal, Hyperplasia, Lymphoid |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>4 2.3</b> |
| Mediastinal, Pigmentation          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 1.5</b> |
| Pancreatic, Hyperplasia, Lymphoid  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 2.0</b> |
| Lymph Node, Mandibular             | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | <b>+ 1</b>   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |  |  |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|--|--|
|                              | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               |  |  |
|                              | 6 | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3               |  |  |
|                              | 7 | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 2 | 2               |  |  |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |  |  |
| <b>25000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |  |  |
| <b>ANIMAL ID</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               |  |  |
|                              | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5               |  |  |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | <b>* TOTALS</b> |  |  |

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |     |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|
| Hyperplasia, Lymphoid            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 1   | 1.0 |
| Lymph Node, Mesenteric           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |
| Ectasia                          |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1   | 3.0 |
| Hemorrhage                       |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1   | 1.0 |
| Hyperplasia, Lymphoid            |   |   |   | 2 | 1 |   |   | 2 |   |   |   |   |   |   | 2 |   | 1 | 3 | 2 | 2 |   |   |   | 2 | 2 | 1 | 23 | 2.0 |     |
| Pigmentation                     |   |   |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   | 1 | 1 | 1 | 1 | 17 | 1.0 |     |
| Spleen                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |
| Fibrosis                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   | 2 |   |   |   |   |   |    | 2   | 2.0 |
| Hematopoietic Cell Proliferation |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3   | 3.0 |
| Hyperplasia, Lymphoid, Focal     |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |     |
| Pigmentation                     | 1 | 1 | 1 | 3 | 3 | 2 | 1 | 1 | 1 | 2 |   | 1 | 3 | 1 | 1 | 1 | 3 | 3 | 2 |   | 2 |   |   | 3 | 3 | 2 | 42 | 2.0 |     |
| Lymphoid Follicle, Atrophy       |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |     |
| Lymphoid Follicle, Hyperplasia   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   | 6  | 2.3 |     |
| Thymus                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |     |     |

**INTEGUMENTARY SYSTEM**

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |  |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|--|
| Mammary Gland             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |     |  |
| Hyperplasia               |   |   | 1 | 2 |   |   |   | 1 |   |   |   |   |   | 1 | 1 |   |   |   |   | 2 |   |   |   |   | 2 |   | 13 | 1.3 |  |
| Duct, Ectasia             |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 4  | 1.5 |  |
| Skin                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |  |
| Cyst Epithelial Inclusion |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  |     |  |
| Fibrosis                  |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |  |
| Hyperkeratosis            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 4.0 |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|
|                              | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               | 7 |
|                              | 6 | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 3               | 3 |
|                              | 7 | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 2               | 2 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
| <b>25000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
|                              | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               | 1 |
|                              | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4               | 5 |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9               | 0 |
|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |   |

|                        |   |              |
|------------------------|---|--------------|
| Ulcer                  | 2 | <b>1 2.0</b> |
| Epidermis, Hyperplasia |   | <b>1 2.0</b> |

**MUSCULOSKELETAL SYSTEM**

|      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b> |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|

**NERVOUS SYSTEM**

|                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |              |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|--------------|
| Brain            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>    |              |
| Compression      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 | <b>1 2.0</b> |              |
| Hemorrhage       | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 1 | 1 | 1 |   |              | <b>6 1.0</b> |
| Necrosis         |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 2.0</b> |
| Peripheral Nerve |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>2</b>     |
| Spinal Cord      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>2</b>     |

**RESPIRATORY SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |               |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---------------|
| Lung                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |               |
| Hemorrhage                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>4 1.3</b>  |
| Infiltration Cellular, Histiocyte | 1 |   | 1 | 1 | 1 | 1 |   |   | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 2 | 1 |   | 1 |   | <b>43 1.0</b> |               |
| Inflammation, Chronic             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |               | <b>2 1.0</b>  |
| Alveolar Epithelium, Hyperplasia  |   |   |   | 1 |   |   |   | 3 | 2 |   |   | 1 | 1 |   |   |   | 2 |   |   |   |   |   | 2 | 2 |   |               | <b>17 1.8</b> |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                                     | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0   | 0      |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|--------|
|   | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7   | 7      |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| FISCHER 344 RATS MALE<br>25000 PPM<br>ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0   | 0      |
|   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0   | 0      |
| 1   | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1   | 1      |
| 2   | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4   | 5      |
| 6   | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9   | 0      |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| <b>* TOTALS</b>                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| Nose  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 50     |
| Foreign Body                                    |   |   |   |   |   |   | 1 |   |   | 1 |   |   | 2 | 1 |   |   | 1 |   |   |   |   | 1 |     | 7 1.3  |
| Inflammation, Chronic                           |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 2 | 1 |   | 1   | 6 1.2  |
| Goblet Cell, Hyperplasia                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     | 1 2.0  |
| Respiratory Epithelium, Metaplasia, Squamous    |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |     | 1 1.0  |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| Trachea   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 50     |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| <b>SPECIAL SENSES SYSTEM</b>                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| Eye   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 48     |
| Cataract  |   |   | 1 |   | 1 |   | 2 | 1 |   |   | 1 | 4 | 1 |   |   |   |   |   | 1 |   |   | 1 | 1   | 18 1.4 |
| Edema   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |     | 1 4.0  |
| Inflammation, Chronic                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |     | 1 1.0  |
| Retinal Detachment                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     | 1 3.0  |
| Bilateral, Cataract                             |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     | 6 1.3  |
| Retina, Degeneration                            |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |     | 3 3.0  |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| Harderian Gland                                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 50     |
| Hyperplasia, Focal                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |     | 1 1.0  |
| Inflammation, Chronic                           |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |     | 2 2.0  |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| <b>URINARY SYSTEM</b>                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| .....   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |        |
| Kidney  | + | + | A | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | 48     |
| Cyst  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3   | 1 3.0  |
| Mineralization                                  |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 1 |   |   |   |   |   |   |   |   | 1 1 | 7 1.0  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                          | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0  |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|----|
|                                      | 6 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               | 7  |
|                                      | 6 | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 4 | 2 | 0 | 9 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 3               | 3  |
|                                      | 7 | 1 | 6 | 1 | 1 | 0 | 0 | 7 | 9 | 9 | 7 | 9 | 4 | 1 | 1 | 0 | 0 | 9 | 9 | 9 | 9 | 9 | 9 | 2               | 2  |
| <b>FISCHER 344 RATS MALE</b>         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0  |
| <b>25000 PPM</b>                     | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0  |
| ANIMAL ID                            | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               | 1  |
|                                      | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4               | 5  |
|                                      | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9               | 0  |
|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |    |
| Nephropathy                          | 1 | 1 |   | 1 | 2 | 1 | 1 |   | 1 | 2 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1               | 1  |
| Renal Tubule, Pigmentation           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |                 |    |
| Transitional Epithelium, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 2 | 2 | 1 | 1               |    |
| Urinary Bladder                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +               | 50 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
l .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                        | 0     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|                                    | 7 7 7 7 7 7 6 7 7 7 7 7 7 6 7 7 7 5 7 7 7 7 7 7 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS MALE<br>50000 PPM | 3 0 3 3 3 3 3 3 3 3 2 2 2 1 4 3 3 3 9 1 2 2 3 3 3 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 1 2 1 1 1 1 8 0 0 9 9 9 1 5 0 0 0 1 0 9 9 1 1 1 1 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                          | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 5 5 5 5 5 5 5 5 6 6 6 6 6 6 6 6 6 6 6 7 7 7 7 7 7 7 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                    | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

males  
(cont...)

ALIMENTARY SYSTEM

|                           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Esophagus                 | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Cecum    | + + + + + + + + + + + + + + A + + + + + + + + + + M + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Colon    | + + + + + + + + + + + + + + A + + + + + + + + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Edema                     | 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ulcer                     | 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Rectum   | + + + + + + + + + + + + + + A + + + + + + + + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Edema                     | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fibrosis                  | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhage                |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhage, Chronic       | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Duodenum | + + + + + + + + + + + + + + A + + + + + + + + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Ileum    | + + + + + + + + + + + + + + A + + + + + + + + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Jejunum  | + + + + + + + + + + + + + + A + + + + + + + + + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Perforation               | 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Liver                     | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Angiectasis               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Basophilic Focus          | X       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                                       | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7               |
|                                       | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 4 | 3 | 3 | 3 | 9 | 1 | 2 | 2 | 3 | 3 | 3 | 3 | 3 |                 |
|                                       | 1 | 2 | 1 | 1 | 1 | 1 | 8 | 0 | 0 | 9 | 9 | 9 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 9 | 9 | 1 | 1 | 1 | 1 | 1 |                 |
| .....                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| FISCHER 344 RATS MALE<br>50000 PPM    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| ANIMAL ID                             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               |
|                                       | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7               |
|                                       | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   | males (cont...) |
| Clear Cell Focus                      |   |   | X | X | X | X |   | X | X |   |   | X |   | X | X |   |   | X | X | X | X | X | X | X | X | X |                 |
| Eosinophilic Focus                    |   |   | X | X | X | X |   | X |   | X |   |   |   |   |   |   |   |   |   |   | X | X |   |   |   |   |                 |
| Hepatodiaphragmatic Nodule            |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Infarct                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   | 4 |                 |
| Infiltration Cellular, Mixed Cell     |   | 1 | 1 | 1 |   |   |   | 1 |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Mixed Cell Focus                      |   |   |   |   |   | X |   | X |   | X |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Necrosis, Focal                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |                 |
| Bile Duct, Hyperplasia                |   | 1 |   |   | 2 | 1 | 2 |   |   |   |   |   | 1 | 3 |   |   |   |   |   |   |   | 1 |   |   |   | 1 |                 |
| Hepatocyte, Vacuolization Cytoplasmic |   |   |   |   |   |   | 3 |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Serosa, Fibrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |                 |
| .....                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Mesentery                             |   | + |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |                 |
| Accessory Spleen                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Fat, Necrosis                         |   | 3 |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| .....                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Pancreas                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |                 |
| Atrophy                               | 1 |   |   |   | 2 | 1 | 2 | 1 | 1 |   |   |   |   | 3 |   | 2 |   | 2 |   |   | 2 |   | 1 | 3 |   | 1 |                 |
| Metaplasia, Hepatocyte                |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Acinus, Hyperplasia, Focal            |   |   | 2 |   |   |   |   |   |   | 2 |   |   |   |   |   |   | 3 |   |   |   | 1 | 3 |   |   |   |   |                 |
| Duct, Ectasia                         | 1 |   |   | 2 | 1 | 1 | 1 | 1 | 1 |   |   |   | 4 | 1 |   |   | 2 |   |   | 2 |   |   | 3 |   | 1 | 2 |                 |
| .....                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Salivary Glands                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |                 |
| Atrophy                               |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 1 |   | 2 | 1 |   |   |   |   |   |   | 1 |                 |
| Hyperplasia, Lymphoid                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| .....                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| Stomach, Forestomach                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |                 |
| Edema                                 |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |                 |
| Ulcer                                 |   |   |   |   |   | 4 |   |   |   |   | 2 |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |                 |
| Epithelium, Hyperplasia               |   | 1 |   |   |   | 2 |   |   |   |   |   |   | 1 | 2 |   |   |   |   |   |   |   |   |   |   |   |   |                 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
|                              | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 4 | 3 | 3 | 3 | 9 | 1 | 2 | 2 | 3 | 3 | 3 | 3 |
|                              | 1 | 2 | 1 | 1 | 1 | 1 | 8 | 0 | 0 | 9 | 9 | 9 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 9 | 9 | 1 | 1 | 1 | 1 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>50000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>ANIMAL ID</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
|                              | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 |
|                              | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

males (cont...)

|                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Stomach, Glandular  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Edema               |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Erosion             |   |   |   |   |   |   |   |   |   | 4 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer               |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |
| Glands, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |

**CARDIOVASCULAR SYSTEM**

|                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Blood Vessel       |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   | + |
| Heart              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cardiomyopathy     | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |   | 2 | 1 |   |   | 1 |   | 1 | 2 | 1 | 1 | 1 |   | 1 | 1 |
| Thrombosis         |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |
| Valve, Hyperplasia |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |

**ENDOCRINE SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Accessory Adrenal Cortical Nodule |   |   |   |   |   | 1 | 2 |   | 1 | 1 |   |   |   |   |   |   | 2 |   | 1 |   |   |   | 1 | 1 |   |
| Degeneration, Fatty               | 2 |   |   |   |   |   | 2 |   | 1 | 2 |   |   |   | 2 | 1 | 2 | 1 |   |   |   | 1 |   | 1 |   |   |
| Hyperplasia, Focal                |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |
| Hypertrophy, Focal                |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Necrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 1 | 4 | 1 | 1 |   |   | 3 |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

| DAY ON TEST |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|-------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|             |  | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
|             |  | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 4 | 3 | 3 | 3 | 9 | 1 | 2 | 2 | 3 | 3 | 3 | 3 |
|             |  | 1 | 2 | 1 | 1 | 1 | 1 | 8 | 0 | 0 | 9 | 9 | 9 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 9 | 9 | 1 | 1 | 1 |

**FISCHER 344 RATS MALE**  
ANIMAL ID  
**50000 PPM**

| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------------|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
| 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1                  |
| 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6                  |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | males<br>(cont...) |

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Islets, Pancreatic                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | M | + | + | + | + | + | + | + |
| Pituitary Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars Distalis, Cyst               |   |   |   | 1 | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |
| Pars Distalis, Hyperplasia        |   |   |   |   | 4 |   | 3 |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   | 3 |
| Pars Distalis, Hyperplasia, Focal |   |   | 1 |   |   |   |   | 1 | 3 |   | 4 | 1 |   |   |   |   |   |   |   |   | 3 |   |   |   |   |
| Pars Intermedia, Cyst             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thyroid Gland                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + |   |
| Degeneration, Cystic              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |
| Ultimobranchial Cyst              |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   | 2 |
| C-cell, Hyperplasia               | 1 |   | 1 | 1 |   |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   | 3 | 3 |   | 1 |   |   |   |

**GENERAL BODY SYSTEM**

|                       |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |
|-----------------------|--|--|--|--|--|--|---|--|--|--|--|--|--|--|--|---|--|--|--|--|--|--|--|--|--|
| Tissue NOS            |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic |  |  |  |  |  |  | 4 |  |  |  |  |  |  |  |  | + |  |  |  |  |  |  |  |  |  |

**GENITAL SYSTEM**

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Epididymis      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Granuloma Sperm |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Preputial Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst            |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 59

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                        |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|------------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------------|
| FISCHER 344 RATS MALE<br>50000 PPM | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|                                    |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|                                    |           | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1                  |
|                                    |           | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6                  |
|                                    |           | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   |   | males<br>(cont...) |

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hyperplasia Inflammation, Chronic       | 1 | 2 |   | 2 |   | 2 | 2 |   | 1 | 2 | 2 | 2 |   |   |   | 3 | 1 | 2 |   | 2 |   | 2 | 1 | 1 | 2 | 2 | 1 |
| Prostate Fibrosis Inflammation, Chronic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Epithelium, Hyperplasia                 | 2 | 3 | 1 |   |   |   |   |   |   |   |   |   |   |   |   | 2 | 2 |   |   | 3 |   | 3 |   | 1 |   |   |   |
| Seminal Vesicle                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Testes Atrophy                          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Germinal Epithelium, Atrophy            |   |   |   | 4 |   |   | 2 |   |   |   |   | 2 |   |   |   | 3 |   |   |   | 1 |   | 1 |   |   |   |   | 4 |
| Interstitial Cell, Hyperplasia          |   |   |   |   |   | 1 |   |   |   |   |   | 2 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |

HEMATOPOIETIC SYSTEM

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow Hyperplasia         | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Lymph Node Mediastinal, Abscess |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |
| Lymph Node, Mandibular Ectasia  | M | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph Node, Mesenteric Atrophy  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                  | 0 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
|------------------------------|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|
|                              | 7 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
|                              | 0 |  |  |  |  | 3 |  |  |  |  | 2 |  |  |  |  | 1 |  |  |  |  | 4 |  |  |  |  | 3 |  |  |  |  | 9 |  |  |  |  | 1 |  |  |  |  | 2 |  |  |  |  | 3 |  |  |  |  | 3 |  |  |  |  |
|                              | 1 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| <b>FISCHER 344 RATS MALE</b> | 0 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| <b>50000 PPM</b>             | 0 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| ANIMAL ID                    | 1 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
|                              | 5 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
|                              | 1 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |

males (cont...)

|                                  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
|----------------------------------|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|---|--|--|--|--|
| Ectasia                          |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Hemorrhage                       |   |  |  |  |  | 1 |  |  |  |  |   |  |  |  |  |   |  |  |  |  | 1 |  |  |  |  |   |  |  |  |  |
| Hyperplasia, Lymphoid            |   |  |  |  |  | 2 |  |  |  |  | 1 |  |  |  |  | 2 |  |  |  |  | 2 |  |  |  |  | 1 |  |  |  |  |
| Hyperplasia, Reticulum Cell      |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Pigmentation                     | 1 |  |  |  |  |   |  |  |  |  | 1 |  |  |  |  | 1 |  |  |  |  |   |  |  |  |  | 1 |  |  |  |  |
| Spleen                           | + |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Fibrosis                         | + |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Hematopoietic Cell Proliferation |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Necrosis                         | 3 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Pigmentation                     | 3 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Lymphoid Follicle, Hyperplasia   | 1 |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |
| Thymus                           | + |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |   |  |  |  |  |

**INTEGUMENTARY SYSTEM**

|                           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Mammary Gland             | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fibrosis                  | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia               | 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Duct, Ectasia             | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Skin                      | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cyst Epithelial Inclusion | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**MUSCULOSKELETAL SYSTEM**

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                                     | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|   | 7 7 7 7 7 7 6 7 7 7 7 7 7 6 7 7 7 5 7 7 7 7 7 7 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS MALE<br>50000 PPM<br>ANIMAL ID | 3 0 3 3 3 3 3 3 3 3 2 2 2 1 4 3 3 3 9 1 2 2 3 3 3 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 1 2 1 1 1 1 8 0 0 9 9 9 1 5 0 0 0 1 0 9 9 1 1 1 1 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 5 5 5 5 5 5 5 5 5 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | <b>males (cont...)</b>                              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Bone +

NERVOUS SYSTEM

|                            |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Brain                      | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Compression                | + 4 + + + + + + + + + + + + + + + 2 + + 4 + 3 + + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Developmental Malformation |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Gliosis, Focal             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhage                 | 1 + 1 + + + + + + + + + + + + + + + 1 1 + + + + +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Peripheral Nerve           | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Spinal Cord                | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

RESPIRATORY SYSTEM

|                                     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Lung                                | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infiltration Cellular, Histiocyte   | 1 1 1 1 1 1 1 2 1 1 1 2 1 1 1 1 1 + + 1 + 1 1 2 1     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic               | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Metaplasia, Osseous                 | 1 +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Alveolar Epithelium, Hyperplasia    | + 1 + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Nose                                | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Foreign Body                        | 2 +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic               | 2 2 1 +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Goblet Cell, Hyperplasia            | +     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Respiratory Epithelium, Hyperplasia | 2 +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                              | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 |   |
|                              | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 4 | 3 | 3 | 3 | 9 | 1 | 2 | 2 | 3 | 3 | 3 |   |
|                              | 1 | 2 | 1 | 1 | 1 | 1 | 8 | 0 | 0 | 9 | 9 | 9 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 9 | 9 | 1 | 1 | 1 |   |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>50000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>ANIMAL ID</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |
|                              | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |   |
|                              | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

males  
(cont...)

