

**Experiment Number:** 00058 - 03

**Test Type:** CHRONIC

**Route:** GAVAGE

**Species/Strain:** RATS/HSD

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

Black Cohosh

**CAS Number:** 84776-26-1

**Date Report Requested:** 10/07/2020

**Time Report Requested:** 11:17:00

**First Dose M/F:** 07/03/12 / 07/02/12

**Lab:** BAT

Rats Final 1

**NTP Study Number:** C00058B  
**Lock Date:** 10/02/2018  
**Cage Range:** ALL  
**Date Range:** ALL  
**Reasons For Removal:** ALL  
**Removal Date Range:** ALL  
**Treatment Groups:** Include ALL  
**Study Gender:** Both  
**TDMSE Version:** 3.0.2.3\_002  
**PWG Approval Date:** NONE

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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		
<b>HARLAN SPRAGUE DAWLEY RATS MALE</b>		7	7	7	6	6	7	7	5	6	5	7	5	7	6	6	7	6	6	7	5	7	7	5	6	7	
	<b>0 mg/kg male</b>	3	2	3	7	5	0	3	9	8	6	1	7	1	4	4	3	2	4	1	3	3	3	7	7	3	
		1	6	0	4	4	4	0	8	0	2	8	3	1	3	6	0	4	6	1	8	0	0	7	2	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	0	
		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
		0	0	0	0	0	0	0	0	0	0	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	
		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>

ALIMENTARY SYSTEM

Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine Large, Cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Erosion											2														
Inflammation, Acute																					1				
Inflammation, Chronic											1														
Inflammation, Chronic Active																								3	
Mineral											2													3	
Polyarteritis Nodosa											2								2						2
Ulcer																								3	
Intestine Large, Colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Inflammation, Chronic																									
Parasite Metazoan																									
Polyarteritis Nodosa																									2
Lymphoid Tissue, Hyperplasia																									
Intestine Large, Rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyarteritis Nodosa																									2
Intestine Small, Duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyarteritis Nodosa																									2
Intestine Small, Ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Polyarteritis Nodosa																									
Intestine Small, Jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

\* .. 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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HARLAN SPRAGUE DAWLEY RATS MALE 0 mg/kg male	DAY ON TEST																				ANIMAL ID	males (cont...)																												
	0 7 3 1	0 7 2 6	0 7 3 0	0 6 7 4	0 6 5 4	0 7 0 4	0 7 3 0	0 5 9 8	0 6 8 0	0 5 6 2	0 7 1 8	0 5 7 3	0 6 1 1	0 6 4 3	0 7 6 0	0 6 2 4	0 6 4 6	0 7 1 1	0 5 3 8	0 7 3 0			0 7 3 0	0 5 7 7	0 6 7 2	0 7 3 1																								
Polyarteritis Nodosa																						2																												
Liver																																																		
Angiectasis																																																		
Clear Cell Focus	X	X		X X		X		X		X		X		X		X		X		X		X																												
Eosinophilic Focus																																																		
Mixed Cell Focus																																																		
Necrosis	3																							1	2		1 2		2																					
Polyarteritis Nodosa																						1																												
Artery, Inflammation, Chronic Active																																																		
Bile Duct, Cyst																						X																												
Bile Duct, Dilation																						3																												
Bile Duct, Hyperplasia	2		1	1	1	1		1	1	1	1	1 1		1 1		2		1																																
Pancreas																																																		
Polyarteritis Nodosa																						2																												
Acinus, Atrophy																						1 2																												
Acinus, Hyperplasia	2																							1	4		1																							
Salivary Glands																																																		
Atrophy																																																		
Stomach, Forestomach																																																		
Inflammation, Granulomatous																																																		
Inflammation, Chronic																																																		
Mineral																																																		
Polyarteritis Nodosa																																																		
Epithelium, Hyperplasia																																																		
Epithelium, Hyperplasia, Basal Cell																																																		

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

+ .. Tissue examined microscopically

X .. Lesion present

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HARLAN SPRAGUE DAWLEY RATS MALE 0 mg/kg male	DAY ON TEST																									males (cont...)
	0 7 3 1	0 7 2 6	0 7 3 0	0 6 7 4	0 6 5 4	0 7 0 4	0 7 3 0	0 5 9 8	0 6 8 0	0 5 6 2	0 7 1 8	0 5 7 3	0 6 4 3	0 6 4 6	0 7 3 0	0 6 2 4	0 6 4 6	0 7 1 8	0 5 3 0	0 7 3 0	0 5 7 2	0 6 7 1	0 7 3 1			
ANIMAL ID	0 0 0 0 1	0 0 0 0 2	0 0 0 0 3	0 0 0 0 4	0 0 0 0 5	0 0 0 0 6	0 0 0 0 7	0 0 0 0 8	0 0 0 0 9	0 0 0 0 0	0 0 0 0 1	0 0 0 0 2	0 0 0 0 3	0 0 0 0 4	0 0 0 0 5	0 0 0 0 6	0 0 0 0 7	0 0 0 0 8	0 0 0 0 9	0 0 0 0 0	0 0 0 0 1	0 0 0 0 2	0 0 0 0 3	0 0 0 0 4	0 0 0 0 5	

Bilateral, Hyperplasia, Focal

4

Islets, Pancreatic  
Atrophy  
Hyperplasia

+  
3

Parathyroid Gland  
Hyperplasia, Diffuse

+ + + + + + + + + + + + + + + + + M + + + + +  
1 3 2 2 3

Pituitary Gland  
Inflammation, Chronic Active  
Pars Distalis, Hyperplasia

+  
3 1

Thyroid Gland  
Ectopic Thymus  
C-cell, Hyperplasia

+  
1 2 4 3 1

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

Epididymis  
Atrophy  
Bilateral, Atrophy

+  
2 2

Preputial Gland  
Duct, Hyperplasia, Squamous

+  
3

Prostate

+ +

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| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male | DAY ON TEST      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | ANIMAL ID | males<br>(cont...) |                       |                  |
|--|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|-----------|--------------------|-----------------------|------------------|
|  | 0<br>7<br>3<br>1 | 0<br>7<br>2<br>6 | 0<br>7<br>3<br>0 | 0<br>6<br>7<br>4 | 0<br>6<br>5<br>4 | 0<br>7<br>0<br>4 | 0<br>7<br>3<br>0 | 0<br>5<br>9<br>8 | 0<br>6<br>8<br>0 | 0<br>5<br>2<br>8 | 0<br>7<br>1<br>3 | 0<br>5<br>7<br>1 | 0<br>6<br>4<br>3 | 0<br>6<br>4<br>6 | 0<br>7<br>2<br>4 | 0<br>6<br>6<br>1 | 0<br>5<br>3<br>8 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>5<br>7<br>7 |           |                    | 0<br>6<br>7<br>2      | 0<br>7<br>3<br>1 |
|  | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0         | 0                  | 0<br>0<br>0<br>0<br>1 |                  |

Hyperplasia  
Inflammation, Chronic Active

1  
1 1 1 3

Seminal Vesicle  
Inflammation, Chronic Active

+ +

Testis  
Granuloma Sperm

+  
1

Mineral  
Polyarteritis Nodosa  
Bilateral, Germinal Epithelium, Degeneration  
Germinal Epithelium, Degeneration  
Interstitial Cell, Hyperplasia

2  
4 1 2 2 1 2 1 1 1 1 2 3 1 2 3 1 3 4 3  
1 3 1 4 3 1 4 3 3 4 2

HEMATOPOIETIC SYSTEM

Bone Marrow  
Hemorrhage  
Hypercellularity

+  
3 3 3 2 3 3 4 2 1 4 2 4 3 2 1  
3 3 3 2 3 3 4 2 1 4 2 4 3 2 1

Lymph Node  
Lumbar, Hyperplasia, Lymphoid  
Mediastinal, Infiltration Cellular, Histiocyte  
Mediastinal, Thrombus  
Renal, Hemorrhage

+  
+  
1 X

Lymph Node, Mandibular  
Hyperplasia, Lymphoid  
Infiltration Cellular, Plasma Cell

+  
+ +

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| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male | DAY ON TEST           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | males<br>(cont...)    |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
|  | 0<br>7<br>3<br>1      | 0<br>7<br>2<br>6      | 0<br>7<br>3<br>0      | 0<br>6<br>7<br>4      | 0<br>6<br>5<br>4      | 0<br>7<br>0<br>4      | 0<br>7<br>3<br>0      | 0<br>5<br>9<br>8      | 0<br>6<br>8<br>0      | 0<br>5<br>6<br>2      | 0<br>7<br>1<br>8      | 0<br>5<br>7<br>3      | 0<br>6<br>4<br>6      | 0<br>6<br>4<br>0      | 0<br>7<br>3<br>4      | 0<br>6<br>2<br>4      | 0<br>7<br>1<br>6      | 0<br>5<br>3<br>8      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>0      | 0<br>5<br>7<br>7      | 0<br>6<br>7<br>2      | 0<br>7<br>3<br>1      |                       |                       |
| ANIMAL ID  | 0<br>0<br>0<br>0<br>1 | 0<br>0<br>0<br>0<br>2 | 0<br>0<br>0<br>0<br>3 | 0<br>0<br>0<br>0<br>4 | 0<br>0<br>0<br>0<br>5 | 0<br>0<br>0<br>0<br>6 | 0<br>0<br>0<br>0<br>7 | 0<br>0<br>0<br>0<br>8 | 0<br>0<br>0<br>0<br>9 | 0<br>0<br>0<br>0<br>0 | 0<br>0<br>0<br>0<br>1 | 0<br>0<br>0<br>0<br>2 | 0<br>0<br>0<br>0<br>3 | 0<br>0<br>0<br>0<br>4 | 0<br>0<br>0<br>0<br>5 | 0<br>0<br>0<br>0<br>6 | 0<br>0<br>0<br>0<br>7 | 0<br>0<br>0<br>0<br>8 | 0<br>0<br>0<br>0<br>9 | 0<br>0<br>0<br>0<br>0 | 0<br>0<br>0<br>0<br>1 | 0<br>0<br>0<br>0<br>2 | 0<br>0<br>0<br>0<br>3 | 0<br>0<br>0<br>0<br>4 | 0<br>0<br>0<br>0<br>5 |

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lymph Node, Mesenteric Atrophy                                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Lymphoid Infiltration Cellular, Histiocyte Necrosis |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Spleen                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Extramedullary Hematopoiesis | 2 | 2 | 2 | 3 | 3 | 3 | 2 | 2 |   | 3 | 2 | 2 | 2 | 4 | 3 |   | 2 | 2 | 3 | 2 | 4 | 3 | 1 | 2 |
| Pigment                      | 2 | 1 | 1 | 1 |   |   | 2 | 1 | 2 | 2 |   | 1 | 2 | 1 |   | 1 | 1 | 1 |   | 1 |   |   | 1 | 1 |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| White Pulp, Atrophy          |   | 2 |   |   |   |   |   |   |   | 3 |   |   |   | 4 |   |   |   |   | 3 | 2 |   |   | 2 | 4 |

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thymus                    | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Atrophy                   | 2 | 4 | 2 | 3 |   | 4 | 1 | 2 | 4 | 4 | 4 | 3 | 4 | 3 | 4 |   | 2 | 4 | 4 | 2 | 2 | 4 | 4 | 1 |
| Ectopic Parathyroid Gland |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**INTEGUMENTARY SYSTEM**

|               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + |
| Galactocele   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Hyperplasia   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Skin                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst Epithelial Inclusion    |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Granulomatous  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. 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

|   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                                  |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------------------------------|
| <b>HARLAN SPRAGUE DAWLEY RATS</b><br><b>MALE</b><br><b>0 mg/kg male</b> | DAY ON TEST | 0731  | 0736  | 0770  | 0774  | 0775  | 0783  | 0788  | 0790  | 0792  | 0798  | 0799  | 0799  | 0803  | 0804  | 0806  | 0807  | 0808  | 0811  | 0813  | 0817  | 0817  | 0823  | 0824  | 0826  | 0827  | 0831  | 0832  | <b>males</b><br><b>(cont...)</b> |
|   | ANIMAL ID   | 00001 | 00002 | 00003 | 00004 | 00005 | 00006 | 00007 | 00008 | 00009 | 00010 | 00011 | 00012 | 00013 | 00014 | 00015 | 00016 | 00017 | 00018 | 00019 | 00020 | 00021 | 00022 | 00023 | 00024 | 00025 | 00026 | 00027 |                                  |
|   |             | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |                                  |

**MUSCULOSKELETAL SYSTEM**

|      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

**NERVOUS SYSTEM**

|            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
| Brain      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |
| Hemorrhage |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |

**RESPIRATORY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
| Lung  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |
| Infiltration Cellular, Histiocyte             |   |   | 1 |   |   |   | 2 | 1 |   |   | 3 | 1 |   |   |   |   | 1 | 1 | 1 | 1 |   |   |   | 1 | 1 |   |   |   |  |
| Inflammation, Granulomatous                   | 1 |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 | 1 |   |   |   |   |   | 1 |   |   |  |
| Inflammation, Acute                           |   |   |   |   |   |   |   |   |   |   | 3 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Mineral                                       |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   |  |
| Alveolar Epithelium, Hyperplasia              |   |   |   | 2 |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Alveolus, Foreign Body                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Interstitial, Fibrosis                        |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Perivascular, Infiltration Cellular, Lymphoid |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Nose  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |
| Foreign Body                                  |   | X | X |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Inflammation, Suppurative                     |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |  |
| Inflammation, Acute                           |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Inflammation, Chronic                         |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Inflammation, Chronic Active                  |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Nasolacrimal Duct, Inflammation, Suppurative  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Nasolacrimal Duct, Inflammation, Chronic      | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |

\* .. 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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Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male | DAY ON TEST      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                       | ANIMAL ID | males<br>(cont...) |
|--|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|-----------------------|-----------|--------------------|
|  | 0<br>7<br>3<br>1 | 0<br>7<br>2<br>6 | 0<br>7<br>3<br>0 | 0<br>6<br>7<br>4 | 0<br>6<br>5<br>4 | 0<br>7<br>0<br>4 | 0<br>7<br>3<br>0 | 0<br>5<br>9<br>8 | 0<br>6<br>8<br>0 | 0<br>5<br>6<br>2 | 0<br>7<br>1<br>8 | 0<br>5<br>7<br>3 | 0<br>6<br>4<br>1 | 0<br>6<br>4<br>6 | 0<br>7<br>3<br>4 | 0<br>6<br>2<br>6 | 0<br>7<br>1<br>1 | 0<br>5<br>3<br>8 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>5<br>7<br>7 | 0<br>6<br>7<br>2 | 0<br>7<br>3<br>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<br>0<br>0<br>0<br>1 |           |                    |

Nasolacrimal Duct, Inflammation, Chronic Active

1

Olfactory Epithelium, Metaplasia, Respiratory  
Respiratory Epithelium, Hyperplasia

Trachea

+ +

SPECIAL SENSES SYSTEM

Eye

+ +

Cataract

1

Cornea, Inflammation, Acute

3

3

2

Cornea, Inflammation, Chronic

2

Cornea, Inflammation, Chronic Active

Retina, Degeneration

2 2

1

Retina, Fibrosis

1

Harderian Gland

+ +

Atrophy

Zymbal's Gland

+

URINARY SYSTEM

Kidney

+ +

Calculus Micro Observation Only

Hemorrhage

4

Hyperplasia, Oncocytic

Infarct

1

Nephropathy, Chronic Progressive

3 3 4 4 4 3 2 4 4 4 4 4 4 2 4 4 4 4 4 4 3 2 3 4 4

Polyarteritis Nodosa

1

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

+ .. Tissue examined microscopically

M .. Missing tissue

1-4 .. Lesion qualified as:

X .. Lesion present

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Black Cohosh

CAS Number: 84776-26-1

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Lab: BAT

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|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|  | 0731        | 0732  | 0733  | 0734  | 0735  | 0736  | 0737  | 0738  | 0739  | 0740  | 0741  | 0742  | 0743  | 0744  | 0745  | 0746  | 0747  | 0748  | 0749  | 0750  | 0751  | 0752  | 0753  | 0754  |          |
| ANIMAL ID  | 00026       | 00027 | 00028 | 00029 | 00030 | 00031 | 00032 | 00033 | 00034 | 00035 | 00036 | 00037 | 00038 | 00039 | 00040 | 00041 | 00042 | 00043 | 00044 | 00045 | 00046 | 00047 | 00048 | 00049 | 00050    |

**ALIMENTARY SYSTEM**

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |       |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-------|
| Esophagus                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Intestine Large, Cecum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Erosion                      |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |    | 3 1.7 |
| Inflammation, Acute          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0 |
| Inflammation, Chronic        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |    | 2 1.0 |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 3.0 |
| Mineral                      |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3 2.3 |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3 2.0 |
| Ulcer                        |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 2.5 |
| Intestine Large, Colon       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Inflammation, Chronic        |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0 |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1     |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 2.0 |
| Lymphoid Tissue, Hyperplasia |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 3.0 |
| Intestine Large, Rectum      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 1.5 |
| Intestine Small, Duodenum    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 2.0 |
| Intestine Small, Ileum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |       |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |    | 1 1.0 |
| Intestine Small, Jejunum     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |

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X .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

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Lab: BAT

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|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-------|-----|
|  | 07<br>31    | 07<br>20 | 07<br>30 | 07<br>31 | 06<br>16 | 06<br>18 | 06<br>23 | 06<br>29 | 06<br>32 | 07<br>08 | 07<br>11 | 07<br>13 | 06<br>22 | 06<br>28 | 07<br>05 | 07<br>11 | 07<br>14 | 05<br>09 | 06<br>04 | 06<br>06 |          | 06<br>11 | 06<br>13 | 06<br>20 | 06<br>27 | 06<br>30 |       |     |
| ANIMAL ID  | 00026       | 00027    | 00028    | 00029    | 00030    | 00031    | 00032    | 00033    | 00034    | 00035    | 00036    | 00037    | 00038    | 00039    | 00040    | 00041    | 00042    | 00043    | 00044    | 00045    | 00046    | 00047    | 00048    | 00049    | 00050    |          |       |     |
| Polyarteritis Nodosa                               |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        | 2 2.0 |     |
| Liver  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       | 1 3.0 |     |
| Angiectasis  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 19    | 3.0 |
| Clear Cell Focus                                   | X           |          | X        | X        |          |          |          |          |          | X        | X        | X        |          |          |          |          |          |          |          |          | X        | X        |          | X        |          |          | 5     |     |
| Eosinophilic Focus                                 |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | X        | X        |          |          |          |          | 2     |     |
| Mixed Cell Focus                                   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | X        |          |          |          |          |          | 8     | 1.6 |
| Necrosis   | 1           |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          | 2     | 1.0 |
| Polyarteritis Nodosa                               |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1     | 2.0 |
| Artery, Inflammation, Chronic Active               |             |          |          |          |          |          |          |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          | 4     |     |
| Bile Duct, Cyst                                    |             |          |          | X        |          |          | X        |          | X        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 3     | 2.7 |
| Bile Duct, Dilation                                |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 27    | 1.1 |
| Bile Duct, Hyperplasia                             | 1           | 1        | 2        | 1        |          |          | 1        |          |          | 1        |          | 1        | 1        | 1        |          | 1        |          |          |          |          | 1        | 1        |          | 1        | 1        |          | 50    |     |
| Pancreas   | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       | 6 1.7 |     |
| Polyarteritis Nodosa                               |             |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          | 5     | 1.4 |
| Acinus, Atrophy                                    |             |          |          | 1        |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 9     | 2.3 |
| Acinus, Hyperplasia                                |             |          | 4        | 3        |          |          | 1        | 1        |          |          |          |          |          |          |          |          |          | 4        |          |          |          |          |          |          |          |          | 50    |     |
| Salivary Glands                                    | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       | 1 2.0 |     |
| Atrophy  |             |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1     | 2.0 |
| Stomach, Forestomach                               | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       | 1 1.0 |     |
| Inflammation, Granulomatous                        |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          | 2     | 1.5 |
| Inflammation, Chronic                              |             |          |          |          |          |          |          |          |          | 2        |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          | 1     | 1.0 |
| Mineral  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          | 1     | 2.0 |
| Polyarteritis Nodosa                               |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          | 1     | 2.0 |
| Epithelium, Hyperplasia                            |             |          |          |          |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1     | 2.0 |
| Epithelium, Hyperplasia, Basal Cell                |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 3        |          | 1     | 3.0 |

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|  | 07<br>31    | 07<br>20 | 07<br>23 | 07<br>31 | 06<br>16 | 06<br>18 | 06<br>23 | 06<br>29 | 06<br>32 | 07<br>08 | 07<br>11 | 07<br>13 | 06<br>22 | 04<br>28 | 06<br>27 | 05<br>05 | 03<br>09 | 05<br>14 | 06<br>16 | 06<br>23 | 06<br>26 | 07<br>03 | 06<br>07 | 06<br>10 |          | 06<br>17 |
| ANIMAL ID  | 00026       | 00027    | 00028    | 00029    | 00030    | 00031    | 00032    | 00033    | 00034    | 00035    | 00036    | 00037    | 00038    | 00039    | 00040    | 00041    | 00042    | 00043    | 00044    | 00045    | 00046    | 00047    | 00048    | 00049    | 00050    |          |

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| Stomach, Glandular                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Infiltration Cellular, Lymphocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Inflammation, Chronic             |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Mineral                           |   | 4 |   |   | 2 | 2 |   |   |   |   |   | 3 |   |   |   |   |   | 2 | 2 |   |   |   | 3 |   |   | 15 |

CARDIOVASCULAR SYSTEM

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| Blood Vessel         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 32 |
| Mineral              |   | 2 |   |   | 3 |   |   |   |   |   |   | 2 |   |   |   |   |   | 1 | 1 |   |   |   | 2 |   |   | 14 |
| Intima, Hyperplasia  |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Heart                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Cardiomyopathy       | 1 | 3 | 2 | 1 | 1 |   |   | 1 | 1 | 1 |   | 3 |   |   |   | 1 |   | 2 | 2 |   | 1 | 1 | 2 |   | 1 | 37 |
| Mineral              |   | 1 |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  |
| Polyarteritis Nodosa |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 2  |
| Atrium, Thrombus     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   | 2  |

ENDOCRINE SYSTEM

|                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |
|-------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| Adrenal Cortex                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Degeneration, Cystic          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 5  |
| Hyperplasia, Focal            |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 6  |
| Hypertrophy, Focal            |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Necrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 1 |   |   | 2  |
| Vacuolization Cytoplasmic     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Bilateral, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Adrenal Medulla               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hyperplasia, Focal            |   | 1 |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 1 |   | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male                      | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|   | 0731        | 0732  | 0733  | 0734  | 0735  | 0736  | 0737  | 0738  | 0739  | 0740  | 0741  | 0742  | 0743  | 0744  | 0745  | 0746  | 0747  | 0748  | 0749  | 0750  | 0751  | 0752  | 0753  | 0754  |          |
| ANIMAL ID   | 00026       | 00027 | 00028 | 00029 | 00030 | 00031 | 00032 | 00033 | 00034 | 00035 | 00036 | 00037 | 00038 | 00039 | 00040 | 00041 | 00042 | 00043 | 00044 | 00045 | 00046 | 00047 | 00048 | 00049 | 00050    |
| Bilateral, Hyperplasia, Focal   |             |       |       | 2     |       |       |       |       | 3     |       |       |       |       |       | 2     |       |       |       |       |       |       |       |       |       | 5        |
| Islets, Pancreatic Atrophy  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |
| Hyperplasia   |             |       |       |       |       |       |       |       | 1     |       |       |       |       |       |       |       |       |       |       |       |       |       | 4     |       | 1        |
| Parathyroid Gland Hyperplasia, Diffuse                                  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 49       |
| Pituitary Gland Inflammation, Chronic Active Pars Distalis, Hyperplasia |             | 4     |       |       | 4     |       |       |       | 3     |       |       | 4     |       |       |       |       |       | 4     | 3     |       |       |       | 2     | 3     | 13       |
| Pituitary Gland Inflammation, Chronic Active Pars Distalis, Hyperplasia | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |
| Thyroid Gland Ectopic Thymus  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 1        |
| C-cell, Hyperplasia   |             | 4     |       | 2     |       | 3     |       |       | 3     |       |       |       |       | 3     |       |       |       |       |       |       |       |       |       |       | 9        |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| Epididymis Atrophy                          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Bilateral, Atrophy                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |
| Preputial Gland Duct, Hyperplasia, Squamous | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Prostate                                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

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

+ .. Tissue examined microscopically

X .. Lesion present

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

Black Cohosh

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male | DAY ON TEST |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | * TOTALS |          |          |          |          |          |          |          |     |
|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----|
|  | 07<br>31    | 07<br>20 | 07<br>30 | 07<br>31 | 06<br>16 | 06<br>18 | 06<br>23 | 06<br>29 | 06<br>32 | 07<br>08 | 07<br>11 | 07<br>13 | 06<br>22 | 06<br>28 | 07<br>05 | 07<br>11 | 07<br>14 | 05<br>09 | 06<br>04 | 06<br>06 |          | 06<br>06 | 07<br>03 | 06<br>03 | 07<br>03 | 06<br>07 | 06<br>07 | 06<br>07 |     |
| ANIMAL ID  | 00026       | 00027    | 00028    | 00029    | 00030    | 00031    | 00032    | 00033    | 00034    | 00035    | 00036    | 00037    | 00038    | 00039    | 00040    | 00041    | 00042    | 00043    | 00044    | 00045    | 00046    | 00047    | 00048    | 00049    | 00050    | 00051    | 00052    |          |     |
| Hyperplasia  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        | 1.0 |
| Inflammation, Chronic Active                       | 2           |          |          |          |          | 3        | 3        |          | 2        |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          | 9        | 2.0 |
| Seminal Vesicle                                    | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       |     |
| Inflammation, Chronic Active                       |             |          |          |          |          |          | 2        |          | 2        |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 3        | 2.0 |
| Testis   | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       |     |
| Granuloma Sperm                                    |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        | 1.0 |
| Mineral  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        |          |          |          |          |          | 1        | 2.0 |
| Polyarteritis Nodosa                               |             |          | 1        |          | 2        |          | 2        | 1        | 1        |          |          | 1        |          |          | 3        |          | 2        | 2        |          |          |          |          | 2        | 1        |          |          |          | 24       | 1.6 |
| Bilateral, Germinal Epithelium, Degeneration       |             |          | 3        |          |          |          | 1        | 1        |          |          |          |          |          |          |          |          | 2        |          | 4        |          |          |          | 1        |          |          |          |          | 14       | 2.4 |
| Germinal Epithelium, Degeneration                  | 1           |          |          |          |          |          |          |          |          |          |          | 2        |          | 1        | 1        |          |          |          |          |          |          | 3        |          | 4        | 2        |          |          | 12       | 2.2 |
| Interstitial Cell, Hyperplasia                     |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        | 2.0 |
| <b>HEMATOPOIETIC SYSTEM</b>                        |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |     |
| Bone Marrow  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       |     |
| Hemorrhage   |             |          | 3        |          | 4        |          |          |          | 2        |          | 2        |          |          |          |          |          |          | 1        |          |          |          |          | 4        |          | 4        |          |          | 10       | 2.8 |
| Hypercellularity                                   | 2           | 2        |          |          | 2        | 4        | 1        | 3        |          | 4        |          |          |          | 3        | 1        |          | 1        | 2        |          |          | 1        |          |          | 1        |          |          |          | 28       | 2.4 |
| Lymph Node   |             |          |          |          |          |          |          | +        | +        |          |          |          |          |          |          |          |          |          |          |          |          | +        |          |          |          |          |          | 5        |     |
| Lumbar, Hyperplasia, Lymphoid                      |             |          |          |          |          |          | 3        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        | 3.0 |
| Mediastinal, Infiltration Cellular, Histiocyte     |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        | 1.0 |
| Mediastinal, Thrombus                              |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |     |
| Renal, Hemorrhage                                  |             |          |          |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        | 2.0 |
| Lymph Node, Mandibular                             | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | 50       |     |
| Hyperplasia, Lymphoid                              |             |          |          |          |          |          |          |          |          |          |          |          |          |          | 4        |          |          |          |          |          |          |          |          |          |          |          |          | 1        | 4.0 |
| Infiltration Cellular, Plasma Cell                 |             |          |          | 2        |          | 4        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        | 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:  
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Experiment Number: 00058 - 03

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Black Cohosh

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male | DAY ON TEST |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | * TOTALS |          |
|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|  | 07<br>31    | 07<br>30 | 07<br>30 | 07<br>31 | 06<br>16 | 06<br>18 | 06<br>23 | 06<br>29 | 06<br>32 | 07<br>08 | 07<br>11 | 07<br>13 | 06<br>22 | 07<br>04 | 06<br>08 | 06<br>15 | 06<br>21 | 06<br>28 | 06<br>30 | 07<br>03 | 06<br>06 | 06<br>13 | 06<br>20 | 06<br>27 |          | 07<br>03 |
| ANIMAL ID  | 00026       | 00027    | 00028    | 00029    | 00030    | 00031    | 00032    | 00033    | 00034    | 00035    | 00036    | 00037    | 00038    | 00039    | 00040    | 00041    | 00042    | 00043    | 00044    | 00045    | 00046    | 00047    | 00048    | 00049    | 00050    |          |

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |       |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Lymph Node, Mesenteric Atrophy                                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50    |
| Hyperplasia, Lymphoid Infiltration Cellular, Histiocyte Necrosis |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   | 3     |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0 |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 4.0 |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0 |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0 |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Spleen                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Extramedullary Hematopoiesis | 3 |   | 2 | 2 |   | 2 | 1 | 2 |   | 2 | 2 | 3 |   | 2 | 2 | 2 | 2 | 3 | 2 | 2 |   | 2 |   | 2 |   |   | 41 2.3 |
| Pigment                      | 1 | 2 | 1 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 1 |   | 2 |   | 1 | 1 | 1 | 1 |   | 1 | 1 | 2 | 1 | 2 |   |   | 38 1.3 |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |
| White Pulp, Atrophy          |   | 3 |   |   | 4 |   | 2 |   |   |   |   | 3 | 4 |   |   |   | 3 |   | 2 | 2 |   | 4 |   | 4 |   |   | 17 3.0 |