Trachea +

**SPECIAL SENSES SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye                   | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + |
| Cataract              |   |   | 1 | 1 |   | 1 | 1 |   | 1 |   |   | 4 | 1 |   | 1 |   |   |   |   |   |   |   |   |   |
| Edema                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Cataract   | 1 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 2 |   |   | 1 |   |   |   |   |
| Retina, Degeneration  |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Harderian Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Focal    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |
| Inflammation, Chronic |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Zymbal's Gland        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**URINARY SYSTEM**

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney                               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Suppurative            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Metaplasia, Osseous                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineralization                       |   |   | 1 |   |   | 1 | 1 | 1 |   |   |   |   | 1 |   |   |   | 1 | 2 |   |   | 1 | 1 |   |   |
| Nephropathy                          | 2 | 3 | 1 | 1 | 1 | 1 |   | 1 | 1 |   | 1 | 1 | 2 | 1 | 2 |   | 2 | 2 | 2 | 2 | 1 | 1 | 2 | 1 |
| Renal Tubule, Dilatation             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia | 2 | 2 |   |   | 2 |   |   |   |   |   |   | 1 |   |   |   | 2 |   |   |   |   |   |   | 1 |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 63

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                                      | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | males<br>(cont...) |
|--|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------------|
|  | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                    |
| 7  | 7         | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 0                  |
| 3  | 0         | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 4 | 3 | 3 | 3 | 9 | 1 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 0                  |
| 1  | 2         | 1 | 1 | 1 | 1 | 8 | 0 | 0 | 9 | 9 | 9 | 1 | 5 | 0 | 0 | 0 | 1 | 0 | 9 | 9 | 1 | 1 | 1 | 1 | 1 | 0                  |
| .....  |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                    |
| <b>FISCHER 344 RATS MALE</b><br><b>50000 PPM</b> | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|  | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|  | 1         | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0                  |
|  | 5         | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 0                  |
|  | 1         | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 0                  |
| Urinary Bladder                                  | +         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |                    |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

l .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked



|                                       | DAY ON TEST |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
|---------------------------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                                       | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
|                                       | 7           | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 |                 |
|                                       | 1           | 3 | 3 | 1 | 3 | 7 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 |                 |
|                                       | 1           | 1 | 0 | 4 | 0 | 6 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 6 | 9 | 9 | 9 | 9 | 9 | 8 | 2 | 2 | 2 | 1 |                 |
| <b>FISCHER 344 RATS MALE</b>          | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>50000 PPM</b>                      | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| ANIMAL ID                             | 1           | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |                 |
|                                       | 7           | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 |                 |
|                                       | 6           | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | <b>* TOTALS</b> |
| Clear Cell Focus                      |             | X | X |   | X |   |   | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | <b>33</b>       |
| Eosinophilic Focus                    |             | X | X |   | X | X |   |   | X | X |   | X | X |   | X |   |   |   |   | X |   |   | X | X | <b>19</b>       |
| Hepatodiaphragmatic Nodule            |             |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   | X |   |   |   | <b>3</b>        |
| Infarct                               |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 4.0</b>    |
| Infiltration Cellular, Mixed Cell     |             | 1 | 1 |   |   |   | 1 | 1 |   |   |   |   |   |   | 1 |   | 1 | 1 | 1 |   | 1 |   | 1 |   | <b>15 1.0</b>   |
| Mixed Cell Focus                      |             |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>5</b>        |
| Necrosis, Focal                       |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 2.0</b>    |
| Bile Duct, Hyperplasia                |             | 3 |   |   |   | 1 | 1 |   |   |   |   |   |   | 1 | 1 |   |   |   | 1 | 1 | 2 | 1 |   |   | <b>17 1.4</b>   |
| Hepatocyte, Vacuolization Cytoplasmic |             |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   | <b>4 2.3</b>    |
| Serosa, Fibrosis                      |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 4.0</b>    |
| Mesentery                             |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>+ 6</b>      |
| Accessory Spleen                      |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2</b>        |
| Fat, Necrosis                         |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>3 4 2.8</b>  |
| Pancreas                              |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>+ 50</b>     |
| Atrophy                               |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>30 1.6</b>   |
| Metaplasia, Hepatocyte                |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 2.0</b>    |
| Acinus, Hyperplasia, Focal            |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>9 2.0</b>    |
| Duct, Ectasia                         |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>27 1.7</b>   |
| Salivary Glands                       |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>+ 50</b>     |
| Atrophy                               |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>9 1.2</b>    |
| Hyperplasia, Lymphoid                 |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>    |
| Stomach, Forestomach                  |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>+ 50</b>     |
| Edema                                 |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>3 2.0</b>    |
| Ulcer                                 |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>3 3.3</b>    |
| Epithelium, Hyperplasia               |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>5 1.4</b>    |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
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 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Milk thistle extract  
 CAS Number: 84604-20-6

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                 |  |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|--|
|                              | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 |                 |  |
|                              | 1 | 3 | 3 | 1 | 3 | 7 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 |                 |  |
|                              | 1 | 1 | 0 | 4 | 0 | 6 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 6 | 9 | 9 | 9 | 9 | 9 | 8 | 2 | 2 | 2 | 1 |                 |  |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |  |
| ANIMAL ID                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |  |
| <b>50000 PPM</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |                 |  |
|                              | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 |                 |  |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | <b>* TOTALS</b> |  |

|                     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |              |  |  |  |           |              |  |
|---------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|--|--|--------------|--|--|--|-----------|--------------|--|
| Stomach, Glandular  | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |              |  |  |  | <b>50</b> |              |  |
| Edema               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |              |  |  |  |           | <b>1 2.0</b> |  |
| Erosion             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |              |  |  |  |           | <b>2 2.5</b> |  |
| Ulcer               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |              |  |  |  |           | <b>3 1.7</b> |  |
| Glands, Hyperplasia |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 |  |  | <b>1 4.0</b> |  |  |  |           |              |  |

CARDIOVASCULAR SYSTEM

|                    |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |               |              |  |              |
|--------------------|---|---|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|---|---|---|---|---------------|--------------|--|--------------|
| Blood Vessel       |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   | <b>2</b>      |              |  |              |
| Heart              | + |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   | <b>50</b>     |              |  |              |
| Cardiomyopathy     | 2 | 1 | 1 |  | 2 | 1 | 2 | 1 | 2 | 2 | 1 | 1 | 2 | 1 | 2 | 1 | 1 | 1 | 1 |  | 2 | 1 | 2 | 1 | <b>42 1.3</b> |              |  |              |
| Thrombosis         | 1 |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   |               | <b>2 2.5</b> |  |              |
| Valve, Hyperplasia |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |   |   |   |   | 1             |              |  | <b>3 1.7</b> |

ENDOCRINE SYSTEM

|                                   |   |  |  |   |  |   |   |   |  |  |  |   |   |   |   |   |  |   |  |  |  |   |   |   |               |              |  |              |
|-----------------------------------|---|--|--|---|--|---|---|---|--|--|--|---|---|---|---|---|--|---|--|--|--|---|---|---|---------------|--------------|--|--------------|
| Adrenal Cortex                    | + |  |  |   |  |   |   |   |  |  |  |   |   |   |   |   |  |   |  |  |  |   |   |   | <b>50</b>     |              |  |              |
| Accessory Adrenal Cortical Nodule |   |  |  | 1 |  | 1 | 2 | 1 |  |  |  |   | 1 | 1 |   | 1 |  |   |  |  |  |   | 4 |   | <b>16 1.4</b> |              |  |              |
| Degeneration, Fatty               |   |  |  | 2 |  | 2 | 1 |   |  |  |  |   |   |   | 1 |   |  |   |  |  |  | 2 |   |   | <b>15 1.5</b> |              |  |              |
| Hyperplasia, Focal                |   |  |  |   |  | 1 |   |   |  |  |  |   | 3 |   |   |   |  | 1 |  |  |  |   | 2 |   | <b>6 1.8</b>  |              |  |              |
| Hypertrophy, Focal                |   |  |  |   |  |   |   |   |  |  |  |   |   |   |   |   |  |   |  |  |  |   |   |   |               | <b>1 2.0</b> |  |              |
| Necrosis                          |   |  |  |   |  |   |   |   |  |  |  |   |   |   |   |   |  |   |  |  |  |   |   |   | 1             |              |  | <b>1 1.0</b> |
| Adrenal Medulla                   | + |  |  |   |  |   |   |   |  |  |  |   |   |   |   |   |  |   |  |  |  |   |   |   | <b>50</b>     |              |  |              |
| Hyperplasia                       | 3 |  |  |   |  | 1 | 3 |   |  |  |  | 2 | 3 | 1 | 1 |   |  | 2 |  |  |  |   |   | 3 | <b>15 2.1</b> |              |  |              |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue

M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

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TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                              | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 |                 |
|                              | 1 | 3 | 3 | 1 | 3 | 7 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                 |
|                              | 1 | 1 | 0 | 4 | 0 | 6 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 6 | 9 | 9 | 9 | 9 | 8 | 2 | 2 | 2 | 1 | 1 | 1 |                 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>50000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>ANIMAL ID</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |                 |
|                              | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |                 |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | <b>* TOTALS</b> |

Islets, Pancreatic + **50**

Parathyroid Gland + + + + + + + + + + M + **47**

Pituitary Gland + **50**

Pars Distalis, Cyst 2 3 **5 2.0**

Pars Distalis, Hyperplasia 4 **5 3.4**

Pars Distalis, Hyperplasia, Focal 3 2 1 4 2 1 1 2 **15 2.0**

Pars Intermedia, Cyst 2 2 **2 2.0**

Thyroid Gland + **49**

Degeneration, Cystic 1 1 1 **4 1.0**

Ultimobranchial Cyst 2 2 **4 1.5**

C-cell, Hyperplasia 3 1 1 2 1 2 1 3 **16 1.6**

**GENERAL BODY SYSTEM**

Tissue NOS 2

Inflammation, Chronic 1 **4.0**

**GENITAL SYSTEM**

Epididymis + **50**

Granuloma Sperm 4 **1 4.0**

Preputial Gland + **50**

Cyst 1 **3.0**

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 68



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|
|                              | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7               | 7 |
|                              | 1 | 3 | 3 | 1 | 3 | 7 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3               | 3 |
|                              | 1 | 1 | 0 | 4 | 0 | 6 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 6 | 9 | 9 | 9 | 9 | 9 | 8 | 2 | 2 | 2               | 1 |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
| <b>50000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |
| ANIMAL ID                    | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               | 2 |
|                              | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9               | 0 |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8               | 9 |
|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |   |

|                                  |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |              |
|----------------------------------|---|---|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|--------------|
| Ectasia                          |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b> |              |
| Hemorrhage                       |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1            | <b>3 1.0</b> |
| Hyperplasia, Lymphoid            | 1 | 2 |   |  | 2 |   | 3 |   | 2 |   |   |   |   | 2 |   | 2 |   |   | 2 | 2 |   |   | 2 | 2 |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |              |
| Hyperplasia, Reticulum Cell      |   | 3 |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |              |
| Pigmentation                     |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | 1 | 1 |   |   |   |   |   |   | 1 |   |   |   | 1 |   |   |   |   | <b>9 1.0</b> |              |
| Spleen                           |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + | + | + | + | +             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>    |              |
| Fibrosis                         |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |              | <b>2 2.5</b> |
| Hematopoietic Cell Proliferation |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |              | <b>2 1.5</b> |
| Necrosis                         |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 3.0</b> |
| Pigmentation                     |   | 3 | 2 |  |   | 3 | 2 | 3 | 3 | 3 | 2 | 3 | 2 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 3 | 1 | 2 | 3 | 1 | <b>45 2.2</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |              |
| Lymphoid Follicle, Hyperplasia   |   | 2 |   |  |   |   |   |   |   |   |   |   |   |   | 1 | 2 |   |   |   |   |   | 3 |   | 2 | 2 |   | <b>7 1.9</b>  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |              |
| Thymus                           |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + | + | + | + | +             |   | + |   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +            | <b>42</b>    |

**INTEGUMENTARY SYSTEM**

|                           |   |  |   |   |  |   |   |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |           |              |
|---------------------------|---|--|---|---|--|---|---|--|--|--|--|--|---|--|--|--|---|--|--|--|--|--|---|---|---|---------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|-----------|--------------|
| Mammary Gland             |   |  |   |   |  |   |   |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  | + | + | + | +             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>49</b> |           |              |
| Fibrosis                  |   |  |   |   |  |   |   |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |           | <b>1 3.0</b> |
| Hyperplasia               | 1 |  | 1 | 2 |  | 1 |   |  |  |  |  |  |   |  |  |  | 2 |  |  |  |  |  |   | 2 |   | <b>13 1.7</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |           |              |
| Duct, Ectasia             |   |  |   | 4 |  |   | 4 |  |  |  |  |  | 4 |  |  |  |   |  |  |  |  |  |   | 4 |   | <b>14 2.7</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |           |              |
| Skin                      |   |  |   |   |  |   |   |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  | + | + | + | +             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +         | <b>50</b> |              |
| Cyst Epithelial Inclusion |   |  |   |   |  |   |   |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |   |   |               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |           | <b>2</b>     |

**MUSCULOSKELETAL SYSTEM**

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue

M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

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| DAY ON TEST                  | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|                              | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 |          |
|                              | 1 | 3 | 3 | 1 | 3 | 7 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3        |
|                              | 1 | 1 | 0 | 4 | 0 | 6 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 6 | 9 | 9 | 9 | 9 | 9 | 8 | 2 | 2 | 2 | 1 | 1        |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |
| <b>50000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |
| <b>ANIMAL ID</b>             | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2        |
|                              | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0        |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0        |

Bone + 50

**NERVOUS SYSTEM**

|                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Brain                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Compression                |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   | 6 3.2  |
| Developmental Malformation |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0  |
| Gliosis, Focal             |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |
| Hemorrhage                 | 1 | 1 | 1 |   | 1 |   |   | 1 |   |   | 1 | 1 | 1 |   |   |   |   |   |   |   | 1 |   |   |   | 13 1.0 |
| Peripheral Nerve           |   |   |   |   |   |   |   |   |   |   | + | + |   |   |   |   | + |   |   |   |   |   |   |   | 5      |
| Spinal Cord                |   |   |   |   |   |   |   |   |   |   | + | + |   |   |   |   | + |   |   |   |   |   |   |   | 5      |

**RESPIRATORY SYSTEM**

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Lung                                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Infiltration Cellular, Histiocyte   | 1 | 1 |   | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 |   | 1 | 1 |   |   |   | 1 |   |   | 1 | 1 | 1 | 39 1.1 |
| Inflammation, Chronic               |   |   |   |   |   |   |   |   |   |   | 1 | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   | 6 1.2  |
| Metaplasia, Osseous                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   | 1 |   |   |   | 4 1.3  |
| Alveolar Epithelium, Hyperplasia    | 1 |   |   |   | 2 | 1 |   |   |   |   | 1 |   | 4 |   |   |   |   |   | 1 |   | 1 | 1 |   |   | 13 1.5 |
| Nose                                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Foreign Body                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1 | 5 1.2  |
| Inflammation, Chronic               |   |   |   |   | 1 |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   | 9 1.2  |
| Goblet Cell, Hyperplasia            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |
| Respiratory Epithelium, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                  | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|                              | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 |          |
|                              | 1 | 3 | 3 | 1 | 3 | 7 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 |          |
|                              | 1 | 1 | 0 | 4 | 0 | 6 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 6 | 9 | 9 | 9 | 9 | 9 | 8 | 2 | 2 | 2 | 1 |          |
| <b>FISCHER 344 RATS MALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| <b>50000 PPM</b>             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| ANIMAL ID                    | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |          |
|                              | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |          |
|                              | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0        |

Trachea + 50

**SPECIAL SENSES SYSTEM**

|                       |   |         |        |
|-----------------------|---|---------|--------|
| Eye                   | + | 49      |        |
| Cataract              | 1   |         | 20 1.6 |
| Edema                 |   | 4       | 3 3.7  |
| Bilateral, Cataract   |   | 4       | 6 1.7  |
| Retina, Degeneration  |   | 4 4 1 4 | 5 2.8  |
| Harderian Gland       | + | 50      |        |
| Hyperplasia, Focal    |   | 4       | 3 2.3  |
| Inflammation, Chronic |   | 1 1 1   | 4 1.0  |
| Zymbal's Gland        |   |         | 1      |

**URINARY SYSTEM**

|                                      |   |   |        |
|--------------------------------------|---|---|--------|
| Kidney                               | + | 50  |        |
| Inflammation, Suppurative            |   | 1   | 2 1.0  |
| Metaplasia, Osseous                  |   |   | 1 2.0  |
| Mineralization                       | 1   | 1 1 1 1                                       | 20 1.1 |
| Nephropathy                          |   | 1 1 1 1 1 1 2 2 2 2 1 1 2 1 1 1 2 2 1 1 2 1 1 | 46 1.4 |
| Renal Tubule, Dilatation             |   | 2   | 1 2.0  |
| Transitional Epithelium, Hyperplasia | 1 1   | 1 1 1 1 1 1 1 1 1 1 1 1 1 1                   | 18 1.2 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL  
 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

| DAY ON TEST           |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |           |   |
|-----------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|-----------|---|
| ANIMAL ID             |  | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7               | 7 | 7         |   |
| 50000 PPM             |  | 1 | 3 | 3 | 1 | 3 | 7 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3               | 3 | 3         |   |
|                       |  | 1 | 1 | 0 | 4 | 0 | 6 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 6 | 9 | 9 | 9 | 9 | 9 | 8 | 2 | 2               | 2 | 1         | 1 |
| FISCHER 344 RATS MALE |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 | 0         |   |
| ANIMAL ID             |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 | 0         |   |
| 50000 PPM             |  | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1               | 1 | 1         |   |
|                       |  | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9               | 9 | 0         |   |
|                       |  | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7               | 8 | 9         |   |
|                       |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |   |           |   |
| Urinary Bladder       |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +               | + | <b>50</b> |   |

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

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
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TDMS No. 20008 - 03

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                          |   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                      |   | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 |   |
| FISCHER 344 RATS FEMALE<br>ANIMAL ID |   | 3 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |   |
|                                      |   | 5 | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |
| <b>0 PPM</b>                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|                                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|                                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |
|                                      | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females (cont...)

ALIMENTARY SYSTEM

|                                       |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------------|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus                             | +       |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Cecum                | + + + + + A + + + + + + + + + + + + + + + A + + + + + |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Colon                | + + + + + A + + + + + + + + + + + + + + + A + + + + + |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Rectum               | + + + + + A + + + + + + + + + + + + + + + A + + + + + |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Duodenum             | + + + + + A + + + + + + + + + + + + + + + A + + + + + |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Ileum                | + + + + + A + + + + + + + + + + + + + + + A + + M + + |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Jejunum              | + + + + + A + + + + + + + + + + + + + + + A + + + + + |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Liver                                 | + |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Angiectasis                           |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Basophilic Focus                      | X   |  | X | X | X |   | X | X | X | X |   | X | X | X | X | X | X | X | X |   | X | X |   | X | X |
| Clear Cell Focus                      |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Eosinophilic Focus                    |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hepatodiaphragmatic Nodule            |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infiltration Cellular, Mixed Cell     | 1   |  | 2 |   | 1 |   | 2 | 1 | 1 | 1 |   | 1 |   | 1 | 2 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 |
| Mixed Cell Focus                      |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Necrosis, Focal                       | 1   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bile Duct, Hyperplasia                | 1   |  | 1 | 1 | 1 | 2 |   | 2 | 2 |   | 1 |   | 2 | 1 | 1 | 2 |   |   |   | 1 | 1 | 3 | 1 | 1 |   |
| Hepatocyte, Vacuolization Cytoplasmic | 2 4 3 3   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

l .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 |   |
|                                | 3 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |
|                                | 5 | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>0 PPM</b>                   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 |

females (cont...)

|   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Serosa, Fibrosis                        |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mesentery                               |  | + | + |   |   | + |   |   |   |   |   |   | + |   |   |   |   |   | + |   | + |   |   |   |
| Accessory Spleen                        |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Fat, Necrosis                           |  |   |   | 2 |   |   | 1 |   |   |   |   |   | 2 |   |   |   |   |   | 2 |   | 1 |   |   |   |
| Pancreas                                |  | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Atrophy                                 |  | 1 | 1 | 2 | 2 | 1 |   |   |   |   |   | 2 | 1 | 1 | 1 |   |   |   | 2 |   |   | 1 |   |   |
| Metaplasia, Hepatocyte                  |  |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Acinus, Hyperplasia, Focal              |  |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Duct, Ectasia                           |  | 3 | 1 | 1 |   |   |   | 1 |   |   | 1 |   | 1 |   | 1 | 3 |   |   |   |   | 1 |   |   |   |
| Salivary Glands                         |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Angiectasis                             |  |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Atrophy                                 |  |   | 1 |   |   | 1 |   |   |   |   |   |   |   |   | 1 | 1 |   |   | 1 |   |   |   |   | 1 |
| Infiltration Cellular                   |  |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Stomach, Forestomach                    |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Edema                                   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Erosion                                 |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                                   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Epithelium, Hyperplasia                 |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Stomach, Glandular                      |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Erosion                                 |  |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 1 |
| Infiltration Cellular, Mononuclear Cell |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                                   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                                 | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
|   | 7   | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 |  |
|   | 3   | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |  |
|   | 5   | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |  |
| <b>FISCHER 344 RATS FEMALE</b><br>ANIMAL ID | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |  |
|   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |  |
|   | 2   | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |  |
|   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |  |
|   | 1   | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 |  |

females (cont...)