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Thymus                    | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | M | + | M | + | + | + | + | + | 46     |
| Atrophy                   | 2 | 4 | 2 | 1 | 4 | 2 | 4 | 4 | 3 | 1 | 3 |   | 2 | 3 |   | 1 | 2 | 4 | 3 |   | 2 |   | 4 | 2 | 4 |   | 43 2.9 |
| Ectopic Parathyroid Gland |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   | 2 3.0  |
| Polyarteritis Nodosa      |   |   |   |   | 2 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0  |

INTEGUMENTARY SYSTEM

|               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |       |
|---------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-------|
| Mammary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |       |
| Galactocele   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 2.0 |
| Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0 |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |       |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-------|
| Skin                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Cyst Epithelial Inclusion    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1     |
| Inflammation, Granulomatous  |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 4.0 |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |    | 1 3.0 |
| Ulcer                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |    | 1 3.0 |

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

+ .. Tissue examined microscopically

X .. Lesion present

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First Dose M/F: 07/03/12 / 07/02/12  
Lab: BAT

|  | 0<br>7<br>3<br>1      | 0<br>7<br>2<br>0      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>1      | 0<br>6<br>1<br>6      | 0<br>6<br>9<br>8      | 0<br>6<br>9<br>3      | 0<br>6<br>9<br>2      | 0<br>7<br>1<br>8      | 0<br>7<br>3<br>1      | 0<br>7<br>3<br>1      | 0<br>6<br>2<br>1      | 0<br>4<br>8<br>7      | 0<br>6<br>7<br>5      | 0<br>1<br>3<br>5      | 0<br>7<br>3<br>5      | 0<br>3<br>4<br>9      | 0<br>5<br>6<br>4      | 0<br>6<br>6<br>2      | 0<br>6<br>6<br>3      | 0<br>7<br>6<br>3      | 0<br>7<br>6<br>3      | 0<br>6<br>7<br>0      | 0<br>6<br>7<br>6      |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|--|--|----------|---|-----|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|-----|-----|
| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | * TOTALS |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
| ANIMAL ID  | 0<br>0<br>0<br>2<br>6 | 0<br>0<br>0<br>2<br>7 | 0<br>0<br>0<br>2<br>8 | 0<br>0<br>0<br>3<br>9 | 0<br>0<br>0<br>3<br>0 | 0<br>0<br>0<br>3<br>1 | 0<br>0<br>0<br>3<br>2 | 0<br>0<br>0<br>3<br>3 | 0<br>0<br>0<br>3<br>4 | 0<br>0<br>0<br>3<br>5 | 0<br>0<br>0<br>3<br>6 | 0<br>0<br>0<br>3<br>7 | 0<br>0<br>0<br>3<br>8 | 0<br>0<br>0<br>3<br>9 | 0<br>0<br>0<br>4<br>0 | 0<br>0<br>0<br>4<br>1 | 0<br>0<br>0<br>4<br>2 | 0<br>0<br>0<br>4<br>3 | 0<br>0<br>0<br>4<br>4 | 0<br>0<br>0<br>4<br>5 | 0<br>0<br>0<br>4<br>6 | 0<br>0<br>0<br>4<br>7 | 0<br>0<br>0<br>4<br>8 | 0<br>0<br>0<br>4<br>9 |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
| Nasolacrimal Duct, Inflammation, Chronic Active    |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | 1        | 2 | 1.0 |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
| Olfactory Epithelium, Metaplasia, Respiratory      |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          | 2 | 1   | 2.0 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
| Respiratory Epithelium, Hyperplasia                |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | 1        | 1 | 1.0 |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
| Trachea  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | +        | + | +   | +   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |     |     |
| <b>SPECIAL SENSES SYSTEM</b>                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
| Eye  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | +        | + | +   | +   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |     |     |
| Cataract   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 1.0 |     |     |
| Cornea, Inflammation, Acute                        |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 5   | 2.4 |     |
| Cornea, Inflammation, Chronic                      |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |    |   | 2   | 1.5 |     |
| Cornea, Inflammation, Chronic Active               |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   | 4   |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   | 1   | 4.0 |     |
| Retina, Degeneration                               |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   | 3   | 1.7 |     |
| Retina, Fibrosis                                   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   | 1   | 1.0 |     |
| Harderian Gland                                    |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | +        | + | +   | +   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | + | 50  |     |     |
| Atrophy  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   | 2   | 1   | 2.0 |
| Zymbal's Gland                                     |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   | 2   |     |     |
| <b>URINARY SYSTEM</b>                              |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |     |     |
| Kidney   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | +        | + | +   | +   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | + | 50  |     |     |
| Calculus Micro Observation Only                    |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     | 1   |     |
| Hemorrhage   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     | 1   | 4.0 |
| Hyperplasia, Oncocytic                             |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   | 4   |     |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     | 2   | 3.0 |
| Infarct  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     | 1   | 1.0 |
| Nephropathy, Chronic Progressive                   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  | 3        | 4 | 3   | 3   | 4 | 4 | 3 | 4 | 4 | 2 | 3 | 4 | 2 | 4 | 2 | 4 | 2 | 4 | 4 | 3 | 2 | 4 | 4 | 3 | 4  |   | 50  | 3.4 |     |
| Polyarteritis Nodosa                               |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |          |   |     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     | 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

Experiment Number: 00058 - 03  
 Test Type: CHRONIC  
 Route: GAVAGE  
 Species/Strain: RATS/HSD

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 Black Cohosh  
 CAS Number: 84776-26-1

Date Report Requested: 10/07/2020  
 Time Report Requested: 11:17:00  
 First Dose M/F: 07/03/12 / 07/02/12  
 Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>0 mg/kg male | DAY ON TEST      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | * TOTALS |
|--|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|----------|
|  | 0<br>7<br>3<br>1 | 0<br>7<br>2<br>0 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>1 | 0<br>6<br>1<br>6 | 0<br>6<br>1<br>8 | 0<br>6<br>9<br>3 | 0<br>6<br>9<br>2 | 0<br>7<br>1<br>8 | 0<br>7<br>3<br>1 | 0<br>7<br>3<br>1 | 0<br>6<br>2<br>1 | 0<br>4<br>8<br>1 | 0<br>6<br>7<br>8 | 0<br>1<br>5<br>5 | 0<br>7<br>3<br>1 | 0<br>3<br>5<br>4 | 0<br>5<br>9<br>3 | 0<br>6<br>4<br>2 | 0<br>6<br>6<br>3 | 0<br>7<br>3<br>1 | 0<br>6<br>3<br>1 | 0<br>7<br>3<br>0 | 0<br>6<br>7<br>6 |          |
|  | 0<br>0<br>0<br>6 | 0<br>0<br>0<br>7 | 0<br>0<br>0<br>8 | 0<br>0<br>0<br>9 | 0<br>0<br>0<br>0 | 0<br>0<br>0<br>1 | 0<br>0<br>0<br>2 | 0<br>0<br>0<br>3 | 0<br>0<br>0<br>4 | 0<br>0<br>0<br>5 | 0<br>0<br>0<br>6 | 0<br>0<br>0<br>7 | 0<br>0<br>0<br>8 | 0<br>0<br>0<br>9 | 0<br>0<br>0<br>0 | 0<br>0<br>0<br>1 | 0<br>0<br>0<br>2 | 0<br>0<br>0<br>3 | 0<br>0<br>0<br>4 | 0<br>0<br>0<br>5 | 0<br>0<br>0<br>6 | 0<br>0<br>0<br>7 | 0<br>0<br>0<br>8 | 0<br>0<br>0<br>9 |          |
| 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        |
| Pelvis, Dilation                                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2        |
| Pelvis, Inflammation, Acute                        |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2        |
| Pelvis, Inflammation, Chronic Active               |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2        |
| Renal Tubule, Accumulation, Hyaline Droplet        |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 4        |
| Renal Tubule, Cyst                                 |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 4        |
| Renal Tubule, Dilation                             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 2        |
| Urinary Bladder                                    |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 50       |
| Inflammation, Chronic                              |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 4        |
| Perivascular, Infiltration Cellular, Lymphocyte    |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|   |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |                    |    |
|---|-------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|--------------------|----|
| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST | 04 | 06 | 06 | 07 | 07 | 06 | 06 | 05 | 06 | 07 | 06 | 06 | 07 | 07 | 07 | 05 | 07 | 06 | 07 | 02 | 07 | 07 | 05 | 04 | males<br>(cont...) |    |
|   | ANIMAL ID   | 08 | 03 | 06 | 02 | 03 | 04 | 08 | 09 | 01 | 03 | 03 | 06 | 01 | 01 | 01 | 03 | 05 | 03 | 01 | 03 | 07 | 03 | 03 | 06 |                    | 07 |
|   |             | 08 | 07 | 06 | 04 | 00 | 04 | 00 | 06 | 07 | 00 | 00 | 09 | 01 | 03 | 01 | 00 | 03 | 00 | 08 | 01 | 04 | 01 | 01 | 00 |                    | 05 |

ALIMENTARY SYSTEM

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum          | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Erosion                         |   |   |   |   |   |   |   |   |   |   | 1 |   | 2 |   |   |   |   |   |   |   |   |   |   | 1 |
| Infiltration Cellular, Lymphoid |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic           |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |
| Inflammation, Chronic Active    |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineral                         |   |   |   |   |   |   | 1 |   |   |   | 1 |   | 3 |   |   |   |   |   |   |   | 2 |   |   |   |
| Polyarteritis Nodosa            |   |   |   |   |   |   | 2 |   |   |   | 2 |   | 1 |   |   |   |   |   |   |   | 1 |   | 3 |   |
| Ulcer                           |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Colon          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Infiltration Cellular, Lymphoid |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineral                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |
| Parasite Metazoan               |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   | X |   |   |   |
| Polyarteritis Nodosa            |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |
| Lymphoid Tissue, Hyperplasia    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |
| Intestine Large, Rectum         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parasite Metazoan               |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |
| Intestine Small, Duodenum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Ileum          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyarteritis Nodosa            |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Jejunum        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

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Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   | ANIMAL ID | males<br>(cont...) |
|---|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|---|-----------|--------------------|
|   | 0<br>4<br>8<br>8 | 0<br>6<br>3<br>7 | 0<br>6<br>6<br>6 | 0<br>7<br>2<br>4 | 0<br>7<br>3<br>0 | 0<br>6<br>4<br>4 | 0<br>6<br>8<br>0 | 0<br>5<br>9<br>6 | 0<br>6<br>1<br>7 | 0<br>7<br>3<br>0 | 0<br>6<br>3<br>0 | 0<br>6<br>6<br>9 | 0<br>7<br>1<br>1 | 0<br>6<br>3<br>1 | 0<br>7<br>1<br>3 | 0<br>7<br>1<br>1 | 0<br>5<br>3<br>3 | 0<br>7<br>1<br>0 | 0<br>6<br>8<br>1 | 0<br>7<br>3<br>4 | 0<br>7<br>3<br>1 | 0<br>5<br>3<br>1 | 0<br>7<br>3<br>0 | 0<br>4<br>7<br>5 |   |           |                    |
| Polyarteritis Nodosa                                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Peyer's Patch, Hyperplasia                          |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           | 2                  |
| Liver   | +                | +                |                  | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | + |           |                    |
| Basophilic Focus                                    |                  |                  | X                |                  |                  |                  |                  |                  |                  |                  |                  |                  | X                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Clear Cell Focus                                    |                  |                  |                  |                  | X                |                  |                  |                  |                  | X                |                  |                  |                  | X                |                  | X                |                  | X                |                  | X                |                  |                  |                  | X                |   | X         | X                  |
| Eosinophilic Focus                                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  | X                |                  |   |           |                    |
| Extramedullary Hematopoiesis                        |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   | 1         |                    |
| Fatty Change, Focal                                 |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Hepatodiaphragmatic Nodule                          |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Inflammation, Granulomatous                         |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           | 4                  |
| Mixed Cell Focus                                    |                  |                  |                  |                  | X                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Necrosis  |                  |                  | 2                |                  |                  |                  |                  |                  |                  |                  | 2                |                  |                  |                  |                  |                  | 3                |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Bile Duct, Cyst                                     |                  |                  | X                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Bile Duct, Dilation                                 |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Bile Duct, Hyperplasia                              |                  |                  | 1                |                  | 1                | 1                |                  |                  |                  | 1                | 1                |                  |                  |                  |                  |                  | 1                |                  |                  | 1                |                  |                  |                  |                  |   |           |                    |
| Centrilobular, Necrosis                             |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Mesentery   |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Hemorrhage  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           |                    |
| Pigment   |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           | 2                  |
| Polyarteritis Nodosa                                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           | 3                  |
| Pancreas  | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | + |           |                    |
| Polyarteritis Nodosa                                |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           | 2                  |
| Acinus, Atrophy                                     |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   | 1         |                    |
| Acinus, Hyperplasia                                 |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   | 4         | 1 4                |
| Salivary Glands                                     | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | +                | + |           |                    |
| Atrophy   |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   |           | 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

Experiment Number: 00058 - 03

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

Date Report Requested: 10/07/2020

Test Type: CHRONIC

Black Cohosh

Time Report Requested: 11:17:00

Route: GAVAGE

CAS Number: 84776-26-1

First Dose M/F: 07/03/12 / 07/02/12

Species/Strain: RATS/HSD

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 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 |                    |
|   | 4           | 6 | 6 | 7 | 7 | 6 | 6 | 5 | 6 | 7 | 6 | 6 | 6 | 7 | 7 | 7 | 5 | 7 | 6 | 7 | 2 | 7 | 7 | 5 |                    |
| ANIMAL ID   | 8           | 3 | 6 | 2 | 3 | 4 | 8 | 9 | 1 | 3 | 3 | 6 | 1 | 1 | 1 | 3 | 5 | 3 | 1 | 3 | 7 | 3 | 3 | 6 | 7                  |
|   | 8           | 7 | 6 | 4 | 0 | 4 | 0 | 6 | 7 | 0 | 0 | 9 | 1 | 3 | 1 | 0 | 3 | 0 | 8 | 1 | 4 | 1 | 1 | 0 | 5                  |
|   | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|   | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                  |
|   | 0           | 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                  |
|   | 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                  |

Inflammation, Chronic Active

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Stomach, Forestomach                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst, Squamous                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |
| Foreign Body                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infiltration Cellular, Lipocyte     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Inflammation, Acute                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic Active        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineral                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Epithelium, Hyperplasia             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Epithelium, Hyperplasia, Basal Cell |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Stomach, Glandular              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Infiltration Cellular, Lipocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Acute             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineral                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Tongue  
Edema  
Inflammation, Chronic Active

|                             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-----------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Tooth                       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Metaplasia, Osseous         |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Dentine, Degeneration       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pulp, Inflammation, Chronic |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**CARDIOVASCULAR SYSTEM**

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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | males<br>(cont...) |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------------------|
|   | 0488        | 0637  | 0666  | 0724  | 0774  | 0664  | 0568  | 0669  | 0711  | 0663  | 0666  | 0711  | 0771  | 0777  | 0575  | 0773  | 0661  | 0737  | 0773  | 0773  | 0566  | 0747  | 0775  | 0475  |       |                    |
| ANIMAL ID   | 00051       | 00052 | 00053 | 00054 | 00055 | 00056 | 00057 | 00058 | 00059 | 00060 | 00061 | 00062 | 00063 | 00064 | 00065 | 00066 | 00067 | 00068 | 00069 | 00070 | 00071 | 00072 | 00073 | 00074 | 00075 |                    |

|   |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
|---|---|---|---|--|--|---|---|---|---|---|--|---|---|---|---|---|---|---|--|---|---|---|---|---|---|---|---|---|
| Blood Vessel                                    |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Aneurysm  | + | + |   |  |  | + | + | + | + | + |  |   | + |   | + | + | + |   |  | + | + | + |   |   | + |   |   |   |
| Mineral   | 2 | 2 |   |  |  |   | 3 | 1 |   |   |  |   | 2 |   | 4 |   |   | 2 |  |   | 3 |   | 2 |   |   | 2 |   |   |
| Aorta, Dilation                                 |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   | 3 |   |   |   |   | 3 |   |   |
| Heart   |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Cardiomyopathy                                  | 1 | 1 | 2 |  |  | 1 | 2 | 2 | 1 |   |  | 1 | 3 | 2 | 3 | 2 | 3 |   |  | 3 |   | 3 | 2 | 1 | 2 | 2 | 2 | 2 |
| Inflammation, Acute                             |   |   | 1 |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Mineral   | 2 |   |   |  |  |   | 1 |   |   |   |  |   |   |   | 1 |   |   |   |  | 3 |   | 1 |   |   |   |   |   |   |
| Polyarteritis Nodosa                            |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Thrombus  |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Atrium, Thrombus                                |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |
| Perivascular, Infiltration Cellular, Lymphocyte |   |   |   |  |  |   |   |   |   |   |  |   |   |   |   |   |   |   |  |   |   |   |   |   |   |   |   |   |

ENDOCRINE SYSTEM

|                               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|-------------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Adrenal Cortex                |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Degeneration, Cystic          |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia, Focal            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Necrosis                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Thrombus                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Adrenal Medulla               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia, Focal            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Bilateral, Hyperplasia, Focal |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Islets, Pancreatic            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Hyperplasia                   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Parathyroid Gland             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|                               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

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+ .. Tissue examined microscopically

X .. Lesion present

I .. Insufficient tissue

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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | males<br>(cont...) |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------------------|
|   | 0488        | 0637  | 0666  | 0724  | 0770  | 0664  | 0560  | 0665  | 0676  | 0691  | 0733  | 0669  | 0661  | 0713  | 0771  | 0773  | 0553  | 0730  | 0668  | 0771  | 0227  | 0773  | 0773  | 0554  | 0475  |                    |
| ANIMAL ID   | 00051       | 00052 | 00053 | 00054 | 00055 | 00056 | 00057 | 00058 | 00059 | 00060 | 00061 | 00062 | 00063 | 00064 | 00065 | 00066 | 00067 | 00068 | 00069 | 00070 | 00071 | 00072 | 00073 | 00074 | 00075 |                    |

Hyperplasia, Diffuse

2 2 2 2 2 3 2 4 4 3 3 4 2 3

Pituitary Gland  
Pars Distalis, Hyperplasia

+  
1 2 1 2 1 3 1 2

Thyroid Gland  
Polyarteritis Nodosa  
C-cell, Hyperplasia

+  
2 2 2 3

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

Epididymis  
Atrophy  
Granuloma Sperm

+ +

Preputial Gland

+ +

Prostate  
Hyperplasia  
Inflammation, Chronic  
Inflammation, Chronic Active

+  
1 2 3 1

Seminal Vesicle  
Inflammation, Chronic Active  
Mineral

+  
2 3 2

Testis

+ +

\* .. 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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| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  | males<br>(cont...) |
|---|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|--|--------------------|
|   | 0<br>4<br>8<br>8      | 0<br>6<br>3<br>7      | 0<br>6<br>6<br>6      | 0<br>7<br>2<br>4      | 0<br>7<br>3<br>0      | 0<br>6<br>4<br>4      | 0<br>6<br>8<br>0      | 0<br>5<br>9<br>6      | 0<br>6<br>1<br>7      | 0<br>7<br>3<br>0      | 0<br>6<br>3<br>0      | 0<br>6<br>6<br>9      | 0<br>6<br>1<br>1      | 0<br>7<br>1<br>3      | 0<br>7<br>1<br>5      | 0<br>5<br>3<br>0      | 0<br>7<br>1<br>8      | 0<br>6<br>3<br>1      | 0<br>7<br>3<br>4      | 0<br>7<br>3<br>1      | 0<br>7<br>3<br>1      | 0<br>5<br>6<br>0      | 0<br>4<br>7<br>5      |                       |  |                    |
| ANIMAL ID   | 0<br>0<br>0<br>5<br>1 | 0<br>0<br>0<br>5<br>2 | 0<br>0<br>0<br>5<br>3 | 0<br>0<br>0<br>5<br>4 | 0<br>0<br>0<br>5<br>5 | 0<br>0<br>0<br>5<br>6 | 0<br>0<br>0<br>5<br>7 | 0<br>0<br>0<br>5<br>8 | 0<br>0<br>0<br>5<br>9 | 0<br>0<br>0<br>6<br>0 | 0<br>0<br>0<br>6<br>1 | 0<br>0<br>0<br>6<br>2 | 0<br>0<br>0<br>6<br>3 | 0<br>0<br>0<br>6<br>4 | 0<br>0<br>0<br>6<br>5 | 0<br>0<br>0<br>6<br>6 | 0<br>0<br>0<br>6<br>7 | 0<br>0<br>0<br>6<br>8 | 0<br>0<br>0<br>6<br>9 | 0<br>0<br>0<br>7<br>0 | 0<br>0<br>0<br>7<br>1 | 0<br>0<br>0<br>7<br>2 | 0<br>0<br>0<br>7<br>3 | 0<br>0<br>0<br>7<br>4 |  |                    |
| Polyarteritis Nodosa                                | 1                     |                       | 2                     | 1                     |                       | 2                     | 2                     |                       | 3                     |                       | 2                     | 1                     | 3                     | 2                     |                       |                       | 2                     |                       |                       | 2                     | 2                     | 1                     | 2                     |                       |  |                    |
| Bilateral, Germinal Epithelium, Degeneration        |                       | 3                     |                       |                       |                       | 1                     | 4                     |                       | 1                     | 4                     | 1                     | 2                     |                       | 1                     | 3                     | 1                     |                       |                       |                       |                       |                       |                       | 2                     |                       |  |                    |
| Germinal Epithelium, Degeneration                   |                       |                       | 1                     |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1                     |                       | 1                     |                       |                       | 2                     |                       |  |                    |
| Interstitial Cell, Hyperplasia                      |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 2                     |                       |                       |                       |                       |                       |                       |  |                    |

HEMATOPOIETIC SYSTEM

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage                         | 1 | 1 |   |   |   | 1 | 3 | 3 |   |   |   | 3 | 3 | 3 |   |   | 1 |   | 1 |   |   |   |   | 2 |
| Hypercellularity                   |   | 3 | 2 |   | 1 | 1 | 2 | 2 |   | 1 | 2 | 3 |   |   | 3 | 1 |   |   | 2 | 4 | 1 | 1 | 2 |   |
| Myelofibrosis                      |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |
| Lymph Node                         |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mediastinal, Hemorrhage            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal, Hemorrhage                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal, Pigment                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lymph Node, Mandibular             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Infiltration Cellular, Plasma Cell |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lymph Node, Mesenteric             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Lymphoid              |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |
| Spleen                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Extramedullary Hematopoiesis       |   | 3 | 2 | 1 | 2 | 2 | 1 | 1 |   | 2 |   | 1 | 1 | 2 | 3 | 2 |   | 2 |   | 2 | 3 | 1 | 2 | 2 |
| Hemorrhage                         |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pigment                            | 2 |   | 1 | 2 | 1 | 2 | 2 | 1 |   | 1 | 2 | 1 | 1 |   | 1 | 1 | 2 | 1 | 2 | 1 |   | 1 | 1 | 1 |
| White Pulp, Atrophy                | 4 | 4 |   | 2 |   | 2 | 3 | 4 |   |   | 3 | 4 | 3 |   |   |   | 4 | 3 |   | 2 |   |   | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | males<br>(cont...) |
|---|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|--------------------|
|   | 0488        | 0637 | 0662 | 0774 | 0773 | 0664 | 0668 | 0559 | 0667 | 0671 | 0666 | 0666 | 0777 | 0777 | 0777 | 0555 | 0777 | 0666 | 0777 | 0227 | 0777 | 0775 | 0484 | 0485 |      |                    |
| ANIMAL ID   | 0001        | 0002 | 0003 | 0004 | 0005 | 0006 | 0007 | 0008 | 0009 | 0010 | 0011 | 0012 | 0013 | 0014 | 0015 | 0016 | 0017 | 0018 | 0019 | 0020 | 0021 | 0022 | 0023 | 0024 | 0025 |                    |
|   | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |                    |

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thymus Atrophy            | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Ectopic Parathyroid Gland | 4 | 4 | 1 | 4 | 1 | 4 | 4 | 4 |   | 1 |   |   | 4 | 1 | 3 | 1 | 4 |   | 4 | 2 | 3 | 1 | 3 | 4 | 3 |
| Polyarteritis Nodosa      |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

INTEGUMENTARY SYSTEM

|                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland Hyperplasia      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + |
| Mineral                        |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Skin Cyst Epithelial Inclusion | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Chronic Active   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

MUSCULOSKELETAL SYSTEM

|           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Cyst | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|           |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

NERVOUS SYSTEM

|                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain Hemorrhage | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Necrosis         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Nerve Trigeminal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Peripheral Nerve |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| DAY ON TEST                     |     |           |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |   |
|---------------------------------|-----|-----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|
|                                 |     | 0 4       | 0 6 | 0 6 | 0 7 | 0 7 | 0 6 | 0 6 | 0 5 | 0 6 | 0 7 | 0 6 | 0 6 | 0 7 | 0 7 | 0 7 | 0 5 | 0 7 | 0 6 | 0 7 | 0 2 | 0 7 | 0 7 | 0 5 | 0 4 |   |
| HARLAN SPRAGUE DAWLEY RATS MALE |     | 8         | 3   | 6   | 2   | 3   | 4   | 8   | 9   | 1   | 3   | 3   | 6   | 1   | 1   | 1   | 3   | 5   | 3   | 1   | 3   | 7   | 3   | 3   | 6   | 7 |
|                                 |     | 8         | 7   | 6   | 4   | 0   | 4   | 0   | 6   | 7   | 0   | 0   | 9   | 1   | 3   | 1   | 0   | 3   | 0   | 8   | 1   | 4   | 1   | 1   | 0   | 5 |
| 75 mg/kg male                   |     |           |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |   |
|                                 |     | 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 5                             | 0 5 | 0 5       | 0 5 | 0 5 | 0 5 | 0 5 | 0 5 | 0 5 | 0 5 | 0 5 | 0 6 | 0 6 | 0 6 | 0 6 | 0 6 | 0 6 | 0 7 | 0 7 | 0 7 | 0 7 | 0 7 | 0 7 | 0 7 | 0 7 | 0 7 |   |
| 1 1                             | 2 2 | 3 3       | 4 4 | 5 5 | 6 6 | 7 7 | 8 8 | 9 9 | 0 0 | 1 1 | 2 2 | 3 3 | 4 4 | 5 5 | 6 6 | 7 7 | 8 8 | 9 9 | 0 0 | 1 1 | 2 2 | 3 3 | 4 4 | 5 5 | 6 6 |   |

males (cont...)

Spinal Cord +  
Hemorrhage 3  
Axon, Degeneration 2

RESPIRATORY SYSTEM

|   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lung  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hemorrhage  |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Infiltration Cellular, Histiocyte                 | 2 |   |   |   |   |   |   | 3 |   | 1 |   | 3 |   |   |   | 1 |   |   | 1 | 1 |   |   |   | 1 |
| Inflammation, Granulomatous                       | 1 |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 1 |   |   |   |   |   |   |   | 1 |
| Inflammation, Acute                               |   |   |   |   |   |   |   |   |   |   | 1 | 2 |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineral   | 1 |   |   |   |   |   | 2 |   |   |   | 1 |   | 2 |   |   | 4 |   | 4 |   |   | 2 |   |   | 1 |
| Squamous Metaplasia                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Alveolar Epithelium, Hyperplasia                  |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Alveolus, Fibrosis                                |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |
| Bronchiole, Fibrosis                              |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bronchiole, Foreign Body                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Interstitial, Fibrosis                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Perivascular, Inflammation, Chronic               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Nose  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Foreign Body                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Suppurative                         | 4 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 1 |
| Inflammation, Chronic Active                      |   |   |   |   |   |   | 1 |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |
| Nasolacrimal Duct, Inflammation, Suppurative      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Nasolacrimal Duct, Inflammation, Chronic          | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Nasolacrimal Duct, Inflammation, Chronic Active   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |
| Nasopharyngeal Duct, Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |

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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|  |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| <b>HARLAN SPRAGUE DAWLEY RATS</b><br><b>MALE</b><br><b>75 mg/kg male</b> | 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 |
|  | 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 |
|  |             | 4 | 6 | 6 | 7 | 7 | 6 | 6 | 5 | 6 | 7 | 6 | 6 | 6 | 7 | 7 | 7 | 5 | 7 | 6 | 7 | 2 | 7 | 7 | 5 | 4 |
|  |             | 8 | 3 | 6 | 2 | 3 | 4 | 8 | 9 | 1 | 3 | 3 | 6 | 1 | 1 | 1 | 3 | 5 | 3 | 1 | 3 | 7 | 3 | 3 | 6 | 7 |
|  |             | 8 | 7 | 6 | 4 | 0 | 4 | 0 | 6 | 7 | 0 | 0 | 9 | 1 | 3 | 1 | 0 | 3 | 0 | 8 | 1 | 4 | 1 | 1 | 0 | 5 |

males  
(cont...)