**CARDIOVASCULAR SYSTEM**

|                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Heart              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cardiomyopathy     |   |   | 1 |   | 1 |   | 2 | 1 | 1 | 1 |   | 1 | 1 |   | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 |   |
| Valve, Hyperplasia |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**ENDOCRINE SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                    | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Accessory Adrenal Cortical Nodule |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Degeneration, Fatty               |   | 3 |   |   |   |   |   |   |   | 1 |   |   | 1 | 2 | 1 |   | 1 | 1 | 1 | 2 |   | 2 | 3 |
| Fibrosis                          |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Focal                | 1 |   | 2 |   | 1 |   | 2 |   | 2 | 1 |   | 1 |   | 3 | 2 | 1 |   |   |   | 2 |   |   | 4 |
| Hypertrophy, Focal                |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   |   |   |   |   |   |   |   |   |
| Necrosis                          |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla                   | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                       | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |
| Bilateral, Hyperplasia            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Islets, Pancreatic                | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars Distalis, Angiectasis        |   | 3 |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 | 2 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                    | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7   | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 |   |
|                                | 3   | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |   |
|                                | 5   | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>0 PPM</b>                   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                      | 2   | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                | 1   | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females (cont...)

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pars Distalis, Cyst               |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 1 | 2 |   |   | 2 | 2 | 2 |   |   |   |
| Pars Distalis, Hyperplasia        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Hyperplasia, Focal |   | 1 |   |   | 2 |   |   | 2 |   |   |   |   | 2 |   | 1 | 1 |   |   |   | 2 |   |   |   | 4 |
| Pars Distalis, Hypertrophy        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Intermedia, Angiectasis      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Intermedia, Cyst             |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |
| Rathke's Cleft, Hemorrhage        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thyroid Gland                     | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + |
| Degeneration, Cystic              |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ultimobranchial Cyst              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| C-cell, Hyperplasia               | 1 |   | 1 | 2 |   |   |   |   | 1 | 1 | 2 |   |   |   | 2 |   | 4 |   |   |   |   |   |   | 3 |

**GENERAL BODY SYSTEM**

NONE

**GENITAL SYSTEM**

|                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clitoral Gland              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Abscess                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia                 |   |   | 2 |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |
| Inflammation, Acute         |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic       | 1 |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 4 |   |
| Ovary                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst                        |   |   |   | 4 |   |   |   | 3 | 3 |   | 2 |   |   |   | 2 |   |   |   |   |   | 2 |   |   |   |
| Granulosa Cell, Hyperplasia |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

| DAY ON TEST                    |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DAY ON TEST                    |           | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 | 7 |   |
| DAY ON TEST                    |           | 3 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |   |
| DAY ON TEST                    |           | 5 | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |   |
| <b>FISCHER 344 RATS FEMALE</b> | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|                                | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|                                | ANIMAL ID | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |   |
|                                | ANIMAL ID | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 |   |

females (cont...)

|                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Uterus              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Cystic | 1 | 2 |   |   | 1 |   | 3 | 1 |   | 1 |   |   | 1 |   | 1 | 2 | 1 | 2 |   |   |   | 1 | 1 |   |
| Vagina              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + |

**HEMATOPOIETIC SYSTEM**

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow                                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + |
| Hyperplasia                                    |   |   |   | 4 |   |   |   |   |   |   |   | 1 |   | 4 |   |   |   |   |   |   |   |   |   |   |   |
| Lymph Node                                     |   |   | + |   |   | + |   |   |   |   |   |   |   | + |   |   |   |   |   |   | + |   |   |   | + |
| Mediastinal, Hemorrhage                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Mediastinal, Hyperplasia, Lymphoid             |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 2 |
| Mediastinal, Infiltration Cellular, Histiocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mediastinal, Pigmentation                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   | 3 |
| Pancreatic, Ectasia                            |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pancreatic, Hemorrhage                         |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pancreatic, Pigmentation                       |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lymph Node, Mandibular                         | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M |
| Lymph Node, Mesenteric                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Ectasia  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Fibrosis                                       |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 1 |
| Hyperplasia, Lymphoid                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pigmentation                                   | 2 | 1 |   | 1 | 2 | 1 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 2 | 1 | 2 | 1 | 2 | 2 | 1 | 1 | 1 | 2 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

| DAY ON TEST                    | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
|                                | 7   | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 |  |
|                                | 3   | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |  |
|                                | 5   | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |  |
| <b>FISCHER 344 RATS FEMALE</b> | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |  |
| <b>0 PPM</b>                   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |  |
| <b>ANIMAL ID</b>               | 2   | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |  |
|                                | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |   |  |
|                                | 1   | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 |   |  |

females (cont...)

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Spleen                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hematopoietic Cell Proliferation |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 2 |   |   | 3 | 1 |   |   |   |   |   |
| Hyperplasia, Focal               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |
| Necrosis                         |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pigmentation                     | 4 |   | 4 |   | 3 |   | 3 | 4 | 4 | 4 | 2 | 2 | 3 | 2 | 3 | 4 | 3 | 3 | 4 |   | 4 | 3 | 1 |
| Lymphoid Follicle, Atrophy       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 | 2 |
| Lymphoid Follicle, Hyperplasia   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thymus                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage                       | 2 |   |   |   |   |   | 1 |   | 1 | 1 |   |   | 1 |   |   | 1 |   | 1 |   |   | 1 |   | 2 |

**INTEGUMENTARY SYSTEM**

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia               | 1 |   |   | 4 |   |   |   |   |   |   |   | 2 |   |   | 1 | 2 | 1 |   |   |   |   | 3 |   |
| Hyperplasia, Focal        |   |   |   | 2 |   | 1 | 1 | 2 |   |   | 3 |   |   |   | 1 | 2 |   | 1 |   | 1 |   |   | 1 |
| Duct, Ectasia             | 2 |   | 1 | 3 | 1 | 2 | 3 | 2 | 4 | 1 |   | 3 | 1 | 1 | 3 |   | 3 | 3 | 3 | 2 | 2 | 3 | 3 |
| Duct, Hyperplasia         |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Skin                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst Epithelial Inclusion |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperkeratosis            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |
| Epidermis, Hyperplasia    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |

**MUSCULOSKELETAL SYSTEM**

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Femur, Osteopetrosis |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|             | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 |   |
|             | 3 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |   |
|             | 5 | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |   |

  

| FISCHER 344 RATS FEMALE | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                              |
|-------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------------------------------|
| ANIMAL ID               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                              |
| 0 PPM                   | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |                              |
|                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |   |                              |
|                         | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |                              |
|                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>females<br/>(cont...)</b> |

Skeletal Muscle

+

NERVOUS SYSTEM

Brain

  Compression

  Hemorrhage

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |
|  |   |   |   |   |   |   |   | 1 |   |   |   | 1 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |

Spinal Cord

+

RESPIRATORY SYSTEM

Lung

  Hemorrhage

  Infiltration Cellular, Histiocyte

  Inflammation, Chronic

  Metaplasia, Osseous

  Alveolar Epithelium, Hyperplasia

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|  | 1 | 1 | 1 | 1 | 1 |   |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 |   |
|  |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |
|  | 1 | 1 | 1 |   |   |   |   | 2 | 1 |   |   | 2 | 1 | 1 | 1 |   |   | 2 |   |   | 1 | 3 |   | 2 |   |

Nose

  Inflammation, Chronic

  Goblet Cell, Hyperplasia

  Respiratory Epithelium, Hyperplasia

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|  |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   | 1 |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Trachea

  Inflammation, Acute

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 3 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 6 | 7 | 7 |
|                                | 3 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 8 | 3 | 3 |
|                                | 5 | 7 | 5 | 5 | 5 | 7 | 2 | 2 | 2 | 2 | 2 | 6 | 6 | 6 | 6 | 5 | 0 | 5 | 5 | 4 | 2 | 2 | 7 | 2 |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>0 PPM</b>                   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 |
|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

females (cont...)

**SPECIAL SENSES SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye                   | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Edema                 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Retina, Degeneration  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |
| Harderian Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Focal    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic | 1 |   |   |   |   |   |   | 1 | 1 | 1 |   |   | 1 |   | 1 |   |   |   |   |   |   |   |   |   |

**URINARY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney                                      | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Casts Granular                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Cyst  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |
| Inflammation, Chronic Active                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineralization                              |   |   | 1 | 1 |   |   |   | 1 | 1 | 1 |   | 1 | 1 |   |   | 1 | 1 |   |   | 1 | 1 |   | 1 |   |
| Necrosis                                    |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Nephropathy                                 | 1 | 2 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 |   | 2 | 1 | 1 | 1 | 1 |   |
| Vacuolization Cytoplasmic                   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal Tubule, Accumulation, Hyaline Droplet |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Urinary Bladder                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

Page 81

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |  |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|--|
|                                | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 2               |  |
|                                | 3 | 3 | 3 | 3 | 3 | 6 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 1 | 3 | 3 | 2 | 3 | 3 | 0 |                 |  |
|                                | 5 | 5 | 5 | 5 | 5 | 0 | 3 | 2 | 2 | 2 | 5 | 5 | 5 | 5 | 5 | 5 | 8 | 5 | 5 | 5 | 5 | 5 | 0 |   |                 |  |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |  |
| <b>0 PPM</b>                   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |  |
| ANIMAL ID                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |                 |  |
|                                | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |                 |  |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | <b>* TOTALS</b> |  |

**ALIMENTARY SYSTEM**

|                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |     |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|-----|
| Esophagus                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Intestine Large, Cecum                | + | + | + | + | + | A | + | + | + | + | + | M | + | + | A | + | M | + | + | + | + | + | + | A | 43 |    |     |     |
| Intestine Large, Colon                | + | + | + | + | + | A | A | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | A | 44 |    |     |     |
| Intestine Large, Rectum               | + | + | + | + | + | A | A | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | A | 44 |    |     |     |
| Intestine Small, Duodenum             | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | 46 |    |     |     |
| Intestine Small, Ileum                | + | + | M | + | + | + | A | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | M | A  | 42 |     |     |
| Intestine Small, Jejunum              | + | + | + | + | + | A | A | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | A | 44 |    |     |     |
| Liver                                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Angiectasis                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 1  | 2.0 |     |
| Basophilic Focus                      | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |    | 44 |     |     |
| Clear Cell Focus                      | X |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   | X |   |   |   |   | X |   |   |    | 9  |     |     |
| Eosinophilic Focus                    |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   | X |   |   |   |   |   |   |    | 5  |     |     |
| Hepatodiaphragmatic Nodule            |   |   |   |   | X |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |    | 6  |     |     |
| Infiltration Cellular, Mixed Cell     | 1 | 1 | 2 | 2 | 1 | 2 |   | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 |   | 1 |   | 1 | 1 |   | 1 | 1 | 1 |    | 37 | 1.2 |     |
| Mixed Cell Focus                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |    |    | 3   |     |
| Necrosis, Focal                       |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |    |    | 3   | 1.0 |
| Bile Duct, Hyperplasia                | 1 | 1 | 2 | 1 | 1 |   |   | 1 | 1 | 1 |   | 1 |   | 1 | 2 | 2 | 1 | 2 | 2 | 1 | 3 | 1 | 1 | 1 |    | 37 | 1.4 |     |
| Hepatocyte, Vacuolization Cytoplasmic |   |   |   | 2 |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   | 2 |   |   |    |    | 8   | 2.4 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                             | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |                 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|   | 7   | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 2 | 2 |   |                 |
|   | 3   | 3 | 3 | 3 | 3 | 6 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 1 | 3 | 3 | 2 | 3 | 3 | 0 |   |                 |
|   | 5   | 5 | 5 | 5 | 5 | 0 | 3 | 2 | 2 | 2 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 8 | 5 | 5 | 5 | 5 | 5 | 0 | 0 |   |                 |
| <b>FISCHER 344 RATS FEMALE</b>          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| <b>0 PPM</b>                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| ANIMAL ID                               | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|   | 2   | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2               |
|   | 2   | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5 | 5               |
|   | 6   | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 0 | 0               |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |
| Serosa, Fibrosis                        | 1   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0           |
| Mesentery                               | +   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 10              |
| Accessory Spleen                        | X   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1               |
| Fat, Necrosis                           | 3 1 2   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 8 1.8           |
| Pancreas                                | + + + + + + A + + + + + + + + + + + + + + + + + + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 48              |
| Atrophy                                 | 1 1 2 1 2 1                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 23 1.4          |
| Metaplasia, Hepatocyte                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0           |
| Acinus, Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 1.5           |
| Duct, Ectasia                           | 1 1 1 2 1   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 14 1.4          |
| Salivary Glands                         | +   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 50              |
| Angiectasis                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0           |
| Atrophy                                 | 2   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 12 1.2          |
| Infiltration Cellular                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0           |
| Stomach, Forestomach                    | + + + + + + A + + + + + + + + + + + + + + + + + + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 49              |
| Edema                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0           |
| Erosion                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0           |
| Ulcer                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 4.0           |
| Epithelium, Hyperplasia                 | 2 2   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 2.0           |
| Stomach, Glandular                      | + + + + + + A + + + + + + + + + + + + + + + + + + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 49              |
| Erosion                                 | 1   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 7 1.6           |
| Infiltration Cellular, Mononuclear Cell | 1   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0           |
| Ulcer                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 1.5           |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                    | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |   |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|---|---|
|                                | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 6 | 7 | 7 | 7 |          | 7 | 2 |
|                                | 3 | 3 | 3 | 3 | 3 | 6 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 1 | 3 | 3 | 2 | 3        | 3 | 0 |
|                                | 5 | 5 | 5 | 5 | 5 | 0 | 3 | 2 | 2 | 2 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 8 | 5 | 5 | 5 | 5 | 5        | 0 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        | 0 | 0 |
| ANIMAL ID                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        | 0 | 0 |
| <b>0 PPM</b>                   | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2        | 2 | 2 |
|                                | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4        | 5 | 5 |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0        | 0 | 0 |

**CARDIOVASCULAR SYSTEM**

|                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |
|--------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|
| Heart              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50  |
| Cardiomyopathy     | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 |   |   | 1 | 1 | 1 |   | 1 | 1 | 1 |   |   |   |   |   | 1 | 1 |   |   | 32  |
| Valve, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1.1 |
|                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2.0 |

**ENDOCRINE SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| Adrenal Cortex                    | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Accessory Adrenal Cortical Nodule |   |   | 1 |   |   | 2 |   |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   |   | 1 | 1 |   |   |   |   | 7  |
| Degeneration, Fatty               |   |   |   |   | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   | 2 | 2 |   | 2 |   |   |   |   |   |   | 16 |
| Fibrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Hyperplasia, Focal                | 1 | 2 | 2 |   | 1 |   |   | 2 |   |   |   |   | 1 | 1 |   |   |   |   |   | 1 |   |   |   | 3 |   |   |   | 21 |
| Hypertrophy, Focal                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  |
| Necrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Adrenal Medulla                   | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3  |
| Bilateral, Hyperplasia            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Islets, Pancreatic                | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pituitary Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pars Distalis, Angiectasis        | 2 |   |   | 3 |   | 4 | 4 |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   | 4 |   |   | 10 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

|                                   | DAY ON TEST      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | * TOTALS |                  |                  |     |     |     |
|-----------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|----------|------------------|------------------|-----|-----|-----|
|                                   | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>6<br>6<br>0 | 0<br>6<br>2<br>3 | 0<br>7<br>3<br>2 | 0<br>7<br>3<br>2 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>5<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>6<br>1<br>8 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>2<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 |          | 0<br>7<br>3<br>5 | 0<br>2<br>0<br>0 |     |     |     |
| <b>FISCHER 344 RATS FEMALE</b>    | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0        | 0                | 0                | 0   |     |     |
| 0 PPM                             | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0        | 0                | 0                | 0   |     |     |
| ANIMAL ID                         | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2        | 2                | 2                | 2   |     |     |
|                                   | 2                | 2                | 2                | 2                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 3                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4                | 4        | 4                | 4                | 5   |     |     |
|                                   | 6                | 7                | 8                | 9                | 0                | 1                | 2                | 3                | 4                | 5                | 6                | 7                | 8                | 9                | 0                | 1                | 2                | 3                | 4                | 5                | 6                | 7                | 8                | 9                | 0        |                  |                  |     |     |     |
| Pars Distalis, Cyst               |                  | 1                | 4                |                  |                  | 1                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  | 1                |                  | 4                |                  |                  |          |                  | 12               | 1.9 |     |     |
| Pars Distalis, Hyperplasia        |                  |                  |                  |                  |                  |                  | 3                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |          |                  |                  | 1   | 3.0 |     |
| Pars Distalis, Hyperplasia, Focal |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  |                  | 3                | 2                |                  |          |                  |                  | 12  | 2.0 |     |
| Pars Distalis, Hypertrophy        |                  |                  |                  |                  |                  |                  | 3                |                  |                  |                  |                  |                  |                  |                  |                  | 3                |                  |                  |                  |                  |                  |                  |                  |                  |          |                  |                  | 2   | 3.0 |     |
| Pars Intermedia, Angiectasis      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 3                |                  |                  |                  |                  |                  |                  |                  |                  |                  |          |                  |                  | 1   | 3.0 |     |
| Pars Intermedia, Cyst             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |          |                  |                  | 2   | 1.5 |     |
| Rathke's Cleft, Hemorrhage        |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |          |                  |                  | 2   | 2.0 |     |
| Thyroid Gland                     | +                | +                | +                | +                | +                | +                | A                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +        | +                | +                | 47  |     |     |
| Degeneration, Cystic              |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |          |                  |                  |     | 2   | 1.0 |
| Ultimobranchial Cyst              |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |          |                  |                  |     | 1   | 2.0 |
| C-cell, Hyperplasia               |                  |                  | 1                | 1                |                  | 1                |                  |                  | 1                |                  |                  |                  | 3                |                  | 2                |                  |                  |                  |                  |                  |                  | 4                | 2                |                  | 1        |                  |                  |     | 18  | 1.8 |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

|                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |
|-----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|
| Clitoral Gland              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |
| Abscess                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 |     |
| Hyperplasia                 |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   | 4 |   |   |   |   |   |    | 7 | 2.6 |
| Inflammation, Acute         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 1.0 |
| Inflammation, Chronic       |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 5 | 2.6 |
| Ovary                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |
| Cyst                        |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   | 2 | 2 |   |   |   |   |   |   |   |   |    | 9 | 2.4 |
| Granulosa Cell, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 1.0 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | * TOTALS |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|                                | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 2 |          |
|                                | 3 | 3 | 3 | 3 | 3 | 6 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 1 | 3 | 3 | 2 | 3 | 3 | 0 |   |          |
|                                | 5 | 5 | 5 | 5 | 5 | 0 | 3 | 2 | 2 | 2 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 8 | 5 | 5 | 5 | 5 | 5 | 0 |   |   |          |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |          |
| <b>0 PPM</b>                   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |          |
| <b>ANIMAL ID</b>               | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |          |
|                                | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |   |   |          |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |   |          |

|                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|---------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Uterus              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Hyperplasia, Cystic | 1 | 1 |   |   |   | 1 | 4 |   | 1 | 3 | 2 | 3 |   | 2 | 1 | 1 | 4 | 4 | 2 | 3 | 1 | 2 | 1 | 4 |   | 32 1.8 |
| Vagina              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2      |