Nasopharyngeal Duct, Squamous Metaplasia 3  
 Olfactory Epithelium, Metaplasia, Respiratory  
 Olfactory Epithelium, Squamous Metaplasia  
 Respiratory Epithelium, Hyperplasia 1

Trachea +  
 Mineral 2

**SPECIAL SENSES SYSTEM**

Eye +  
 Inflammation, Chronic  
 Cornea, Inflammation, Acute 1 2  
 Cornea, Inflammation, Chronic  
 Cornea, Inflammation, Chronic Active 2 1 3  
 Retina, Dysplasia 2  
 Retina, Hyperplasia 2

Harderian Gland +  
 Metaplasia 1

Zymbal's Gland

**URINARY SYSTEM**

Kidney +  
 Calculus Micro Observation Only X X  
 Hemorrhage 4  
 Nephropathy, Chronic Progressive 4 4 3 4 3 4 4 4 3 4 4 3 4 4 4 3 2 4 4 4 4  
 Polyarteritis Nodosa 2

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically M .. Missing tissue 1-4 .. Lesion qualified as:  
 X .. Lesion present A .. Autolysis precludes evaluation 1) Minimal 3) Moderate  
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Lab: BAT

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                            |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------------|---|---|
| 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 | <b>males<br/>(cont...)</b> |   |   |
| <b>HARLAN SPRAGUE DAWLEY RATS MALE</b> | 4 | 6 | 6 | 7 | 7 | 6 | 6 | 5 | 6 | 7 | 6 | 6 | 6 | 7 | 7 | 7 | 5 | 7 | 6 | 7 | 2 | 7 | 7 |                            | 0 | 4 |
|  | 8 | 3 | 6 | 2 | 3 | 4 | 8 | 9 | 1 | 3 | 3 | 6 | 1 | 1 | 1 | 3 | 5 | 3 | 1 | 3 | 7 | 3 | 3 |                            | 6 | 7 |
|  | 8 | 7 | 6 | 4 | 0 | 4 | 0 | 6 | 7 | 0 | 0 | 9 | 1 | 3 | 1 | 0 | 3 | 0 | 8 | 1 | 4 | 1 | 1 |                            | 0 | 5 |
| 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 |   |
| 75 mg/kg 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 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                          | 0 |   |
|  | 0 | 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 | 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 |   |

|                                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|--------------------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Pelvis, Inflammation, Chronic Active |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Renal Tubule, Cyst                   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Urinary Bladder                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Chronic Active         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Transitional Epithelium, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST | 0637  | 0433  | 0575  | 0575  | 0680  | 0730  | 0776  | 0668  | 0674  | 0733  | 0779  | 0678  | 0720  | 0737  | 0676  | 0733  | 0559  | 0773  | 0447  | 0665  | 0555  | 0661  | 0678  | * TOTALS |
|   | ANIMAL ID   | 00076 | 00077 | 00078 | 00079 | 00080 | 00081 | 00082 | 00083 | 00084 | 00085 | 00086 | 00087 | 00088 | 00089 | 00090 | 00091 | 00092 | 00093 | 00094 | 00095 | 00096 | 00097 | 00098 |          |
|   |             | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |          |

ALIMENTARY SYSTEM

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |       |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-------|
| Esophagus                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | 50 |       |
| Intestine Large, Cecum          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | 49 |       |
| Erosion                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 4 1.5 |
| Infiltration Cellular, Lymphoid |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |    |    | 1 2.0 |
| Inflammation, Chronic           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2 1.5 |
| Inflammation, Chronic Active    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1 1.0 |
| Mineral                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 4 1.8 |
| Polyarteritis Nodosa            |   |   | 2 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |    |    | 8 1.8 |
| Ulcer                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1 2.0 |
| Intestine Large, Colon          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |       |
| Infiltration Cellular, Lymphoid |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |    |    | 1 2.0 |
| Mineral                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1 3.0 |
| Parasite Metazoan               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2     |
| Polyarteritis Nodosa            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2 1.5 |
| Lymphoid Tissue, Hyperplasia    |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   | 3 |   | 2 |   |   |   |   |   |   |    |    | 4 2.5 |
| Intestine Large, Rectum         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |       |
| Parasite Metazoan               |   |   |   |   |   |   | X |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 3     |
| Polyarteritis Nodosa            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2 2.0 |
| Intestine Small, Duodenum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |       |
| Intestine Small, Ileum          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |       |
| Polyarteritis Nodosa            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1 1.0 |
| Intestine Small, Jejunum        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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  
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Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |      |   |     |    |     |     |     |     |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|------|---|-----|----|-----|-----|-----|-----|
|   | 0637        | 0433  | 0575  | 0575  | 0680  | 0730  | 0770  | 0668  | 0674  | 0711  | 0711  | 0635  | 0729  | 0778  | 0700  | 0673  | 0731  | 0733  | 0559  | 0731  | 0733  | 0447  | 0654  | 0557  |          | 0618 |   |     |    |     |     |     |     |
| ANIMAL ID   | 00076       | 00077 | 00078 | 00079 | 00080 | 00081 | 00082 | 00083 | 00084 | 00085 | 00086 | 00087 | 00088 | 00089 | 00090 | 00091 | 00092 | 00093 | 00094 | 00095 | 00096 | 00097 | 00098 | 00099 | 00100    |      |   |     |    |     |     |     |     |
| Polyarteritis Nodosa                                |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          | 1    | 1 | 1.0 |    |     |     |     |     |
| Peyer's Patch, Hyperplasia                          |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   | 1   | 1  | 2.0 |     |     |     |
| Liver   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +    | + | 50  | 2  |     |     |     |     |
| Basophilic Focus                                    |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 2   |     |     |     |
| Clear Cell Focus                                    |             |       |       |       |       |       |       |       | X     |       |       | X     |       |       | X     |       | X     |       |       | X     |       |       |       |       |          |      |   |     | 13 |     |     |     |     |
| Eosinophilic Focus                                  |             |       |       |       |       |       |       |       | X     |       | X     | X     |       |       | X     |       | X     | X     |       |       |       |       |       |       |          |      |   |     | 7  |     |     |     |     |
| Extramedullary Hematopoiesis                        |             |       |       |       |       |       |       |       |       | 2     |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     | 3  | 1.3 |     |     |     |
| Fatty Change, Focal                                 |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 2     |       |       |       |       |       |       |       |          |      |   |     | 1  | 2.0 |     |     |     |
| Hepatodiaphragmatic Nodule                          |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 1   |     |     |     |
| Inflammation, Granulomatous                         |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 1   | 4.0 |     |     |
| Mixed Cell Focus                                    |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 1   |     |     |     |
| Necrosis  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 3   | 2.3 |     |     |
| Bile Duct, Cyst                                     |             |       |       |       |       |       | X     |       |       |       |       |       | X     |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 4   |     |     |     |
| Bile Duct, Dilation                                 |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 1   | 2.0 |     |     |
| Bile Duct, Hyperplasia                              |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 1   | 1.1 |     |     |
| Centrilobular, Necrosis                             |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 1   | 2.0 |     |     |
| Mesentery   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    | 3   | 1   | 3.0 |     |
| Hemorrhage  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    |     | 1   | 2.0 |     |
| Pigment   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    |     | 1   | 3.0 |     |
| Polyarteritis Nodosa                                |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    |     | 1   | 2.0 |     |
| Pancreas  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +    | + | +   | 50 | 6   | 1.8 |     |     |
| Polyarteritis Nodosa                                |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    |     | 2   | 1.3 |     |
| Acinus, Atrophy                                     |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    |     | 4   | 2.8 |     |
| Acinus, Hyperplasia                                 |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    |     | 9   | 2.8 |     |
| Salivary Glands                                     | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +    | + | +   | 50 | 1   | 2.0 |     |     |
| Atrophy   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |      |   |     |    |     |     | 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:

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| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |       |       |       |       |       |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|-------|-------|-------|-------|-------|
|   | 0637        | 0433  | 0577  | 0578  | 0680  | 0773  | 0776  | 0668  | 0667  | 0776  | 0777  | 0667  | 0776  | 0777  | 0778  | 0667  | 0776  | 0777  | 0559  | 0773  |          | 0447  | 0664  | 0557  | 0661  | 0668  |
| ANIMAL ID   | 00076       | 00077 | 00078 | 00079 | 00080 | 00081 | 00082 | 00083 | 00084 | 00085 | 00086 | 00087 | 00088 | 00089 | 00090 | 00091 | 00092 | 00093 | 00094 | 00095 | 00096    | 00097 | 00098 | 00099 | 00100 | 00101 |
|   | 0           | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0        | 0     | 0     | 0     | 0     | 0     |

|   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |    |     |
|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|----|-----|
| Blood Vessel                                    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 33 |    |     |
| Aneurysm  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1  | 3.0 |
| Mineral   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 15 | 2.2 |
| Aorta, Dilation                                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 2  | 3.0 |
| Heart   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Cardiomyopathy                                  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 40 | 1.8 |
| Inflammation, Acute                             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1  | 1.0 |
| Mineral   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 8  | 2.0 |
| Polyarteritis Nodosa                            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1  | 2.0 |
| Thrombus  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1  |     |
| Atrium, Thrombus                                |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1  |     |
| Perivascular, Infiltration Cellular, Lymphocyte |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1  | 2.0 |

**ENDOCRINE SYSTEM**

|                               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |    |     |
|-------------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|----|-----|
| Adrenal Cortex                |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Degeneration, Cystic          |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 4  | 1.0 |
| Hyperplasia, Focal            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 10 | 1.6 |
| Necrosis                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 3  | 1.7 |
| Thrombus                      |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 2  |     |
| Adrenal Medulla               |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Hyperplasia, Focal            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 9  | 1.6 |
| Bilateral, Hyperplasia, Focal |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 2  | 2.5 |
| Islets, Pancreatic            |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Hyperplasia                   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 3  | 2.0 |
| Parathyroid Gland             |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 47 |    |     |

\* .. 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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 1) Minimal 3) Moderate  
 2) Mild 4) Marked

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| 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             | ANIMAL ID | * TOTALS |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---------------|-----------|----------|
|  | 6 | 4 | 5 | 5 | 6 | 7 | 7 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 5 | 7 | 7 | 4 | 6 | 5 | 6  |               |           |          |
| <b>HARLAN SPRAGUE DAWLEY RATS MALE</b><br><b>75 mg/kg male</b> | 3 | 3 | 7 | 7 | 8 | 3 | 0 | 8 | 5 | 3 | 3 | 5 | 2 | 0 | 3 | 7 | 3 | 3 | 5 | 3 | 3 | 4 | 5 | 5 | 1  | 0             | * TOTALS  |          |
|  | 7 | 3 | 5 | 5 | 0 | 0 | 6 | 7 | 4 | 1 | 1 | 3 | 9 | 8 | 0 | 6 | 1 | 0 | 9 | 1 | 1 | 7 | 4 | 7 | 8  | 0             |           |          |
|  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 0             |           |          |
|  | 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  | 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 | 0  | 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  | 0             |           |          |
| Hyperplasia, Diffuse   | 4 |   | 3 |   | 4 |   |   |   | 2 |   |   | 3 |   | 3 |   |   |   | 3 |   |   |   | 4 | 3 | 2 |    | <b>24 2.9</b> |           |          |
| Pituitary Gland  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |               |           |          |
| Pars Distalis, Hyperplasia                                     |   |   | 2 |   | 2 |   |   |   | 1 |   | 1 |   |   | 1 |   | 2 |   |   |   | 1 |   |   |   |   |    | <b>15 1.5</b> |           |          |
| Thyroid Gland  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |               |           |          |
| Polyarteritis Nodosa   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |    | <b>1 2.0</b>  |           |          |
| C-cell, Hyperplasia  |   |   |   |   |   |   |   | 2 | 1 |   |   | 2 | 2 |   |   |   |   | 1 |   | 3 |   |   |   |   |    | <b>10 2.0</b> |           |          |

**GENERAL BODY SYSTEM**

NONE

**GENITAL SYSTEM**

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |              |  |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--------------|--|
| Epididymis                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | 50           |  |
| Atrophy                      | 2 |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |    | <b>2 2.0</b> |  |
| Granuloma Sperm              |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | <b>1 4.0</b> |  |
| Preputial Gland              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |              |  |
| Prostate                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |              |  |
| Hyperplasia                  |   |   |   |   | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | <b>3 1.0</b> |  |
| Inflammation, Chronic        |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |    | <b>1 1.0</b> |  |
| Inflammation, Chronic Active |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |    | <b>6 1.7</b> |  |
| Seminal Vesicle              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |              |  |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | <b>2 2.5</b> |  |
| Mineral                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | <b>1 2.0</b> |  |
| Testis                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |       |       |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|-------|-------|
|   | 0637        | 0433  | 0573  | 0575  | 0680  | 0730  | 0770  | 0668  | 0667  | 0773  | 0776  | 0672  | 0777  | 0777  | 0777  | 0676  | 0777  | 0575  | 0777  | 0474  |          | 0666  | 0555  |
| ANIMAL ID   | 00076       | 00077 | 00078 | 00079 | 00080 | 00081 | 00082 | 00083 | 00084 | 00085 | 00086 | 00087 | 00088 | 00089 | 00090 | 00091 | 00092 | 00093 | 00094 | 00095 | 00096    | 00097 | 00098 |
|   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |       |       |

|  |   |  |   |  |   |   |  |  |  |   |  |  |   |  |  |   |   |   |   |   |   |  |   |    |     |
|--|---|--|---|--|---|---|--|--|--|---|--|--|---|--|--|---|---|---|---|---|---|--|---|----|-----|
| Polyarteritis Nodosa                         |   |  |   |  | 1 | 2 |  |  |  |   |  |  | 1 |  |  | 2 | 2 | 2 | 2 | 3 | 1 |  | 1 | 25 | 1.8 |
| Bilateral, Germinal Epithelium, Degeneration | 1 |  | 1 |  | 3 |   |  |  |  | 3 |  |  | 4 |  |  | 3 |   | 2 | 3 | 3 |   |  | 3 | 21 | 2.3 |
| Germinal Epithelium, Degeneration            |   |  |   |  |   |   |  |  |  |   |  |  |   |  |  |   |   |   |   |   |   |  |   | 5  | 1.2 |
| Interstitial Cell, Hyperplasia               |   |  |   |  |   | 2 |  |  |  |   |  |  |   |  |  |   |   |   |   |   |   |  |   | 2  | 2.0 |

**HEMATOPOIETIC SYSTEM**

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |     |  |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|--|
| Bone Marrow                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Hemorrhage                         | 2 |   | 2 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 3 | 1 | 1 | 1 |   | 4 | 19 | 1.9 |     |  |
| Hypercellularity                   | 2 |   |   |   | 2 |   |   |   |   | 4 |   |   | 2 | 3 |   |   | 3 | 2 | 3 |   | 1 |   | 2 | 3  | 27  | 2.1 |  |
| Myelofibrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 1.0 |     |  |
| Lymph Node                         | + |   |   | + |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  |     |     |  |
| Mediastinal, Hemorrhage            | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |     |  |
| Renal, Hemorrhage                  |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |     |  |
| Renal, Pigment                     |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |     |  |
| Lymph Node, Mandibular             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Infiltration Cellular, Plasma Cell |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   | 2  | 2.5 |     |  |
| Inflammation                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   | 3 | 2  | 2.5 |     |  |
| Lymph Node, Mesenteric             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Hyperplasia, Lymphoid              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |     |  |
| Spleen                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Extramedullary Hematopoiesis       | 2 | 2 |   |   | 3 | 2 | 2 | 1 | 4 | 2 | 2 | 3 | 3 | 2 | 2 | 2 | 1 | 2 | 1 | 1 | 2 | 2 | 3 | 3  | 41  | 2.0 |  |
| Hemorrhage                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |     |  |
| Pigment                            | 1 | 1 | 2 |   |   | 1 | 1 | 2 |   | 1 | 1 | 1 | 1 | 2 | 1 |   | 2 |   | 2 |   | 1 | 1 | 1 | 1  | 39  | 1.3 |  |
| White Pulp, Atrophy                | 4 |   | 4 |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   | 4 | 3 |   |   |   | 4 | 19 | 3.3 |     |  |

\* .. 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:

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Experiment Number: 00058 - 03

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Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>75 mg/kg male | 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 |   |   |
|   | 6           | 4 | 5 | 5 | 6 | 7 | 7 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 5 | 7 | 7 |          | 4 | 6 | 5 |
| ANIMAL ID   | 3           | 3 | 7 | 7 | 8 | 3 | 0 | 8 | 5 | 3 | 3 | 5 | 2 | 0 | 3 | 7 | 3 | 5 | 3 | 3 | 4        | 5 | 5 | 1 |
|   | 7           | 3 | 5 | 5 | 0 | 0 | 6 | 7 | 4 | 1 | 1 | 3 | 9 | 8 | 0 | 6 | 1 | 0 | 9 | 1 | 1        | 7 | 4 | 8 |
|   | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0        | 0 | 0 | 0 |
|   | 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 |

|                           |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |  |
|---------------------------|---|---|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|--|
| Thymus                    |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 48 |     |  |
| Atrophy                   | + | + |   |  | + | + |   | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  |     |  |
| Ectopic Parathyroid Gland | 4 | 1 | 4 |  | 3 |   | 2 |   | 3 | 1 | 2 | 4 | 2 |   |   | 2 | 1 | 4 | 2 | 2 |   | 1 | 4 | 4  |     |  |
| Polyarteritis Nodosa      |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1  | 1.0 |  |

INTEGUMENTARY SYSTEM

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |  |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|--|
| Mammary Gland                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 48 |     |  |
| Hyperplasia                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | +  |     |  |
| Mineral                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |  |
| Skin                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 50 |     |  |
| Cyst Epithelial Inclusion    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   | 2 |   |    |     |  |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 4.0 |  |
| Ulcer                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 4.0 |  |

MUSCULOSKELETAL SYSTEM

|      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|--|
| Bone |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 50 |  |  |
| Cyst | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  |  |  |
|      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |  |  |

NERVOUS SYSTEM

|                  |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |    |     |  |
|------------------|---|---|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|----|-----|--|
| Brain            |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     | 50 |     |  |
| Hemorrhage       | + | + | + |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | +  |     |  |
| Necrosis         |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   | 2 | 2.5 |    |     |  |
|                  |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     | 2  | 2.0 |  |
| Nerve Trigeminal |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     | 1  |     |  |
| Peripheral Nerve |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     | 1  |     |  |

\* .. 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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 Test Type: CHRONIC  
 Route: GAVAGE  
 Species/Strain: RATS/HSD

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 Black Cohosh  
 CAS Number: 84776-26-1

Date Report Requested: 10/07/2020  
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 Lab: BAT

|  |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| <b>HARLAN SPRAGUE DAWLEY RATS<br/>MALE<br/>75 mg/kg male</b> | 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 | 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 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
|  |             | 7 | 7 | 8 | 9 | 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 | 6 | 7 | 8 | 9 | 0 |

\* TOTALS

Spinal Cord 1  
 Hemorrhage 1 3.0  
 Axon, Degeneration 1 2.0

**RESPIRATORY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |        |       |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|--------|-------|
| Lung  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |        |       |
| Hemorrhage  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 2 3.0  |       |
| Infiltration Cellular, Histiocyte                 | 1 | 1 |   |   |   |   |   |   | 1 | 1 | 1 | 3 | 1 | 1 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 19 1.5 |       |
| Inflammation, Granulomatous                       |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   |   | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   |   | 9 1.0  |        |       |
| Inflammation, Acute                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 1.3  |        |       |
| Mineral   |   |   | 2 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 11 1.9 |        |       |
| Squamous Metaplasia                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0  |       |
| Alveolar Epithelium, Hyperplasia                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 1.0  |       |
| Alveolus, Fibrosis                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 1.0  |       |
| Bronchiole, Fibrosis                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0  |       |
| Bronchiole, Foreign Body                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1      |       |
| Interstitial, Fibrosis                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 1.0  |       |
| Perivascular, Inflammation, Chronic               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 2.0  |       |
| Nose  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |        |       |
| Foreign Body                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |        | 1     |
| Inflammation, Suppurative                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |        | 6 2.2 |
| Inflammation, Chronic Active                      |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 4 1.5  |       |
| Nasolacrimal Duct, Inflammation, Suppurative      |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 3.0  |       |
| Nasolacrimal Duct, Inflammation, Chronic          |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 4 1.3  |       |
| Nasolacrimal Duct, Inflammation, Chronic Active   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 4 1.3  |       |
| Nasopharyngeal Duct, Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        | 1 3.0  |       |

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

Experiment Number: 00058 - 03

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Date Report Requested: 10/07/2020

Test Type: CHRONIC

Black Cohosh

Time Report Requested: 11:17:00

Route: GAVAGE

CAS Number: 84776-26-1

First Dose M/F: 07/03/12 / 07/02/12

Species/Strain: RATS/HSD

Lab: BAT

|   |  | 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                                   |  | 6 | 4 | 5 | 5 | 6 | 7 | 7 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 5 | 7 | 7 | 4 | 6 | 5 | 6      |          |  |
| HARLAN SPRAGUE DAWLEY RATS MALE               |  | 3 | 3 | 7 | 7 | 8 | 3 | 0 | 8 | 5 | 3 | 3 | 5 | 2 | 0 | 3 | 7 | 3 | 5 | 3 | 3 | 4 | 5 | 5 | 1      |          |  |
| 75 mg/kg male                                 |  | 7 | 3 | 5 | 5 | 0 | 0 | 6 | 7 | 4 | 1 | 1 | 3 | 9 | 8 | 0 | 6 | 1 | 0 | 9 | 1 | 1 | 7 | 7 | 8      |          |  |
| 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      | * 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 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1      |          |  |
| Nasopharyngeal Duct, Squamous Metaplasia      |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 3.0  |          |  |
| Olfactory Epithelium, Metaplasia, Respiratory |  |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0  |          |  |
| Olfactory Epithelium, Squamous Metaplasia     |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   | 1 1.0  |          |  |
| Respiratory Epithelium, Hyperplasia           |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0  |          |  |
| Trachea                                       |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |          |  |
| Mineral                                       |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |          |  |
| <b>SPECIAL SENSES SYSTEM</b>                  |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |          |  |
| Eye   |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |          |  |
| Inflammation, Chronic                         |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 1.0  |          |  |
| Cornea, Inflammation, Acute                   |  |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   | 1 |   |   | 2 |   | 5 1.6  |          |  |
| Cornea, Inflammation, Chronic                 |  |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 1.5  |          |  |
| Cornea, Inflammation, Chronic Active          |  |   |   |   |   |   | 2 | 2 |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   | 6 2.0  |          |  |
| Retina, Dysplasia                             |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |          |  |
| Retina, Hyperplasia                           |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |          |  |
| Harderian Gland                               |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |          |  |
| Metaplasia                                    |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 1.0  |          |  |
| Zymbal's Gland                                |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1      |          |  |
| <b>URINARY SYSTEM</b>                         |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |          |  |
| Kidney  |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |          |  |
| Calculus Micro Observation Only               |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2      |          |  |
| Hemorrhage                                    |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 4.0  |          |  |
| Nephropathy, Chronic Progressive              |  | 4 | 3 | 4 | 3 | 4 | 4 | 4 | 3 | 3 | 3 | 2 | 4 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 3 | 3 | 4 | 4 | 50 3.6 |          |  |
| Polyarteritis Nodosa                          |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 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

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1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

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Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|                                      |  | 0 | 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 |     |     |
|--------------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----------|-----|-----|
| DAY ON TEST                          |  | 6 | 4 | 5 | 5 | 6 | 7 | 7 | 6 | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 5 | 7 | 7 | 4 | 6 | 5 | 6  |          |     |     |
| HARLAN SPRAGUE DAWLEY RATS MALE      |  | 3 | 3 | 7 | 7 | 8 | 3 | 0 | 8 | 5 | 3 | 3 | 5 | 2 | 0 | 3 | 7 | 3 | 3 | 5 | 3 | 3 | 4 | 5 | 5 | 1  |          |     |     |
| 75 mg/kg male                        |  | 7 | 3 | 5 | 5 | 0 | 0 | 6 | 7 | 4 | 1 | 1 | 3 | 9 | 8 | 0 | 6 | 1 | 0 | 9 | 1 | 1 | 7 | 4 | 7 | 8  |          |     |     |
| 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  |          |     |     |
|                                      |  | 7 | 7 | 7 | 7 | 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  |          |     |     |
| Pelvis, Inflammation, Chronic Active |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 2.0      |     |     |
| Renal Tubule, Cyst                   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   | X  | 5        |     |     |
| Urinary Bladder                      |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |          |     |     |
| Inflammation, Chronic                |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 1        | 2.0 |     |
| Inflammation, Chronic Active         |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1        | 2.0 |     |
| Polyarteritis Nodosa                 |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1        | 2.0 |     |
| Transitional Epithelium, Hyperplasia |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 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

|                                 |  | DAY ON TEST |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        | males<br>(cont...) |        |        |        |        |    |
|---------------------------------|--|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------------------|--------|--------|--------|--------|----|
| HARLAN SPRAGUE DAWLEY RATS MALE |  | 07          | 06     | 07     | 07     | 07     | 07     | 07     | 07     | 06     | 04     | 06     | 04     | 07     | 06     | 07     | 06     | 05     | 04     | 05     | 06     |                    | 06     | 07     | 07     | 07     | 06 |
| 250 mg/kg male                  |  | 31          | 64     | 30     | 30     | 30     | 11     | 30     | 18     | 54     | 34     | 93     | 13     | 00     | 44     | 00     | 65     | 02     | 89     | 04     | 06     |                    | 01     | 30     | 33     | 30     | 09 |
| ANIMAL ID                       |  | 001100      | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111 | 001111             | 001111 | 001111 | 001111 | 001111 |    |

**ALIMENTARY SYSTEM**

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mineral                      |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |
| Intestine Large, Colon       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mineral                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |
| Ulcer                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |
| Lymphoid Tissue, Hyperplasia |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Rectum      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Intestine Small, Duodenum    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |
| Intestine Small, Ileum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Peyer's Patch, Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |
| Liver                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Basophilic Focus             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Clear Cell Focus             | X |   | X | X | X | X | X | X | X |   |   |   |   |   |   | X |   |   |   |   |   |   | X | X | X | X |

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 X .. Lesion present  
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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | males<br>(cont...) |      |      |               |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|--------------------|------|------|---------------|
|  | 0731        | 0664 | 0760 | 0770 | 0777 | 0777 | 0777 | 0777 | 0668 | 0445 | 0664 | 0443 | 0770 | 0664 | 0776 | 0667 | 0665 | 0445 | 0568 | 0660 | 0664 | 0666 | 0771 | 0777 | 0777 |                    | 0666 | 0669 |               |
| ANIMAL ID  | 0010        | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001 | 0001               | 0001 |      |               |
| Degeneration, Cystic Eosinophilic Focus              |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      | 1    |               |
| Extramedullary Hematopoiesis                         |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | X             |
| Hepatodiaphragmatic Nodule                           |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 1             |
| Necrosis   |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 1             |
| Bile Duct, Cyst                                      |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | X             |
| Bile Duct, Dilatation                                |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 4             |
| Bile Duct, Hyperplasia                               | 2           | 1    | 1    | 1    | 1    |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 1 1 1 1 1 1 1 |
| Mesentery Fat, Necrosis                              |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Oral Mucosa  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Pancreas   |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Polyarteritis Nodosa                                 | 1           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 2 1           |
| Acinus, Atrophy                                      |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 1             |
| Acinus, Hyperplasia                                  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 4 3 2 3       |
| Salivary Glands                                      |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Stomach, Forestomach                                 |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Erosion  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 1             |
| Inflammation, Acute                                  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 1             |
| Inflammation, Chronic                                |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Inflammation, Chronic Active                         |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 2 1           |
| Mineral  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Necrosis   |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      |               |
| Polyarteritis Nodosa                                 |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 1 1           |
| Ulcer  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |      |      | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |                    |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|--------------------|
| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST | 0731 | 0664 | 0730 | 0730 | 0770 | 0770 | 0770 | 0770 | 0668 | 0465 | 0643 | 0740 | 0664 | 0776 | 0665 | 0452 | 0549 | 0664 | 0667 | 0770 | 0770 | 0770 | 0669 | males<br>(cont...) |
|  | ANIMAL ID   | 0010 | 0011 | 0012 | 0013 | 0014 | 0015 | 0016 | 0017 | 0018 | 0019 | 0020 | 0021 | 0022 | 0023 | 0024 | 0025 | 0026 | 0027 | 0028 | 0029 | 0030 | 0031 | 0032 |                    |

Epithelium, Hyperplasia  
Epithelium, Hyperplasia, Basal Cell

1 2  
1

Stomach, Glandular  
Mineral  
Polyarteritis Nodosa

+ + + + + + + + 1 + + + + + + + + + + + + + +  
2 1 2 1 3 3 2

CARDIOVASCULAR SYSTEM

Blood Vessel  
Mineral  
Aorta, Dilation

+  
1 2 1  
2

Heart  
Cardiomyopathy  
Mineral  
Atrium, Thrombus  
Perivascular, Infiltration Cellular, Lymphocyte  
Valve, Inflammation, Chronic

+  
1 2 1 1 1 3 1 1 2 1 1 1 1 1 3 1 3 2 1 1 1 1 1 1  
1 1 X X X 1  
1

ENDOCRINE SYSTEM

Adrenal Cortex  
Amyloid Deposition, Focal  
Degeneration, Cystic  
Hyperplasia, Focal  
Necrosis  
Bilateral, Hyperplasia, Focal

+  
1  
1  
2 2 2 1 1 1

Adrenal Medulla

+ +

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+ .. Tissue examined microscopically  
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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |  | males<br>(cont...) |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|--|--------------------|
|  | 0731        | 0664 | 0760 | 0770 | 0773 | 0777 | 0777 | 0777 | 0664 | 0464 | 0664 | 0473 | 0667 | 0766 | 0565 | 0454 | 0566 | 0666 | 0767 | 0777 | 0777 | 0667 | 0669 |  |                    |
| ANIMAL ID  | 0011        | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 |  |                    |

Hyperplasia, Focal Bilateral, Hyperplasia, Focal 3 2 4 2 1 2

Islets, Pancreatic Hyperplasia +

Parathyroid Gland Hyperplasia, Diffuse + + M M + + + M + + + + + + + + + + + + + + M + + 4 3 4 3 2 2 1 2

Pituitary Gland Pars Distalis, Hyperplasia + 1 3 1 1 3

Thyroid Gland C-cell, Hyperplasia + 2 2 3 4 3

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

Epididymis Inflammation, Chronic Active Polyarteritis Nodosa + 1 1

Preputial Gland Duct, Hyperplasia, Squamous +

Prostate Inflammation, Chronic Hyperplasia + 1 1

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

Experiment Number: 00058 - 03

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Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | males<br>(cont...)    |                       |                       |                       |                       |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
|  | 0<br>7<br>3<br>1      | 0<br>6<br>6<br>4      | 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>0      | 0<br>7<br>3<br>1      | 0<br>6<br>8           | 0<br>4<br>5           | 0<br>6<br>4           | 0<br>4<br>3           | 0<br>7<br>6           | 0<br>6<br>9           | 0<br>3<br>1           | 0<br>6<br>5           | 0<br>4<br>0           | 0<br>5<br>8           | 0<br>6<br>0           | 0<br>7<br>3           |                       | 0<br>7<br>3           | 0<br>7<br>3           | 0<br>6<br>0           |                       |
| ANIMAL ID  | 0<br>0<br>1<br>0<br>1 | 0<br>0<br>1<br>0<br>2 | 0<br>0<br>1<br>0<br>3 | 0<br>0<br>1<br>0<br>4 | 0<br>0<br>1<br>0<br>5 | 0<br>0<br>1<br>0<br>6 | 0<br>0<br>1<br>0<br>7 | 0<br>0<br>1<br>0<br>8 | 0<br>0<br>1<br>0<br>9 | 0<br>0<br>1<br>0<br>0 | 0<br>0<br>1<br>0<br>1 | 0<br>0<br>1<br>0<br>2 | 0<br>0<br>1<br>0<br>3 | 0<br>0<br>1<br>0<br>4 | 0<br>0<br>1<br>0<br>5 | 0<br>0<br>1<br>0<br>6 | 0<br>0<br>1<br>0<br>7 | 0<br>0<br>1<br>0<br>8 | 0<br>0<br>1<br>0<br>9 | 0<br>0<br>1<br>0<br>0 | 0<br>0<br>1<br>0<br>1 | 0<br>0<br>1<br>0<br>2 | 0<br>0<br>1<br>0<br>3 | 0<br>0<br>1<br>0<br>4 | 0<br>0<br>1<br>0<br>5 |

Inflammation, Chronic Active  
Polyarteritis Nodosa

2  
1

2  
1

3  
1

Seminal Vesicle  
Inflammation, Chronic Active  
Metaplasia, Squamous  
Polyarteritis Nodosa

+ +

1  
1

Testis  
Polyarteritis Nodosa  
Bilateral, Germinal Epithelium, Degeneration  
Germinal Epithelium, Degeneration  
Interstitial Cell, Hyperplasia

+ +

1 2 2 3  
1 1 1 2 4 1  
1 4  
2 1  
2

HEMATOPOIETIC SYSTEM

Bone Marrow  
Hemorrhage  
Hypercellularity

+ +

1 3 2 2 1 2 2 4 1 2 2 4 1 3 3 1 1 2 1 1

Lymph Node  
Lumbar, Hemorrhage  
Lumbar, Infiltration Cellular, Histiocyte  
Lumbar, Pigment  
Pancreatic, Infiltration Cellular, Plasma Cell  
Renal, Hemorrhage  
Renal, Pigment

+  
2  
2  
2  
2  
2  
2

Lymph Node, Mandibular  
Atrophy

+ +

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  
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Experiment Number: 00058 - 03  
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Species/Strain: RATS/HSD

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
Black Cohosh  
CAS Number: 84776-26-1

Date Report Requested: 10/07/2020  
Time Report Requested: 11:17:00  
First Dose M/F: 07/03/12 / 07/02/12  
Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | ANIMAL ID | males<br>(cont...) |
|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|--------------------|
|  | 07<br>31    | 06<br>64 | 07<br>30 | 07<br>30 | 07<br>30 | 07<br>31 | 07<br>30 | 07<br>30 | 06<br>48 | 04<br>65 | 04<br>63 | 07<br>43 | 06<br>64 | 07<br>30 | 06<br>64 | 07<br>30 | 06<br>59 | 04<br>42 | 05<br>68 | 06<br>64 | 07<br>30 | 07<br>30 | 07<br>30 | 07<br>30 | 07<br>30 |           |                    |
|  | 001         | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      | 001      |           |                    |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
| Ectasia                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |  |
| Lymph Node, Mesenteric       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + |   |  |
| Spleen                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M |   |  |
| Extramedullary Hematopoiesis | 2 | 3 | 2 | 2 | 2 | 2 | 3 | 2 | 3 | 2 | 1 | 2 | 1 | 2 | 3 | 2 | 3 | 2 | 2 | 2 | 2 | 2 | 1 | 1 |   |   |  |
| Pigment                      | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |   |   |  |
| White Pulp, Atrophy          | 2 |   |   |   |   |   |   |   | 3 | 2 | 4 |   |   |   | 2 |   | 4 | 2 | 3 | 1 |   |   |   |   |   |   |  |
| Thymus                       | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + |   |   |  |
| Atrophy                      | 1 |   | 1 | 1 | 2 | 2 | 4 | 2 | 3 | 3 | 3 | 4 | 3 | 2 | 2 | 2 | 4 | 4 | 4 | 2 |   | 2 | 1 | 1 |   |   |  |
| Cyst                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Ectopic Parathyroid Gland    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |  |

**INTEGUMENTARY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland                             | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                               |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Skin                                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst Epithelial Inclusion                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |
| Inflammation, Granulomatous               |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic Active              |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                                     |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Subcutaneous Tissue, Polyarteritis Nodosa |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**MUSCULOSKELETAL SYSTEM**

|      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

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+ .. Tissue examined microscopically  
X .. Lesion present  
I .. Insufficient tissue

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST      |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |                  |   | ANIMAL ID | males<br>(cont...) |
|--|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|---|-----------|--------------------|
|  | 0<br>7<br>3<br>1 | 0<br>6<br>6<br>4 | 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>1<br>0 | 0<br>7<br>3<br>0 | 0<br>6<br>1<br>8 | 0<br>4<br>3<br>5 | 0<br>6<br>9<br>4 | 0<br>4<br>1<br>3 | 0<br>7<br>3<br>0 | 0<br>6<br>9<br>4 | 0<br>7<br>3<br>0 | 0<br>6<br>5<br>6 | 0<br>4<br>0<br>2 | 0<br>5<br>8<br>9 | 0<br>6<br>0<br>4 | 0<br>6<br>0<br>6 | 0<br>7<br>3<br>1 | 0<br>7<br>3<br>0 | 0<br>7<br>3<br>0 | 0<br>6<br>0<br>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 |           |                    |
|  | 0                | 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                | 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 |           |                    |

|   |   |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|---|--|--|--|---|--|--|--|--|--|---|--|---|--|--|
| Mineral   |   |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  | 3 |  |   |  |  |
| Alveolar Epithelium, Hyperplasia                | 1 |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Bronchiole, Fibrosis                            | 1 |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Peribronchiolar, Fibrosis                       |   |  |  |  |  |  |  |  |  |  |  |  |  | 2 |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Nose  | + |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Foreign Body                                    |   |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Inflammation, Acute                             |   |  |  |  |  |  |  |  |  |  |  |  |  | 1 |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Inflammation, Chronic                           | 1 |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  | 1 |  |  |
| Inflammation, Chronic Active                    |   |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  | 1 |  |   |  |  |
| Nasolacrimal Duct, Inflammation, Chronic        | 1 |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Nasolacrimal Duct, Inflammation, Chronic Active |   |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  | 1 |  |  |  |  |  |   |  | 1 |  |  |
| Respiratory Epithelium, Hyperplasia             |   |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Respiratory Epithelium, Squamous Metaplasia     |   |  |  |  |  |  |  |  |  |  |  |  |  | 2 |  |  |  |   |  |  |  |  |  |   |  |   |  |  |
| Trachea   | + |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |  |   |  |  |  |  |  |   |  |   |  |  |

SPECIAL SENSES SYSTEM

|                                      |   |  |  |   |  |   |  |   |  |  |  |  |  |  |   |  |  |  |  |   |  |  |   |  |   |  |   |  |   |  |  |
|--------------------------------------|---|--|--|---|--|---|--|---|--|--|--|--|--|--|---|--|--|--|--|---|--|--|---|--|---|--|---|--|---|--|--|
| Eye                                  | + |  |  |   |  |   |  |   |  |  |  |  |  |  |   |  |  |  |  |   |  |  |   |  |   |  |   |  |   |  |  |
| Inflammation, Acute                  |   |  |  |   |  |   |  |   |  |  |  |  |  |  |   |  |  |  |  | 2 |  |  |   |  |   |  |   |  |   |  |  |
| Cornea, Inflammation, Acute          | 2 |  |  |   |  |   |  |   |  |  |  |  |  |  |   |  |  |  |  |   |  |  |   |  |   |  |   |  |   |  |  |
| Cornea, Inflammation, Chronic Active | 1 |  |  | 2 |  | 3 |  | 3 |  |  |  |  |  |  |   |  |  |  |  |   |  |  | 1 |  | 2 |  | 4 |  | 2 |  |  |
| Retina, Degeneration                 |   |  |  |   |  |   |  |   |  |  |  |  |  |  |   |  |  |  |  |   |  |  |   |  |   |  |   |  |   |  |  |
| Harderian Gland                      | + |  |  |   |  |   |  |   |  |  |  |  |  |  |   |  |  |  |  |   |  |  |   |  |   |  |   |  |   |  |  |
| Atrophy                              |   |  |  |   |  |   |  |   |  |  |  |  |  |  | 1 |  |  |  |  |   |  |  |   |  |   |  |   |  |   |  |  |
| Metaplasia                           |   |  |  |   |  |   |  |   |  |  |  |  |  |  |   |  |  |  |  |   |  |  |   |  |   |  |   |  |   |  |  |

\* .. 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

Experiment Number: 00058 - 03

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Date Report Requested: 10/07/2020

Test Type: CHRONIC

Black Cohosh

Time Report Requested: 11:17:00

Route: GAVAGE

CAS Number: 84776-26-1

First Dose M/F: 07/03/12 / 07/02/12

Species/Strain: RATS/HSD

Lab: BAT

|                                 |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                 |   |   |   |   |   |   |
|---------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|---|---|---|---|---|
| HARLAN SPRAGUE DAWLEY 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 | 0 | 0               | 0 | 0 | 0 | 0 |   |   |
| 250 mg/kg male                  |  | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 4 | 6 | 4 | 7 | 6 | 7 | 6 | 5 | 4 | 5 | 6 | 6 | 7 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 6               | 6 | 6 | 6 | 6 |   |   |
| DAY ON TEST                     |  | 3 | 6 | 3 | 3 | 3 | 3 | 1 | 3 | 1 | 3 | 9 | 1 | 3 | 9 | 3 | 1 | 9 | 0 | 8 | 0 | 0 | 3 | 3 | 3 | 0 | 3 | 3 | 0 | 0               | 0 | 0 | 0 | 0 |   |   |
| ANIMAL ID                       |  | 1 | 4 | 0 | 0 | 0 | 0 | 1 | 0 | 8 | 5 | 4 | 3 | 0 | 4 | 0 | 6 | 5 | 2 | 9 | 4 | 6 | 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 | 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 | 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 | 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 | 2 | 3 | 3 | 4 | 4 | 5 |                 |   |   |   |   |   |   |
|                                 |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | males (cont...) |   |   |   |   |   |   |

Zymbal's Gland

+

URINARY SYSTEM

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney                               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Amphophilic/Vacuolar Hyperplasia     |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Nephropathy, Chronic Progressive     | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 2 | 4 | 2 | 4 | 4 | 4 | 4 | 2 | 1 | 4 | 4 | 4 | 4 | 4 | 3 | 3 | 4 | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pelvis, Inflammation, Acute          |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pelvis, Inflammation, Chronic Active |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal Tubule, Cyst                   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |
| Urinary Bladder                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Infiltration Cellular, Lymphocyte    |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. 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

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1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked



Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| DAY ON TEST | HARLAN SPRAGUE DAWLEY RATS MALE |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | * TOTALS |      |      |
|-------------|---------------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|
|             | 0693                            | 0725 | 0771 | 0522 | 0494 | 0445 | 0773 | 0773 | 0667 | 0768 | 0673 | 0558 | 0733 | 0733 | 0733 | 0669 | 0662 | 0547 | 0668 | 0599 |          | 0673 | 0733 |
| ANIMAL ID   | 0011                            | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011     | 0011 | 0011 |
|             | 2                               | 2    | 2    | 2    | 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    |      |      |      |      |      |      |          |      |      |

**ALIMENTARY SYSTEM**

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |       |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-------|
| Esophagus                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Intestine Large, Cecum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Mineral                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0 |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 2.0 |
| Intestine Large, Colon       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Mineral                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0 |
| Parasite Metazoan            |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1     |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 1.0 |
| Ulcer                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 2.0 |
| Lymphoid Tissue, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |    | 2 3.0 |
| Intestine Large, Rectum      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1     |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0 |
| Intestine Small, Duodenum    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |       |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3 1.7 |
| Intestine Small, Ileum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Intestine Small, Jejunum     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Peyer's Patch, Hyperplasia   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 4.0 |
| Liver                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Basophilic Focus             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |    | 1     |
| Clear Cell Focus             |   | X |   |   |   |   | X | X | X | X | X | X | X | X |   |   |   | X |   |   | X | X |   |    | 24    |

\* .. 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | * TOTALS |      |      |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|
|  | 0693        | 0725 | 0731 | 0521 | 0448 | 0445 | 0770 | 0771 | 0666 | 0667 | 0753 | 0757 | 0773 | 0773 | 0669 | 0662 | 0542 | 0725 | 0668 | 0552 |          | 0669 | 0773 |
| ANIMAL ID  | 0011        | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011     | 0011 | 0011 |
| Degeneration, Cystic Eosinophilic Focus              |             |      |      |      |      |      | 1    |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Extramedullary Hematopoiesis                         |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Hepatodiaphragmatic Nodule                           |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Necrosis   |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Bile Duct, Cyst                                      |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Bile Duct, Dilation                                  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Bile Duct, Hyperplasia                               |             |      |      | 1    | 1    |      |      |      | 1    | 1    | 1    | 1    |      | 1    | 1    | 1    |      | 1    | 1    |      | 1        |      |      |
| Mesentery Fat, Necrosis                              |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Oral Mucosa  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Pancreas   |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Polyarteritis Nodosa                                 |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Acinus, Atrophy                                      |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Acinus, Hyperplasia                                  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Salivary Glands                                      |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Stomach, Forestomach                                 |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Erosion  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Inflammation, Acute                                  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Inflammation, Chronic                                |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Inflammation, Chronic Active                         |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Mineral  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Necrosis   |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Polyarteritis Nodosa                                 |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |
| Ulcer  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |      |      |

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

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Black Cohosh

CAS Number: 84776-26-1

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Lab: BAT

|  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST | 0693  | 0725  | 0773  | 0752  | 0744  | 0744  | 0777  | 0777  | 0666  | 0776  | 0766  | 0775  | 0777  | 0777  | 0666  | 0665  | 0777  | 0666  | 0555  | 0666  | 0777  | 0773  | 0773  | * TOTALS |
|  | ANIMAL ID   | 00126 | 00078 | 00009 | 00002 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 | 00001 |          |
|  |             | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     | 1     |          |

|                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |     |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|-----|
| Epithelium, Hyperplasia             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 | 3  | 1  | 5   | 2.2 |
| Epithelium, Hyperplasia, Basal Cell |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1   | 1.0 |
| Stomach, Glandular                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Mineral                             |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 | 1 |   |   |   |   |   |   |    | 10 | 1.9 |     |
| Polyarteritis Nodosa                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |    |    | 1   | 2.0 |

CARDIOVASCULAR SYSTEM

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  |    |     |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|--|---|--|--|--|--|--|--|--|--|---|---|---|---|--|---|---|---|---|----|--|----|-----|
| Blood Vessel                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | + | + | +  |    | +   |  | + |  |  |  |  |  |  |  |  | + | + | + | + |  | + | + | + | + | 32 |  |    |     |
| Mineral   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  | 13 | 1.3 |
| Aorta, Dilation                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  | 1  | 2.0 |
| Heart   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  |    |     |
| Cardiomyopathy                                  | 2 | 1 |   |   | 1 | 2 | 2 |   | 2 | 1 | 1 | 1 | 1 | 1 | 1 |   | 1 | 2 | 2 | 1 |   | 1 | 2 | 2 | 1 |    | 40 | 1.4 |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  |    |     |
| Mineral   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  | 1  | 1.0 |
| Atrium, Thrombus                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  | 4  |     |
| Perivascular, Infiltration Cellular, Lymphocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  | 2  | 1.0 |
| Valve, Inflammation, Chronic                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |  |   |  |  |  |  |  |  |  |  |   |   |   |   |  |   |   |   |   |    |  | 1  | 1.0 |

ENDOCRINE SYSTEM

|                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |     |
|-------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|-----|
| Adrenal Cortex                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |     |
| Amyloid Deposition, Focal     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 | 1.0 |
| Degeneration, Cystic          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 5 | 1.0 |
| Hyperplasia, Focal            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 8 | 1.1 |
| Necrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 4 | 1.5 |
| Bilateral, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 | 2.0 |
| Adrenal Medulla               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male               | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |       |       |       |                      |      |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|-------|-------|-------|----------------------|------|
|  | 0693        | 0725  | 0771  | 0521  | 0448  | 0445  | 0770  | 0771  | 0666  | 0677  | 0666  | 0775  | 0777  | 0777  | 0666  | 0666  | 0554  | 0776  | 0665  | 0552  |          | 0668  | 0559  | 0667  | 0773                 | 0773 |
| ANIMAL ID  | 00126       | 00117 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111 | 00111    | 00111 | 00111 | 00111 | 00111                |      |
| Hyperplasia, Focal<br>Bilateral, Hyperplasia, Focal                | 2           |       |       |       |       |       |       | 4     |       |       | 2     | 1     |       | 3     |       | 1     |       | 4     |       |       |          |       | 2     | 1     | 13 2.2<br>3 2.3      |      |
| Islets, Pancreatic<br>Hyperplasia                                  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +     | +     | +     | 50<br>1 1.0          |      |
| Parathyroid Gland<br>Hyperplasia, Diffuse                          | +           | +     | +     | +     | +     | +     | M     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +     | M     | +     | 44<br>16 2.3         |      |
| Pituitary Gland<br>Pars Distalis, Hyperplasia                      | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +     | +     | +     | 50<br>15 1.7         |      |
| Thyroid Gland<br>C-cell, Hyperplasia                               | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +     | +     | +     | 50<br>9 3.1          |      |
| <b>GENERAL BODY SYSTEM</b>   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |       |       |       |                      |      |
| NONE   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |       |       |       |                      |      |
| <b>GENITAL SYSTEM</b>  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |       |       |       |                      |      |
| Epididymis<br>Inflammation, Chronic Active<br>Polyarteritis Nodosa | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +     | +     | +     | 50<br>1 1.0<br>2 1.0 |      |
| Preputial Gland<br>Duct, Hyperplasia, Squamous                     | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +     | +     | +     | 50<br>1 3.0          |      |
| Prostate<br>Hyperplasia<br>Inflammation, Chronic                   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +        | +     | +     | +     | 50<br>2 1.0<br>5 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

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| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | * TOTALS |      |      |      |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|------|
|  | 0693        | 0725 | 0771 | 0522 | 0494 | 0445 | 0770 | 0773 | 0667 | 0671 | 0768 | 0638 | 0535 | 0733 | 0773 | 0669 | 0662 | 0574 | 0762 | 0588 |          | 0659 | 0673 | 0733 |
| ANIMAL ID  | 0011        | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011     | 0011 | 0011 | 0011 |
|  | 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    | 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    |

Inflammation, Chronic Active Polyarteritis Nodosa 1 4 2.0 2 1.0

Seminal Vesicle + 50  
 Inflammation, Chronic Active 1 1.0  
 Metaplasia, Squamous 2 1 2.0  
 Polyarteritis Nodosa 1 2 1.0

Testis + 50  
 Polyarteritis Nodosa 3 1 3 3 1 2 1 2 1 1 2 2 24 1.8  
 Bilateral, Germinal Epithelium, Degeneration 4 2 1 4 2 3 3 3 3 3 4 4 4 4 4 4 4 4 4 4 4 4 4 5 19 2.1  
 Germinal Epithelium, Degeneration 3 6 2.0  
 Interstitial Cell, Hyperplasia 3 2 2.5

**HEMATOPOIETIC SYSTEM**

Bone Marrow + 50  
 Hemorrhage 4 1 15 2.0  
 Hypercellularity 2 3 1 2 1 1 1 2 2 2 2 1 30 1.9

Lymph Node + 3  
 Lumbar, Hemorrhage 1 2.0  
 Lumbar, Infiltration Cellular, Histiocyte 1 2.0  
 Lumbar, Pigment 1 2.0  
 Pancreatic, Infiltration Cellular, Plasma Cell 2 1 2.0  
 Renal, Hemorrhage 1 2.0  
 Renal, Pigment 1 2.0

Lymph Node, Mandibular + 50  
 Atrophy 1 4.0

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
 + .. Tissue examined microscopically M .. Missing tissue 1-4 .. Lesion qualified as:  
 X .. Lesion present A .. Autolysis precludes evaluation 1) Minimal 3) Moderate  
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|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|------|------|
|  | 0693        | 0725 | 0771 | 0521 | 0448 | 0445 | 0770 | 0771 | 0667 | 0768 | 0673 | 0758 | 0773 | 0777 | 0661 | 0665 | 0554 | 0772 | 0668 | 0552 |          | 0662 | 0559 | 0667 | 0773 |
| ANIMAL ID  | 0011        | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011     | 0011 | 0011 | 0011 | 0011 |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |    |     |   |     |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|----|-----|---|-----|---|---|---|---|---|---|---|---|---|---|
| Ectasia                      | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     | 2  | 3.0 |   |     |   |   |   |   |   |   |   |   |   |   |
| Lymph Node, Mesenteric       | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     | 49 |     |   |     |   |   |   |   |   |   |   |   |   |   |
| Spleen                       | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     | 49 |     |   |     |   |   |   |   |   |   |   |   |   |   |
| Extramedullary Hematopoiesis | 2 | 1 | 2 |   | 2 | 1 | 2 | 3 | 3 | 2 | 3 | 2 |   | 2 | 2 | 2 |   | 1 | 1  | 2   | 2  | 2   | 2 | 2   |   |   |   |   |   |   |   |   |   |   |
| Pigment                      | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 1 |   | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 2 | 2 | 1  | 1   | 1  | 1   | 1 | 2   |   |   |   |   |   |   |   |   |   |   |
| White Pulp, Atrophy          | 3 |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   | 4 | 4 | 13 | 2.8 |    |     |   |     |   |   |   |   |   |   |   |   |   |   |
| Thymus                       | M | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | +   | +  | +   | + |     |   |   |   |   |   |   |   |   |   |   |
| Atrophy                      | 4 |   | 2 |   | 3 | 2 |   |   |   |   |   |   |   |   |   |   | 1 | 2 | 1  | 3   | 1  | 3   | 2 | 1   | 3 | 4 | 4 | 3 | 3 | 2 | 2 | 2 | 2 | 3 |
| Cyst                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     | X  |     | 1 |     |   |   |   |   |   |   |   |   |   |   |
| Ectopic Parathyroid Gland    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     | X  |     | 2 |     |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |    |     | 1 | 1.0 |   |   |   |   |   |   |   |   |   |   |

**INTEGUMENTARY SYSTEM**

|   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |     |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|-----|
| Mammary Gland                             | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 49 |     |
| Hyperplasia                               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1  | 2.0 |
| Skin                                      | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |     |
| Cyst Epithelial Inclusion                 |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1   |
| Inflammation, Granulomatous               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1  | 3.0 |
| Inflammation, Chronic Active              |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1  | 3.0 |
| Ulcer                                     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1  | 2.0 |
| Subcutaneous Tissue, Polyarteritis Nodosa |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1  | 1.0 |

**MUSCULOSKELETAL SYSTEM**

|      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |  |
|------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|--|
| Bone | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |  |
|------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|--|

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|----------------|---------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|----------|
|                | 0693                            | 0725   | 0771   | 0521   | 0448   | 0445   | 0770   | 0773   | 0666   | 0767   | 0668   | 0753   | 0773   | 0773   | 0666   | 0666   | 0554   | 0772   | 0662   | 0558   | 0669   | 0667   | 0733   | 0733   |          |
| ANIMAL ID      | 001126                          | 000178 | 000008 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 | 000000 |          |
| 250 mg/kg 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      |          |

|                                  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |     |     |
|----------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|-----|-----|
| Mineral                          |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 | 3.0 |     |
| Alveolar Epithelium, Hyperplasia | 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   | 2   | 1.5 |
| Bronchiole, Fibrosis             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 1.0 |
| Peribronchiolar, Fibrosis        |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   | 1   | 2.0 |

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|
| Nose  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |
| Foreign Body                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 |     |
| Inflammation, Acute                             | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 | 1.0 |
| Inflammation, Chronic                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 | 1.0 |
| Inflammation, Chronic Active                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |    | 3 | 1.0 |
| Nasolacrimal Duct, Inflammation, Chronic        |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 | 1.0 |
| Nasolacrimal Duct, Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |    | 4 | 1.3 |
| Respiratory Epithelium, Hyperplasia             |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |    | 1 | 1.0 |
| Respiratory Epithelium, Squamous Metaplasia     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 2.0 |

|         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |
|---------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |
|---------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|

SPECIAL SENSES SYSTEM

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|
| Eye                                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |
| Inflammation, Acute                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Cornea, Inflammation, Acute          | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2  | 2.0 |
| Cornea, Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |    | 11 | 2.2 |
| Retina, Degeneration                 |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |    | 1  | 1.0 |

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|
| Harderian Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |
| Atrophy         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 | 1.0 |
| Metaplasia      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 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



Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|
| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>250 mg/kg male | DAY ON TEST | 0693 | 0725 | 0773 | 0522 | 0449 | 0444 | 0773 | 0776 | 0667 | 0673 | 0753 | 0773 | 0773 | 0666 | 0666 | 0554 | 0776 | 0556 | 0673 | 0773 | 0773 | * TOTALS |
|  | ANIMAL ID   | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 |          |
|  |             | 2678 | 2789 | 2311 | 2330 | 3311 | 3332 | 3333 | 3334 | 3335 | 3336 | 3337 | 3338 | 3339 | 4400 | 4411 | 4422 | 4433 | 4444 | 4455 | 4466 | 4477 |          |

Zymbal's Gland

1

URINARY SYSTEM

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |     |     |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|-----|
| Kidney                               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |     |
| Amphophilic/Vacuolar Hyperplasia     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |     |     |
| Nephropathy, Chronic Progressive     | 4 | 4 | 4 | 1 | 3 | 1 | 4 | 2 | 4 | 3 | 4 | 4 | 4 | 3 | 4 | 3 | 4 | 4 | 3 | 4 | 2 | 1 | 4 | 2  | 3   | 50  | 3.4 |
| Pelvis, Inflammation, Acute          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1   | 1.0 |     |
| Pelvis, Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1   | 2.0 |     |
| Renal Tubule, Cyst                   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  |     |     |     |
| Urinary Bladder                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |     |
| Infiltration Cellular, Lymphocyte    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 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

Experiment Number: 00058 - 03  
 Test Type: CHRONIC  
 Route: GAVAGE  
 Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL  
 Black Cohosh  
 CAS Number: 84776-26-1

Date Report Requested: 10/07/2020  
 Time Report Requested: 11:17:00  
 First Dose M/F: 07/03/12 / 07/02/12  
 Lab: BAT

| DAY ON TEST | HARLAN SPRAGUE DAWLEY RATS MALE |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                          | 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                        |                          |                    |
| 7           | 6                               | 7 | 5 | 6 | 7 | 6 | 5 | 6 | 5 | 6 | 5 | 7 | 6 | 5 | 6 | 6 | 7 | 7 | 4 | 6 | 6 | 7 | 6 | 7                        | 000000000000000000000000 |                    |
| 3           | 1                               | 3 | 0 | 4 | 2 | 3 | 8 | 1 | 6 | 3 | 9 | 3 | 9 | 6 | 8 | 0 | 1 | 3 | 4 | 2 | 5 | 3 | 6 | 3                        | 000000000000000000000000 |                    |
| 0           | 3                               | 0 | 2 | 3 | 5 | 2 | 6 | 1 | 4 | 3 | 8 | 1 | 3 | 9 | 2 | 7 | 8 | 0 | 2 | 0 | 0 | 0 | 3 | 0                        | 000000000000000000000000 |                    |
| 0           | 0                               | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0                        | 000000000000000000000000 |                    |
| 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                        | 111111111111111111111111 |                    |
| 5           | 5                               | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 555555555566666666777777 |                          |                    |
| 1           | 2                               | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 123456789012345678901234 |                          |                    |