**HEMATOPOIETIC SYSTEM**

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Bone Marrow                                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49     |
| Hyperplasia                                    |   |   |   |   |   | 4 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 5 3.0  |
| Lymph Node                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 9      |
| Mediastinal, Hemorrhage                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.5  |
| Mediastinal, Hyperplasia, Lymphoid             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 2.3  |
| Mediastinal, Infiltration Cellular, Histiocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 3.0  |
| Mediastinal, Pigmentation                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 2.8  |
| Pancreatic, Ectasia                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 3.0  |
| Pancreatic, Hemorrhage                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |
| Pancreatic, Pigmentation                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |
| Lymph Node, Mandibular                         | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 1      |
| Lymph Node, Mesenteric                         | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49     |
| Ectasia  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0  |
| Fibrosis                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |
| Hemorrhage                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0  |
| Hyperplasia, Lymphoid                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0  |
| Pigmentation                                   | 2 | 2 | 2 | 2 | 1 | 1 |   | 2 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | 2 | 1 | 2 | 1 | 2 | 1 |   | 2 | 1 | 1 | 47 1.5 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

|                                  | DAY ON TEST |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |
|----------------------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|                                  | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| <b>FISCHER 344 RATS FEMALE</b>   | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| <b>0 PPM</b>                     | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| <b>ANIMAL ID</b>                 | 2           | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |          |
|                                  | 2           | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |          |
|                                  | 6           | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |          |
| Spleen                           | +           | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49       |
| Hematopoietic Cell Proliferation |             |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   | 5 1.8    |
| Hyperplasia, Focal               |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0    |
| Necrosis                         |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0    |
| Pigmentation                     | 3           | 4 | 4 | 2 | 4 | 4 |   | 4 | 2 | 4 | 4 | 3 | 4 | 4 | 3 | 4 | 2 | 3 | 4 | 2 | 1 |   | 4 | 3 | 43 3.2   |
| Lymphoid Follicle, Atrophy       |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   | 1 2.0    |
| Lymphoid Follicle, Hyperplasia   |             |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 1.5    |
| Thymus                           | +           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50       |
| Hemorrhage                       |             | 1 |   |   | 1 |   |   |   |   |   |   | 1 | 1 |   | 1 | 3 |   |   |   |   |   |   | 1 |   | 17 1.2   |
| <b>INTEGUMENTARY SYSTEM</b>      |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |
| Mammary Gland                    | +           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50       |
| Hyperplasia                      | 2           |   |   | 1 |   |   | 2 | 4 | 2 |   |   |   | 2 | 2 | 1 | 2 |   | 3 | 3 | 3 | 2 |   |   |   | 20 2.2   |
| Hyperplasia, Focal               | 2           |   |   | 1 | 1 |   |   | 2 | 2 |   |   |   | 2 |   | 1 | 2 |   |   | 1 | 2 |   |   |   |   | 20 1.6   |
| Duct, Ectasia                    | 2           | 2 | 3 | 3 | 2 | 2 | 1 | 3 | 2 | 3 | 2 | 2 | 2 | 1 | 3 | 2 | 2 | 2 | 3 | 3 |   | 2 |   | 2 | 44 2.2   |
| Duct, Hyperplasia                |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0    |
| Skin                             | +           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50       |
| Cyst Epithelial Inclusion        | X           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1        |
| Hyperkeratosis                   |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0    |
| Epidermis, Hyperplasia           |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0    |
| <b>MUSCULOSKELETAL SYSTEM</b>    |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |
| Bone                             | +           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50       |
| Femur, Osteopetrosis             |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0    |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 6 | 7 | 7 | 7 | 7 |
|                                | 3 | 3 | 3 | 3 | 3 | 6 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 1 | 3 | 3 | 2 | 3 |
|                                | 5 | 5 | 5 | 5 | 5 | 0 | 3 | 2 | 2 | 2 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 8 | 5 | 5 | 5 | 5 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>0 PPM</b>                   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>ANIMAL ID</b>               | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |   |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |   |
| <b>* TOTALS</b>                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Skeletal Muscle

1

### NERVOUS SYSTEM

Brain

+ + + + + + + + 4 + + + + + + + + + + + + + + + + 50

Compression

4

2

4

1

5 3.0

Hemorrhage

1

4 1.0

Spinal Cord

1

### RESPIRATORY SYSTEM

Lung

+ 50

Hemorrhage

2

1

1

3 1.3

Infiltration Cellular, Histiocyte

1 1 1 1 1 1 1 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1

45 1.0

Inflammation, Chronic

1 1.0

Metaplasia, Osseous

1 1.0

Alveolar Epithelium, Hyperplasia

1 3 1 1 1 1 1 1 2 1 1 2 1 1 2

25 1.4

Nose

+ 50

Inflammation, Chronic

1

2

2

2

7 1.6

Goblet Cell, Hyperplasia

1

1 1.0

Respiratory Epithelium, Hyperplasia

2

2 1.5

Trachea

+ 50

Inflammation, Acute

1

1 1.0

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                                | 7 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 2 |                 |
|                                | 3 | 3 | 3 | 3 | 3 | 6 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 1 | 3 | 3 | 2 | 3 | 3 |                 |
|                                | 5 | 5 | 5 | 5 | 5 | 0 | 3 | 2 | 2 | 2 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 8 | 5 | 5 | 5 | 5 | 5 | 0 |                 |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>0 PPM</b>                   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>ANIMAL ID</b>               | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |                 |
|                                | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |                 |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0               |
|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |

**SPECIAL SENSES SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Eye                   | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48     |
| Edema                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |
| Retina, Degeneration  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |
| Harderian Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Hyperplasia, Focal    |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0  |
| Inflammation, Chronic |   |   |   |   |   |   | 1 |   |   | 1 | 1 |   |   | 1 |   | 1 |   |   |   |   |   |   |   | 1 | 12 1.0 |

**URINARY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |        |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|--------|
| Kidney                                      | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48     |        |
| Casts Granular                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 3.0  |
| Cyst  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0  |
| Inflammation, Chronic Active                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 4.0  |
| Mineralization                              |   |   |   |   |   |   |   |   |   |   | 1 | 1 |   |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |   |   | 21 1.0 |        |
| Necrosis                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 1.0  |
| Nephropathy                                 | 1 | 1 | 1 | 3 | 1 |   |   | 1 |   |   |   | 1 | 1 | 1 | 1 | 2 |   | 2 |   |   |   | 1 |   | 1 | 1      | 36 1.2 |
| Vacuolization Cytoplasmic                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |        | 2 1.5  |
| Renal Tubule, Accumulation, Hyaline Droplet |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |        | 1 3.0  |
| Transitional Epithelium, Hyperplasia        |   |   |   |   | 3 |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |        | 3 2.0  |
| Urinary Bladder                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +      | 50     |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
l .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked  
Page 89

| DAY ON TEST                    | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 5 | 7 | 7 | 7 | 7 | 7 | 5 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 |
| 9                              | 3 | 3 | 3 | 3 | 2 | 9 | 7 | 3 | 3 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 |   |
| 2                              | 6 | 6 | 6 | 6 | 5 | 9 | 2 | 7 | 2 | 2 | 9 | 6 | 6 | 6 | 5 | 5 | 5 | 5 | 5 | 0 | 2 | 2 | 2 | 2 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>12500 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |   |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females (cont...)

**ALIMENTARY SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus                         | +         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Cecum            | + + + + + + + + + A + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Colon            | + + + + + + + + + A + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Rectum           | + + + + + + + + + A + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Duodenum         | + + + + + + + + + A + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Ileum            | + + + + + + + + + A + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Jejunum          | + + + + + + + + + A + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Liver                             | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Angiectasis                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Basophilic Focus                  | X   | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Clear Cell Focus                  |   |   |   | X | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Eosinophilic Focus                | X   | X |   |   |   |   | X | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hematopoietic Cell Proliferation  |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hepatodiaphragmatic Nodule        |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infiltration Cellular, Mixed Cell | 1   | 1 |   |   |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mixed Cell Focus                  |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |
| Necrosis, Focal                   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bile Duct, Hyperplasia            |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   | 1 |   | 3 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

|  | DAY ON TEST      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   | females<br>(cont...) |
|--|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|---|---|----------------------|
|  | 0<br>5<br>9<br>2 | 0<br>7<br>3<br>6 | 0<br>7<br>3<br>6 | 0<br>7<br>3<br>6 | 0<br>7<br>2<br>5 | 0<br>7<br>9<br>5 | 0<br>6<br>7<br>2 | 0<br>6<br>3<br>7 | 0<br>6<br>3<br>2 | 0<br>7<br>3<br>2 | 0<br>7<br>3<br>2 | 0<br>6<br>3<br>9 | 0<br>7<br>3<br>6 | 0<br>7<br>3<br>6 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>7<br>3<br>5 | 0<br>6<br>3<br>0 | 0<br>7<br>3<br>2 | 0<br>7<br>3<br>3 | 0<br>7<br>3<br>4 | 0<br>7<br>3<br>5 |   |   |                      |
| <b>FISCHER 344 RATS FEMALE</b>               | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0 |   |                      |
| <b>12500 PPM</b>                             | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0 |   |                      |
| ANIMAL ID                                    | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2                | 2 |   |                      |
|  | 5                | 5                | 5                | 5                | 5                | 5                | 5                | 5                | 6                | 6                | 6                | 6                | 6                | 6                | 6                | 6                | 6                | 6                | 6                | 6                | 7                | 7                | 7                | 7 |   |                      |
|  | 1                | 2                | 3                | 4                | 5                | 6                | 7                | 8                | 9                | 0                | 1                | 2                | 3                | 4                | 5                | 6                | 7                | 8                | 9                | 0                | 1                | 2                | 3                | 4 | 5 |                      |
| Hepatocyte, Vacuolization Cytoplasmic        | 2                |                  |                  |                  |                  |                  |                  | 4                |                  |                  | 4                | 1                | 3                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Hepatocyte, Vacuolization Cytoplasmic, Focal |                  |                  |                  |                  | X                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Mesentery                                    |                  |                  |                  |                  | +                |                  |                  |                  |                  |                  | +                |                  |                  |                  |                  |                  | +                |                  |                  |                  |                  |                  | +                |   |   |                      |
| Accessory Spleen                             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | X                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Fat, Necrosis                                |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  | 2                |   |   |                      |
| Pancreas                                     | +                | +                | +                | +                | +                | +                | +                | +                | A                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                |   |   |                      |
| Atrophy                                      |                  |                  |                  |                  | 1                | 4                |                  |                  |                  | 1                | 3                |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  | 1                | 2 | 2 |                      |
| Acinus, Hyperplasia, Focal                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Duct, Ectasia                                |                  | 1                | 1                | 3                |                  |                  |                  | 2                |                  | 1                |                  |                  | 1                | 1                |                  |                  |                  |                  |                  | 2                |                  | 2                |                  | 3 |   |                      |
| Salivary Glands                              | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                |   |   |                      |
| Atrophy                                      |                  |                  |                  |                  | 1                |                  |                  | 1                |                  | 2                |                  |                  |                  |                  | 1                |                  |                  |                  |                  | 2                |                  | 1                |                  |   |   |                      |
| Hyperplasia, Lymphoid                        |                  |                  |                  |                  |                  |                  |                  | 1                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Stomach, Forestomach                         | +                | +                | +                | +                | +                | +                | +                | +                | A                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                |   |   |                      |
| Edema  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Inflammation, Chronic Active                 |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 1                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Ulcer  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 4                |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Epithelium, Hyperplasia                      |                  |                  |                  |                  |                  |                  |                  | 1                |                  |                  |                  | 2                | 4                | 1                |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Stomach, Glandular                           | +                | +                | +                | +                | +                | +                | +                | +                | A                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                |   |   |                      |
| Edema  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Erosion                                      |                  |                  |                  |                  | 2                |                  |                  | 1                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Ulcer  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |
| Tongue                                       |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |   |                      |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 5 | 7 | 7 | 7 | 7 | 7 | 5 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 |   |
|                                | 9 | 3 | 3 | 3 | 3 | 2 | 9 | 7 | 3 | 3 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 3 |   |
|                                | 2 | 6 | 6 | 6 | 6 | 5 | 9 | 2 | 7 | 2 | 2 | 9 | 6 | 6 | 6 | 5 | 5 | 5 | 5 | 0 | 2 | 2 | 2 | 2 | 2 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>12500 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |   |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   |
|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

females (cont...)

Hyperplasia

CARDIOVASCULAR SYSTEM

Blood Vessel

+

Heart

Cardiomyopathy  
Thrombosis  
Valve, Hyperplasia

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|   |   | 1 | 1 | 1 |   | 1 | 2 | 1 | 1 | 1 | 1 |   |   |   |   | 1 | 1 | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 |
|   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

ENDOCRINE SYSTEM

Adrenal Cortex

Accessory Adrenal Cortical Nodule  
Degeneration, Fatty  
Hyperplasia, Focal  
Hypertrophy, Focal  
Necrosis

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|   |   |   | 1 |   |   |   |   |   | 1 |   |   |   |   |   | 1 |   |   |   |   | 1 |   |   |   |   | 1 |
|   |   |   |   | 2 |   | 2 | 2 |   |   | 1 |   |   |   |   | 1 | 1 |   | 1 |   |   |   |   | 1 |   | 3 |
|   | 1 |   | 2 | 2 | 1 |   |   |   |   |   |   |   |   |   | 1 | 1 |   | 1 |   |   |   |   |   |   |   |
|   |   |   |   | 3 |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |

Adrenal Medulla

Hyperplasia  
Infiltration Cellular, Lipocyte

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 2 |   |   |   | 1 |   |   | 1 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Islets, Pancreatic

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

Parathyroid Gland

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                          | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|--------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|                                      | 5 7 7 7 7 7 5 6 6 7 7 6 7 7 7 7 7 7 6 7 7 7 7 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS FEMALE<br>12500 PPM | 9 3 3 3 3 2 9 7 3 3 2 1 3 3 3 3 3 3 3 6 3 3 3 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 2 6 6 6 6 5 9 2 7 2 2 9 6 6 6 5 5 5 5 0 2 2 2 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                            | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 5 5 5 5 5 5 5 5 6 6 6 6 6 6 6 6 6 6 6 6 7 7 7 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | females (cont...)                                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

|                                     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Pituitary Gland                     | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pars Distalis, Angiectasis          |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pars Distalis, Cyst                 | 4 4 2 4 2 2 1 1 2 4 2                             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pars Distalis, Cyst, Multiple       | X   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pars Distalis, Hyperplasia          | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pars Distalis, Hyperplasia, Focal   | 2 3 1 2 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pars Intermedia, Angiectasis        | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pars Intermedia, Cyst               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Rathke's Cleft, Hemorrhage          | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Thyroid Gland                       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Degeneration, Cystic                | 1 1 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ultimobranchial Cyst                | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| C-cell, Hyperplasia                 | 1 3 1 1 1 2                                       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Follicular Cell, Hyperplasia, Focal |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**GENERAL BODY SYSTEM**

NONE

**GENITAL SYSTEM**

|                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Clitoral Gland        | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cyst                  | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia           | 4 1 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ovary                 | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
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 1) Minimal 3) Moderate  
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TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 5 | 7 | 7 | 7 | 7 | 7 | 5 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 |   |
|                                | 9 | 3 | 3 | 3 | 3 | 2 | 9 | 7 | 3 | 3 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 |   |
|                                | 2 | 6 | 6 | 6 | 6 | 5 | 9 | 2 | 7 | 2 | 2 | 9 | 6 | 6 | 6 | 5 | 5 | 5 | 5 | 0 | 2 | 2 | 2 | 2 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>12500 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |   |
|                                | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |   |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females (cont...)

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cyst<br>Granulosa Cell, Hyperplasia |   |   |   |   | 2 |   |   | 2 |   |   |   |   | 2 | 4 |   |   |   |   |   | 3 |   |   |   | 4 |
| Uterus                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Decidual Reaction                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Cystic                 | 1 | 2 | 2 | 2 | 1 |   | 1 |   |   | 2 | 2 |   | 1 |   | 3 | 1 | 4 | 1 | 4 |   | 2 | 1 | 2 | 1 |
| Vagina                              |   |   |   |   |   |   |   |   |   |   |   |   | + | + |   |   |   |   |   |   |   |   |   |   |

HEMATOPOIETIC SYSTEM

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Hyperplasia                        |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   | 2 |   |   |   | 4 |   |   |   |   |
| Lymph Node                         | + |   |   |   |   |   |   |   |   |   |   | + | + |   | + |   |   |   |   | + | + |   |   |   |   |
| Deep Cervical, Hemorrhage          | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Deep Cervical, Pigmentation        | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mediastinal, Ectasia               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mediastinal, Hemorrhage            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mediastinal, Hyperplasia, Lymphoid |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pancreatic, Hemorrhage             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |
| Pancreatic, Hyperplasia, Lymphoid  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |
| Lymph Node, Mandibular             | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | + | M | M | M | M | M |
| Ectasia                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |
| Hyperplasia, Lymphoid              | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infiltration Cellular, Histiocyte  | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

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BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked  
Page 94



| DAY ON TEST                          | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females (cont...) |
|--------------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------------------|
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                   |
| 5                                    | 7         | 7 | 7 | 7 | 7 | 5 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 0 | 0                 |
| 9                                    | 3         | 3 | 3 | 3 | 2 | 9 | 7 | 3 | 3 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 0 | 0                 |
| 2                                    | 6         | 6 | 6 | 6 | 5 | 9 | 2 | 7 | 2 | 2 | 9 | 6 | 6 | 6 | 5 | 5 | 5 | 5 | 5 | 0 | 2 | 2 | 2 | 2 | 0 | 0                 |
| .....                                |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| FISCHER 344 RATS FEMALE<br>12500 PPM | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                 |
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                 |
|                                      | 2         | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2                 |
|                                      | 5         | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7                 |
|                                      | 1         | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 0                 |

MUSCULOSKELETAL SYSTEM

|                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Bone                 | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Femur, Osteopetrosis | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

NERVOUS SYSTEM

|                  |   |  |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |   |
|------------------|---|--|---|--|--|--|--|--|--|--|--|--|---|--|--|--|--|--|--|--|--|--|--|--|--|---|
| Brain            | + |  |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |   |
| Compression      | 4 |  | 3 |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  | + |
| Hemorrhage       |   |  |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  | 1 |
| Peripheral Nerve |   |  |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |   |
| Spinal Cord      |   |  |   |  |  |  |  |  |  |  |  |  | + |  |  |  |  |  |  |  |  |  |  |  |  | + |

RESPIRATORY SYSTEM

|                                   |   |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
|-----------------------------------|---|---|---|---|---|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|
| Lung                              | + |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
| Congestion                        | + |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
| Hemorrhage                        | + |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
| Infiltration Cellular, Histiocyte | 1 | 1 | 1 | 1 | 1 | 1 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 |
| Metaplasia, Osseous               |   |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
| Alveolar Epithelium, Hyperplasia  | 1 | 1 |   |   | 1 |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2 |
| Nose                              | + |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |
| Foreign Body                      |   |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |

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+ .. Tissue examined microscopically  
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1) Minimal 3) Moderate  
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TDMS No. 20008 - 03  
 Test Type: CHRONIC  
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 Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST  |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |           | 5 | 7 | 7 | 7 | 7 | 5 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 |
|  |           | 9 | 3 | 3 | 3 | 3 | 2 | 9 | 7 | 3 | 3 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 |
|  |           | 2 | 6 | 6 | 6 | 6 | 5 | 9 | 2 | 7 | 2 | 2 | 9 | 6 | 6 | 6 | 5 | 5 | 5 | 5 | 0 | 2 | 2 | 2 |
| <b>FISCHER 344 RATS FEMALE</b><br><b>12500 PPM</b> | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|  |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|  |           | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
|  |           | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 |
|  |           | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 |

females  
(cont...)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Hemorrhage                               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic                    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Goblet Cell, Hyperplasia                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Nasolacrimal Duct, Cyst                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Nasolacrimal Duct, Hyperplasia, Squamous |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Respiratory Epithelium, Hyperplasia      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Trachea                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

SPECIAL SENSES SYSTEM

|                       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Eye                   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cataract              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Edema                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Cornea, Hyperplasia   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Retina, Degeneration  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Harderian Gland       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia, Focal    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Zymbal's Gland        |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

URINARY SYSTEM

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST  | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females<br>(cont...) |
|--|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|
|  | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
| 5  | 7         | 7 | 7 | 7 | 7 | 7 | 5 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 0 |                      |
| 9  | 3         | 3 | 3 | 3 | 2 | 9 | 7 | 3 | 3 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 0 |                      |
| 2  | 6         | 6 | 6 | 6 | 5 | 9 | 2 | 7 | 2 | 2 | 9 | 6 | 6 | 6 | 5 | 5 | 5 | 5 | 5 | 0 | 2 | 2 | 2 | 2 | 0 |                      |
| <hr/>  |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                      |
| <b>FISCHER 344 RATS FEMALE</b><br><b>12500 PPM</b> | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
|  | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
|  | 2         | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |                      |
|  | 5         | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |                      |
|  | 1         | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |                      |
| Kidney   | +         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |                      |
| Infarct  |           |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |                      |
| Inflammation                                       |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                      |
| Mineralization                                     |           | 1 |   | 1 | 2 | 1 |   |   |   | 1 |   | 1 | 2 |   | 1 |   | 2 |   | 1 |   |   | 1 | 1 | 1 |   |                      |
| Nephropathy  | 2         | 2 | 1 | 1 | 1 | 1 | 1 | 1 |   | 2 | 1 | 3 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 3 |                      |
| Renal Tubule, Accumulation, Hyaline Droplet        |           |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 | 4 |   |   |   |   |   |   |   |   |   |                      |
| Transitional Epithelium, Hyperplasia               |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |                      |
| <hr/>  |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                      |
| Urinary Bladder                                    | +         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |                      |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue

M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

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|                                |                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| DAY ON TEST                    | 7               | 7 | 7 | 4 | 7 | 6 | 7 | 4 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 |   |
|                                | 3               | 3 | 3 | 7 | 3 | 1 | 3 | 5 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 1 | 3 | 3 |   |
|                                | 6               | 6 | 6 | 7 | 6 | 8 | 2 | 9 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 9 | 5 | 9 | 5 | 5 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>12500 PPM</b>               | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                      | 2               | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 |   |
|                                | 7               | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |   |
|                                | 6               | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |
|                                | <b>* TOTALS</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**ALIMENTARY SYSTEM**

|                                   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |
|-----------------------------------|---|---|---|---|---|---|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|
| Esophagus                         | +     |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b>     |
| Intestine Large, Cecum            | + A + + + + |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>48</b>     |
| Intestine Large, Colon            | + + + + + A + A + + + + + + + + + + + + + A A + + +   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>45</b>     |
| Intestine Large, Rectum           | + + + + + A + A + + + + + + + + + + + + + A A + + +   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>45</b>     |
| Intestine Small, Duodenum         | + + + + + + + A + + + + + + + + + + + + + A + + +     |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>47</b>     |
| Intestine Small, Ileum            | + + + + + A + A + + + + + + + + + + + + + A A + + +   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>45</b>     |
| Intestine Small, Jejunum          | + + + + + A + + + + + + + + + + + + + + + A A + + +   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>46</b>     |
| Liver                             | +     |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>50</b>     |
| Angiectasis                       |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 2.0</b>  |
| Basophilic Focus                  | X   | X | X | X | X | X | X |  | X | X | X | X |   | X | X | X | X | X | X |   | X | X | X |               |
| Clear Cell Focus                  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>10</b>     |
| Eosinophilic Focus                |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>13</b>     |
| Hematopoietic Cell Proliferation  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 1.0</b>  |
| Hepatodiaphragmatic Nodule        |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>5</b>      |
| Infiltration Cellular, Mixed Cell | 1   | 1 | 1 |   | 1 | 1 |   |  | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |               |
| Mixed Cell Focus                  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>34 1.0</b> |
| Necrosis, Focal                   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>6</b>      |
| Bile Duct, Hyperplasia            |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 1.5</b>  |
|                                   |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>10 1.7</b> |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |               |                 |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|-----------------|
|  | 7 | 7 | 7 | 4 | 7 | 6 | 7 | 4 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 |               |                 |
|  | 3 | 3 | 3 | 7 | 3 | 1 | 3 | 5 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 1 | 3 |               |                 |
|  | 6 | 6 | 6 | 7 | 6 | 8 | 2 | 9 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 9 | 5 | 9 | 5 |               |                 |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| <b>FISCHER 344 RATS FEMALE</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |               |                 |
| <b>12500 PPM</b>                             | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |               |                 |
| <b>ANIMAL ID</b>                             | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 |               |                 |
|  | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |               |                 |
|  | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0             | <b>* TOTALS</b> |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| Hepatocyte, Vacuolization Cytoplasmic        |   |   |   |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 2 |   | 2 |   | <b>9 2.2</b>  |                 |
| Hepatocyte, Vacuolization Cytoplasmic, Focal |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2</b>      |                 |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| Mesentery                                    | + |   | + |   |   |   |   |   |   |   |   |   |   | + | + |   |   |   |   |   |   | + | + |   | <b>10</b>     |                 |
| Accessory Spleen                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1</b>      |                 |
| Fat, Necrosis                                | 2 |   | 2 |   |   |   |   |   |   |   | 2 | 2 |   |   |   |   |   |   |   |   | 2 |   |   |   | <b>8 2.0</b>  |                 |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| Pancreas                                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | <b>48</b>     |                 |
| Atrophy                                      |   | 2 | 2 | 1 |   |   |   | 1 | 2 |   |   |   |   | 1 | 1 |   |   |   | 1 | 1 |   | 1 | 1 |   | <b>19 1.6</b> |                 |
| Acinus, Hyperplasia, Focal                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | <b>1 1.0</b>  |                 |
| Duct, Ectasia                                |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 1 | 2 |   |   |   |   |   |   | 4 |   | <b>14 1.8</b> |                 |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| Salivary Glands                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |                 |
| Atrophy                                      |   |   | 1 |   |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 |   | <b>10 1.2</b> |                 |
| Hyperplasia, Lymphoid                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |                 |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| Stomach, Forestomach                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | +             | <b>48</b>       |
| Edema  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 4.0</b>  |                 |
| Inflammation, Chronic Active                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |                 |
| Ulcer  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 4.0</b>  |                 |
| Epithelium, Hyperplasia                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | <b>5 1.8</b>  |                 |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| Stomach, Glandular                           | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | +             | <b>47</b>       |
| Edema  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 2.0</b>  |                 |
| Erosion                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 1.5</b>  |                 |
| Ulcer  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 2.0</b>  |                 |
| -----  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |                 |
| Tongue                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>+ 1</b>    |                 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked



| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 7 | 7 | 4 | 7 | 6 | 7 | 4 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 |
|                                | 3 | 3 | 3 | 7 | 3 | 1 | 3 | 5 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 1 | 3 |
|                                | 6 | 6 | 6 | 7 | 6 | 8 | 2 | 9 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 9 | 5 | 9 | 5 |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>12500 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                      | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 |
|                                | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| <b>* TOTALS</b>                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Pituitary Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Pars Distalis, Angiectasis        |   |   |   |   |   |   |   |   |   | 1 |   |   |   | 3 |   |   | 3 |   |   |   |   |   |   |   | 6 3.2  |
| Pars Distalis, Cyst               |   |   |   | 3 | 2 | 3 |   |   |   |   | 1 |   |   |   | 1 |   | 1 |   | 1 |   | 2 |   |   |   | 18 2.1 |
| Pars Distalis, Cyst, Multiple     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1      |
| Pars Distalis, Hyperplasia        |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   | 2 3.5  |
| Pars Distalis, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   | 1 |   |   |   | 4 |   | 3 |   | 1 |   |   |   |   |   |   | 9 2.1  |
| Pars Intermedia, Angiectasis      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0  |
| Pars Intermedia, Cyst             |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   | 1 |   |   |   |   |   |   |   |   |   | 2 1.5  |
| Rathke's Cleft, Hemorrhage        |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0  |

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Thyroid Gland                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | 49     |
| Degeneration, Cystic                |   |   |   |   | 2 |   |   |   |   | 1 |   |   |   | 1 | 1 |   |   |   |   |   |   |   | 1 |   | 8 1.1  |
| Ultimobranchial Cyst                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |
| C-cell, Hyperplasia                 | 2 | 2 |   |   |   |   |   | 4 |   |   | 2 | 2 | 1 | 1 |   | 1 | 1 |   |   |   |   |   |   |   | 17 1.6 |
| Follicular Cell, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 |   |   | 1 |   | 1 |   |   | 3 1.0  |

**GENERAL BODY SYSTEM**

NONE

**GENITAL SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |       |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Clitoral Gland        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | 49    |
| Cyst                  |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   | 2 3.5 |
| Hyperplasia           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 2.3 |
| Inflammation, Chronic |   |   |   |   |   | 1 | 2 |   |   |   |   |   | 3 |   |   | 2 |   |   |   |   |   |   | 2 |   |   |   | 6 2.0 |
| Ovary                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | 49    |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 102

| DAY ON TEST | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |
|-------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|             | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| 7           | 7         | 7 | 4 | 7 | 6 | 7 | 4 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 8        |
| 3           | 3         | 3 | 7 | 3 | 1 | 3 | 5 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 1 | 3 | 2        |
| 6           | 6         | 6 | 7 | 6 | 8 | 2 | 9 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 9 | 5 | 9 | 5 | 0        |

**FISCHER 344 RATS FEMALE**

**12500 PPM**

|                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |  |   |   |  |  |  |  |  |  |  |  |  |    |     |   |     |
|-----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|--|---|---|--|--|--|--|--|--|--|--|--|----|-----|---|-----|
| Cyst                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 2 |  |   |   |  |  |  |  |  |  |  |  |  | 8  | 2.6 |   |     |
| Granulosa Cell, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |  | 2 | 1 |  |  |  |  |  |  |  |  |  |    |     | 2 | 1.5 |
| Uterus                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | 49 |   |  |   |   |  |  |  |  |  |  |  |  |  |    |     |   |     |
| Decidual Reaction           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |  |   |   |  |  |  |  |  |  |  |  |  | 1  | 3.0 |   |     |
| Hemorrhage                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |  |   |   |  |  |  |  |  |  |  |  |  | 1  | 4.0 |   |     |
| Hyperplasia, Cystic         | 1 |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |  |   |   |  |  |  |  |  |  |  |  |  | 30 | 2.0 |   |     |
| Vagina                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |  |   |   |  |  |  |  |  |  |  |  |  | 2  |     |   |     |

**HEMATOPOIETIC SYSTEM**

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   |     |     |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|--|--|--|--|--|--|--|--|--|--|--|---|-----|-----|
| Bone Marrow                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |  |  |  |  |  |  |  |  |  |  |  |   | 5   | 3.0 |
| Hyperplasia                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   |     |
| Lymph Node                         |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 8   |     |
| Deep Cervical, Hemorrhage          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 2.0 |
| Deep Cervical, Pigmentation        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 4.0 |
| Mediastinal, Ectasia               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 2   | 2.0 |
| Mediastinal, Hemorrhage            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 3   | 3.0 |
| Mediastinal, Hyperplasia, Lymphoid |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 3   | 2.7 |
| Pancreatic, Hemorrhage             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 2.0 |
| Pancreatic, Hyperplasia, Lymphoid  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 3.0 |
| Lymph Node, Mandibular             | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 3 |    |  |  |  |  |  |  |  |  |  |  |  |  | 1 | 1.0 |     |
| Ectasia                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 2.0 |
| Hyperplasia, Lymphoid              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 2.0 |
| Infiltration Cellular, Histiocyte  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 2.0 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 7 | 7 | 4 | 7 | 6 | 7 | 4 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 |   |
|                                | 3 | 3 | 3 | 7 | 3 | 1 | 3 | 5 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 1 | 3 |   |
|                                | 6 | 6 | 6 | 7 | 6 | 8 | 2 | 9 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 9 | 5 | 9 | 5 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>12500 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>ANIMAL ID</b>               | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 |   |
|                                | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |   |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |
|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| <b>* TOTALS</b>                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|--------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Pigmentation |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |        |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|--------|
| Lymph Node, Mesenteric           | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | +      | 48     |
| Ectasia                          |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0  |
| Hemorrhage                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 1 |   |   |   |   |   |        | 4 1.0  |
| Hyperplasia, Lymphoid            |   |   |   |   |   | 3 | 1 |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |        | 9 1.8  |
| Pigmentation                     | 2 | 1 | 1 | 1 | 1 | 1 | 1 |   | 1 | 2 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |   |   | 39 1.2 |        |
| Spleen                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +      | 50     |
| Hematopoietic Cell Proliferation |   |   |   |   | 2 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 5 2.2  |
| Pigmentation                     | 3 | 4 | 3 | 3 | 3 | 4 | 3 |   |   | 3 | 3 | 4 |   | 4 | 2 | 4 | 3 | 3 | 2 | 2 | 4 |   | 3 | 4 | 3 | 42 3.0 |        |
| Lymphoid Follicle, Atrophy       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |        | 1 1.0  |
| Lymphoid Follicle, Hyperplasia   |   |   |   |   | 2 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |        | 5 1.6  |
| Thymus                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +      | 49     |
| Hemorrhage                       | 2 | 2 |   |   | 1 | 2 | 1 |   |   | 2 | 2 | 1 |   |   |   |   |   |   | 2 |   |   |   |   |   | 1 |        | 15 1.5 |

### INTEGUMENTARY SYSTEM

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Mammary Gland             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Hyperplasia               | 3 |   |   |   | 2 | 2 |   |   |   | 2 |   |   |   |   |   |   |   | 1 | 2 |   | 2 | 2 | 3 |   |   |   | 17 1.8 |
| Hyperplasia, Focal        | 1 | 1 |   |   |   | 2 | 2 |   |   | 2 |   |   |   | 2 | 2 | 2 |   | 2 | 1 | 2 |   | 1 |   | 1 |   |   | 26 1.6 |
| Duct, Ectasia             | 2 | 2 |   |   |   | 4 | 2 |   |   | 2 | 1 | 1 | 1 | 3 | 1 | 3 | 2 | 2 |   | 1 |   | 2 | 3 | 3 |   |   | 37 2.0 |
| Skin                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Cyst Epithelial Inclusion |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1      |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

l .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                                       | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------|
|   | 7 7 7 4 7 6 7 4 7 7 7 7 6 7 7 7 7 7 7 7 6 7 6 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
| FISCHER 344 RATS FEMALE<br>12500 PPM<br>ANIMAL ID | 3 3 3 7 3 1 3 5 3 3 3 3 6 3 3 3 3 3 3 3 0 3 1 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 6 6 6 7 6 8 2 9 2 2 2 2 0 2 2 2 2 2 2 2 9 5 9 5   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 2 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 7 7 7 7 8 8 8 8 8 8 8 8 8 8 9 9 9 9 9 9 9 9 9 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | * TOTALS |

MUSCULOSKELETAL SYSTEM

|                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |       |
|----------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|-------|
| Bone                 | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |       |
| Femur, Osteopetrosis |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2  | 1 2.0 |

NERVOUS SYSTEM

|                  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |   |   |   |       |
|------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|---|---|---|-------|
| Brain            | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |   |   |   |       |
| Compression      | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 4  | 1 | 3 | 4 | 9 3.0 |
| Hemorrhage       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1  | 2 | 1 | 1 | 7 1.1 |
| Peripheral Nerve | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |   |   |   | 4     |
| Spinal Cord      | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |   |   |   | 5     |

RESPIRATORY SYSTEM

|                                   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |   |   |  |        |       |
|-----------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|---|---|--|--------|-------|
| Lung                              | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |   |   |  |        |       |
| Congestion                        |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2  |   |   |  |        | 2 2.0 |
| Hemorrhage                        |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1  |   | 1 |  | 3      | 4 1.5 |
| Infiltration Cellular, Histiocyte | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |   |   |  | 44 1.0 |       |
| Metaplasia, Osseous               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |   | 1 |  |        | 1 1.0 |
| Alveolar Epithelium, Hyperplasia  | 1 1 1 2 1 1 1 2 3 1 2 1 1 1 1                   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |   |   |  | 25 1.3 |       |
| Nose                              | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |   |   |  |        |       |
| Foreign Body                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2  | 1 |   |  |        | 3 1.3 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                    |                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|--------------------------------|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                                |                  | 7 | 7 | 7 | 4 | 7 | 6 | 7 | 4 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7               |
|                                |                  | 3 | 3 | 3 | 7 | 3 | 1 | 3 | 5 | 3 | 3 | 3 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 1 | 3               |
|                                |                  | 6 | 6 | 6 | 7 | 6 | 8 | 2 | 9 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 9 | 5 | 9 | 5               |
| <b>FISCHER 344 RATS FEMALE</b> | <b>ANIMAL ID</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
| <b>12500 PPM</b>               |                  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               |
|                                |                  | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3               |
|                                |                  | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0               |
|                                |                  | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8               |
|                                |                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |

|  |  |  |  |  |  |   |  |  |   |   |  |  |  |   |  |  |   |   |   |   |  |  |  |              |
|--|--|--|--|--|--|---|--|--|---|---|--|--|--|---|--|--|---|---|---|---|--|--|--|--------------|
| Hemorrhage                               |  |  |  |  |  |   |  |  |   |   |  |  |  |   |  |  |   |   |   |   |  |  |  | <b>1 3.0</b> |
| Inflammation, Chronic                    |  |  |  |  |  | 2 |  |  | 2 | 2 |  |  |  | 2 |  |  | 1 | 2 | 1 |   |  |  |  | <b>9 1.8</b> |
| Goblet Cell, Hyperplasia                 |  |  |  |  |  |   |  |  |   |   |  |  |  |   |  |  |   |   |   |   |  |  |  | <b>1 1.0</b> |
| Nasolacrimal Duct, Cyst                  |  |  |  |  |  |   |  |  |   |   |  |  |  |   |  |  |   |   |   |   |  |  |  | <b>1 2.0</b> |
| Nasolacrimal Duct, Hyperplasia, Squamous |  |  |  |  |  |   |  |  |   |   |  |  |  |   |  |  |   | 3 |   |   |  |  |  | <b>1 3.0</b> |
| Respiratory Epithelium, Hyperplasia      |  |  |  |  |  | 2 |  |  |   | 1 |  |  |  |   |  |  |   |   |   | 1 |  |  |  | <b>5 1.6</b> |