**ALIMENTARY SYSTEM**

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Erosion                      |   | 3 |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Acute          |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic        |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic Active |   | 3 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mineral                      |   | 3 |   | 1 | 2 |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa         |   | 2 |   | 2 |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ulcer                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Colon       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Parasite Metazoan            |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa         |   |   |   |   | 1 |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Rectum      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |
| Intestine Small, Duodenum    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Ileum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Jejunum     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyarteritis Nodosa         |   |   |   |   | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male | DAY ON TEST |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | males<br>(cont...) |
|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|--------------------|
|  | 07<br>30    | 06<br>13 | 07<br>30 | 05<br>02 | 06<br>43 | 07<br>25 | 06<br>32 | 05<br>86 | 06<br>11 | 05<br>44 | 06<br>33 | 05<br>88 | 06<br>11 | 05<br>43 | 06<br>39 | 05<br>68 | 06<br>02 | 07<br>88 | 06<br>74 | 07<br>42 | 06<br>60 | 05<br>50 | 06<br>30 | 07<br>63 | 06<br>70 |                    |
| ANIMAL ID  | 001151      | 001152   | 001153   | 001154   | 001155   | 001156   | 001157   | 001158   | 001159   | 001160   | 001161   | 001162   | 001163   | 001164   | 001165   | 001166   | 001167   | 001168   | 001169   | 001170   | 001171   | 001172   | 001173   | 001174   | 001175   | 001176             |
| Peyer's Patch, Hyperplasia                           |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Liver  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                  |
| Basophilic Focus                                     |             |          | X        |          |          |          |          |          |          |          |          | X        | X        |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Clear Cell Focus                                     | X           | X        | X        |          |          |          |          | X        |          |          |          | X        |          |          |          |          |          |          | X        |          |          |          | X        |          | X        |                    |
| Degeneration, Cystic                                 |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Eosinophilic Focus                                   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Extramedullary Hematopoiesis                         |             |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |                    |
| Fatty Change, Focal                                  |             |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Hepatodiaphragmatic Nodule                           |             |          |          |          |          |          |          |          |          |          |          |          |          |          | X        |          |          |          |          |          |          |          |          |          |          |                    |
| Mixed Cell Focus                                     |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | X        |          |          |          |          |          |          |          |          |                    |
| Necrosis   |             |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |                    |
| Polyarteritis Nodosa                                 |             |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Bile Duct, Cyst                                      | X           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Bile Duct, Hyperplasia                               |             | 1        |          |          |          | 1        |          |          |          |          |          |          |          | 1        | 2        | 1        | 1        | 1        | 1        | 1        | 2        | 1        |          | 1        | 1        |                    |
| Bile Duct, Inflammation, Chronic Active              |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        |          |          |          |          |                    |
| Centrilobular, Degeneration                          |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Pancreas   | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                  |
| Polyarteritis Nodosa                                 | 1           | 1        |          |          |          |          |          |          |          |          |          |          |          | 1        |          | 1        |          |          |          |          |          |          |          |          | 2        |                    |
| Acinus, Atrophy                                      |             |          |          |          |          | 1        | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Acinus, Hyperplasia                                  |             |          |          |          | 3        | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |                    |
| Duct, Cyst   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Salivary Glands                                      | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                  |
| Stomach, Forestomach                                 | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                  |
| Edema  |             | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Inflammation, Chronic                                |             |          |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                    |
| Inflammation, Chronic Active                         |             |          |          | 1        |          | 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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M .. Missing tissue

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1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

Experiment Number: 00058 - 03

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

Date Report Requested: 10/07/2020

Test Type: CHRONIC

Black Cohosh

Time Report Requested: 11:17:00

Route: GAVAGE

CAS Number: 84776-26-1

First Dose M/F: 07/03/12 / 07/02/12

Species/Strain: RATS/HSD

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male | DAY ON TEST |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | males<br>(cont...) |    |
|--|-------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|--------------------|----|
|  | 07          | 06 | 07 | 05 | 06 | 07 | 06 | 05 | 06 | 05 | 06 | 05 | 07 | 06 | 05 | 06 | 06 | 07 | 07 | 04 | 06 | 06 | 07 | 06 |                    | 07 |
|  | 30          | 13 | 03 | 00 | 04 | 02 | 03 | 08 | 01 | 06 | 03 | 09 | 03 | 09 | 06 | 08 | 00 | 01 | 03 | 04 | 02 | 00 | 05 | 03 |                    | 06 |
|  | 00          | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00                 |    |
|  | 11          | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11                 |    |
|  | 51          | 52 | 53 | 54 | 55 | 56 | 55 | 55 | 55 | 56 | 56 | 56 | 56 | 56 | 56 | 56 | 56 | 56 | 56 | 57 | 57 | 57 | 57 | 57 | 57                 |    |

Polyarteritis Nodosa  
Epithelium, Hyperplasia  
Epithelium, Hyperplasia, Basal Cell

2 2 3

Stomach, Glandular  
Mineral

+  
4 3 3 3 1 1 1 2

**CARDIOVASCULAR SYSTEM**

Blood Vessel  
Mineral  
Aorta, Dilation  
Carotid Artery, Polyarteritis Nodosa  
Pulmonary Artery, Thrombus

+  
4 2 2 1 2 2 3 1 1 3 4 1 2 2 2 3 2 2 2 2 1

Heart  
Cardiomyopathy  
Inflammation, Chronic Active  
Mineral  
Atrium, Thrombus  
Valve, Thrombus

+  
2 2 1 2 3 1 1 1 3 4 3 1 2 2 2 3 2 2 2 2 1  
3 1 1 X

**ENDOCRINE SYSTEM**

Adrenal Cortex  
Angiectasis  
Degeneration, Cystic  
Hyperplasia, Focal  
Necrosis  
Thrombus

+  
1 1 2 1 2 X 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

|                                 |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                    |
|---------------------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------------|
| HARLAN SPRAGUE DAWLEY 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 | males<br>(cont...) |
| 750 mg/kg male                  |  | 7 | 6 | 7 | 5 | 6 | 7 | 6 | 5 | 6 | 5 | 6 | 7 | 6 | 5 | 6 | 6 | 7 | 7 | 4 | 6 | 6 | 7 | 6 | 7 | 6 | 7 |   |                    |
| ANIMAL ID                       |  | 3 | 1 | 3 | 0 | 4 | 2 | 3 | 8 | 1 | 6 | 3 | 9 | 3 | 9 | 6 | 8 | 0 | 1 | 3 | 4 | 2 | 5 | 3 | 6 | 3 | 0 |   |                    |

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Vacuolization Cytoplasmic<br>Bilateral, Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla<br>Hyperplasia, Focal<br>Bilateral, Hyperplasia, Focal  | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|   | 1 | 4 |   | 1 |   | 2 |   |   |   |   |   |   | 4 | 1 |   |   | 2 |   |   | 4 |   |   |   |   |   |   | 1 |   |
| Islets, Pancreatic<br>Hyperplasia                                       | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |
| Parathyroid Gland<br>Hyperplasia, Diffuse                               | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + |   |
|   | 3 |   |   | 4 |   |   |   |   | 4 |   |   | 3 |   |   | 2 | 3 |   |   |   |   |   | 3 |   |   | 2 |   |   |   |
| Pituitary Gland<br>Pars Distalis, Hyperplasia<br>Pars Nervosa, Thrombus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |
|   | 2 |   |   |   |   | 1 | 1 |   |   |   | 4 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |
| Thyroid Gland<br>Polyarteritis Nodosa<br>C-cell, Hyperplasia            | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   |   | 2 |   |   |   |   |   |   |   | 4 |   |   | 3 |   |   |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Epididymis<br>Atrophy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 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  
 M .. Missing tissue  
 A .. Autolysis precludes evaluation  
 BLANK .. Not examined microscopically  
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Experiment Number: 00058 - 03

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Black Cohosh

CAS Number: 84776-26-1

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Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male | DAY ON TEST |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        | males<br>(cont...) |
|--|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------------------|
|  | 0730        | 0613   | 0730   | 0502   | 0643   | 0765   | 0682   | 0558   | 0661   | 0566   | 0653   | 0738   | 0611   | 0703   | 0569   | 0682   | 0767   | 0677   | 0442   | 0662   | 0665   | 0733   | 0664   | 0763   | 0673   |                    |
| ANIMAL ID  | 001151      | 000122 | 000033 | 000044 | 000055 | 000066 | 000077 | 000088 | 000099 | 000000 | 000011 | 000022 | 000033 | 000044 | 000055 | 000066 | 000077 | 000088 | 000099 | 000000 | 000011 | 000022 | 000033 | 000044 | 000055 |                    |

Duct, Hyperplasia, Squamous

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Prostate                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic        |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 1 |   |   |
| Inflammation, Chronic Active |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Seminal Vesicle              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Chronic Active |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Testis                                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Edema  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Granuloma Sperm                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa                         | 2 | 2 |   |   | 2 |   |   |   |   | 1 |   |   | 3 | 2 | 1 |   | 2 |   |   |   | 1 | 2 |   | 1 |
| Bilateral, Germinal Epithelium, Degeneration |   | 1 |   |   | 2 |   |   |   | 3 |   |   | 1 |   |   |   | 1 |   |   |   |   |   |   |   |   |
| Germinal Epithelium, Degeneration            | 1 |   |   | 4 |   | 1 | 3 |   |   |   | 1 |   | 1 | 1 |   |   |   |   | 1 |   |   |   |   |   |
| Interstitial Cell, Hyperplasia               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

HEMATOPOIETIC SYSTEM

|                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage       |   | 3 |   | 2 | 3 | 1 |   |   | 2 |   | 1 |   | 1 | 4 | 2 | 4 |   |   | 1 | 2 | 1 |   |   |   |
| Hypercellularity |   |   |   | 3 | 2 | 1 |   |   | 1 | 4 |   | 2 | 2 |   |   | 2 |   |   | 2 | 2 | 1 |   | 2 | 1 |
| Necrosis         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

|                                  |  |  |  |  |  |   |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------------------------------|--|--|--|--|--|---|--|--|--|--|---|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Lymph Node                       |  |  |  |  |  | + |  |  |  |  | + |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lumbar, Hyperplasia, Plasma Cell |  |  |  |  |  | 2 |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Lumbar, Lymphatic Sinus, Ectasia |  |  |  |  |  | 2 |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mediastinal, Hemorrhage          |  |  |  |  |  | 2 |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mediastinal, Pigment             |  |  |  |  |  | 2 |  |  |  |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |

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

+ .. Tissue examined microscopically

X .. Lesion present

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|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------------------------|
| <b>HARLAN SPRAGUE DAWLEY RATS MALE</b><br><b>750 mg/kg male</b> | DAY ON TEST | 0730  | 0633  | 0730  | 0562  | 0673  | 0668  | 0552  | 0661  | 0564  | 0653  | 0793  | 0638  | 0569  | 0662  | 0770  | 0774  | 0422  | 0665  | 0673  | 0663  | 0763  | 0767  | <b>males (cont...)</b> |
|   | ANIMAL ID   | 00151 | 00012 | 00013 | 00014 | 00015 | 00016 | 00017 | 00018 | 00019 | 00020 | 00021 | 00022 | 00023 | 00024 | 00025 | 00026 | 00027 | 00028 | 00029 | 00030 | 00031 | 00032 |                        |

Renal, Ectasia

4

Lymph Node, Mandibular  
Hyperplasia, Lymphoid  
Infiltration Cellular, Plasma Cell

+ + + + + 2 + + + + + + + + + + + + + + + + + +  
2  
2 2

Lymph Node, Mesenteric  
Atrophy

+ +

Spleen  
Extramedullary Hematopoiesis  
Necrosis  
Pigment  
White Pulp, Atrophy

+  
3 2 2 3 1 2 3 2 2 2 2 2 2 2 2 2 3 2 2 2 1 2  
1 2 1 1 2 1 2 2 1 1 1 1 1 2 2 1 1 2 1 1 2  
4 4 1 4 3 4 4 4 3 4 3 3 3 4 4 3 3

Thymus  
Atrophy  
Hyperplasia, Lymphoid

+  
1 4 4 4 3 4 2 4 3 3 3 4 3 3 3 4 4 2 4 4 1

**INTEGUMENTARY SYSTEM**

Mammary Gland

+ + + + + + M + + + + + + + + + + + + + + + + +

Skin  
Cyst Epithelial Inclusion  
Edema  
Foreign Body  
Hemorrhage  
Inflammation, Granulomatous  
Inflammation, Chronic Active

+  
X  
2 X 2 4 2 3 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

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|   |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                                  |   |
|---|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------------------|---|
| <b>HARLAN SPRAGUE DAWLEY RATS</b><br><b>MALE</b><br><b>750 mg/kg male</b> | 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 | 5 | 6 | 7 | 6 | 5 | 6 | 5 | 6 | 7 | 6 | 5 | 6 | 6 | 7 | 7 | 4 | 6 | 6 | 7 | 6 | 7 | 0                                |   |
|   |             | 3 | 1 | 3 | 0 | 4 | 2 | 3 | 8 | 1 | 6 | 3 | 9 | 3 | 9 | 6 | 8 | 0 | 1 | 3 | 4 | 2 | 5 | 3 | 6 | 3                                |   |
|   |             | 0 | 3 | 0 | 2 | 3 | 5 | 2 | 6 | 1 | 4 | 3 | 8 | 1 | 3 | 9 | 2 | 7 | 8 | 0 | 2 | 0 | 0 | 0 | 3 | 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                                |   |
|   |             | 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 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |                                  |   |
|   |             | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4                                | 5 |
|   |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>males</b><br><b>(cont...)</b> |   |

|                        |   |  |  |  |   |  |   |   |   |
|------------------------|---|--|--|--|---|--|---|---|---|
| Ulcer                  | 4 |  |  |  | 3 |  |   | 4 | 2 |
| Epidermis, Hyperplasia | 2 |  |  |  |   |  | 1 | 2 |   |

**MUSCULOSKELETAL SYSTEM**

|                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |
|----------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|--|--|
| Bone                 | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |
| Osteopetrosis        | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |
| Skeletal Muscle      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | + |  |  |
| Degeneration         |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2 |  |  |
| Polyarteritis Nodosa |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |  |

**NERVOUS SYSTEM**

|                                |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |   |  |  |
|--------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|--|---|--|--|
| Brain                          | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  |   |  |  |
| Gliososis                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 2 |  |  |
| Inflammation, Chronic Active   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 2 |  |  |
| Necrosis                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 2 |  | 3 |  |  |
| Peripheral Nerve               |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | + |  |  |
| Degeneration                   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 2 |  |  |
| Axon, Sciatic, Degeneration    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 2 |  |  |
| Axon, Tibial, Degeneration     |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 3 |  |  |
| Axon, Trigeminal, Degeneration |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 2 |  |  |
| Trigeminal, Fibrosis           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 2 |  |  |
| Spinal Cord                    |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | + |  |  |
| Axon, Degeneration             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |   |  | 2 |  |  |

**RESPIRATORY SYSTEM**

\* .. 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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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| 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 |
| 7           | 6 | 7 | 5 | 6 | 7 | 6 | 5 | 6 | 5 | 6 | 5 | 7 | 6 | 5 | 6 | 6 | 7 | 7 | 4 | 6 | 6 | 7 | 6 | 7 | 6 | 7 | 6 | 7 |   |
| 3           | 1 | 3 | 0 | 4 | 2 | 3 | 8 | 1 | 6 | 3 | 9 | 3 | 9 | 6 | 8 | 0 | 1 | 3 | 4 | 2 | 5 | 3 | 6 | 3 | 6 | 3 | 0 |   |   |
| 0           | 3 | 0 | 2 | 3 | 5 | 2 | 6 | 1 | 4 | 3 | 8 | 1 | 3 | 9 | 2 | 7 | 8 | 0 | 2 | 0 | 0 | 0 | 3 | 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 |   |   |
| 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 | 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 | 6 | 7 | 8 |   |   |

males (cont...)

|                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
|--------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|--|--|
| Cornea, Inflammation, Chronic        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |  |  |  |
| Cornea, Inflammation, Chronic Active | 1 | 1 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Optic Nerve, Polyarteritis Nodosa    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Harderian Gland Atrophy              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |  |  |
| Inflammation, Suppurative            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |  |  |  |

URINARY SYSTEM

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|--|--|
| Kidney                                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |  |  |
| Amphophilic/Vacuolar Hyperplasia            |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Cyst  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Hemorrhage                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Infarct                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Inflammation, Chronic                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Nephropathy, Chronic Progressive            | 3 | 4 | 3 | 4 | 4 | 4 | 3 | 3 | 4 | 2 | 3 | 4 | 3 | 4 | 1 | 4 | 3 | 3 | 3 | 4 | 4 | 2 | 3 | 4 | 2 |   |   |  |  |  |
| Renal Tubule, Accumulation, Hyaline Droplet |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Renal Tubule, Cyst                          |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   | X | X |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Urinary Bladder                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |  |  |
| Inflammation, Chronic                       |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |
| Polyarteritis Nodosa                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |  |  |

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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male | DAY ON TEST           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | * TOTALS              |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
|  | 0<br>7<br>1<br>1      | 0<br>7<br>3<br>1      | 0<br>4<br>3<br>4      | 0<br>6<br>7<br>2      | 0<br>7<br>1<br>3      | 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>5<br>0      | 0<br>7<br>3<br>0      | 0<br>4<br>4<br>9      | 0<br>7<br>3<br>0      | 0<br>6<br>4<br>3      | 0<br>6<br>6<br>9      | 0<br>5<br>2<br>0      | 0<br>7<br>0<br>5      | 0<br>4<br>4<br>1      | 0<br>7<br>3<br>1      | 0<br>7<br>5<br>4      | 0<br>6<br>5<br>3      | 0<br>6<br>1<br>4      | 0<br>7<br>3<br>1      | 0<br>6<br>7<br>4      | 0<br>7<br>3<br>1      |                       |
| ANIMAL ID  | 0<br>0<br>1<br>7<br>6 | 0<br>0<br>1<br>7<br>7 | 0<br>0<br>1<br>7<br>8 | 0<br>0<br>1<br>7<br>9 | 0<br>0<br>1<br>8<br>0 | 0<br>0<br>1<br>8<br>1 | 0<br>0<br>1<br>8<br>2 | 0<br>0<br>1<br>8<br>3 | 0<br>0<br>1<br>8<br>4 | 0<br>0<br>1<br>8<br>5 | 0<br>0<br>1<br>8<br>6 | 0<br>0<br>1<br>8<br>7 | 0<br>0<br>1<br>8<br>8 | 0<br>0<br>1<br>8<br>8 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>1<br>9<br>9 | 0<br>0<br>2<br>9<br>0 |

### ALIMENTARY SYSTEM

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |     |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|-----|
| Esophagus                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | 50 |     |     |
| Intestine Large, Cecum       | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | 49 |     |     |
| Erosion                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2   | 2.0 |
| Inflammation, Acute          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1   | 1.0 |
| Inflammation, Chronic        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1   | 2.0 |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |    |    | 3   | 2.7 |
| Mineral                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |    |    | 5   | 1.6 |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |    |    | 4   | 1.8 |
| Ulcer                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |    |    | 1   | 3.0 |
| Intestine Large, Colon       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |    |    | 1   | 1.0 |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1   |     |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |    |    | 3   | 1.3 |
| Intestine Large, Rectum      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |    | 2  |     |     |
| Intestine Small, Duodenum    | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | 49 |    |     |     |
| Polyarteritis Nodosa         |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |     |
| Intestine Small, Ileum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |    | 1  | 1.0 |     |
| Intestine Small, Jejunum     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 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

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Experiment Number: 00058 - 03

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Black Cohosh

CAS Number: 84776-26-1

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male | DAY ON TEST |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | * TOTALS |    |    |    |        |
|--|-------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----------|----|----|----|--------|
|  | 07          | 07 | 04 | 06 | 07 | 07 | 07 | 07 | 06 | 07 | 04 | 07 | 06 | 06 | 05 | 07 | 04 | 07 | 07 | 05 |          | 06 | 06 | 07 | 06     |
| ANIMAL ID  | 00          | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00       | 00 | 00 | 00 | 00     |
| Peyer's Patch, Hyperplasia                           |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 3.0  |
| Liver  | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +        | +  | +  | +  | 50     |
| Basophilic Focus                                     |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 4      |
| Clear Cell Focus                                     |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 17     |
| Degeneration, Cystic                                 |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 1.0  |
| Eosinophilic Focus                                   |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1      |
| Extramedullary Hematopoiesis                         |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 3 1.3  |
| Fatty Change, Focal                                  |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 1.0  |
| Hepatodiaphragmatic Nodule                           |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 3      |
| Mixed Cell Focus                                     |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 2      |
| Necrosis   |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 2 2.5  |
| Polyarteritis Nodosa                                 |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 1.0  |
| Bile Duct, Cyst                                      |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1      |
| Bile Duct, Hyperplasia                               |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 18 1.1 |
| Bile Duct, Inflammation, Chronic Active              |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 2.0  |
| Centrilobular, Degeneration                          |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 2.0  |
| Pancreas   | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +        | +  | +  | +  | 50     |
| Polyarteritis Nodosa                                 |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 10 1.5 |
| Acinus, Atrophy                                      |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 4 1.3  |
| Acinus, Hyperplasia                                  |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 6 1.8  |
| Duct, Cyst   |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1      |
| Salivary Glands                                      | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +        | +  | +  | +  | 50     |
| Stomach, Forestomach                                 | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +        | +  | +  | +  | 50     |
| Edema  |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 2.0  |
| Inflammation, Chronic                                |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 1 2.0  |
| Inflammation, Chronic Active                         |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |    |    |    | 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

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|--|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|
|  | 07          | 07  | 04  | 06  | 07  | 07  | 07  | 07  | 06  | 07  | 04  | 07  | 06  | 06  | 05  | 07  | 04  | 07  | 07  | 05  | 06  | 06  | 07  | 06  |          | 07  |
| ANIMAL ID  | 001         | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 | 001 |          |     |
| Polyarteritis Nodosa                                 | 2           |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1        | 2.0 |
| Epithelium, Hyperplasia                              |             |     |     |     |     |     |     | 1   |     | 1   |     |     |     |     |     |     |     | 1   |     |     |     | 2   |     |     | 7        | 1.7 |
| Epithelium, Hyperplasia, Basal Cell                  |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 2   |     |     |     |     |     |     | 1        | 2.0 |
| Stomach, Glandular                                   | +           | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | 50       |     |
| Mineral  |             |     |     | 2   | 2   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 3   |     |     |     | 10       | 2.4 |
| <b>CARDIOVASCULAR SYSTEM</b>                         |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |          |     |
| Blood Vessel   |             | +   | +   | +   | +   |     | +   |     | +   | +   | +   | +   | +   | +   | +   | +   |     |     | +   |     | +   | +   |     | +   | 33       |     |
| Mineral  |             | 1   |     | 2   | 2   |     |     |     | 1   |     |     |     |     |     |     |     |     |     | 4   |     |     |     |     |     | 11       | 2.0 |
| Aorta, Dilation                                      |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1        | 3.0 |
| Carotid Artery, Polyarteritis Nodosa                 |             |     |     |     |     |     |     |     |     | 2   |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1        | 2.0 |
| Pulmonary Artery, Thrombus                           |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | X   |     |     |     | 1        |     |
| Heart  | +           | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | 50       |     |
| Cardiomyopathy                                       | 2           | 2   | 1   | 2   | 1   |     |     | 1   |     | 1   | 2   | 1   |     | 1   | 2   | 2   |     | 2   | 2   | 3   | 1   | 2   | 1   | 1   | 37       | 1.7 |
| Inflammation, Chronic Active                         |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1        | 4.0 |
| Mineral  |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1   |     |     |     |     |     | 3        | 1.7 |
| Atrium, Thrombus                                     |             |     |     |     |     |     |     |     | X   | X   |     |     |     | X   |     |     |     |     |     |     |     |     |     |     | 3        |     |
| Valve, Thrombus                                      |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1        |     |
| <b>ENDOCRINE SYSTEM</b>                              |             |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |          |     |
| Adrenal Cortex                                       | +           | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | +   | 50       |     |
| Angiectasis  |             | 2   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 1        | 2.0 |
| Degeneration, Cystic                                 |             |     |     |     | 1   | 1   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 4        | 1.0 |
| Hyperplasia, Focal                                   |             |     |     |     | 3   | 2   |     |     |     | 1   |     |     |     | 2   |     |     | 2   |     |     |     |     | 1   |     |     | 9        | 1.7 |
| Necrosis   |             |     |     |     |     |     |     |     |     | 1   |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 3        | 1.3 |
| Thrombus   |             | X   |     |     |     |     |     |     | X   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male                    | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | * TOTALS              |
|---|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----------------------|
|   | 07          | 07   | 04   | 06   | 07   | 07   | 07   | 07   | 06   | 07   | 04   | 07   | 06   | 06   | 05   | 07   | 04   | 07   | 07   | 05   | 06   | 06   | 07   | 06   |                       |
| ANIMAL ID   | 0011        | 0011 | 0014 | 0022 | 0033 | 0033 | 0033 | 0050 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 |                       |
| Vacuolization Cytoplasmic<br>Bilateral, Hyperplasia, Focal              |             |      |      | 1    |      |      | 1    |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | 1 2.0<br>5 1.2        |
| Adrenal Medulla<br>Hyperplasia, Focal<br>Bilateral, Hyperplasia, Focal  | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | 50<br>15 2.0<br>4 2.8 |
| Islets, Pancreatic<br>Hyperplasia                                       | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | 50<br>3 2.3           |
| Parathyroid Gland<br>Hyperplasia, Diffuse                               | M           | +    | M    | +    | +    | M    | M    | +    | M    | M    | +    | +    | +    | +    | M    | +    | M    | +    | +    | +    | +    | +    | +    | +    | 39<br>14 2.6          |
| Pituitary Gland<br>Pars Distalis, Hyperplasia<br>Pars Nervosa, Thrombus | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | 50<br>15 1.9<br>1     |
| Thyroid Gland<br>Polyarteritis Nodosa<br>C-cell, Hyperplasia            | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | 50<br>1 2.0<br>6 2.7  |

**GENERAL BODY SYSTEM**

NONE

**GENITAL SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |             |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------------|
| Epididymis<br>Atrophy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50<br>1 2.0 |
| Preputial Gland       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50          |

\* .. 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  
 BLANK .. Not examined microscopically  
 1-4 .. Lesion qualified as:  
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**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**

Black Cohosh

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Date Report Requested: 10/07/2020

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

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|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|
|  | 07          | 07   | 04   | 06   | 07   | 07   | 07   | 07   | 06   | 07   | 04   | 07   | 06   | 06   | 05   | 07   | 04   | 07   | 07   | 05   | 06   | 06   | 07   | 06   |          |
| ANIMAL ID  | 0011        | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 |          |

|  |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  |     |        |
|--|---|---|--|---|---|---|--|---|---|---|--|--|--|--|--|--|--|--|--|---|---|---|---|--|-----|--------|
| Duct, Hyperplasia, Squamous                  |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 2   | 1 2.0  |
| Prostate                                     | + |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 50  |        |
| Hyperplasia                                  |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 1 1 | 3 1.0  |
| Inflammation, Chronic                        |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 1   | 2 1.0  |
| Inflammation, Chronic Active                 |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 2   | 4 1.8  |
| Seminal Vesicle                              | + |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 50  |        |
| Inflammation, Chronic Active                 |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 1   | 1 3.0  |
| Testis                                       | + |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 50  |        |
| Edema  |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 3   | 1 3.0  |
| Granuloma Sperm                              |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 1   | 1 1.0  |
| Polyarteritis Nodosa                         | 2 | 2 |  | 2 | 2 | 1 |  | 1 | 1 | 2 |  |  |  |  |  |  |  |  |  | 2 | 2 | 2 | 2 |  | 23  | 1.7    |
| Bilateral, Germinal Epithelium, Degeneration |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 3   | 10 2.2 |
| Germinal Epithelium, Degeneration            |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 3   | 16 1.5 |
| Interstitial Cell, Hyperplasia               |   |   |  |   |   |   |  |   |   |   |  |  |  |  |  |  |  |  |  |   |   |   |   |  | 2   | 1 2.0  |

**HEMATOPOIETIC SYSTEM**

|                                  |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   |     |        |     |  |
|----------------------------------|---|---|--|---|---|--|--|---|---|--|---|---|---|--|--|--|--|--|--|---|---|---|---|---|-----|--------|-----|--|
| Bone Marrow                      | + |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   | 50  |        |     |  |
| Hemorrhage                       |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   | 4 4 | 21 2.3 |     |  |
| Hypercellularity                 | 1 | 2 |  | 2 | 2 |  |  | 1 | 2 |  | 2 | 1 | 3 |  |  |  |  |  |  | 2 | 1 | 2 | 2 | 3 | 1   | 29     | 1.8 |  |
| Necrosis                         |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   | 3   | 1 3.0  |     |  |
| Lymph Node                       |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   | +   | +      | 4   |  |
| Lumbar, Hyperplasia, Plasma Cell |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   |     | 1 2.0  |     |  |
| Lumbar, Lymphatic Sinus, Ectasia |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   |     | 1 2.0  |     |  |
| Mediastinal, Hemorrhage          |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   |     | 1 2.0  |     |  |
| Mediastinal, Pigment             |   |   |  |   |   |  |  |   |   |  |   |   |   |  |  |  |  |  |  |   |   |   |   |   |     | 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

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Black Cohosh

CAS Number: 84776-26-1

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | * TOTALS |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|
|  | 0711        | 0713 | 0714 | 0716 | 0717 | 0717 | 0717 | 0717 | 0716 | 0717 | 0714 | 0716 | 0716 | 0715 | 0717 | 0714 | 0717 | 0717 | 0715 | 0716 | 0716 | 0717 | 0716 | 0717 |          |
| ANIMAL ID  | 0011        | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 |          |

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |                                     |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-------------------------------------|
| Renal, Ectasia  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3  | 2 3.5                               |
| Lymph Node, Mandibular<br>Hyperplasia, Lymphoid<br>Infiltration Cellular, Plasma Cell | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 50 | 1 2.0<br>2 2.0                      |
| Lymph Node, Mesenteric<br>Atrophy   | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + |    |                                     |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  | 48<br>1 4.0                         |
| Spleen<br>Extramedullary Hematopoiesis<br>Necrosis<br>Pigment<br>White Pulp, Atrophy  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |    |                                     |
|   | 2 | 3 | 2 |   |   | 2 | 2 | 2 | 2 | 2 |   | 2 |   | 2 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |    |                                     |
|   | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 1 |   | 1 |   | 1 |   | 1 | 1 |   | 2 |   | 1 | 1 | 1 | 2 | 1 | 2 |    |                                     |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  | 39 2.1<br>1 3.0<br>40 1.4<br>17 3.4 |
| Thymus<br>Atrophy<br>Hyperplasia, Lymphoid  | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |    |                                     |
|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 49<br>40 3.0<br>1 2.0               |

**INTEGUMENTARY SYSTEM**

|   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |  |
|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|--|
| Mammary Gland   | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 48 |  |
| Skin<br>Cyst Epithelial Inclusion<br>Edema<br>Foreign Body<br>Hemorrhage<br>Inflammation, Granulomatous<br>Inflammation, Chronic Active | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 | 1<br>1 2.0<br>1<br>1 2.0<br>1 2.0<br>6 3.3 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
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|--|-------------|------|-----------|------|-----|------|-----|------|-----|------|-----|------|-----|------|-----|------|-----|------|-----|------|-----|------|----------|---|---|
|  | 0-7         | 7-11 | 0-7       | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 | 0-7 | 7-11 |          |   |   |
|  | 1           | 3    | 3         | 7    | 1   | 3    | 3   | 3    | 5   | 3    | 4   | 3    | 4   | 6    | 2   | 0    | 4   | 3    | 3   | 5    | 5   | 1    | 3        | 7 | 3 |
|  | 1           | 1    | 1         | 2    | 3   | 1    | 1   | 1    | 0   | 0    | 9   | 0    | 3   | 9    | 0   | 5    | 1   | 1    | 1   | 4    | 3   | 4    | 4        | 3 | 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 |
|  | 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 |

|                        |   |   |     |
|------------------------|---|---|-----|
| Ulcer                  | 2 | 5 | 3.0 |
| Epidermis, Hyperplasia |   | 3 | 1.7 |

MUSCULOSKELETAL SYSTEM

|                      |   |    |       |
|----------------------|---|----|-------|
| Bone                 | + | 50 |       |
| Osteopetrosis        |   | 3  | 1 3.0 |
| Skeletal Muscle      |   | +  |       |
| Degeneration         |   |    | 1 2.0 |
| Polyarteritis Nodosa |   | 1  | 1 1.0 |

NERVOUS SYSTEM

|                                |   |    |       |
|--------------------------------|---|----|-------|
| Brain                          | + | 50 |       |
| Gliosis                        |   |    | 1 2.0 |
| Inflammation, Chronic Active   |   |    | 1 2.0 |
| Necrosis                       |   |    | 2 2.5 |
| Peripheral Nerve               |   | +  | 2     |
| Degeneration                   |   |    | 1 2.0 |
| Axon, Sciatic, Degeneration    |   |    | 1 2.0 |
| Axon, Tibial, Degeneration     |   |    | 1 3.0 |
| Axon, Trigeminal, Degeneration |   | 1  | 2 1.5 |
| Trigeminal, Fibrosis           |   |    | 1 2.0 |
| Spinal Cord                    |   | +  | 2     |
| Axon, Degeneration             |   |    | 1 2.0 |

RESPIRATORY SYSTEM

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Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>MALE<br>750 mg/kg male | DAY ON TEST |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | * TOTALS |    |    |    |    |
|--|-------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----------|----|----|----|----|
|  | 07          | 07 | 04 | 06 | 07 | 07 | 07 | 07 | 06 | 07 | 04 | 07 | 06 | 06 | 05 | 07 | 04 | 07 | 07 | 05 |          | 06 | 06 | 07 | 06 |
| ANIMAL ID  | 1           | 3  | 3  | 7  | 1  | 3  | 3  | 3  | 5  | 3  | 4  | 3  | 4  | 6  | 2  | 0  | 4  | 3  | 3  | 5  | 5        | 1  | 3  | 7  | 3  |
|  | 1           | 1  | 4  | 2  | 3  | 1  | 1  | 1  | 0  | 0  | 9  | 0  | 3  | 9  | 0  | 5  | 1  | 1  | 1  | 4  | 3        | 4  | 1  | 4  | 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  |
|  | 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  |

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|
| Lung                              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |
| Infiltration Cellular, Histiocyte | 1 | 2 | 1 |   |   | 1 | 1 |   | 2 |   | 4 |   |   |   | 3 |   |   |   |   |   |   | 1 | 1 | 1 | 1  | 26 | 1.7 |
| Inflammation, Granulomatous       |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 |   |   | 2 |   |   |   |   | 1 |    | 9  | 1.1 |
| Inflammation, Acute               |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Inflammation, Chronic Active      |   |   | 2 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |    | 4  | 1.8 |
| Mineral                           |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |    | 5  | 1.4 |
| Polyarteritis Nodosa              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Thrombus                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |    | 2  |     |
| Alveolar Epithelium, Hyperplasia  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2  | 1.0 |
| Alveolar Epithelium, Hypertrophy  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 1.0 |
| Bronchiole, Fibrosis              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Interstitialium, Fibrosis         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Pleura, Fibrosis                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 1.0 |

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|
| Nose  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |
| Inflammation, Suppurative                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |    | 3 | 2.0 |
| Inflammation, Chronic Active                    |   |   |   |   |   |   | 1 |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 4 | 1.3 |
| Nasolacrimal Duct, Inflammation, Chronic        |   |   | 1 |   |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |    | 5 | 1.0 |
| Nasolacrimal Duct, Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |    | 5 | 1.6 |
| Olfactory Epithelium, Degeneration              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |    | 1 | 2.0 |
| Respiratory Epithelium, Hyperplasia             |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |    | 2 | 1.5 |
| Respiratory Epithelium, Squamous Metaplasia     |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 1.0 |

|         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |
|---------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
|---------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|

SPECIAL SENSES SYSTEM

|                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |
|-----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|
| Eye                         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |
| Cornea, Inflammation, Acute |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |    | 4 | 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

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|  | 07          | 07 | 04 | 06 | 07 | 07 | 07 | 07 | 06 | 07 | 04 | 07 | 06 | 06 | 05 | 07 | 04 | 07 | 07 | 05 | 06 | 06 | 07 | 06 | 07 |          |  |
| ANIMAL ID  | 1           | 3  | 3  | 7  | 1  | 3  | 3  | 3  | 5  | 3  | 4  | 3  | 4  | 6  | 2  | 0  | 4  | 3  | 3  | 5  | 5  | 1  | 3  | 7  | 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           | 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  |          |  |
| Cornea, Inflammation, Chronic                        | 1           |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 2 2.5    |  |
| Cornea, Inflammation, Chronic Active                 |             |    |    |    |    |    |    |    | 3  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 4 1.5    |  |
| Optic Nerve, Polyarteritis Nodosa                    |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1  |    |    |    |    |    |    | 1 1.0    |  |
| Harderian Gland                                      | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50       |  |
| Atrophy  |             | 2  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 2.0    |  |
| Inflammation, Suppurative                            |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 3.0    |  |
| <b>URINARY SYSTEM</b>                                |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |  |
| Kidney   | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50       |  |
| Amphophilic/Vacuolar Hyperplasia                     |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 3.0    |  |
| Cyst   |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | X  |    |    |    |    |    | 1        |  |
| Hemorrhage   |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 2.0    |  |
| Infarct  |             |    |    |    |    |    |    |    |    |    |    | 1  |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 1.0    |  |
| Inflammation, Chronic                                |             |    |    |    | 1  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 1.0    |  |
| Nephropathy, Chronic Progressive                     | 4           | 4  | 2  | 4  | 4  | 3  | 3  | 4  | 4  | 3  | 4  | 3  | 2  | 3  | 4  | 3  | 3  | 4  | 4  | 4  | 4  | 4  | 3  | 2  | 3  | 50 3.3   |  |
| Renal Tubule, Accumulation, Hyaline Droplet          |             |    |    |    |    |    |    |    |    |    |    |    | 3  |    |    |    |    |    |    |    |    |    |    |    |    | 2 2.0    |  |
| Renal Tubule, Cyst                                   |             |    | X  | X  |    |    |    | X  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 6        |  |
| Urinary Bladder                                      | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50       |  |
| Inflammation, Chronic                                |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 2.0    |  |
| Polyarteritis Nodosa                                 |             | 2  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 2.0    |  |

\*\*\* 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

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| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>0 mg/kg female | DAY ON TEST |   | ANIMAL ID |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | females<br>(cont...) |   |   |   |   |   |   |   |   |   |   |   |   |
|--|-------------|---|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|
|  | 0           | 7 | 0         | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 7 | 0 |                      | 7 | 0 | 7 |   |   |   |   |   |   |   |   |   |
|  | 3           | 0 | 3         | 0 | 7 | 0 | 8 | 0 | 3 | 9 | 0 | 9 | 6 | 7 | 0 | 8 | 0 | 9 | 0 | 3 | 0 | 3 | 2 | 2 | 2 | 2 | 2 | 2                    | 0 | 0 | 3 | 3 | 3 | 1 | 2 | 2 | 7 | 2 | 2 |   |
|  | 0           | 0 | 0         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 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           | 0 | 2         | 0 | 2 | 0 | 2 | 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 | 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 | 6 | 7 | 8                    | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |   |

ALIMENTARY SYSTEM

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
| Esophagus                                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |  |
| Intestine Large, Cecum                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |  |
| Intestine Large, Colon<br>Parasite Metazoan  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |  |
| Intestine Large, Rectum<br>Parasite Metazoan | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |  |
| Intestine Small, Duodenum                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |  |
| Intestine Small, Ileum                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |
| Intestine Small, Jejunum                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |  |
| Liver  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |  |
| Angiectasis                                  |   |   |   |   |   | 2 |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Basophilic Focus                             |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |  |
| Clear Cell Focus                             | X | X |   |   | X |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |  |
| Eosinophilic Focus                           |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |  |
| Extramedullary Hematopoiesis                 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |  |
| Necrosis                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |  |
| Bile Duct, Cyst                              |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |  |
| Bile Duct, Hyperplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |  |
| Centrilobular, Necrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
| Hepatocyte, Hyperplasia                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |  |

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>0 mg/kg female | DAY ON TEST |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | ANIMAL ID | females<br>(cont...) |      |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----------|----------------------|------|
|  | 0730        | 0730 | 0738 | 0730 | 0739 | 0736 | 0735 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0736 | 0735 | 0737 | 0735 | 0737 | 0736 | 0737 | 0736 |           |                      | 0737 |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002201               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002202               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002203               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002204               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002205               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002206               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002207               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002208               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002209               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002210               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002211               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002212               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002213               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002214               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002215               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002216               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002217               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002218               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002219               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002220               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002221               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002222               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002223               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002224               |      |
|  | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0         | 002225               |      |

Oval Cell, Hyperplasia

Mesentery  
Hemorrhage

Pancreas  
Basophilic Focus  
Polyarteritis Nodosa  
Acinus, Atrophy

Salivary Glands

Stomach, Forestomach  
Inflammation, Acute  
Inflammation, Chronic  
Inflammation, Chronic Active  
Mineral  
Ulcer  
Epithelium, Hyperplasia

Stomach, Glandular  
Mineral

CARDIOVASCULAR SYSTEM

Blood Vessel

Heart  
Cardiomyopathy

\* .. 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|  |                   |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--|-------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>0 mg/kg female | DAY ON TEST       | 0730 | 0730 | 0573 | 0743 | 0656 | 0575 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0656 | 0575 | 0777 | 0575 | 0777 | 0676 | 0777 | 0766 | 0777 |      |
|  | ANIMAL ID         | 0020 | 0021 | 0022 | 0023 | 0024 | 0025 | 0026 | 0027 | 0028 | 0029 | 0030 | 0031 | 0032 | 0033 | 0034 | 0035 | 0036 | 0037 | 0038 | 0039 | 0040 | 0041 | 0042 | 0043 |
|  | females (cont...) |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |

**ENDOCRINE SYSTEM**

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Angiectasis                     |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Degeneration, Cystic            |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |
| Hyperplasia, Focal              |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hypertrophy, Focal              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |
| Infiltration Cellular, Lipocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Metaplasia, Osseous             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thrombus                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Degeneration, Cystic |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Hyperplasia, Focal   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Islets, Pancreatic              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Parathyroid Gland               | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | + | + | + | + | + |
| Pituitary Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars Distalis, Hyperplasia      |   | 3 | 3 | 1 |   |   |   | 1 | 2 |   |   |   |   |   | 2 |   |   | 2 |   |   |   | 2 | 2 | 2 |
| Thyroid Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, Hyperplasia             |   | 2 |   |   |   |   |   |   |   | 2 | 2 |   | 1 |   | 3 |   |   | 4 | 2 |   |   |   |   |   |
| Follicle, Cyst                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**GENERAL BODY 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  
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Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| 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 |
|-----------------------|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                       | <b>HARLAN SPRAGUE DAWLEY RATS FEMALE</b> | 7 | 7 | 5 | 7 | 4 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 5 | 7 | 6 | 7 | 7 | 6 | 7 |
| <b>0 mg/kg female</b> | 3  | 3 | 7 | 3 | 9 | 0 | 9 | 3 | 0 | 3 | 2 | 2 | 2 | 2 | 0 | 0 | 3 | 3 | 3 | 1 | 2 | 2 | 7 | 2 |   |
|                       | 0  | 0 | 8 | 0 | 9 | 6 | 7 | 0 | 8 | 0 | 9 | 9 | 9 | 9 | 0 | 4 | 0 | 6 | 0 | 8 | 9 | 9 | 7 | 9 |   |
| 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 | 1 | 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 | 5 |

females (cont...)

NONE

**GENITAL SYSTEM**

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clitoral Gland                   | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Squamous Metaplasia              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ovary                            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Atrophy                          | 2 | 2 | 3 |   |   | 2 |   |   |   | 2 |   | 2 | 2 | 3 |   |   |   | 2 | 1 | 2 |   | 2 | 2 | 2 | 1 |
| Cyst                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |
| Bursa, Cyst                      |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Follicle, Cyst                   | X |   | X |   | X |   |   |   | X |   |   |   |   |   |   |   |   | X |   |   |   | X |   |   |   |
| Follicle, Cyst, Multiple         |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Periovarian Tissue, Cyst         |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |
| Rete Ovarii, Cyst                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Uterus                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Dilation                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |
| Hemorrhage                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |
| Hyperplasia, Atypical            | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |
| Inflammation, Acute              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |
| Inflammation, Chronic Active     |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | 2 |
| Squamous Metaplasia              | 1 | 1 | 2 |   |   |   |   |   | 3 |   |   |   | 1 | 1 |   |   |   | 2 | 2 |   |   | 2 |   |   |   |
| Thrombus                         |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |
| Cervix, Hyperplasia, Squamous    |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Cervix, Hyperplasia, Stromal     |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |
| Cervix, Hypertrophy, Stromal     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Endometrium, Hyperplasia, Cystic | 4 | 1 |   |   |   | 1 |   | 2 |   |   |   |   | 2 | 2 |   |   |   | 1 |   |   |   | 1 |   |   |   |
| Vagina                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

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

Experiment Number: 00058 - 03  
 Test Type: CHRONIC  
 Route: GAVAGE  
 Species/Strain: RATS/HSD

**P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL**  
 Black Cohosh  
 CAS Number: 84776-26-1

Date Report Requested: 10/07/2020  
 Time Report Requested: 11:17:00  
 First Dose M/F: 07/03/12 / 07/02/12  
 Lab: BAT

| 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 |   |
|----------------|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                | HARLAN SPRAGUE DAWLEY RATS FEMALE | 7 | 7 | 5 | 7 | 4 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 5 | 7 | 6 | 7 | 7 | 6 |
| 0 mg/kg female | 3                                 | 3 | 7 | 3 | 9 | 0 | 9 | 3 | 0 | 3 | 2 | 2 | 2 | 2 | 2 | 0 | 0 | 3 | 3 | 3 | 1 | 2 | 2 | 7 | 2 |
| 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 |
|                | 2                                 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
|                | 0                                 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 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 |
|                | <b>females (cont...)</b>          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Inflammation, Acute

**HEMATOPOIETIC SYSTEM**

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Hemorrhage                   |   |   |   |   |   |   |   |   |   | 2 | 1 |   |   |   | 2 |   |   |   |   | 1 |   | 1 |   |   |   |
| Hypercellularity             |   |   |   | 4 |   | 4 | 4 | 3 | 1 | 4 |   | 1 | 1 | 3 |   | 1 | 4 | 4 |   |   | 2 | 4 |   | 3 |   |
| Lymph Node, Mandibular       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Lymph Node, Mesenteric       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Spleen                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Extramedullary Hematopoiesis | 2 | 2 | 3 | 2 | 3 | 3 | 3 | 2 | 3 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 2 | 1 | 2 | 3 | 2 | 2 | 2 | 2 |   |
| Pigment                      | 1 | 1 |   | 1 |   |   |   | 1 |   | 1 | 2 | 2 | 1 | 1 | 1 |   |   | 2 | 2 | 1 |   | 1 | 1 | 1 |   |
| White Pulp, Atrophy          |   |   |   |   |   | 1 | 2 |   | 1 |   |   |   |   |   |   |   | 2 |   | 3 |   |   |   |   | 2 |   |
| Thymus                       | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Atrophy                      | 1 | 1 | 1 | 1 | 2 |   | 3 | 2 | 2 | 1 | 2 | 2 |   | 1 | 2 | 3 | 3 | 2 | 2 | 2 | 1 | 1 | 2 | 3 | 1 |

**INTEGUMENTARY SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland         | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Galactocoele          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia           |   |   |   |   |   |   |   | 2 |   | 2 | 2 | 3 |   |   | 2 |   |   |   |   |   | 2 |   |   | 2 |
| Hyperplasia, Atypical | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Skin                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**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



Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|   |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |                  |   |   |   |   |   |   |   |   |   |   |
|---|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------------------|---|---|---|---|---|---|---|---|---|---|
| <b>HARLAN SPRAGUE DAWLEY RATS</b><br><b>FEMALE</b><br><br><b>0 mg/kg female</b> | 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                | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   |
|   |             | 7 | 7 | 5 | 7 | 4 | 6 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 5 | 7 | 6 | 7 | 7 | 6 | 7 | 6 | 7 | 7 | 6                | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 |
|   |             | 3 | 3 | 7 | 3 | 9 | 0 | 9 | 3 | 0 | 3 | 2 | 2 | 2 | 2 | 2 | 0 | 0 | 3 | 3 | 3 | 1 | 2 | 2 | 7 | 2 | 7 | 2 | 7                | 2 | 7 | 2 | 7 | 2 | 7 | 2 | 7 | 2 | 7 |
| 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 |
|   | 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 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
|   | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 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 | 6 | 7 | 8 | 9                | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|   |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>females</b>   |   |   |   |   |   |   |   |   |   |   |
|   |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>(cont...)</b> |   |   |   |   |   |   |   |   |   |   |

Bone +

**NERVOUS SYSTEM**

Brain +  
 Necrosis  
 Glial Cell, Hyperplasia

**RESPIRATORY SYSTEM**

Lung +  
 Infiltration Cellular, Histiocyte 2 2 1 1 2 1 1 2 2 2 1 3 2 4 2 2 1 3 1 1  
 Inflammation, Granulomatous 1 1  
 Inflammation, Acute  
 Inflammation, Chronic Active 1  
 Alveolar Epithelium, Hyperplasia 1  
 Bronchiole, Hyperplasia  
 Nose +  
 Inflammation, Acute 2  
 Inflammation, Chronic 1  
 Nasolacrimal Duct, Inflammation, Chronic 1 1 1

**SPECIAL SENSES SYSTEM**

Eye +  
 Harderian Gland +

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



Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>0 mg/kg female | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|  | 0730        | 0733  | 0735  | 0737  | 0739  | 0763  | 0767  | 0769  | 0772  | 0775  | 0776  | 0777  | 0778  | 0779  | 0780  | 0781  | 0782  | 0783  | 0784  | 0785  | 0786  | 0787  | 0788  | 0789  | 0790  |          |
| ANIMAL ID  | 00226       | 00227 | 00228 | 00229 | 00230 | 00231 | 00232 | 00233 | 00234 | 00235 | 00236 | 00237 | 00238 | 00239 | 00240 | 00241 | 00242 | 00243 | 00244 | 00245 | 00246 | 00247 | 00248 | 00249 | 00250 |          |
|  | 0           | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |          |

**ALIMENTARY SYSTEM**

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |         |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------|
| Esophagus                                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50      |
| Intestine Large, Cecum                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50      |
| Intestine Large, Colon<br>Parasite Metazoan  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50<br>1 |
| Intestine Large, Rectum<br>Parasite Metazoan | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50<br>1 |
| Intestine Small, Duodenum                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50      |
| Intestine Small, Ileum                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50      |
| Intestine Small, Jejunum                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50      |
| Liver  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50      |
| Angiectasis                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0   |
| Basophilic Focus                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X | X |   |   |   |   |   |   | 4       |
| Clear Cell Focus                             | X |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   | X |   | X |   |   |   |   |   | 15      |
| Eosinophilic Focus                           |   | X |   |   | X | X |   |   |   |   | X |   |   |   |   |   | X |   |   |   |   |   | X |   | 10      |
| Extramedullary Hematopoiesis                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 3 1.3   |
| Necrosis                                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   | 4 2.3   |
| Bile Duct, Cyst                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X | X | 4       |
| Bile Duct, Hyperplasia                       |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   |   |   | 1 | 1 |   |   |   |   |   | 1 |   | 11 1.1  |
| Centrilobular, Necrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 1 2.0   |
| Hepatocyte, Hyperplasia                      |   |   |   |   |   |   |   |   |   |   |   | 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

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1) Minimal 3) Moderate

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Experiment Number: 00058 - 03

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Black Cohosh

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Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>0 mg/kg female | DAY ON TEST |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | * TOTALS |       |       |
|--|-------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|----------|-------|-------|
|  | 0700226     | 0700227 | 0700228 | 0700229 | 0700230 | 0700231 | 0700232 | 0700233 | 0700234 | 0700235 | 0700236 | 0700237 | 0700238 | 0700239 | 0700240 | 0700241 | 0700242 | 0700243 | 0700244 | 0700245 | 0700246 | 0700247 | 0700248 | 0700249 | 0700250 |          |       |       |
| ANIMAL ID  | 00226       | 00227   | 00228   | 00229   | 00230   | 00231   | 00232   | 00233   | 00234   | 00235   | 00236   | 00237   | 00238   | 00239   | 00240   | 00241   | 00242   | 00243   | 00244   | 00245   | 00246   | 00247   | 00248   | 00249   | 00250   |          |       |       |
| Oval Cell, Hyperplasia                                 |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1        | 1 1.0 |       |
| Mesentery Hemorrhage                                   |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |          | 1     | 1 3.0 |
| Pancreas Basophilic Focus                              | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | 50       | 1     |       |
| Pancreas Polyarteritis Nodosa                          |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |          | 1     | 1 1.0 |
| Pancreas Acinus, Atrophy                               |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 2        | 3 1.3 |       |
| Salivary Glands  | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | 50       |       |       |
| Stomach, Forestomach Inflammation, Acute               | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | 50       | 1 2.0 |       |
| Stomach, Forestomach Inflammation, Chronic             |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 2        | 2 1.0 |       |
| Stomach, Forestomach Inflammation, Chronic Active      |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1        | 1 3.0 |       |
| Stomach, Forestomach Mineral Ulcer                     |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1        | 1 1.0 |       |
| Stomach, Forestomach Epithelium, Hyperplasia           |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 3        | 3 3.0 |       |
| Stomach, Glandular Mineral                             | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | 50       | 2 1.0 |       |
|  |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 1        |       |       |
| <b>CARDIOVASCULAR SYSTEM</b>                           |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |          |       |       |
| Blood Vessel   | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +        | 49    |       |
| Heart Cardiomyopathy                                   | +           | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | +       | 50       | 4 1.0 |       |
|  |             |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         | 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  
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|  |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |          |
|--|-------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----------|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>0 mg/kg female | DAY ON TEST | 07 | 07 | 05 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 05 | 07 | 05 | 05 | * TOTALS |
|  |             | 30 | 33 | 33 | 33 | 33 | 99 | 22 | 22 | 55 | 22 | 11 | 00 | 55 | 22 | 22 | 77 | 22 | 11 | 88 | 23 | 55 | 33 | 22 |          |
|  | ANIMAL ID   | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 |          |

NONE

GENITAL SYSTEM

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    |     |     |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|----|-----|-----|
| Clitoral Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |  |    |     |     |
| Squamous Metaplasia              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  | 3  | 1   | 3.0 |
| Ovary                            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |    |     |     |
| Atrophy                          | 2 | 2 |   | 2 | 2 | 2 | 2 |   |   | 2 | 2 |   |   | 2 | 3 | 2 | 3 | 2 | 2 |   | 2 | 2 |   |   |    |  | 32 | 2.1 |     |
| Cyst                             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 1   |     |
| Bursa, Cyst                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 1   |     |
| Follicle, Cyst                   |   |   |   | X |   |   |   |   | X |   |   | X | X |   |   |   |   | X |   |   |   |   | X |   |    |  |    | 12  |     |
| Follicle, Cyst, Multiple         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 1   |     |
| Periovarian Tissue, Cyst         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 1   |     |
| Rete Ovarii, Cyst                |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |    |  |    | 1   |     |
| Uterus                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |    |     |     |
| Dilation                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |    |  |    | 2   | 4.0 |
| Hemorrhage                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 1   | 3.0 |
| Hyperplasia, Atypical            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |    |  |    | 3   | 1.3 |
| Inflammation, Acute              |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 2   | 1.5 |
| Inflammation, Chronic Active     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |    |  |    | 4   | 1.5 |
| Squamous Metaplasia              | 1 | 1 |   | 2 | 3 |   |   |   |   | 1 |   |   |   | 4 | 2 | 1 | 3 |   | 2 |   | 1 | 1 |   |   |    |  |    | 21  | 1.8 |
| Thrombus                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 1   |     |
| Cervix, Hyperplasia, Squamous    |   |   |   |   | 1 |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 3   | 1.7 |
| Cervix, Hyperplasia, Stromal     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |    | 1   | 4.0 |
| Cervix, Hypertrophy, Stromal     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |    |  |    | 1   | 2.0 |
| Endometrium, Hyperplasia, Cystic | 1 |   |   | 2 | 1 | 2 |   |   |   | 2 | 2 |   | 1 |   | 2 |   | 1 |   | 2 |   | 1 |   |   |   |    |  |    | 19  | 1.6 |
| Vagina                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |    |     |     |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically M .. Missing tissue 1-4 .. Lesion qualified as:  
X .. Lesion present A .. Autolysis precludes evaluation 1) Minimal 3) Moderate  
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Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>0 mg/kg female | 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    |      |      |
| ANIMAL ID  | 0730        | 0730 | 0753 | 0773 | 0773 | 0679 | 0772 | 0772 | 0675 | 0779 | 0775 | 0676 | 0775 | 0672 | 0772 | 0677 | 0772 | 0771 | 0688 | 0773 | 0575     | 0773 | 0572 | 0572 |
|  | 0022        | 0022 | 0022 | 0022 | 0022 | 0033 | 0033 | 0022 | 0033 | 0033 | 0022 | 0033 | 0033 | 0022 | 0022 | 0022 | 0044 | 0044 | 0044 | 0044 | 0022     | 0022 | 0022 | 0022 |
|  | 67          | 78   | 89   | 90   | 01   | 22   | 33   | 23   | 44   | 55   | 66   | 77   | 88   | 99   | 00   | 11   | 22   | 33   | 44   | 55   | 66       | 77   | 88   | 99   |

Inflammation, Acute

1 1 1.0

HEMATOPOIETIC SYSTEM

|                              |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |    |     |
|------------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|----|-----|
| Bone Marrow                  | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Hemorrhage                   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 10 | 1.2 |
| Hypercellularity             |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 31 | 2.8 |
| Lymph Node, Mandibular       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Lymph Node, Mesenteric       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Spleen                       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Extramedullary Hematopoiesis |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 47 | 2.3 |
| Pigment                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 35 | 1.3 |
| White Pulp, Atrophy          |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 9  | 2.1 |
| Thymus                       | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 49 |    |     |
| Atrophy                      |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 46 | 1.8 |

INTEGUMENTARY SYSTEM

|                       |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |    |     |
|-----------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|----|-----|
| Mammary Gland         | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |
| Galactocele           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 2  | 4.0 |
| Hyperplasia           |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 13 | 2.0 |
| Hyperplasia, Atypical |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    | 1  | 3.0 |
| Skin                  | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 50 |    |     |

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:

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2) Mild 4) Marked

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|--|-------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|--------|--|----------|
|  | 07          | 07 | 05 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 07 | 06 | 07 | 07 | 05 | 07 | 05 | 05     |  |          |
| ANIMAL ID  | 00          | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00     |  |          |
| Bone   | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50     |  |          |
| <b>NERVOUS SYSTEM</b>                                  |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |        |  |          |
| Brain  | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50     |  |          |
| Necrosis   |             |    | 2  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 2.0  |  |          |
| Glial Cell, Hyperplasia                                |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 2  |    |    | 1 2.0  |  |          |
| <b>RESPIRATORY SYSTEM</b>                              |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |        |  |          |
| Lung   | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50     |  |          |
| Infiltration Cellular, Histiocyte                      | 2           | 1  | 1  | 2  | 2  | 2  | 1  | 1  | 2  |    | 1  | 2  | 1  |    | 1  | 2  | 3  | 1  |    |    | 3  | 2  | 1  | 39 1.7 |  |          |
| Inflammation, Granulomatous                            |             | 1  |    | 1  |    |    |    |    |    |    |    |    |    | 1  |    |    |    |    |    |    |    |    |    | 7 1.0  |  |          |
| Inflammation, Acute                                    |             |    |    |    |    |    |    | 1  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 1.0  |  |          |
| Inflammation, Chronic Active                           |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 1.0  |  |          |
| Alveolar Epithelium, Hyperplasia                       | 2           |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1  |    |    | 4 1.3  |  |          |
| Bronchiole, Hyperplasia                                |             |    |    |    |    |    | 1  |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 1.0  |  |          |
| Nose   | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50     |  |          |
| Inflammation, Acute                                    |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 2.0  |  |          |
| Inflammation, Chronic                                  |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 1 1.0  |  |          |
| Nasolacrimal Duct, Inflammation, Chronic               | 1           |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | 4 1.0  |  |          |
| Trachea  | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50     |  |          |
| <b>SPECIAL SENSES SYSTEM</b>                           |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |        |  |          |
| Eye  | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50     |  |          |
| Harderian Gland  | +           | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | +  | 50     |  |          |