Trachea + 50

**SPECIAL SENSES SYSTEM**

|                       |  |  |  |  |  |  |   |   |   |   |  |  |  |  |  |  |   |   |  |  |   |  |   |   |              |
|-----------------------|--|--|--|--|--|--|---|---|---|---|--|--|--|--|--|--|---|---|--|--|---|--|---|---|--------------|
| Eye                   |  |  |  |  |  |  |   |   |   |   |  |  |  |  |  |  |   |   |  |  |   |  |   |   | <b>48</b>    |
| Cataract              |  |  |  |  |  |  |   |   |   |   |  |  |  |  |  |  |   |   |  |  |   |  |   |   | <b>6 3.2</b> |
| Edema                 |  |  |  |  |  |  | 1 |   |   |   |  |  |  |  |  |  | 2 |   |  |  |   |  | 4 |   | <b>4 3.0</b> |
| Inflammation, Chronic |  |  |  |  |  |  |   | 1 |   |   |  |  |  |  |  |  |   |   |  |  |   |  |   |   | <b>1 1.0</b> |
| Cornea, Hyperplasia   |  |  |  |  |  |  |   | 2 |   |   |  |  |  |  |  |  |   |   |  |  |   |  |   |   | <b>1 2.0</b> |
| Retina, Degeneration  |  |  |  |  |  |  |   |   |   |   |  |  |  |  |  |  |   | 2 |  |  |   |  |   | 4 | <b>5 3.6</b> |
| Harderian Gland       |  |  |  |  |  |  |   |   |   |   |  |  |  |  |  |  |   |   |  |  |   |  |   |   | <b>49</b>    |
| Hyperplasia, Focal    |  |  |  |  |  |  |   |   | 1 |   |  |  |  |  |  |  |   |   |  |  |   |  |   | 1 | <b>2 1.0</b> |
| Inflammation, Chronic |  |  |  |  |  |  |   |   |   | 1 |  |  |  |  |  |  |   |   |  |  | 1 |  |   | 2 | <b>7 1.1</b> |
| Zymbal's Gland        |  |  |  |  |  |  |   |   |   |   |  |  |  |  |  |  |   |   |  |  |   |  |   |   | <b>1</b>     |

**URINARY SYSTEM**

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
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TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                                       | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | * TOTALS |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------|
|   | 7 7 7 4 7 6 7 4 7 7 7 6 7 7 7 7 7 7 7 7 6 7 6 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
| FISCHER 344 RATS FEMALE<br>12500 PPM<br>ANIMAL ID | 3 3 3 7 3 1 3 5 3 3 3 3 6 3 3 3 3 3 3 3 0 3 1 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 6 6 6 7 6 8 2 9 2 2 2 2 0 2 2 2 2 2 2 2 9 5 9 5   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
| Kidney  | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 49       |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 7 7 7 7 8 8 8 8 8 8 8 8 8 8 9 9 9 9 9 9 9 9 9 9   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
| Infarct   | + A + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 3 2.0    |
| Inflammation                                      | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 1.0    |
| Mineralization                                    | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 28 1.1   |
| Nephropathy                                       | 2 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 45 1.3   |
| Renal Tubule, Accumulation, Hyaline Droplet       | 4 4   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 4 4.0    |
| Transitional Epithelium, Hyperplasia              | 3 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 3 2.0    |
| Urinary Bladder                                   | + A + + + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 49       |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
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x .. Lesion present  
I .. Insufficient tissue  
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BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked  
Page 107

| DAY ON TEST                          | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females (cont...) |
|--------------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------------------|
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                   |
| 7                                    | 6         | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 5 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 0 |                   |
| 3                                    | 7         | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 6 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 6 | 3 | 8 |   |                   |
| 2                                    | 6         | 2 | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 3 | 7 | 5 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 7 | 5 | 0 |   |                   |
| .....                                |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| FISCHER 344 RATS FEMALE<br>25000 PPM | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                   |
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                   |
|                                      | 3         | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                   |
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                   |
|                                      | 1         | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |                   |

ALIMENTARY SYSTEM

|                                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|---------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Esophagus                             | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Cecum                | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Colon                | + A |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Large, Rectum               | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Duodenum             | + A |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Ileum                | + A |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Intestine Small, Jejunum              | + A |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Liver                                 | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Angiectasis                           | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Basophilic Focus                      | X   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Clear Cell Focus                      | X   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Eosinophilic Focus                    | X   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hematopoietic Cell Proliferation      | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hepatodiaphragmatic Nodule            | X X   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infiltration Cellular, Mixed Cell     | 1 1 1 1 1 1 2 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mixed Cell Focus                      | X   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Bile Duct, Hyperplasia                | 1 2 1 3 4 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hepatocyte, Vacuolization Cytoplasmic | 2 1 2 4 2 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 5 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 0 |   |
|                                | 3 | 7 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 6 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 6 | 3 | 8 |
|                                | 2 | 6 | 2 | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 3 | 7 | 5 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 7 | 5 | 0 |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>25000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANIMAL ID                      | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females (cont...)

|  |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
|--|---|--|--|--|--|--|--|--|--|--|---|--|--|--|--|---|--|--|--|--|-------|--|--|--|--|
| Hepatocyte, Vacuolization Cytoplasmic, Focal | X   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Mesentery Fat, Necrosis                      | +   |  |  |  |  |  |  |  |  |  | 2 |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Oral Mucosa Pharyngeal, Hyperplasia          |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  | + |  |  |  |  |       |  |  |  |  |
| Pancreas Atrophy                             | + |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Acinus, Hyperplasia, Focal                   | 2 3 1 1 2 1 |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Duct, Ectasia                                | 3 2 2 1 |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Salivary Glands Atrophy                      | + |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Stomach, Forestomach Edema                   |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  | +     |  |  |  |  |
| Epithelium, Hyperplasia                      |   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  | 3 2 3 |  |  |  |  |
| Stomach, Glandular Erosion                   | + |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Inflammation                                 | 2 |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Ulcer Epithelium, Hyperplasia                | 2 |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |
| Tongue                                       | +   |  |  |  |  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |       |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
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 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DAY ON TEST                                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 5 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 0 |
| FISCHER 344 RATS FEMALE<br>25000 PPM<br>ANIMAL ID | 3 | 7 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 6 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 6 | 3 |
|   | 2 | 6 | 2 | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 3 | 7 | 5 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 7 | 5 |
| 25000 PPM<br>ANIMAL ID                            | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 25000 PPM<br>ANIMAL ID                            | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
|   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
|   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 |

females (cont...)

Tooth I

CARDIOVASCULAR SYSTEM

|                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Blood Vessel   | + |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |
| Heart          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cardiomyopathy | 1 | 2 |   |   |   |   | 1 | 1 |   | 2 |   |   | 1 | 1 |   | 1 |   | 2 | 2 | 2 |   | 1 |   |
| Thrombosis     |   |   |   |   |   |   |   |   |   |   | 1 | 2 |   |   |   |   |   |   |   |   |   |   |   |

ENDOCRINE SYSTEM

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Accessory Adrenal Cortical Nodule |   |   |   |   |   |   |   |   |   | 2 |   |   | 2 | 2 | 1 |   | 1 | 1 |   | 2 |   |   |   |
| Degeneration, Fatty               | 3 | 1 | 2 |   |   |   | 2 |   |   |   | 1 |   |   | 3 | 2 |   | 2 |   | 1 | 4 | 4 | 1 |   |
| Hyperplasia, Focal                | 1 |   | 2 |   |   |   | 1 | 1 |   |   |   |   | 1 |   | 2 | 1 |   |   | 2 | 1 |   |   |   |
| Hypertrophy, Focal                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |
| Necrosis                          |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Capsule, Hyperplasia              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |
| Islets, Pancreatic                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | M |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 5 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 0 |   |
|  | 3 | 7 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 6 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 6 | 3 | 8 |
|  | 2 | 6 | 2 | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 3 | 7 | 5 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 7 | 5 | 0 |
| <b>FISCHER 344 RATS FEMALE</b><br><b>25000 PPM</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|  | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |   |
|  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |   |
|  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 |
| Pituitary Gland                                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Pars Distalis, Angiectasis                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Cyst                                | 2 | 4 |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 | 3 |   | 2 |   |
| Pars Distalis, Hyperplasia                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Hyperplasia, Focal                  |   |   | 3 |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 2 |   |   |   |   |   |   |   |   |
| Pars Distalis, Hypertrophy                         |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Intermedia, Cyst                              |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 |   |   |   |   |
| Rathke's Cleft, Hemorrhage                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thyroid Gland                                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Degeneration, Cystic                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |
| Ultimobranchial Cyst                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |
| C-cell, Hyperplasia                                | 1 |   |   | 2 |   |   |   | 1 |   |   | 1 |   | 2 |   | 1 | 1 |   |   |   | 4 |   |   | 3 |   |   |

females  
(cont...)

**GENERAL BODY SYSTEM**

|                            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Tissue NOS                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fat, Necrosis              |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Fat, Mediastinum, Necrosis |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**GENITAL SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clitoral Gland        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst                  | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Squamous |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Inflammation, Acute   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   | 4 |
| Inflammation, Chronic |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 | 1 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
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 x .. Lesion present  
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 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 111

|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                          |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------------------|
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                        |
| DAY ON TEST                    | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 5 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 0                        |
|                                | 3 | 7 | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 6 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 6 | 3 | 8                        |
|                                | 2 | 6 | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 3 | 7 | 5 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 7 | 5 | 0                        |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                        |
| <b>25000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                        |
| ANIMAL ID                      | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3                        |
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2                        |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3                        |
|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>females (cont...)</b> |

|                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ovary Cyst                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|                            |   |   |   | 3 |   | 2 |   |   | 2 |   |   |   | 2 |   | 2 |   | 3 |   |   |   | 2 | 2 |   |   |
| Uterus Hyperplasia, Cystic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|                            | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 1 | 2 | 2 | 4 |   | 3 | 1 |   | 1 |   | 2 | 2 |   |   | 2 | 1 |   |
| Vagina                     |   | + |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + |

**HEMATOPOIETIC SYSTEM**

|                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Depletion Cellular                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Hyperplasia                           |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   | 3 | 2 |   |   |
| Infiltration Cellular, Histiocyte     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Myelofibrosis                         |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lymph Node                            |   | + |   |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   | + |
| Mediastinal, Hemorrhage               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Mediastinal, Hyperplasia, Plasma Cell |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Lymph Node, Mandibular                | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Hemorrhage                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Lymphoid                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lymph Node, Mesenteric                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Ectasia                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage                            |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 112

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 5 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 0 |   |
|                                | 3 | 7 | 3 | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 6 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 6 | 3 | 8 |
|                                | 2 | 6 | 2 | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 3 | 7 | 5 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 7 | 5 | 0 |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>25000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| <b>ANIMAL ID</b>               | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females (cont...)

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hyperplasia, Lymphoid Pigmentation |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |
|                                    |   | 1 |   |   | 1 | 2 | 2 | 2 | 1 | 1 |   | 2 | 1 |   | 1 | 3 | 1 | 1 |   |   | 1 |   |   | 1 |   |
| Spleen                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hematopoietic Cell Proliferation   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pigmentation                       |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |
| Lymphoid Follicle, Hyperplasia     |   |   |   |   |   |   |   |   |   | 2 |   |   |   | 4 |   | 4 | 3 | 3 | 3 | 2 |   | 3 | 3 | 3 | 3 |
|                                    |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |
| Thymus                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst                               | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage                         | 1 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 2 |

**INTEGUMENTARY SYSTEM**

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                      | 2 |   |   |   |   | 3 | 2 |   |   |   | 2 | 3 | 3 |   | 2 | 3 | 1 | 2 |   | 1 |   |   | 1 | 2 |   |
| Hyperplasia, Focal Duct, Ectasia |   |   | 2 |   |   |   |   | 1 |   | 2 | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
|                                  |   | 1 | 4 | 2 | 2 | 2 |   | 1 |   | 2 | 2 | 2 | 1 | 2 | 1 | 1 |   |   |   | 2 | 1 | 2 | 3 | 2 | 2 |
| Skin                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst Epithelial Inclusion        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|                                  |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**MUSCULOSKELETAL SYSTEM**

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Femur, Osteopetrosis |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked  
Page 113

| DAY ON TEST                          | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|--------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|                                      | 7 6 7 7 7 7 7 7 5 7 7 5 7 6 7 7 7 7 7 7 7 6 7 7 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FISCHER 344 RATS FEMALE<br>25000 PPM | 3 7 3 3 3 3 3 3 0 0 0 6 3 6 3 3 3 3 3 0 3 3 6 3 8 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 2 6 2 2 2 2 2 2 7 3 3 7 5 0 5 5 5 5 5 3 5 5 7 5 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ANIMAL ID                            | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 0 0 0 0 0 0 0 0 0 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                                      | 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

females (cont...)

Skeletal Muscle +

**NERVOUS SYSTEM**

| Brain                      | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Compression                | 1 4 3 4 2 2                                       |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Developmental Malformation |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Gliosis                    | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhage                 | 1 1 1 1 1 1 1                                     |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Necrosis                   | 3 4 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Peripheral Nerve           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Spinal Cord                |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**RESPIRATORY SYSTEM**

| Lung                              | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Congestion                        | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hemorrhage                        | 2 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia, Lymphoid             | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Infiltration Cellular, Histiocyte | 1   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Suppurative         | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inflammation, Chronic             | 2 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Alveolar Epithelium, Hyperplasia  | 1 2 1 1 1 1 2 2 2 1 1 1                           |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Nose                              | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
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 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 5 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 0 |
|                                | 3 | 7 | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 6 | 3 | 6 | 3 | 3 | 3 | 3 | 3 | 0 | 3 | 3 | 6 | 3 | 8 |   |
|                                | 2 | 6 | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 3 | 7 | 5 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 5 | 5 | 7 | 5 | 0 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>25000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>ANIMAL ID</b>               | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |   |
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |   |   |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 |   |

females (cont...)

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Foreign Body                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Inflammation, Chronic                    | 2 |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   | 2 |   |   |   |   |   | 1 |
| Goblet Cell, Hyperplasia                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |
| Nasolacrimal Duct, Hyperplasia, Squamous |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |
| Respiratory Epithelium, Hyperplasia      | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Trachea                                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**SPECIAL SENSES SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cataract              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Edema                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Cornea, Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Retina, Degeneration  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Harderian Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Atrophy               |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic | 4 |   | 1 |   |   |   | 1 |   |   | 1 |   |   |   |   |   |   |   | 1 |   | 1 |   |   |   |   |
| Zymbal's Gland        |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   | + |

**URINARY SYSTEM**

|        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|--------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

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 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 115

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                                 |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |   |   |
|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FISCHER 344 RATS FEMALE                     |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |   |   |
| 25000 PPM                                   |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |   |   |
| ANIMAL ID                                   |  | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |   |   |   |
|   |  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |   |   |
|   |  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   |
| Cyst  |  |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infarct                                     |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic                       |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineralization                              |  |   |   |   |   | 1 | 1 | 1 |   |   |   | 1 | 1 | 1 |   |   | 1 | 1 | 1 |   |   |   |   |   |   |   |   |
| Nephropathy                                 |  | 1 |   | 1 | 2 | 1 | 2 | 1 | 1 |   |   | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 2 |   |   | 2 |   | 1 | 1 | 2 | 2 |
| Bilateral, Infarct                          |  |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal Tubule, Accumulation, Hyaline Droplet |  |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |
| Renal Tubule, Necrosis                      |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia        |  |   |   |   |   |   |   |   | 1 |   |   | 2 |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |
| Urinary Bladder                             |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

females (cont...)

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue

M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

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| DAY ON TEST                                       | 0 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | * TOTALS |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------|
|   | 6 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
| FISCHER 344 RATS FEMALE<br>25000 PPM<br>ANIMAL ID | 7 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 4 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 7 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |

**ALIMENTARY SYSTEM**

|                                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |        |
|---------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--------|
| Esophagus                             | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50     |
| Intestine Large, Cecum                | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 49     |
| Intestine Large, Colon                | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 48     |
| Intestine Large, Rectum               | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 49     |
| Intestine Small, Duodenum             | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 48     |
| Intestine Small, Ileum                | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 48     |
| Intestine Small, Jejunum              | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 48     |
| Liver                                 | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 49     |
| Angiectasis                           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 3.0  |
| Basophilic Focus                      | X |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 44     |
| Clear Cell Focus                      | X |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 17     |
| Eosinophilic Focus                    | X |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 11     |
| Hematopoietic Cell Proliferation      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 1.0  |
| Hepatodiaphragmatic Nodule            |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 4      |
| Infiltration Cellular, Mixed Cell     | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 36 1.1 |
| Mixed Cell Focus                      | X |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 11     |
| Bile Duct, Hyperplasia                | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 10 1.3 |
| Hepatocyte, Vacuolization Cytoplasmic | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 8 1.9  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                                  | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|
|  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |
| FISCHER 344 RATS FEMALE                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |
| 25000 PPM                                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |
| ANIMAL ID                                    | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3        |
|  | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3        |
|  | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0        |
| Hepatocyte, Vacuolization Cytoplasmic, Focal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1        |
| Mesentery                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4        |
| Fat, Necrosis                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 2.3    |
| Oral Mucosa                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1        |
| Pharyngeal, Hyperplasia                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0    |
| Pancreas                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 49       |
| Atrophy                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 25 1.2   |
| Acinus, Hyperplasia, Focal                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0    |
| Duct, Ectasia                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 16 1.4   |
| Salivary Glands                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 50       |
| Atrophy                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 13 1.1   |
| Stomach, Forestomach                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 49       |
| Edema  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0    |
| Epithelium, Hyperplasia                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.5    |
| Stomach, Glandular                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 49       |
| Erosion                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0    |
| Inflammation                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0    |
| Ulcer  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0    |
| Epithelium, Hyperplasia                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 1 3.0  |
| Tongue                                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1        |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

|   |                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DAY ON TEST                                       | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   | 6               | 7 | 7 | 4 | 7 | 7 | 7 | 4 | 7 | 4 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 |
|   | 4               | 3 | 3 | 7 | 3 | 3 | 3 | 5 | 3 | 8 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 1 | 8 | 3 | 3 | 3 | 3 |
|   | 7               | 6 | 6 | 7 | 6 | 5 | 5 | 1 | 5 | 4 | 6 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 1 | 7 | 6 | 6 | 6 | 6 |
| FISCHER 344 RATS FEMALE<br>25000 PPM<br>ANIMAL ID | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   | 0               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|   | 3               | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
|   | 2               | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |
|   | 6               | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |
|   | <b>* TOTALS</b> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Tooth **0**

**CARDIOVASCULAR SYSTEM**

Blood Vessel **2**

Heart **50**

  Cardiomyopathy **28 1.3**

  Thrombosis **2 1.5**

**ENDOCRINE SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|
| Adrenal Cortex                    | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | <b>49</b>     |
| Accessory Adrenal Cortical Nodule | 1 |   |   |   |   |   |   |   |   |   | 1 |   | 1 |   |   | 1 |   |   |   |   |   |   |   | <b>11 1.4</b> |
| Degeneration, Fatty               | 1 |   |   | 1 |   |   |   |   | 2 | 1 |   |   | 1 |   |   | 1 | 1 | 2 | 2 | 2 |   |   | 1 | <b>24 1.8</b> |
| Hyperplasia, Focal                |   |   | 1 |   |   |   |   |   |   |   |   |   | 2 |   | 1 |   | 2 | 1 |   |   |   | 2 | 1 | <b>21 1.5</b> |
| Hypertrophy, Focal                |   |   |   |   |   | 2 | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |
| Necrosis                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 3.0</b>  |
| Capsule, Hyperplasia              |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |
| Adrenal Medulla                   | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | M | + | + | <b>48</b>     |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 | 2 |   |   |   |   |   | <b>3 1.7</b>  |
| Islets, Pancreatic                | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | <b>49</b>     |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | <b>47</b>     |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