\* .. 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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|---|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| <b>HARLAN SPRAGUE DAWLEY RATS<br/>FEMALE<br/>0 mg/kg female</b> | 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 | 5 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 5 | 7 | 5 | 5 |
|   |                 | 3 | 3 | 3 | 3 | 3 | 9 | 2 | 2 | 5 | 2 | 1 | 0 | 5 | 2 | 2 | 7 | 2 | 1 | 8 | 2 | 3 | 5 | 3 | 2 |
| 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 |
|   | 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 | 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> |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

Lacrimal Gland  
Inflammation, Granulomatous 1  
1 3.0

**URINARY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Kidney                                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |
| Nephropathy, Chronic Progressive            | 1 | 1 |   | 1 | 1 | 2 | 1 | 2 | 1 | 1 | 2 | 3 | 2 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 |   | 43 1.3 |
| Pelvis, Dilation                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   | 1 2.0  |
| Renal Tubule, Accumulation, Hyaline Droplet |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 1.5  |
| 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  
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|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------------------|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | DAY ON TEST | 0634  | 0730  | 0730  | 0691  | 0665  | 0772  | 0772  | 0772  | 0772  | 0772  | 0633  | 0337  | 0568  | 0678  | 0777  | 0777  | 0777  | 0777  | 0777  | 0777  | 0676  | 0773  | 0673  | 0767  | 0773  | females<br>(cont...) |
|   | ANIMAL ID   | 00251 | 00252 | 00253 | 00254 | 00255 | 00256 | 00257 | 00258 | 00259 | 00260 | 00261 | 00262 | 00263 | 00264 | 00265 | 00266 | 00267 | 00268 | 00269 | 00270 | 00271 | 00272 | 00273 | 00274 | 00275 |                      |

ALIMENTARY SYSTEM

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum<br>Polyarteritis Nodosa                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Colon<br>Parasite Metazoan<br>Polyarteritis Nodosa  | + | + | + | + | + | + | + | + | + | + | X | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Rectum<br>Parasite Metazoan<br>Polyarteritis Nodosa | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Duodenum  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Ileum   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Angiectasis  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Basophilic Focus   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Clear Cell Focus   |   |   |   |   |   |   |   |   |   | X | X |   |   |   |   |   |   |   |   |   | X |   | X |   |   |   |
| Eosinophilic Focus   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   | X | X |   |   |   |   |   |   |   |   | X |
| Extramedullary Hematopoiesis   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hepatodiaphragmatic Nodule   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Mixed Cell Focus   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |
| Necrosis   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
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I .. Insufficient tissue  
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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 |           |                      |
|   | 6           | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 3 | 3 | 5 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7         |                      |
|   | 3           | 3 | 3 | 9 | 0 | 2 | 1 | 2 | 2 | 2 | 0 | 3 | 9 | 8 | 4 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 1 | 3 |           |                      |
|   | 4           | 0 | 0 | 1 | 5 | 9 | 2 | 9 | 9 | 9 | 0 | 2 | 7 | 8 | 8 | 0 | 0 | 2 | 0 | 0 | 6 | 0 | 4 | 0 |           |                      |
|   | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |           |                      |
|   | 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 |           |                      |
|   | 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 |           |                      |

Pigment 4 X  
 Regeneration  
 Bile Duct, Cyst X X  
 Bile Duct, Hyperplasia 1 1 1 1 1 1 1  
 Centrilobular, Necrosis  
 Hepatocyte, Hypertrophy 3  
 Hepatocyte, Multinucleated 3  
 Serosa, Fibrosis

Pancreas +  
 Polyarteritis Nodosa 2  
 Acinus, Atrophy 3  
 Acinus, Hyperplasia, Focal 2

Salivary Glands +  
 Atrophy 2

Stomach, Forestomach +  
 Inflammation, Acute  
 Polyarteritis Nodosa 2  
 Ulcer  
 Epithelium, Hyperplasia

Stomach, Glandular +  
 Mineral 1 1

**CARDIOVASCULAR SYSTEM**

Blood Vessel +  
 Media, Hypertrophy

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

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | DAY ON TEST           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | females<br>(cont...)  |                       |                       |
|---|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
|   | ANIMAL ID             |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
|   | 0<br>6<br>3<br>4      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>0      | 0<br>6<br>9<br>1      | 0<br>6<br>0<br>5      | 0<br>7<br>2<br>9      | 0<br>7<br>1<br>2      | 0<br>7<br>2<br>9      | 0<br>7<br>2<br>9      | 0<br>7<br>2<br>9      | 0<br>6<br>0<br>0      | 0<br>3<br>3<br>7      | 0<br>5<br>8<br>8      | 0<br>6<br>4<br>8      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>1      | 0<br>7<br>3<br>3      | 0<br>7<br>2<br>6      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>0      | 0<br>6<br>1<br>4      | 0<br>7<br>3<br>0      |                       |                       |                       |
|   | 0<br>0<br>2<br>5<br>1 | 0<br>0<br>2<br>5<br>2 | 0<br>0<br>2<br>5<br>3 | 0<br>0<br>2<br>5<br>4 | 0<br>0<br>2<br>5<br>5 | 0<br>0<br>2<br>5<br>6 | 0<br>0<br>2<br>5<br>7 | 0<br>0<br>2<br>5<br>8 | 0<br>0<br>2<br>5<br>9 | 0<br>0<br>2<br>6<br>0 | 0<br>0<br>2<br>6<br>1 | 0<br>0<br>2<br>6<br>2 | 0<br>0<br>2<br>6<br>3 | 0<br>0<br>2<br>6<br>4 | 0<br>0<br>2<br>6<br>5 | 0<br>0<br>2<br>6<br>6 | 0<br>0<br>2<br>6<br>7 | 0<br>0<br>2<br>6<br>8 | 0<br>0<br>2<br>6<br>9 | 0<br>0<br>2<br>7<br>0 | 0<br>0<br>2<br>7<br>1 | 0<br>0<br>2<br>7<br>2 | 0<br>0<br>2<br>7<br>3 | 0<br>0<br>2<br>7<br>4 | 0<br>0<br>2<br>7<br>5 |

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Heart                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cardiomyopathy                    |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 1 | 1 |   |
| Infiltration Cellular, Histiocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Atrium, Thrombus                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

ENDOCRINE SYSTEM

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Angiectasis                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |
| Degeneration, Cystic            |   |   |   |   |   |   |   |   |   |   |   | 1 | 1 |   |   |   | 1 | 1 |   |   |   | 1 | 1 |   |
| Extramedullary Hematopoiesis    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |
| Necrosis                        |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thrombus                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Degeneration, Cystic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   | 1 |
| Adrenal Medulla                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 2 | 3 |
| Necrosis                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |
| Islets, Pancreatic              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |
| Parathyroid Gland               | + | + | + | + | M | + | M | + | M | + | + | + | M | + | M | + | + | + | + | + | + | + | M | + |
| Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Diffuse            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Pituitary Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cyst                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

\* .. 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|   |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | 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 | 0 | 0 |
|   | ANIMAL ID   | 6 | 7 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 6 | 3 | 3 | 5 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 7 | 7 |   |
|   |             | 3 | 3 | 3 | 9 | 0 | 2 | 1 | 2 | 2 | 2 | 0 | 3 | 9 | 8 | 4 | 3 | 3 | 1 | 3 | 3 | 3 | 3 | 3 | 1 | 4 | 3 | 3 | 1 | 3 | 0 |

females  
(cont...)

|                            |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |     |  |   |  |     |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------------------------|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-----|--|---|--|-----|--|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Pars Distalis, Hyperplasia | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 1 4 |  | 2 |  | 4 1 |  | 3 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Thyroid Gland              | + |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | M   |  | + |  |     |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| C-cell, Hyperplasia        | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 4   |  | 3 |  | +   |  |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

GENERAL BODY SYSTEM

Peritoneum

GENITAL SYSTEM

|                                  |   |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
|----------------------------------|---|---|---|---|---|---|---|--|--|---|---|---|---|--|---|---|---|--|---|---|---|---|---|---|---|--|--|---|--|--|
| Clitoral Gland                   | + |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Ovary                            | + |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Atrophy                          | 4 | 3 |   | 2 | 2 | 2 | 4 |  |  |   | 2 | 3 | 3 |  | 2 | 2 | 2 |  | 3 | 2 | 4 | 2 | 2 | 2 | 2 |  |  |   |  |  |
| Bursa, Cyst                      | X |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Follicle, Cyst                   | X |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Periovarian Tissue, Cyst         | X |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Uterus                           | + |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Adenomyosis                      | 2 |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Dilation                         | 4 |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Hyperplasia, Atypical            | 2 |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Inflammation, Chronic            | 1 |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Inflammation, Chronic Active     | 1 |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Squamous Metaplasia              | 1 |   | 1 |   | 2 |   |   |  |  | 1 | 1 |   |   |  | 1 | 1 |   |  | 1 | 2 |   | 2 | 1 | 2 | 2 |  |  |   |  |  |
| Ulcer                            |   |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Cervix, Cyst, Squamous           |   |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Cervix, Hyperplasia, Squamous    |   |   |   |   |   |   |   |  |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |   |  |  |   |  |  |
| Endometrium, Hyperplasia, Cystic | 2 | 1 |   | 2 | 1 |   |   |  |  |   | 1 | 1 |   |  |   | 1 | 1 |  |   | 1 | 1 | 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  
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|   |             |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |
|---|-------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | DAY ON TEST | 0<br>6<br>3<br>4      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>0      | 0<br>6<br>9<br>1      | 0<br>6<br>0<br>5      | 0<br>7<br>2<br>9      | 0<br>7<br>1<br>2      | 0<br>7<br>2<br>9      | 0<br>7<br>2<br>9      | 0<br>6<br>2<br>0      | 0<br>3<br>9<br>7      | 0<br>5<br>8<br>8      | 0<br>6<br>4<br>8      | 0<br>7<br>3<br>0      | 0<br>7<br>1<br>2      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>6      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>0      | 0<br>6<br>1<br>4      | 0<br>7<br>3<br>0      |                       |                       |                       |
|   | ANIMAL ID   | 0<br>0<br>2<br>5<br>1 | 0<br>0<br>2<br>5<br>2 | 0<br>0<br>2<br>5<br>3 | 0<br>0<br>2<br>5<br>4 | 0<br>0<br>2<br>5<br>5 | 0<br>0<br>2<br>5<br>6 | 0<br>0<br>2<br>5<br>7 | 0<br>0<br>2<br>5<br>8 | 0<br>0<br>2<br>5<br>9 | 0<br>0<br>2<br>5<br>0 | 0<br>0<br>2<br>6<br>1 | 0<br>0<br>2<br>6<br>2 | 0<br>0<br>2<br>6<br>3 | 0<br>0<br>2<br>6<br>4 | 0<br>0<br>2<br>6<br>5 | 0<br>0<br>2<br>6<br>6 | 0<br>0<br>2<br>6<br>7 | 0<br>0<br>2<br>6<br>8 | 0<br>0<br>2<br>6<br>9 | 0<br>0<br>2<br>7<br>0 | 0<br>0<br>2<br>7<br>1 | 0<br>0<br>2<br>7<br>2 | 0<br>0<br>2<br>7<br>3 | 0<br>0<br>2<br>7<br>4 |

females  
(cont...)

Vagina  
Hyperplasia, Squamous  
Inflammation, Chronic Active

+ +

HEMATOPOIETIC SYSTEM

Bone Marrow  
Hypercellularity

+  
4 1 2 2 4 4 3 4 3 4

Lymph Node  
Lumbar, Hemorrhage  
Lumbar, Sinus, Ectasia  
Mediastinal, Hemorrhage  
Mediastinal, Infiltration Cellular, Plasma Cell

+

Lymph Node, Mandibular

+ +

Lymph Node, Mesenteric

+ +

Spleen  
Extramedullary Hematopoiesis  
Hemorrhage  
Pigment  
White Pulp, Atrophy

+  
2 2 2 2 2 3 2 2 2 1 3 3 1 2 2 3 3 2 3 2 2 2  
2  
2 1 2 2 2 1 2 2 1 2 2 2 1 2 1 1 1 1 1 2  
2 2 2 1 1 2 3 2 2 2 3 2 1 2 1 2

Thymus  
Atrophy

+  
3 2 2 1 2 2 2 2 1 1 2 3 2 2 2 3 2 1 2 1 2

INTEGUMENTARY SYSTEM

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
X .. Lesion present  
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|  |                   |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|--|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| <b>HARLAN SPRAGUE DAWLEY RATS FEMALE</b><br><b>75 mg/kg female</b> | DAY ON TEST       | 0634  | 0730  | 0730  | 0691  | 0665  | 0772  | 0772  | 0772  | 0772  | 0772  | 0663  | 0335  | 0338  | 0567  | 0677  | 0777  | 0777  | 0777  | 0777  | 0272  | 0773  | 0773  | 0630  | 0773  | 0667  | 0776  | 0777  |
|  | ANIMAL ID         | 00251 | 00252 | 00253 | 00254 | 00255 | 00256 | 00257 | 00258 | 00259 | 00260 | 00261 | 00262 | 00263 | 00264 | 00265 | 00266 | 00267 | 00268 | 00269 | 00270 | 00271 | 00272 | 00273 | 00274 | 00275 | 00276 | 00277 |
|  | females (cont...) |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |

|                           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skin                      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

MUSCULOSKELETAL SYSTEM

|      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

NERVOUS SYSTEM

|       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|-------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

RESPIRATORY SYSTEM

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lung   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Infiltration Cellular, Histiocyte Inflammation, Granulomatous          |   | 1 | 2 |   | 2 | 1 |   | 1 | 3 |   | 2 | 1 | 1 | 2 | 1 | 2 | 1 | 1 | 3 |   |   | 1 | 3 |   |   | 2 |   |   |
| Inflammation, Chronic Active Squamous Metaplasia                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Alveolar Epithelium, Hyperplasia                                       |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Alveolar Epithelium, Metaplasia, Respiratory Peribronchiolar, Fibrosis |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Nose   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Suppurative  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Respiratory Epithelium, Hyperplasia                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Trachea  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

\* .. 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

|  |             |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |
|--|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| <b>HARLAN SPRAGUE DAWLEY RATS</b><br><b>FEMALE</b><br><b>75 mg/kg female</b> | DAY ON TEST | 0634   | 0730   | 0730   | 0691   | 0665   | 0772   | 0772   | 0772   | 0772   | 0772   | 0633   | 0333   | 0568   | 0674   | 0773   | 0773   | 0773   | 0773   | 0773   | 0773   | 0626   | 0733   | 0733   | 0614   | 0767   |
|  | ANIMAL ID   | 00251  | 00252  | 00253  | 00254  | 00255  | 00256  | 00257  | 00258  | 00259  | 00260  | 00261  | 00262  | 00263  | 00264  | 00265  | 00266  | 00267  | 00268  | 00269  | 00270  | 00271  | 00272  | 00273  | 00274  | 00275  |
|  | Sex         | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female | Female |

females (cont...)

**SPECIAL SENSES SYSTEM**

|                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye Phthisis Bulbi | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian Gland    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**URINARY SYSTEM**

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Nephropathy, Chronic Progressive | 4 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 3 | 3 | 1 | 2 |   |   |   |   |   |
| Pelvis, Dilation                 |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |
| Pelvis, Inflammation, Acute      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Renal Tubule, Dilation           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |
| Urinary Bladder                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Acute              |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |
| Inflammation, Chronic Active     |   |   |   |   |   |   |   |   |   | 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 | 0 |
|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|---|---|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female |  | 7 | 6 | 3 | 7 | 7 | 4 | 5 | 6 | 7 | 7 | 7 | 3 | 6 | 7 | 6 | 7 | 6 | 5 | 7 | 4 | 7 | 6 | 7               | 6 | 7 | 6 |
|   |  | 2 | 7 | 8 | 2 | 2 | 9 | 1 | 1 | 3 | 1 | 2 | 0 | 7 | 2 | 2 | 3 | 3 | 6 | 7 | 3 | 8 | 2 | 3               | 2 | 7 | 5 |
|   |  | 9 | 5 | 6 | 9 | 9 | 9 | 2 | 5 | 0 | 2 | 9 | 2 | 2 | 9 | 9 | 0 | 0 | 3 | 0 | 0 | 2 | 9 | 3               | 9 | 5 |   |
| 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 |
|   |  | 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 |   |
|   |  | 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> |   |   |   |

ALIMENTARY SYSTEM

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   |   |              |    |       |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|---|---|---|---|--------------|----|-------|
| Esophagus  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
| Intestine Large, Cecum<br>Polyarteritis Nodosa                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   |   | <b>1 2.0</b> |    |       |
| Intestine Large, Colon<br>Parasite Metazoan<br>Polyarteritis Nodosa  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   |   | <b>1</b>     |    |       |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   |   | <b>1 2.0</b> |    |       |
| Intestine Large, Rectum<br>Parasite Metazoan<br>Polyarteritis Nodosa | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
|  |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   | X |   |              |    | 4     |
|  |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   |   |              |    | 2 1.5 |
| Intestine Small, Duodenum  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
| Intestine Small, Ileum   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
| Intestine Small, Jejunum   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
| Liver  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +   | + | + | + | + | +            | +  | 50    |
| Angiectasis  | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   |   |              | 1  | 1.0   |
| Basophilic Focus   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   | X |   |              |    | 3     |
| Clear Cell Focus   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   | X |   |   |   |     | 6 |   |   |   |              |    |       |
| Eosinophilic Focus   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   | 5 |   |   |     |   |   |   |   |              |    |       |
| Extramedullary Hematopoiesis   |   |   |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   |   |   |   | 1 | 1.2 |   |   |   |   |              |    |       |
| Hepatodiaphragmatic Nodule   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   | X | 2            |    |       |
| Mixed Cell Focus   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |     |   |   |   | 1 |              |    |       |
| Necrosis   |   |   |   |   |   |   |   | 2 | 2 |   |   |   |   | 3 | 1 | 2 |   |   |   | 2   | 2 |   |   | 3 | 1            | 10 | 2.0   |

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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|   | 079         | 067   | 038   | 072   | 072   | 049   | 051   | 061   | 073   | 073   | 073   | 036   | 067   | 072   | 062   | 073   | 063   | 057   | 073   | 048   | 076   | 073   | 067   | 067   |          |
| ANIMAL ID   | 00276       | 00077 | 00088 | 00029 | 00029 | 00089 | 00001 | 00002 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 |          |

|                            |   |  |  |   |  |  |  |   |  |  |   |   |  |  |  |   |   |  |  |  |  |   |  |    |     |     |
|----------------------------|---|--|--|---|--|--|--|---|--|--|---|---|--|--|--|---|---|--|--|--|--|---|--|----|-----|-----|
| Pigment                    |   |  |  |   |  |  |  |   |  |  |   |   |  |  |  |   |   |  |  |  |  |   |  |    | 3   | 2.5 |
| Regeneration               |   |  |  |   |  |  |  |   |  |  |   |   |  |  |  |   |   |  |  |  |  |   |  |    | 1   | 2.0 |
| Bile Duct, Cyst            |   |  |  | X |  |  |  | X |  |  |   |   |  |  |  |   |   |  |  |  |  |   |  | 7  |     |     |
| Bile Duct, Hyperplasia     | 1 |  |  | 1 |  |  |  |   |  |  |   | 1 |  |  |  | 2 | 1 |  |  |  |  | 1 |  | 14 | 1.1 |     |
| Centrilobular, Necrosis    |   |  |  |   |  |  |  |   |  |  | 2 |   |  |  |  |   |   |  |  |  |  |   |  | 1  | 2.0 |     |
| Hepatocyte, Hypertrophy    |   |  |  |   |  |  |  |   |  |  |   |   |  |  |  |   |   |  |  |  |  |   |  | 1  | 3.0 |     |
| Hepatocyte, Multinucleated |   |  |  |   |  |  |  |   |  |  |   |   |  |  |  |   |   |  |  |  |  |   |  | 1  | 3.0 |     |
| Serosa, Fibrosis           |   |  |  |   |  |  |  |   |  |  |   |   |  |  |  |   |   |  |  |  |  | 1 |  | 1  | 1.0 |     |

|                            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |
|----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Pancreas                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |
| Polyarteritis Nodosa       |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 1.5 |
| Acinus, Atrophy            |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   | 2  | 2.5 |
| Acinus, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Salivary Glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |
| Atrophy         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |

|                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |
|-------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Stomach, Forestomach    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |
| Inflammation, Acute     |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |
| Polyarteritis Nodosa    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |
| Ulcer                   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |
| Epithelium, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   | 1 |   |   | 2  | 1.5 |

|                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |
|--------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Stomach, Glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |
| Mineral            |   |   |   |   |   | 2 |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 4  | 1.3 |

CARDIOVASCULAR SYSTEM

|                    |   |   |   |   |  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |
|--------------------|---|---|---|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Blood Vessel       | + | + | + | + |  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |     |
| Media, Hypertrophy |   |   |   |   |  |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   | 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:

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Experiment Number: 00058 - 03

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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|   | 079         | 067   | 038   | 072   | 072   | 049   | 051   | 061   | 073   | 071   | 073   | 036   | 067   | 072   | 062   | 073   | 063   | 057   | 073   | 048   | 077   | 066   | 077   | 067   |          |
| ANIMAL ID   | 00276       | 00077 | 00008 | 00022 | 00022 | 00028 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 | 00022 |          |
|   | 0           | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |          |
|   | 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     |          |
|   | 7           | 7     | 7     | 7     | 8     | 8     | 8     | 8     | 8     | 8     | 8     | 8     | 8     | 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     |          |

|                                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  |   |     |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|---|-----|
| Heart                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |  |   |     |
| Cardiomyopathy                    |   |   | 1 |   |   | 1 |   | 2 |   |   |   |   |   |   | 1 |   |   |   |   |   | 1 |   |   |   |    |  | 9 | 1.1 |
| Infiltration Cellular, Histiocyte |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |  | 1 | 2.0 |
| Atrium, Thrombus                  |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |    |  | 1 |     |

ENDOCRINE SYSTEM

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |    |     |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|----|-----|
| Adrenal Cortex                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |    |     |
| Angiectasis                     |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2  | 2.0 |
| Degeneration, Cystic            |   |   |   |   | 1 |   |   |   |   |   | 1 |   | 1 | 1 |   |   |   |   |   |   |   |   | 1 |   |    |    | 11 | 1.0 |
| Extramedullary Hematopoiesis    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 2 |   |   |   |   |   |    |    | 2  | 1.5 |
| Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2  | 1.5 |
| Necrosis                        |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2  | 3.0 |
| Thrombus                        |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1  |     |
| Bilateral, Degeneration, Cystic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |    |    | 3  | 1.3 |
| Adrenal Medulla                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |    |     |
| Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   | 1 |   |   |   |   |   |   |   |   |    |    | 7  | 1.6 |
| Necrosis                        |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1  | 4.0 |
| Islets, Pancreatic              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |    |     |
| Hyperplasia                     |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 2  | 1.5 |
| Parathyroid Gland               | + | M | + | M | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | +  | 40 |    |     |
| Hyperplasia, Focal              |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1  | 1.0 |
| Hyperplasia, Diffuse            |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |    |    | 1  | 2.0 |
| Pituitary Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |    |     |
| Cyst                            |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |        | * TOTALS |    |  |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|----------|----|--|
|   | 079         | 067   | 038   | 072   | 072   | 049   | 051   | 061   | 073   | 071   | 072   | 030   | 067   | 072   | 062   | 073   | 063   | 057   | 073   | 048   | 072   | 063   | 072   | 067    |          |    |  |
| ANIMAL ID   | 00276       | 00077 | 00088 | 00022 | 00022 | 00088 | 00088 | 00022 | 00033 | 00044 | 00055 | 00066 | 00077 | 00088 | 00099 | 00000 | 00011 | 00022 | 00033 | 00044 | 00055 | 00066 | 00077 | 00088  | 00099    |    |  |
| Pars Distalis, Hyperplasia                              |             |       | 1     | 2     | 1     |       | 2     | 1     |       |       | 1     |       |       |       |       |       |       | 3     | 1     | 1     | 2     |       |       | 1      | 18 1.8   |    |  |
| Thyroid Gland   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +      | 49       |    |  |
| C-cell, Hyperplasia                                     | 1           |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 2      | 6 2.0    |    |  |
| <b>GENERAL BODY SYSTEM</b>                              |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |        |          |    |  |
| Peritoneum  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |        |          | 2  |  |
| <b>GENITAL SYSTEM</b>                                   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |        |          |    |  |
| Clitoral Gland  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | M     | +     | M     | +     | +      | +        | 48 |  |
| Ovary   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +      | 50       |    |  |
| Atrophy   | 2           | 2     | 2     | 2     |       | 2     |       |       | 3     | 2     | 3     | 2     | 3     |       | 3     | 2     | 2     | 2     | 2     | 2     |       | 2     | 4     | 2      | 39 2.4   |    |  |
| Bursa, Cyst   |             |       |       |       |       |       |       |       |       |       | X     |       |       |       |       |       |       |       |       |       |       |       |       |        | 2        |    |  |
| Follicle, Cyst  |             |       |       |       | X     |       |       |       |       |       |       |       |       |       |       |       |       | X     |       |       |       |       |       |        | 7        |    |  |
| Periovarian Tissue, Cyst                                |             |       |       |       |       | X     |       |       |       |       |       |       | X     |       |       |       |       |       |       |       |       |       |       |        | 3        |    |  |
| Uterus  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +      | 50       |    |  |
| Adenomyosis   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 2 1.5    |    |  |
| Dilation  |             |       |       |       |       |       |       |       |       |       |       | 2     |       |       |       |       |       |       |       |       |       | 4     |       |        | 3 3.3    |    |  |
| Hyperplasia, Atypical                                   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 4 1.5    |    |  |
| Inflammation, Chronic                                   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |        | 1 1.0    |    |  |
| Inflammation, Chronic Active                            |             |       |       |       |       |       |       |       |       |       |       | 3     |       |       |       |       | 2     |       |       |       | 4     |       |       |        | 5 2.4    |    |  |
| Squamous Metaplasia                                     | 1           |       | 1     | 1     |       | 1     | 1     |       |       |       | 3     |       |       | 2     | 1     |       | 1     | 1     |       |       | 2     |       | 1     | 25 1.4 |          |    |  |
| Ulcer   |             |       |       |       |       |       |       |       |       |       |       | 1     |       |       |       |       |       |       |       |       |       |       |       |        | 1 1.0    |    |  |
| Cervix, Cyst, Squamous                                  |             |       |       |       |       |       |       |       |       |       | X     |       |       |       |       |       |       |       |       |       |       |       |       |        | 1        |    |  |
| Cervix, Hyperplasia, Squamous                           |             |       |       |       |       |       |       |       |       |       | 2     |       |       |       |       |       |       |       |       |       |       |       |       |        | 1 2.0    |    |  |
| Endometrium, Hyperplasia, Cystic                        | 2           |       | 1     | 1     |       | 1     | 1     |       | 2     |       |       |       |       | 1     | 1     |       | 1     |       | 2     |       | 1     |       | 2     | 26 1.3 |          |    |  |

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

+ .. Tissue examined microscopically

X .. Lesion present

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BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

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Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

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First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female | DAY ON TEST | 079   | 065   | 0386  | 0729  | 0729  | 0492  | 0515  | 0611  | 0730  | 0772  | 0773  | 0367  | 0672  | 0673  | 0736  | 0577  | 0748  | 0772  | 0663  | 0739  | 0673  | 0729  | 0676  | 0757  | * TOTALS |
|   | ANIMAL ID   | 00276 | 00077 | 00088 | 00099 | 00010 | 00011 | 00012 | 00013 | 00014 | 00015 | 00016 | 00017 | 00018 | 00019 | 00020 | 00021 | 00022 | 00023 | 00024 | 00025 | 00026 | 00027 | 00028 | 00029 |          |
|   |             | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |          |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |   |     |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|
| Vagina                       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |   |     |
| Hyperplasia, Squamous        |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 2.0 |
| Inflammation, Chronic Active |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 | 2.0 |

HEMATOPOIETIC SYSTEM

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |     |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|-----|
| Bone Marrow                                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Hypercellularity                                | 1 | 4 | 4 |   |   | 4 | 4 | 4 |   | 4 |   | 4 | 3 | 3 | 4 | 1 | 4 | 3 | 4 | 4 | 4 | 3 | 3 | 2 | 4 |    | 31 | 3.3 |     |
| Lymph Node                                      |   |   | + |   |   |   |   |   |   |   |   |   |   | + |   |   |   |   |   |   |   |   |   |   |   | 6  |    |     |     |
| Lumbar, Hemorrhage                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |    |    | 1   | 2.0 |
| Lumbar, Sinus, Ectasia                          |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |    |    | 1   | 3.0 |
| Mediastinal, Hemorrhage                         |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1   | 3.0 |
| Mediastinal, Infiltration Cellular, Plasma Cell |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1   | 3.0 |
| Lymph Node, Mandibular                          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Lymph Node, Mesenteric                          | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Spleen  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |    |     |     |
| Extramedullary Hematopoiesis                    | 2 | 4 | 3 | 2 | 2 | 3 | 2 | 3 | 2 | 4 | 2 | 3 | 3 | 2 | 3 | 2 | 3 | 3 | 4 | 2 | 3 | 2 | 3 | 2 | 3 |    | 48 | 2.4 |     |
| Hemorrhage                                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    | 1   | 2.0 |
| Pigment   | 2 |   |   |   | 2 | 1 |   | 1 |   | 2 |   | 2 |   | 2 | 1 | 1 | 2 |   | 1 |   |   | 1 | 1 | 1 |   |    | 34 | 1.5 |     |
| White Pulp, Atrophy                             |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   | 3 |   |   |   |   |   |   |   | 4 |   |   |    | 10 | 2.3 |     |
| Thymus  | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |    |     |     |
| Atrophy   | 1 | 2 | 1 | 1 |   |   | 3 | 3 | 3 | 2 | 2 | 1 | 3 | 2 | 4 | 1 | 3 | 3 | 3 | 2 | 2 | 1 | 4 | 1 | 2 |    | 44 | 2.0 |     |