  1) Minimal  3) Moderate

  2) Mild     4) Marked



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 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

| DAY ON TEST                                       | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | * TOTALS |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----------|
|   | 6 7 7 4 7 7 7 4 7 4 7 7 7 7 7 7 7 7 7 7 6 7 7 7   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
| FISCHER 344 RATS FEMALE<br>25000 PPM<br>ANIMAL ID | 4 3 3 7 3 3 3 5 3 8 3 2 3 3 3 3 3 3 3 3 1 8 3 3 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 7 6 6 7 6 5 5 1 5 4 6 5 6 6 6 6 6 6 6 6 1 7 6 6 6 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 0   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 2 2 2 2 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |
|   | 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 4 4 4 4 4 5 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |          |

|                     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |        |
|---------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--------|
| Ovary               | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50     |
| Cyst                |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 19 2.3 |
| Uterus              | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50     |
| Hyperplasia, Cystic | 1 4 3 2 2 3 1 2 2 2 1 2 2 2 1 2 2 3             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 33 2.0 |
| Vagina              |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 3      |

**HEMATOPOIETIC SYSTEM**

|                                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |       |
|---------------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-------|
| Bone Marrow                           | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50    |
| Depletion Cellular                    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 3.0 |
| Hyperplasia                           | 4 3 4 1 3   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 8 3.0 |
| Infiltration Cellular, Histiocyte     | 1 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2 1.5 |
| Myelofibrosis                         |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 2.0 |
| Lymph Node                            | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 5     |
| Mediastinal, Hemorrhage               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2 3.0 |
| Mediastinal, Hyperplasia, Plasma Cell |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 3.0 |
| Lymph Node, Mandibular                | M M M M M M M M M M M A M M M M M M M + M M M M + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2     |
| Hemorrhage                            |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 1.0 |
| Hyperplasia, Lymphoid                 |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 2.0 |
| Lymph Node, Mesenteric                | +   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50    |
| Ectasia                               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 2.0 |
| Hemorrhage                            | 2   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 3 1.7 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                                       | 0   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|   | 6 7 7 4 7 7 7 4 7 4 7 7 7 7 7 7 7 7 7 7 6 7 7 7   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
| FISCHER 344 RATS FEMALE<br>25000 PPM<br>ANIMAL ID | 4 3 3 7 3 3 3 5 3 8 3 2 3 3 3 3 3 3 3 3 1 8 3 3 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
|   | 7 6 6 7 6 5 5 1 5 4 6 5 6 6 6 6 6 6 6 6 1 7 6 6 6 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
|   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
|   | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
|   | 3   | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                 |
|   | 2   | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |                 |
|   | 6   | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | <b>* TOTALS</b> |

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|
| Hyperplasia, Lymphoid Pigmentation |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   | 2 | <b>5 1.8</b>  |
|                                    |   |   | 1 |   |   | 1 | 1 | 1 | 1 |   | 2 |   | 1 | 1 |   | 1 | 1 |   | 1 | 1 |   | 2 | 2 | <b>29 1.3</b> |
| Spleen                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Hematopoietic Cell Proliferation   | 3 |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   | 2 | 1 | <b>7 1.9</b>  |
| Pigmentation                       |   | 3 | 2 | 1 |   | 2 | 4 | 3 | 4 |   | 3 |   | 3 | 2 | 1 | 2 | 2 | 3 | 2 | 2 | 3 | 3 | 3 | <b>37 2.7</b> |
| Lymphoid Follicle, Hyperplasia     | 3 |   |   | 1 |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   | 1 | 2 |   | <b>7 1.9</b>  |
| Thymus                             | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | <b>48</b>     |
| Cyst                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   | <b>2 2.0</b>  |
| Hemorrhage                         |   | 2 |   |   |   | 1 |   | 1 |   | 1 |   | 1 | 1 |   | 2 |   | 1 |   |   |   |   |   | 1 | <b>13 1.2</b> |

**INTEGUMENTARY SYSTEM**

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|
| Mammary Gland                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Hyperplasia                      | 4 | 2 | 2 |   | 2 |   | 3 |   | 2 |   |   |   |   | 2 | 3 |   |   |   |   | 2 |   | 2 | 2 | <b>24 2.2</b> |
| Hyperplasia, Focal Duct, Ectasia | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 |   | 2 | 1 | <b>11 1.4</b> |
|                                  | 3 |   | 1 | 1 | 1 | 2 | 4 |   | 2 |   |   | 1 | 2 |   |   | 2 | 2 | 2 | 1 | 3 |   | 2 | 2 | <b>36 1.9</b> |
| Skin                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Cyst Epithelial Inclusion        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1</b>      |

**MUSCULOSKELETAL SYSTEM**

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|
| Bone                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>    |
| Femur, Osteopetrosis |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 4.0</b> |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |   |                 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                                | 6 | 7 | 7 | 4 | 7 | 7 | 7 | 4 | 7 | 4 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 |                 |
|                                | 4 | 3 | 3 | 7 | 3 | 3 | 3 | 5 | 3 | 8 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 1 | 8 | 3 | 3 | 3 |                 |
|                                | 7 | 6 | 6 | 7 | 6 | 5 | 5 | 1 | 5 | 4 | 6 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 1 | 7 | 6 | 6 | 6 |                 |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>25000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>ANIMAL ID</b>               | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                 |
|                                | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |                 |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | <b>* TOTALS</b> |

Skeletal Muscle 1

**NERVOUS SYSTEM**

|                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |        |
|----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--------|
| Brain                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |        |
| Compression                |   |   |   |   | 2 |   | 2 |   |   |   |   |   |   |   | 2 |   |   |   |   |   | 2 | 4 |   |   | 4  | 12 2.7 |
| Developmental Malformation |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 2.0  |
| Gliosis                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 3.0  |
| Hemorrhage                 |   |   | 1 |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 8 1.0  |
| Necrosis                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 3.5  |
| Peripheral Nerve           |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | +  | 3      |
| Spinal Cord                |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | +  | 3      |

**RESPIRATORY SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |       |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|-------|
| Lung                              | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | 49     |       |
| Congestion                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0 |
| Hemorrhage                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 2 1.5 |
| Hyperplasia, Lymphoid             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0 |
| Infiltration Cellular, Histiocyte | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 45 1.0 |       |
| Inflammation, Suppurative         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0 |
| Inflammation, Chronic             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 2 2.0 |
| Alveolar Epithelium, Hyperplasia  |   | 1 | 1 | 1 |   | 2 | 1 | 2 |   |   | 1 |   | 1 | 2 | 1 | 1 |   | 2 |   |   | 1 | 1 | 1 | 1 | 1 | 29 1.3 |       |
| Nose                              | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | 49     |       |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue

M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

Page 123

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

|                                | DAY ON TEST |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
|--------------------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                                | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
|                                | 6           | 7 | 7 | 4 | 7 | 7 | 7 | 4 | 7 | 4 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 |                 |
|                                | 4           | 3 | 3 | 7 | 3 | 3 | 3 | 5 | 3 | 8 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 1 | 8 | 3 | 3 | 3 |                 |
|                                | 7           | 6 | 6 | 7 | 6 | 5 | 5 | 1 | 5 | 4 | 6 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 1 | 7 | 6 | 6 | 6 |                 |
| <b>FISCHER 344 RATS FEMALE</b> | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>25000 PPM</b>               | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>ANIMAL ID</b>               | 3           | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                 |
|                                | 2           | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |                 |
|                                | 6           | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | <b>* TOTALS</b> |

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              |                |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|----------------|
| Foreign Body                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b> |                |
| Inflammation, Chronic                       |   | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>2 7 1.6</b> |
| Goblet Cell, Hyperplasia                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 1.0</b>   |
| Nasolacrimal Duct, Hyperplasia,<br>Squamous |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 2.0</b>   |
| Respiratory Epithelium, Hyperplasia         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |              | <b>1 2.0</b>   |
| Trachea                                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +            | <b>50</b>      |

SPECIAL SENSES SYSTEM

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |              |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|--------------|
| Eye                   | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | <b>49</b>     |              |
| Cataract              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 | 4 | <b>3 4.0</b>  |              |
| Edema                 |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 | 3 | <b>3 3.3</b>  |              |
| Inflammation, Chronic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 1.0</b> |
| Cornea, Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 1.0</b> |
| Retina, Degeneration  |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   | 3 | 4 | <b>3 3.7</b>  |              |
| Harderian Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>50</b>    |
| Atrophy               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 3.0</b> |
| Inflammation, Chronic |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 |   |   |   |   |   |   |   |   | 1 | <b>10 1.3</b> |              |
| Zymbal's Gland        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>2</b>     |

URINARY SYSTEM

|        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |           |
|--------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | <b>49</b> |
|--------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked  
Page 124

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST  | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |        |
|--|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|--------|
|  | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |        |
| 6  | 7         | 7 | 4 | 7 | 7 | 7 | 4 | 7 | 4 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 |          |        |
| 4  | 3         | 3 | 7 | 3 | 3 | 3 | 5 | 3 | 8 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 1 | 8 | 3 | 3 | 3 |          |        |
| 7  | 6         | 6 | 7 | 6 | 5 | 5 | 1 | 5 | 4 | 6 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 1 | 7 | 6 | 6 | 6 |          |        |
| <hr/>  |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |        |
| <b>FISCHER 344 RATS FEMALE</b><br><b>25000 PPM</b> | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |        |
|  | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          |        |
|  | 3         | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |          |        |
|  | 2         | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |          |        |
| 6  | 7         | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |          |        |
| Cyst   |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0    |        |
| Infarct  |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0    |        |
| Inflammation, Chronic                              |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0    |        |
| Mineralization                                     |           |   |   |   | 1 | 1 | 1 |   | 2 |   | 1 |   |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 30 1.1   |        |
| Nephropathy  | 1         | 1 | 2 | 1 | 1 | 1 | 2 |   | 2 | 1 | 2 |   | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 2 | 1        | 43 1.4 |
| Bilateral, Infarct                                 |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0    |        |
| Renal Tubule, Accumulation, Hyaline Droplet        |           |   |   |   | 3 |   | 4 |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   | 3 |   |   | 6 3.5    |        |
| Renal Tubule, Necrosis                             |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 1.5    |        |
| Transitional Epithelium, Hyperplasia               |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 1.5    |        |
| <hr/>  |           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |        |
| Urinary Bladder                                    | +         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50       |        |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked





TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|             | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 |
|             | 2 | 2 | 9 | 2 | 2 | 3 | 3 | 3 | 6 | 3 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 |
|             | 9 | 9 | 3 | 9 | 9 | 6 | 6 | 6 | 4 | 6 | 9 | 9 | 9 | 2 | 9 | 9 | 6 | 6 | 6 | 6 | 8 | 9 | 6 | 6 |

  

| FISCHER 344 RATS FEMALE<br>50000 PPM | ANIMAL ID | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                      |           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|                                      |           | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
|                                      |           | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
|                                      |           | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females  
(cont...)

|                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Blood Vessel   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Heart          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cardiomyopathy | 1 | 1 | 2 | 1 |   | 1 | 1 |   |   | 1 | 1 | 1 |   | 1 | 1 |   |   | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Thrombosis     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**ENDOCRINE SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Accessory Adrenal Cortical Nodule |   |   |   |   |   |   |   |   | 1 |   |   | 2 |   | 1 | 1 | 2 |   |   |   |   |   |   |   |   |   |   |
| Degeneration, Fatty               |   | 1 |   | 1 | 2 | 2 |   |   |   |   | 1 | 1 |   | 1 | 1 |   |   |   |   | 1 | 2 |   |   | 1 | 1 |   |
| Hyperplasia, Focal                | 1 | 2 |   | 2 | 4 | 2 | 2 | 2 |   |   |   | 2 |   | 2 |   |   |   |   |   | 2 |   |   | 2 | 2 | 2 |   |
| Hypertrophy, Focal                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Capsule, Hyperplasia              |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                       |   |   | 3 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Islets, Pancreatic                | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid Gland                 | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars Distalis, Angiectasis        |   |   | 2 |   |   |   |   |   |   |   |   | 2 | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Cyst               |   | 2 |   |   |   |   |   |   |   | 1 |   | 3 | 2 | 2 |   |   |   |   |   | 1 |   |   |   | 1 |   |   |
| Pars Distalis, Hyperplasia        |   |   |   |   |   |   |   |   |   |   | 3 | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Distalis, Hyperplasia, Focal |   | 2 | 1 |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pars Intermedia, Angiectasis      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 |   |
|                                | 2 | 2 | 9 | 2 | 2 | 3 | 3 | 3 | 6 | 3 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 |   |
|                                | 9 | 9 | 3 | 9 | 9 | 6 | 6 | 6 | 4 | 6 | 9 | 9 | 9 | 2 | 9 | 9 | 6 | 6 | 6 | 6 | 8 | 9 | 6 | 6 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| <b>50000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
| ANIMAL ID                      | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |   |
|                                | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 |   |
|                                | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |

females (cont...)

Rathke's Cleft, Hemorrhage

2

Thyroid Gland  
Degeneration, Cystic  
C-cell, Hyperplasia

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 1 | 1 |   | 1 | 1 | 2 |   |   |   |   |   |   | 1 | 3 | 1 | 1 |   |   | 1 |   | 1 | 1 | 1 | 1 |   |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

Clitoral Gland  
Abscess  
Hyperplasia  
Inflammation, Chronic

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 2 |   |   |   | 2 | 3 |   |   |   |   |   | 2 | 2 |   |   | 3 |   |   |   | 2 | 1 | 3 |   |   |   |

Ovary  
Cyst

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|   |   |   |   |   |   |   |   |   | 2 |   |   | 3 |   |   | 2 |   |   |   | 3 |   |   |   |   |   |

Uterus  
Hyperplasia, Cystic

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| 2 | 2 | 1 | 1 | 1 | 4 |   | 3 |   |   | 1 |   |   | 2 | 1 | 1 | 1 | 3 |   |   | 1 | 1 |   | 2 | 2 | 2 |

Vagina

+

HEMATOPOIETIC SYSTEM

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                      | FISCHER 344 RATS FEMALE |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females (cont...) |
|----------------------------------|-------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------------------|
|                                  | ANIMAL ID               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| 50000 PPM                        | 0                       | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                 |
|                                  | 7                       | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |                   |
|                                  | 2                       | 2 | 9 | 2 | 2 | 3 | 3 | 3 | 6 | 3 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 |                   |
|                                  | 9                       | 9 | 3 | 9 | 9 | 6 | 6 | 6 | 4 | 6 | 9 | 9 | 9 | 2 | 9 | 9 | 6 | 6 | 6 | 6 | 8 | 9 | 6 | 6 | 6 |                   |
| Bone Marrow                      | +                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |                   |
| Hyperplasia                      |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Lymph Node                       |                         |   | + |   |   |   |   |   |   | + |   |   |   |   | + |   |   |   |   |   | + | + |   |   |   |                   |
| Deep Cervical, Ectasia           |                         |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |                   |
| Mediastinal, Hemorrhage          |                         |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Mediastinal, Pigmentation        |                         |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Pancreatic, Hemorrhage           |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |                   |
| Pancreatic, Pigmentation         |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |                   |
| Lymph Node, Mandibular           | M                       | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | M |   |                   |
| Lymph Node, Mesenteric           | +                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |                   |
| Hemorrhage                       |                         | 1 |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 1 |   |   | 1 |   |                   |
| Hyperplasia, Lymphoid            |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Hyperplasia, Reticulum Cell      |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Pigmentation                     | 2                       |   |   |   |   | 2 | 1 | 1 |   | 1 | 1 | 1 |   |   | 1 |   | 1 |   | 1 |   |   |   |   |   |   |                   |
| Spleen                           | +                       | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |                   |
| Fibrosis                         |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |                   |
| Hematopoietic Cell Proliferation |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Necrosis                         |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Pigmentation                     | 3                       | 4 |   | 3 | 3 | 3 | 3 | 3 |   | 2 | 2 | 3 | 4 |   | 4 |   | 2 | 3 | 2 | 4 | 4 | 3 | 2 | 3 |   |                   |
| Lymphoid Follicle, Atrophy       |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |                   |
| Lymphoid Follicle, Hyperplasia   |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Thymus                           | +                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |                   |
| Cyst                             |                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                   |
| Hemorrhage                       | 1                       | 2 | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 2 | 1 |   |   | 1 |   |                   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

|  | DAY ON TEST |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|  | 7           | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 |   |
|  | 2           | 2 | 9 | 2 | 2 | 3 | 3 | 3 | 6 | 3 | 2 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 |
|  | 9           | 9 | 3 | 9 | 9 | 6 | 6 | 6 | 4 | 6 | 9 | 9 | 9 | 2 | 9 | 9 | 6 | 6 | 6 | 6 | 8 | 9 | 6 | 6 | 6 |

  

| FISCHER 344 RATS FEMALE<br>50000 PPM | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females<br>(cont...) |
|--------------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
|                                      | 3         | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                      |
|                                      | 5         | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 |                      |
|                                      | 1         | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |                      |

**INTEGUMENTARY SYSTEM**

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia               |   |   | 3 |   | 2 | 2 |   | 1 |   | 1 |   |   |   |   | 2 | 2 |   |   |   | 2 | 2 |   |   | 3 |
| Hyperplasia, Focal        | 1 | 1 |   |   | 3 |   |   |   |   | 2 |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   | 2 |
| Duct, Ectasia             | 2 | 2 | 3 | 2 | 3 | 3 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 2 | 3 | 1 |   | 1 | 4 |   | 2 | 4 | 2 |   |
| Skin                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst Epithelial Inclusion |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperkeratosis            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   | 4 |   |
| Ulcer                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |
| Epidermis, Hyperplasia    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   | 2 |   |

**MUSCULOSKELETAL SYSTEM**

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Femur, Osteopetrosis |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**NERVOUS SYSTEM**

|                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Compression    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage     |   |   |   |   |   |   |   | 1 | 1 |   |   | 1 |   |   |   | 1 |   | 1 |   |   |   | 3 | 4 | 2 |
| Mineralization |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Necrosis       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue

M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked

Page 131

| DAY ON TEST | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|             | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7           | 7         | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 |
| 2           | 2         | 9 | 2 | 2 | 3 | 3 | 3 | 6 | 3 | 2 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 |
| 9           | 9         | 3 | 9 | 9 | 6 | 6 | 6 | 4 | 6 | 9 | 9 | 9 | 2 | 9 | 9 | 6 | 6 | 6 | 6 | 6 | 8 | 9 | 6 | 6 | 6 |

  

| FISCHER 344 RATS FEMALE<br>50000 PPM | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females<br>(cont...) |
|--------------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|
|                                      | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
| 0                                    | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
| 3                                    | 3         | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                      |
| 5                                    | 5         | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |                      |
| 1                                    | 2         | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |   |                      |

Peripheral Nerve

+

Spinal Cord

+

**RESPIRATORY SYSTEM**

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lung                                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage                          | 1 |   |   | 3 |   |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 2 |
| Infiltration Cellular, Histiocyte   | 1 | 1 |   | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Inflammation, Chronic               | 1 |   |   |   | 2 | 1 | 2 |   |   |   |   | 2 |   | 2 |   |   |   |   |   |   |   |   |   |   | 2 |
| Metaplasia, Osseous                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Alveolar Epithelium, Hyperplasia    | 2 | 1 |   | 2 | 2 |   | 3 |   |   | 1 | 1 | 2 |   |   | 4 | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| Nose                                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Foreign Body                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 2 |   |   |   |
| Inflammation, Chronic               |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   | 2 |   |   |   |
| Nasolacrimal Duct, Cyst             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Respiratory Epithelium, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Trachea                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**SPECIAL SENSES SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cataract              |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |
| Edema                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

| DAY ON TEST                    | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females<br>(cont...) |
|--------------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|
|                                | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
| 7                              | 7         | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 6 | 6 | 7 | 7 |                      |
| 2                              | 2         | 9 | 2 | 2 | 3 | 3 | 3 | 6 | 3 | 2 | 2 | 2 | 2 | 2 | 1 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 |                      |
| 9                              | 9         | 3 | 9 | 9 | 6 | 6 | 6 | 4 | 6 | 9 | 9 | 9 | 2 | 9 | 9 | 6 | 6 | 6 | 6 | 8 | 9 | 6 | 6 | 6 | 6 |                      |
| <b>FISCHER 344 RATS FEMALE</b> | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
| <b>50000 PPM</b>               | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                      |
|                                | 3         | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |                      |
|                                | 5         | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 |   |                      |
|                                | 1         | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 |                      |

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Retina, Degeneration  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |
| Harderian Gland       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Focal    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
|                       |   |   | 1 |   | 1 |   |   |   |   | 1 | 1 |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |

**URINARY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infarct                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineralization                              | 1 | 1 |   | 1 | 1 | 1 | 1 | 1 |   | 1 |   | 1 | 1 | 1 |   |   |   |   | 1 | 1 |   | 1 | 1 | 1 | 1 |   |
| Nephropathy                                 | 2 | 2 |   | 2 | 1 | 1 | 1 | 1 |   | 2 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |   |
| Renal Tubule, Accumulation, Hyaline Droplet |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal Tubule, Hyperplasia                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Renal Tubule, Necrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Urinary Bladder                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
 Page 133

TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                    | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
|                                | 7   | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 5 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 |   | 7               |
|                                | 3   | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 4 | 6 | 3 | 3 | 3 | 0 | 4 | 3 | 3 | 2 | 3 | 3 | 3 |                 |
|                                | 6   | 6 | 6 | 3 | 6 | 5 | 5 | 5 | 5 | 4 | 2 | 2 | 6 | 7 | 2 | 5 | 5 | 3 | 7 | 5 | 6 | 1 | 6 | 6 | 6 |                 |
| <b>FISCHER 344 RATS FEMALE</b> | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| <b>50000 PPM</b>               | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |                 |
| ANIMAL ID                      | 3   | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 |                 |
|                                | 7   | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |                 |
|                                | 6   | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | <b>* TOTALS</b> |

**ALIMENTARY SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |           |              |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|-----------|--------------|
| Esophagus                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>50</b> |              |
| Intestine Large, Cecum<br>Edema   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>49</b> | <b>1 4.0</b> |
| Intestine Large, Colon<br>Ulcer   | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>46</b> | <b>1 4.0</b> |
| Intestine Large, Rectum           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>48</b> |              |
| Intestine Small, Duodenum         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>48</b> |              |
| Intestine Small, Ileum            | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>46</b> |              |
| Intestine Small, Jejunum          | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>46</b> |              |
| Liver                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>50</b> |              |
| Basophilic Focus                  | X | X |   |   | X | X | X | X | X | X | X | X | X | X | X | X | X | X |   |   | X | X | X | X | X             | <b>43</b> |              |
| Clear Cell Focus                  | X |   |   |   | X | X |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   | X | <b>21</b>     |           |              |
| Eosinophilic Focus                |   | X |   |   | X |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   | X | X | X |   |               | <b>11</b> |              |
| Hepatodiaphragmatic Nodule        |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   | X |   |   |               | <b>5</b>  |              |
| Infiltration Cellular, Mixed Cell | 1 | 2 |   |   | 1 |   | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | <b>39 1.1</b> |           |              |
| Mixed Cell Focus                  |   | X |   |   |   |   | X | X |   |   |   |   |   | X |   |   | X |   |   |   |   | X | X | X | <b>10</b>     |           |              |
| Necrosis, Focal                   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |           |              |
| Bile Duct, Hyperplasia            |   |   |   |   | 1 |   |   | 1 |   |   |   |   |   |   |   |   |   | 1 |   | 1 |   |   |   |   | <b>8 1.1</b>  |           |              |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
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TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Milk thistle extract

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

Lab: SRI

|  | DAY ON TEST |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |               |                 |          |          |   |   |   |              |   |  |  |               |
|--|-------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------------|-----------------|----------|----------|---|---|---|--------------|---|--|--|---------------|
|  | 0 7 3 6     | 0 7 3 6 | 0 7 3 6 | 0 6 1 3 | 0 7 3 3 | 0 7 3 3 | 0 7 3 3 | 0 7 3 3 | 0 7 3 3 | 0 6 7 3 | 0 7 3 3 | 0 5 4 6 | 0 7 3 3 | 0 7 3 3 | 0 7 3 3 | 0 6 4 3 | 0 7 3 3 | 0 7 2 3 | 0 7 3 2 | 0 7 3 3 | 0 7 3 3 | 0 7 3 3 | 0 6 6 6 |               |                 |          |          |   |   |   |              |   |  |  |               |
| <b>FISCHER 344 RATS FEMALE</b>               | 0           | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0             |                 |          |          |   |   |   |              |   |  |  |               |
| <b>50000 PPM</b>                             | 0           | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0       | 0             |                 |          |          |   |   |   |              |   |  |  |               |
| ANIMAL ID                                    | 3           | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 3       | 4             |                 |          |          |   |   |   |              |   |  |  |               |
|  | 7           | 7       | 7       | 7       | 8       | 8       | 8       | 8       | 8       | 8       | 8       | 8       | 8       | 8       | 9       | 9       | 9       | 9       | 9       | 9       | 9       | 9       | 9       | 0             |                 |          |          |   |   |   |              |   |  |  |               |
|  | 6           | 7       | 8       | 9       | 0       | 1       | 2       | 3       | 4       | 5       | 6       | 7       | 8       | 9       | 0       | 1       | 2       | 3       | 4       | 5       | 6       | 7       | 8       | 9             | <b>* TOTALS</b> |          |          |   |   |   |              |   |  |  |               |
| Hepatocyte, Vacuolization Cytoplasmic        |             |         |         | 2       |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 3       | 4       |               |                 |          |          | 1 |   |   | <b>6 2.3</b> |   |  |  |               |
| Hepatocyte, Vacuolization Cytoplasmic, Focal |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |               | X               | <b>1</b> |          |   |   |   |              |   |  |  |               |
| Mesentery                                    |             |         |         |         |         |         |         |         |         |         | +       |         |         |         |         | +       |         |         | +       | +       |         |         |         |               |                 |          | <b>8</b> |   |   |   |              |   |  |  |               |
| Accessory Spleen                             |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         | X       |         |         |         |         |         |         |         |               | <b>2</b>        |          |          |   |   |   |              |   |  |  |               |
| Fat, Necrosis                                |             |         |         |         |         |         |         |         | 2       |         |         |         |         |         |         | 2       | 2       |         |         |         |         |         |         | <b>6 2.0</b>  |                 |          |          |   |   |   |              |   |  |  |               |
| Pancreas                                     | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | <b>49</b>     |                 |          |          |   |   |   |              |   |  |  |               |
| Atrophy                                      | 1 2         |         | 1 3     |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1       | 2       | 1             | 2 1             |          | 1        | 1 | 1 | 1 | 1            | 1 |  |  | <b>26 1.3</b> |
| Acinus, Hyperplasia, Focal                   |             |         |         |         | 1       | 1       | 1       |         |         |         | 4 1     |         | 1       | 1       |         |         | 1       | 1       | 1       | 1       | 1       | 2       |         |               | <b>17 1.3</b>   |          |          |   |   |   |              |   |  |  |               |
| Duct, Ectasia                                |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |               |                 |          |          |   |   |   |              |   |  |  |               |
| Salivary Glands                              | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | <b>50</b>     |                 |          |          |   |   |   |              |   |  |  |               |
| Atrophy                                      |             |         |         |         |         |         |         |         |         |         | 1       | 1 1     |         | 1 1     |         | 1       | 1       |         |         | 1       | 1       |         |         | <b>16 1.1</b> |                 |          |          |   |   |   |              |   |  |  |               |
| Stomach, Forestomach                         | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | <b>50</b>     |                 |          |          |   |   |   |              |   |  |  |               |
| Edema  |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 3       |         |         |         |         |         |               | <b>1 3.0</b>    |          |          |   |   |   |              |   |  |  |               |
| Erosion                                      | 1           |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |               | <b>1 1.0</b>    |          |          |   |   |   |              |   |  |  |               |
| Ulcer  |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |               | <b>1 4.0</b>    |          |          |   |   |   |              |   |  |  |               |
| Epithelium, Hyperplasia                      |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |               | <b>1 3.0</b>    |          |          |   |   |   |              |   |  |  |               |
| Stomach, Glandular                           | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | <b>49</b>     |                 |          |          |   |   |   |              |   |  |  |               |
| Erosion                                      |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 2       |         |         |         |         |         | <b>1 2.0</b>  |                 |          |          |   |   |   |              |   |  |  |               |
| Ulcer  |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1       | 2       |         |         |         |         | <b>3 1.7</b>  |                 |          |          |   |   |   |              |   |  |  |               |

CARDIOVASCULAR SYSTEM

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                    | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 | 0 |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|---|
|                                | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 5 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7               | 7 | 7 |
|                                | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 4 | 6 | 3 | 3 | 3 | 0 | 4 | 3 | 3 | 2 | 3 | 3               | 3 |   |
|                                | 6 | 6 | 6 | 3 | 6 | 5 | 5 | 5 | 5 | 4 | 2 | 2 | 6 | 7 | 2 | 5 | 5 | 3 | 7 | 5 | 6 | 1 | 6 | 6               | 6 |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |   |
| <b>50000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0               | 0 |   |
| <b>ANIMAL ID</b>               | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3               | 4 |   |
|                                | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9               | 0 |   |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9               | 0 |   |
|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>* TOTALS</b> |   |   |

|                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |               |
|----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|---------------|
| Blood Vessel   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2</b> |               |
| Heart          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +        | <b>50</b>     |
| Cardiomyopathy |   | 1 |   |   |   | 2 | 1 | 2 | 1 | 2 |   | 1 | 1 | 2 |   | 1 | 2 |   | 1 | 1 | 1 | 1 | 1 | 1        | <b>34 1.2</b> |
| Thrombosis     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |          | <b>1 2.0</b>  |

**ENDOCRINE SYSTEM**

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |               |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---------------|
| Adrenal Cortex                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>50</b>     |
| Accessory Adrenal Cortical Nodule |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>7 1.4</b>  |               |
| Degeneration, Fatty               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>22 1.5</b> |               |
| Hyperplasia, Focal                | 2 | 2 | 2 |   |   | 2 | 1 | 2 | 3 |   | 1 | 2 |   |   | 4 | 2 |   |   | 1 | 2 | 1 |   |   | 4             | <b>29 2.0</b> |
| Hypertrophy, Focal                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |               |
| Capsule, Hyperplasia              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 1.0</b>  |               |
| Adrenal Medulla                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>50</b>     |
| Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>6 1.8</b>  |               |
| Islets, Pancreatic                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>49</b>     |
| Parathyroid Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>49</b>     |
| Pituitary Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +             | <b>50</b>     |
| Pars Distalis, Angiectasis        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>7 2.0</b>  |               |
| Pars Distalis, Cyst               | 2 | 2 |   |   |   | 1 |   |   |   |   | 1 | 2 |   | 3 | 1 | 2 |   |   |   |   |   | 2 |   |               | <b>14 1.7</b> |
| Pars Distalis, Hyperplasia        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 2.5</b>  |               |
| Pars Distalis, Hyperplasia, Focal | 1 |   |   |   |   |   |   |   |   |   | 1 | 1 |   |   | 1 | 2 |   |   |   |   |   |   |   |               | <b>8 1.4</b>  |
| Pars Intermedia, Angiectasis      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>2 3.0</b>  |               |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked



TDMS No. 20008 - 03

Test Type: CHRONIC

Route: DOSED FEED

Species/Strain: RATS/F 344/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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

| DAY ON TEST                      | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  |                 |    |     |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----------------|----|-----|
|                                  | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 5 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7  |                 |    |     |
|                                  | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 4 | 6 | 3 | 3 | 3 | 0 | 4 | 3 | 3 | 2 | 3 | 3 | 3 | 3  |                 |    |     |
|                                  | 6 | 6 | 6 | 3 | 6 | 5 | 5 | 5 | 5 | 4 | 2 | 2 | 6 | 7 | 2 | 5 | 5 | 3 | 7 | 5 | 6 | 1 | 6 | 6 | 6 | 6  |                 |    |     |
| <b>FISCHER 344 RATS FEMALE</b>   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  |                 |    |     |
| <b>50000 PPM</b>                 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  |                 |    |     |
| ANIMAL ID                        | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4  |                 |    |     |
|                                  | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0  |                 |    |     |
|                                  | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |    | <b>* TOTALS</b> |    |     |
| Bone Marrow                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |                 |    |     |
| Hyperplasia                      |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 2.0 |
| Lymph Node                       |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   | 8  |                 |    |     |
| Deep Cervical, Ectasia           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 3.0 |
| Mediastinal, Hemorrhage          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 3.0 |
| Mediastinal, Pigmentation        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 3.0 |
| Pancreatic, Hemorrhage           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 2.0 |
| Pancreatic, Pigmentation         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 3.0 |
| Lymph Node, Mandibular           | M | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 2  |                 |    |     |
| Lymph Node, Mesenteric           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |                 |    |     |
| Hemorrhage                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 5  | 1.0 |
| Hyperplasia, Lymphoid            |   |   |   |   |   | 2 |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |    |                 | 2  | 2.0 |
| Hyperplasia, Reticulum Cell      |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 3.0 |
| Pigmentation                     | 1 |   | 1 |   |   |   |   | 1 | 1 | 1 |   |   |   |   | 2 |   |   |   |   | 1 |   |   |   |   | 1 |    |                 | 18 | 1.2 |
| Spleen                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |                 |    |     |
| Fibrosis                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 3.0 |
| Hematopoietic Cell Proliferation |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |    |                 | 2  | 1.5 |
| Necrosis                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |    |                 | 1  | 4.0 |
| Pigmentation                     | 2 | 3 |   |   | 3 | 1 | 3 | 3 | 2 | 3 | 4 | 3 | 1 | 3 | 3 | 3 | 3 |   |   | 3 | 4 | 3 | 4 | 4 | 3 |    |                 | 42 | 3.0 |
| Lymphoid Follicle, Atrophy       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 3.0 |
| Lymphoid Follicle, Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |    |                 | 1  | 1.0 |
| Thymus                           | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | 49 |                 |    |     |
| Cyst                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |    |                 | 1  | 1.0 |
| Hemorrhage                       |   |   |   | 1 |   | 1 |   | 1 |   |   | 2 |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 1 |    |                 | 14 | 1.3 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
x .. Lesion present  
I .. Insufficient tissue  
M .. Missing tissue  
A .. Autolysis precludes evaluation  
BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
2) Mild 4) Marked

| DAY ON TEST                    | 0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | * TOTALS |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|---|
|                                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |          | 0 |
|                                | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 5 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7        |   |
|                                | 3 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 4 | 6 | 3 | 3 | 3 | 0 | 4 | 3 | 3 | 2 | 3 | 3 | 3        |   |
|                                | 6 | 6 | 6 | 3 | 6 | 5 | 5 | 5 | 5 | 4 | 2 | 2 | 6 | 7 | 2 | 5 | 5 | 3 | 7 | 5 | 6 | 1 | 6 | 6 | 6        |   |
| <b>FISCHER 344 RATS FEMALE</b> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |   |
| <b>50000 PPM</b>               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        |   |
| ANIMAL ID                      | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4        |   |
|                                | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0        |   |
|                                | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0        |   |

**INTEGUMENTARY SYSTEM**

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |        |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--------|
| Mammary Gland                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |        |
| Hyperplasia                      |   |   |   | 3 | 2 |   | 2 | 1 | 2 | 1 |   |   |   | 3 |   |   | 3 | 4 | 4 | 2 |   | 4 |   | 2 |    | 23 2.3 |
| Hyperplasia, Focal Duct, Ectasia |   |   | 3 | 3 |   |   | 1 | 1 | 2 |   |   |   |   | 2 | 1 |   |   | 1 |   |   |   |   | 2 |   |    | 20 1.7 |
|                                  |   |   | 3 | 4 | 1 | 1 | 2 | 2 |   | 2 | 2 |   |   | 2 | 2 | 2 | 2 | 1 | 2 |   | 2 | 2 | 2 | 4 |    | 40 2.1 |
| Skin                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |        |
| Cyst Epithelial Inclusion        |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |    | 1      |
| Hyperkeratosis                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 3.0  |
| Ulcer                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 3.0  |
| Epidermis, Hyperplasia           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 2.5  |

**MUSCULOSKELETAL SYSTEM**

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |       |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|-------|
| Bone                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |       |
| Femur, Osteopetrosis |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  | 2 1.5 |

**NERVOUS SYSTEM**

|                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |        |        |
|----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--------|--------|
| Brain          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |        |        |
| Compression    |   |   |   | 3 |   |   |   |   |   | 2 | 4 |   |   | 2 |   |   |   |   |   |   |   |   | 4 | 3 | 4  |        | 10 3.1 |
| Hemorrhage     |   |   |   |   |   |   |   |   | 1 | 3 | 1 |   |   |   |   |   |   | 1 | 1 |   |   |   |   |   |    | 14 1.1 |        |
| Mineralization |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0  |        |
| Necrosis       |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0  |        |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade

+ .. Tissue examined microscopically

x .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

Page 139

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked



TDMS No. 20008 - 03  
 Test Type: CHRONIC  
 Route: DOSED FEED  
 Species/Strain: RATS/F 344/N

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

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

| DAY ON TEST                                 | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|--|---------------|--|--|--|--|--|--|--|--|--|--|--|---|--|--|--|---|--------------|--------------|
|   | 7   | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 5 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
|   | 3   | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 7 | 3 | 3 | 4 | 6 | 3 | 3 | 3 | 0 | 4 | 3 | 3 | 2 | 3 | 3 | 3 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
|   | 6   | 6 | 6 | 3 | 6 | 5 | 5 | 5 | 5 | 4 | 2 | 2 | 6 | 7 | 2 | 5 | 5 | 3 | 7 | 5 | 6 | 1 | 6 | 6 | 6 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| <b>FISCHER 344 RATS FEMALE</b>              | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| <b>50000 PPM</b>                            | 0   | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| ANIMAL ID                                   | 3   | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
|   | 7   | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
|   | 6   | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
|   | <b>* TOTALS</b>                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Retina, Degeneration                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   | 4 |   | <b>3 4.0</b>  |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Harderian Gland                             | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Hyperplasia, Focal                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   | <b>1 3.0</b>  |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Inflammation, Chronic                       |   |   |   |   | 2 | 1 | 1 |   |   |   |   | 2 | 1 |   |   |   |   |   |   | 1 |   |   |   |   |   |               |  | <b>12 1.2</b> |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| <b>URINARY SYSTEM</b>                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Kidney                                      | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Infarct                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   | <b>1 2.0</b>  |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Inflammation, Chronic                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   | <b>1 2.0</b>  |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Mineralization                              |   |   |   |   | 1 | 1 | 1 |   |   |   |   | 1 | 1 |   |   |   |   | 1 |   |   | 2 | 1 | 1 | 1 |   | <b>26 1.0</b> |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Nephropathy                                 |   |   |   |   | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 2 | 1 | 2 | <b>42 1.3</b> |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |
| Renal Tubule, Accumulation, Hyaline Droplet |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  | 3 | <b>1 3.0</b> |              |
| Renal Tubule, Hyperplasia                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   | <b>1 1.0</b> |              |
| Renal Tubule, Necrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  | 2 |  |  |  |   | <b>1 2.0</b> |              |
| Transitional Epithelium, Hyperplasia        |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  | 2 | 2            | <b>4 2.3</b> |
| Urinary Bladder                             | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |  |               |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |              |              |

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

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically  
 x .. Lesion present  
 I .. Insufficient tissue  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
 1) Minimal 3) Moderate  
 2) Mild 4) Marked  
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