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:  
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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>75 mg/kg female                | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |     |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|-----|
|  | 079         | 065   | 038   | 072   | 072   | 049   | 051   | 061   | 070   | 071   | 072   | 030   | 067   | 072   | 062   | 073   | 073   | 066   | 057   | 073   | 048   | 072   | 063   | 076   |          | 076 |
| ANIMAL ID  | 00276       | 00077 | 00008 | 00002 | 00002 | 00008 | 00002 | 00002 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008 | 00008    |     |
| Mammary Gland Hyperplasia  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |     |
|  |             |       |       |       | 2     |       |       |       | 2     |       |       | 1     |       |       | 1     |       |       |       |       |       |       |       |       |       | 8 1.6    |     |
| Skin   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |     |
| <b>MUSCULOSKELETAL SYSTEM</b>  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |     |
| Bone   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |     |
| <b>NERVOUS SYSTEM</b>  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |     |
| Brain  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |     |
| <b>RESPIRATORY SYSTEM</b>  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |     |
| Lung   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |     |
| Infiltration Cellular, Histiocyte Inflammation, Granulomatous          | 2           | 2     | 1     | 1     | 1     |       | 1     |       | 1     |       | 2     |       | 3     | 4     | 2     | 2     | 2     | 2     | 2     |       | 1     | 1     | 2     | 1     | 38 1.7   |     |
| Inflammation, Chronic Active Squamous Metaplasia                       |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 6 1.0    |     |
| Alveolar Epithelium, Hyperplasia                                       |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 1 1.0    |     |
| Alveolar Epithelium, Metaplasia, Respiratory Peribronchiolar, Fibrosis |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 1 1.0    |     |
|  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 2 1.5    |     |
|  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 1 1.0    |     |
|  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 1 3.0    |     |
| Nose   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |     |
| Inflammation, Suppurative  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 2 1.0    |     |
| Respiratory Epithelium, Hyperplasia                                    |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 1 1.0    |     |
| Trachea  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | 50       |     |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
X .. Lesion present  
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1-4 .. Lesion qualified as:  
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|  |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| <b>HARLAN SPRAGUE DAWLEY RATS FEMALE</b><br><b>75 mg/kg female</b> | 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 |   |   |
|  |             | 7 | 6 | 3 | 7 | 7 | 4 | 5 | 6 | 7 | 7 | 7 | 3 | 6 | 7 | 6 | 7 | 6 | 5 | 7 | 4 | 7 | 6 | 7 | 6 |
|  |             | 2 | 7 | 8 | 2 | 2 | 9 | 1 | 1 | 3 | 1 | 2 | 0 | 7 | 2 | 2 | 3 | 3 | 6 | 7 | 3 | 8 | 2 | 3 | 2 |
|  |             | 9 | 5 | 6 | 9 | 9 | 9 | 2 | 5 | 0 | 2 | 9 | 2 | 2 | 9 | 0 | 0 | 3 | 0 | 0 | 2 | 9 | 3 | 9 | 5 |
| 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 |
|  | 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 |
|  | 7           | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 | 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>  |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

**SPECIAL SENSES SYSTEM**

|                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |       |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-------|
| Eye             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Phthisis Bulbi  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |    | 1 2.0 |
| Harderian Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |

**URINARY SYSTEM**

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |        |  |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|--|
| Kidney                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |  |
| Nephropathy, Chronic Progressive | 1 | 1 | 1 | 2 | 2 |   | 1 |   | 2 | 1 | 1 | 1 | 4 | 1 | 1 | 1 | 1 |   | 1 |   | 1 | 1 | 1 |   | 40 1.4 |  |
| Pelvis, Dilation                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 2.0  |  |
| Pelvis, Inflammation, Acute      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   | 1 1.0  |  |
| Renal Tubule, Dilation           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |  |
| Urinary Bladder                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50     |  |
| Inflammation, Acute              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 2.0  |  |
| Inflammation, Chronic Active     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   | 2 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

Experiment Number: 00058 - 03

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Date Report Requested: 10/07/2020

Test Type: CHRONIC

Black Cohosh

Time Report Requested: 11:17:00

Route: GAVAGE

CAS Number: 84776-26-1

First Dose M/F: 07/03/12 / 07/02/12

Species/Strain: RATS/HSD

Lab: BAT

|   |             |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |                |            |
|---|-------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|------------|
| <b>HARLAN SPRAGUE DAWLEY RATS<br/>FEMALE</b><br><br><b>250 mg/kg female</b> | DAY ON TEST | 07<br>22<br>99 | 07<br>22<br>99 | 07<br>22<br>99 | 07<br>22<br>99 | 05<br>73<br>80 | 07<br>63<br>60 | 06<br>65<br>84 | 06<br>67<br>40 | 07<br>73<br>00 | 07<br>73<br>00 | 07<br>73<br>00 | 07<br>73<br>00 | 07<br>73<br>00 | 06<br>64<br>08 | 06<br>66<br>88 | 06<br>66<br>77 | 07<br>71<br>50 | 07<br>73<br>07 | 05<br>94<br>37 | 06<br>62<br>90 | 07<br>69<br>00 | 07<br>62<br>99 |            |
|   | ANIMAL ID   | 003<br>001     | 003<br>002     | 003<br>003     | 003<br>004     | 003<br>005     | 003<br>006     | 003<br>007     | 003<br>008     | 003<br>009     | 003<br>010     | 003<br>011     | 003<br>012     | 003<br>013     | 003<br>014     | 003<br>015     | 003<br>016     | 003<br>017     | 003<br>018     | 003<br>019     | 003<br>020     | 003<br>021     | 003<br>022     | 003<br>023 |
|   |             | 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...)

ALIMENTARY SYSTEM

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum<br>Polyarteritis Nodosa   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Colon<br>Parasite Metazoan<br>Polyarteritis Nodosa<br>Lymphoid Tissue, Hyperplasia                            | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |   |   |   |   |   |   |
|  |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Large, Rectum<br>Parasite Metazoan<br>Polyarteritis Nodosa   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |   |   |   |   |   |   |   |
|  |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Duodenum<br>Polyarteritis Nodosa  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Ileum   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver<br>Angiectasis<br>Basophilic Focus<br>Clear Cell Focus<br>Eosinophilic Focus<br>Extramedullary Hematopoiesis<br>Necrosis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|  |   |   | X |   | X |   |   |   |   |   |   |   |   | X |   |   |   |   | X | X |   |   |   |   |
|  |   |   |   |   |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   | 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



Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>250 mg/kg female | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | females<br>(cont...) |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------------------|
|  | 0729        | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  | 0729  |                      |
| ANIMAL ID  | 00301       | 00302 | 00303 | 00304 | 00305 | 00306 | 00307 | 00308 | 00309 | 00310 | 00311 | 00312 | 00313 | 00314 | 00315 | 00316 | 00317 | 00318 | 00319 | 00320 | 00321 | 00322 | 00323 | 00324 | 00325                |
| Bile Duct, Cyst  |             | X     |       |       |       |       | X     | X     |       |       |       |       | X     |       | X     |       |       |       |       | X     |       | X     |       |       |                      |
| Bile Duct, Dilation                                      |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Bile Duct, Hyperplasia                                   |             |       | 1     | 1     |       | 1     |       |       |       |       |       |       |       | 1     |       |       |       |       |       | 1     |       |       | 1     | 2     |                      |
| Serosa, Fibrosis   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Mesentery  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Oral Mucosa  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Pancreas   | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +                    |
| Basophilic Focus   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Polyarteritis Nodosa                                     |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Salivary Glands  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +                    |
| Polyarteritis Nodosa                                     |             |       |       |       |       |       | 2     |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Stomach, Forestomach                                     | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +                    |
| Inflammation, Chronic                                    |             |       |       |       |       |       | 2     |       |       |       |       |       |       |       |       |       |       |       |       |       | 1     |       |       |       |                      |
| Polyarteritis Nodosa                                     |             |       |       |       |       |       | 2     |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Epithelium, Hyperplasia                                  |             |       |       |       |       |       | 3     |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Stomach, Glandular                                       | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +                    |
| Erosion  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | 2     |       |       |                      |
| Mineral  |             |       |       |       |       | 1     |       |       |       |       |       | 1     |       |       |       |       |       |       |       | 1     |       |       |       |       | 2                    |
| Submucosa, Inflammation, Chronic                         |             | 1     |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Tooth  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Malformation   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |

CARDIOVASCULAR SYSTEM

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

+ .. Tissue examined microscopically

X .. Lesion present

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Experiment Number: 00058 - 03

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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>250 mg/kg female | DAY ON TEST |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | ANIMAL ID | females<br>(cont...) |          |          |          |
|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|----------------------|----------|----------|----------|
|  | 07<br>29    | 07<br>29 | 07<br>29 | 07<br>29 | 05<br>08 | 07<br>00 | 06<br>06 | 06<br>08 | 07<br>04 | 07<br>00 | 07<br>00 | 07<br>00 | 07<br>00 | 07<br>00 | 07<br>00 | 06<br>08 | 06<br>08 | 07<br>05 | 07<br>00 | 05<br>07 |           |                      | 06<br>03 | 07<br>09 | 06<br>00 |
|  | 00<br>31    | 00<br>02 | 00<br>03 | 00<br>04 | 00<br>05 | 00<br>06 | 00<br>07 | 00<br>08 | 00<br>09 | 00<br>00 | 00<br>01 | 00<br>02 | 00<br>03 | 00<br>04 | 00<br>05 | 00<br>06 | 00<br>07 | 00<br>08 | 00<br>09 | 00<br>00 | 00<br>01  | 00<br>02             | 00<br>03 | 00<br>04 | 00<br>05 |

|                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Blood Vessel<br>Mineral | + | + | + | + | + | + |   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart<br>Cardiomyopathy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

ENDOCRINE SYSTEM

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Angiectasis                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Degeneration, Cystic            |   |   | 1 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hyperplasia, Focal              |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Hypertrophy, Focal              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Necrosis                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thrombus                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Degeneration, Cystic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Hypertrophy, Focal   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia, Focal              | 4 | 2 |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Islets, Pancreatic              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Parathyroid Gland               | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | M |
| Pituitary Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars Distalis, Hyperplasia      |   |   | 1 | 4 |   |   |   | 1 |   | 2 |   | 2 | 4 | 4 |   |   | 3 |   | 4 |   |   | 1 | 3 | 3 |
| Thyroid Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

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Black Cohosh

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>250 mg/kg female | DAY ON TEST |          | ANIMAL ID |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | females<br>(cont...) |          |          |   |  |
|--|-------------|----------|-----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------------------|----------|----------|---|--|
|  | 07<br>29    | 07<br>29 | 07<br>29  | 07<br>29 | 05<br>08 | 07<br>00 | 06<br>06 | 06<br>08 | 07<br>04 | 07<br>00 | 07<br>00 | 07<br>00 | 07<br>00 | 07<br>00 | 07<br>00 | 06<br>08 | 06<br>08 | 07<br>05 | 07<br>00 | 05<br>07 | 06<br>03 | 07<br>09 |                      | 06<br>00 | 07<br>02 |   |  |
| Nose   | +           | +        | +         | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        | +        |   |  |
| Foreign Body   |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Inflammation, Suppurative                                |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Inflammation, Acute                                      |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Inflammation, Chronic                                    | 1           |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Nasolacrimal Duct, Inflammation, Chronic                 |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Nasolacrimal Duct, Inflammation, Chronic Active          |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Respiratory Epithelium, Hyperplasia                      |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Respiratory Epithelium, Squamous Metaplasia              |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Trachea  | +           | +        | +         | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        | +        |   |  |
| <b>SPECIAL SENSES SYSTEM</b>                             |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Eye  | +           | +        | +         | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        | +        | + |  |
| Harderian Gland  | +           | +        | +         | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        | +        | + |  |
| Fibrosis   |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| <b>URINARY SYSTEM</b>                                    |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Kidney   | +           | +        | +         | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        | +        | + |  |
| Amphophilic/Vacuolar Hyperplasia                         |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| Nephropathy, Chronic Progressive                         | 1           | 1        | 2         | 1        | 2        | 2        | 4        |          | 2        |          | 1        | 1        |          | 1        |          | 1        | 4        |          | 2        | 2        | 2        | 2        | 1                    | 1        | 2        |   |  |
| Renal Tubule, Cyst                                       |             |          |           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |   |  |
| 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







Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| DAY ON TEST      | HARLAN SPRAGUE DAWLEY RATS FEMALE |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |
|------------------|-----------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|                  | 0644                              | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  | 0730  |          |
| 250 mg/kg 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        |
| ANIMAL ID        | 00326                             | 00327 | 00328 | 00329 | 00330 | 00331 | 00332 | 00333 | 00334 | 00335 | 00336 | 00337 | 00338 | 00339 | 00340 | 00341 | 00342 | 00343 | 00344 | 00345 | 00346 | 00347 | 00348 | 00349 |          |

|                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|
| Blood Vessel Mineral | + | + |   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 | 2  | 1.0 |
| Heart Cardiomyopathy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 13 | 1.2 |

ENDOCRINE SYSTEM

|                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |    |     |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|----|-----|
| Adrenal Cortex                  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 3  | 2.0 |
| Angiectasis                     |   |   | 2 | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 9  | 1.0 |
| Degeneration, Cystic            |   |   |   | 1 |   | 1 |   |   |   |   | 1 |   |   |   |   |   |   | 1 |   |   |   |   |   |   |    | 4  | 1.3 |
| Hyperplasia, Focal              |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Hypertrophy, Focal              |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Necrosis                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Thrombus                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  |     |
| Bilateral, Degeneration, Cystic |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Bilateral, Hypertrophy, Focal   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1  | 2.0 |
| Adrenal Medulla                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 12 | 1.8 |
| Hyperplasia, Focal              |   |   |   |   |   |   | 2 |   |   |   |   |   | 2 |   |   |   |   |   | 2 |   |   |   |   | 1 |    |    |     |
| Islets, Pancreatic              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1  | 3.0 |
| Hyperplasia                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |    |    |     |
| Parathyroid Gland               | M | + | M | M | + | M | + | + | + | + | + | + | + | M | + | + | + | M | M | + | M | + | + | + | 39 |    |     |
| Pituitary Gland                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 19 | 2.6 |
| Pars Distalis, Hyperplasia      |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   | 4 | 1 | 3 | 1 | 2 |   | 3 |    |    |     |
| Thyroid Gland                   | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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



Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| DAY ON TEST      | HARLAN SPRAGUE DAWLEY RATS FEMALE |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |      |     |
|------------------|-----------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|------|-----|
|                  | 0644                              | 0730  | 0730  | 0733  | 0733  | 0722  | 0722  | 0722  | 0736  | 0722  | 0728  | 0722  | 0733  | 0722  | 0733  | 0722  | 0733  | 0722  | 0733  | 0722  | 0733  | 0722  | 0733  | 0722  |          | 0733 |     |
| ANIMAL ID        | 00326                             | 00327 | 00328 | 00329 | 00330 | 00331 | 00332 | 00333 | 00334 | 00335 | 00336 | 00337 | 00338 | 00339 | 00340 | 00341 | 00342 | 00343 | 00344 | 00345 | 00346 | 00347 | 00348 | 00349 | 00350    |      |     |
| 250 mg/kg 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        | 1    | 2.0 |
|                  | 0                                 | 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    | 2.0 |
|                  | 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        | 7    | 2.4 |
|                  | 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        | 30   | 2.1 |
|                  | 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        | 5    | 1.5 |

|                                  |   |   |   |   |   |   |   |   |  |  |   |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   |    |     |     |
|----------------------------------|---|---|---|---|---|---|---|---|--|--|---|--|---|---|---|---|--|---|---|---|--|---|---|---|---|---|---|----|-----|-----|
| Hyperplasia, Stromal             |   |   |   |   |   |   |   |   |  |  |   |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   | 2 | 1  | 2.0 |     |
| Inflammation, Acute              |   |   |   |   |   |   |   |   |  |  |   |  |   |   | 2 | 2 |  |   |   |   |  |   |   |   |   |   |   | 2  | 2   | 2.0 |
| Inflammation, Chronic Active     |   |   |   |   |   | 3 |   | 3 |  |  |   |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   | 7  | 2.4 |     |
| Polyarteritis Nodosa             |   |   |   |   | 1 |   |   |   |  |  |   |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   | 2  | 1.5 |     |
| Squamous Metaplasia              | 4 | 2 | 4 | 1 |   | 2 | 3 | 4 |  |  |   |  |   | 2 |   |   |  | 2 | 3 | 4 |  | 2 |   | 1 | 2 |   |   | 30 | 2.1 |     |
| Thrombus                         |   |   |   |   |   |   |   |   |  |  |   |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   | 5  |     |     |
| Ulcer                            |   |   |   |   |   |   |   | 1 |  |  |   |  |   |   |   |   |  |   | 2 |   |  |   |   |   |   |   |   | 3  | 1.7 |     |
| Cervix, Hyperplasia, Squamous    |   |   |   |   |   |   |   |   |  |  |   |  |   |   |   |   |  |   |   |   |  |   |   |   |   |   |   | 1  | 2.0 |     |
| Cervix, Hyperplasia, Stromal     |   |   |   |   |   |   |   |   |  |  |   |  |   |   |   |   |  |   |   |   |  |   |   |   | 3 |   |   | 1  | 3.0 |     |
| Endometrium, Hyperplasia, Cystic |   |   |   |   |   | 4 | 1 |   |  |  | 1 |  | 1 |   | 2 | 2 |  |   | 1 |   |  |   | 1 | 1 | 1 | 1 |   | 23 | 1.4 |     |

|                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |  |
|---------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|--|
| Vagina              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |  |
| Inflammation, Acute | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 4  | 1.5 |  |

HEMATOPOIETIC SYSTEM

|                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |     |  |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|--|
| Bone Marrow                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Hypercellularity                   | 3 | 3 | 3 | 4 |   | 4 |   |   | 3 |   | 4 | 3 |   | 3 |   | 4 | 2 |   | 2 | 2 |   |   |   | 2 | 2 |   |   | 34 | 2.9 |     |  |
| Lymph Node, Mandibular             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Infiltration Cellular, Plasma Cell |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2   | 2.0 |  |
| Lymph Node, Mesenteric             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Spleen                             | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |     |  |
| Accessory Spleen                   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  |     |     |  |
| Extramedullary Hematopoiesis       |   | 3 | 2 | 3 | 2 | 1 | 2 | 2 | 3 | 2 | 3 | 4 | 2 | 3 | 2 | 1 | 3 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 |   |   | 47 | 2.3 |     |  |
| Hemorrhage                         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |     |  |
| Pigment                            |   | 1 | 2 |   | 2 |   | 1 | 2 |   | 2 |   |   | 1 | 1 | 2 | 2 |   | 2 | 1 | 1 | 1 | 2 | 2 | 1 | 1 |   |   | 37 | 1.4 |     |  |
| White Pulp, Atrophy                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   | 3  | 3.0 |     |  |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically  
X .. Lesion present  
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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>250 mg/kg female           | DAY ON TEST           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | * TOTALS              |                       |                       |                       |                       |   |    |     |     |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|---|----|-----|-----|
|  | 0<br>6<br>4<br>4      | 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>2<br>9      | 0<br>7<br>2<br>9      | 0<br>7<br>2<br>9      | 0<br>3<br>6<br>0      | 0<br>7<br>2<br>9      | 0<br>4<br>8<br>8      | 0<br>7<br>2<br>6      | 0<br>7<br>2<br>3      | 0<br>5<br>2<br>9      | 0<br>7<br>6<br>8      | 0<br>5<br>3<br>8      | 0<br>7<br>2<br>9      | 0<br>6<br>3<br>8      | 0<br>6<br>7<br>0      | 0<br>6<br>3<br>5      |                       | 0<br>7<br>0<br>0      | 0<br>6<br>3<br>0      | 0<br>7<br>3<br>5      | 0<br>7<br>3<br>0      |   |    |     |     |
| ANIMAL ID  | 0<br>0<br>3<br>2<br>6 | 0<br>0<br>3<br>2<br>7 | 0<br>0<br>3<br>2<br>8 | 0<br>0<br>3<br>2<br>9 | 0<br>0<br>3<br>3<br>0 | 0<br>0<br>3<br>3<br>1 | 0<br>0<br>3<br>3<br>2 | 0<br>0<br>3<br>3<br>3 | 0<br>0<br>3<br>3<br>4 | 0<br>0<br>3<br>3<br>5 | 0<br>0<br>3<br>3<br>6 | 0<br>0<br>3<br>3<br>7 | 0<br>0<br>3<br>3<br>8 | 0<br>0<br>3<br>3<br>9 | 0<br>0<br>3<br>4<br>0 | 0<br>0<br>3<br>4<br>1 | 0<br>0<br>3<br>4<br>2 | 0<br>0<br>3<br>4<br>3 | 0<br>0<br>3<br>4<br>4 | 0<br>0<br>3<br>4<br>5 | 0<br>0<br>3<br>4<br>6 | 0<br>0<br>3<br>4<br>7 | 0<br>0<br>3<br>4<br>8 | 0<br>0<br>3<br>4<br>9 | 0<br>0<br>3<br>4<br>0 |   |    |     |     |
| Thymus Atrophy   | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | + | 48 | 43  | 1.9 |
| <b>INTEGUMENTARY SYSTEM</b>  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   |    |     |     |
| Mammary Gland Galactoceles   | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | + | 50 | 4   | 2.5 |
| Mammary Gland Hyperplasia  |                       |                       |                       |                       |                       | 1                     |                       |                       |                       |                       |                       | 1                     |                       |                       |                       |                       |                       |                       |                       |                       | 1                     | 3                     |                       | 4                     |                       |   | 4  | 1.3 |     |
| Skin Inflammation, Chronic   | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | + | 50 | 1   | 2.0 |
| <b>MUSCULOSKELETAL SYSTEM</b>                                      |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   |    |     |     |
| Bone   | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | + | 50 |     |     |
| <b>NERVOUS SYSTEM</b>  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   |    |     |     |
| Brain  | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | + | 50 |     |     |
| <b>RESPIRATORY SYSTEM</b>  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   |    |     |     |
| Lung Infiltration Cellular, Histiocyte Inflammation, Granulomatous | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | + | 50 | 45  | 1.8 |
| Lung Inflammation, Chronic Active                                  |                       |                       |                       |                       | 1                     |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   | 16 | 1.1 |     |
| Lung Alveolar Epithelium, Hyperplasia                              |                       |                       |                       |                       |                       | 2                     |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   | 4  | 1.3 |     |
| Lung Bronchiole, Foreign Body, Multiple                            | 1                     |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   | 1  | 1.0 |     |
| Lung Interstitium, Fibrosis  |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |   | 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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>250 mg/kg female | DAY ON TEST           |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | * TOTALS              |  |  |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|--|--|
|  | 0<br>6<br>4<br>4      | 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>2<br>9      | 0<br>7<br>2<br>9      | 0<br>7<br>2<br>9      | 0<br>7<br>2<br>9      | 0<br>3<br>6<br>0      | 0<br>7<br>2<br>9      | 0<br>4<br>8<br>8      | 0<br>7<br>2<br>9      | 0<br>5<br>3<br>8      | 0<br>7<br>6<br>8      | 0<br>5<br>3<br>8      | 0<br>7<br>2<br>9      | 0<br>6<br>3<br>8      | 0<br>6<br>7<br>7      | 0<br>6<br>3<br>0      | 0<br>7<br>3<br>5      | 0<br>6<br>3<br>0      | 0<br>7<br>3<br>0      |                       |                       |  |  |
| ANIMAL ID  | 0<br>0<br>3<br>2<br>6 | 0<br>0<br>3<br>2<br>7 | 0<br>0<br>3<br>2<br>8 | 0<br>0<br>3<br>3<br>9 | 0<br>0<br>3<br>3<br>0 | 0<br>0<br>3<br>3<br>1 | 0<br>0<br>3<br>3<br>2 | 0<br>0<br>3<br>3<br>3 | 0<br>0<br>3<br>3<br>3 | 0<br>0<br>3<br>3<br>4 | 0<br>0<br>3<br>3<br>5 | 0<br>0<br>3<br>3<br>6 | 0<br>0<br>3<br>3<br>7 | 0<br>0<br>3<br>3<br>8 | 0<br>0<br>3<br>4<br>9 | 0<br>0<br>3<br>4<br>1 | 0<br>0<br>3<br>4<br>2 | 0<br>0<br>3<br>4<br>3 | 0<br>0<br>3<br>4<br>4 | 0<br>0<br>3<br>4<br>4 | 0<br>0<br>3<br>4<br>5 | 0<br>0<br>3<br>4<br>6 | 0<br>0<br>3<br>4<br>7 | 0<br>0<br>3<br>4<br>8 | 0<br>0<br>3<br>4<br>9 |  |  |
| Nose   | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | 50                    |  |  |
| Foreign Body   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 2                     |  |  |
| Inflammation, Suppurative                                |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1 3.0                 |  |  |
| Inflammation, Acute                                      |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 2 2.5                 |  |  |
| Inflammation, Chronic                                    |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1 1.0                 |  |  |
| Nasolacrimal Duct, Inflammation, Chronic                 |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1 2.0                 |  |  |
| Nasolacrimal Duct, Inflammation, Chronic Active          |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1 2.0                 |  |  |
| Respiratory Epithelium, Hyperplasia                      |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 2 2.0                 |  |  |
| Respiratory Epithelium, Squamous Metaplasia              |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1 2.0                 |  |  |
| Trachea  | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | 50                    |  |  |
| <b>SPECIAL SENSES SYSTEM</b>                             |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |
| Eye  | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | 50                    |  |  |
| Harderian Gland  | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | 50                    |  |  |
| Fibrosis   |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1 2.0                 |  |  |
| <b>URINARY SYSTEM</b>                                    |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |  |  |
| Kidney   | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | +                     | 50                    |  |  |
| Amphophilic/Vacuolar Hyperplasia                         |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1 2.0                 |  |  |
| Nephropathy, Chronic Progressive                         | 1                     | 3                     | 3                     | 1                     | 1                     | 1                     | 1                     | 1                     | 1                     | 1                     | 1                     | 1                     | 2                     | 1                     | 1                     | 1                     | 1                     | 2                     | 1                     | 2                     | 1                     | 2                     | 1                     | 2                     | 45 1.6                |  |  |
| Renal Tubule, Cyst                                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       |                       | 1                     |  |  |
| 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:

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Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

|   |             |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |                          |
|---|-------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|--------------------------|
| <b>HARLAN SPRAGUE DAWLEY RATS FEMALE</b><br><b>750 mg/kg female</b> | DAY ON TEST | 07 | 06 | 06 | 04 | 07 | 07 | 06 | 06 | 07 | 00 | 07 | 05 | 07 | 06 | 06 | 05 | 06 | 07 | 07 | 07 | 04 | 05 | 05 | 04 | 05 | <b>females (cont...)</b> |
|   | ANIMAL ID   | 29 | 00 | 02 | 07 | 02 | 02 | 05 | 07 | 02 | 00 | 02 | 00 | 02 | 03 | 01 | 07 | 03 | 03 | 03 | 03 | 03 | 05 | 07 | 07 | 03 |                          |
|   |             | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 | 00 |                          |

**ALIMENTARY SYSTEM**

|   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus                                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum Erosion                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Colon Parasite Metazoan      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Rectum Parasite Metazoan     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Rectum Polyarteritis Nodosa  |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Intestine Small, Duodenum                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Ileum                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum Polyarteritis Nodosa | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver Angiectasis                             | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver Clear Cell Focus                        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Liver Degeneration, Cystic                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Liver Eosinophilic Focus                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Liver Extramedullary Hematopoiesis            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Liver Hepatodiaphragmatic Nodule              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Liver 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:  
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Experiment Number: 00058 - 03

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Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | DAY ON TEST |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | females<br>(cont...) |          |          |
|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------------------|----------|----------|
|  | 07<br>29    | 06<br>00 | 06<br>02 | 04<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 07<br>02 | 07<br>02 | 04<br>05 | 05<br>07 | 05<br>07 |                      | 04<br>05 | 05<br>07 |
| ANIMAL ID  | 00351       | 00352    | 00353    | 00354    | 00355    | 00356    | 00357    | 00358    | 00359    | 00360    | 00361    | 00362    | 00363    | 00364    | 00365    | 00366    | 00367    | 00368    | 00369    | 00370    | 00371    | 00372    | 00373    | 00374    | 00375    | 00376                | 00377    |          |
| Bile Duct, Cyst  |             |          |          |          |          |          |          |          | X        |          |          |          |          |          |          |          |          |          |          | X        |          |          |          |          |          |                      |          |          |
| Bile Duct, Dilation                                      |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Bile Duct, Hyperplasia                                   |             |          |          |          |          |          |          |          | 1        |          |          |          |          |          | 1        |          | 1        | 1        |          |          |          |          |          |          |          |                      | 1        |          |
| Mesentery  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Pancreas   | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | M        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        |          |
| Inflammation, Chronic                                    |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Polyarteritis Nodosa                                     |             |          |          |          |          |          |          |          |          |          |          | 2        |          |          |          |          |          | 2        |          |          |          |          |          |          |          |                      |          |          |
| Acinus, Atrophy  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 4        |          |          |          |          |          |          |          |                      |          |          |
| Salivary Glands  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | M        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        |          |
| Stomach, Forestomach                                     | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        | +        |
| Cyst, Squamous   |             |          |          |          |          |          |          |          | X        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Inflammation, Chronic                                    |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        |          |          |          |          |          |          |          |                      |          |          |
| Inflammation, Chronic Active                             |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Mineral  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Polyarteritis Nodosa                                     |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Ulcer  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Epithelium, Hyperplasia                                  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Stomach, Glandular                                       | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +                    | +        | +        |
| Erosion  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Mineral  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Polyarteritis Nodosa                                     |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Tooth  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Dysplasia  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |
| Inflammation, Chronic                                    |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |                      |          |          |

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

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|  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------------------|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | DAY ON TEST | 0729  | 0600  | 0622  | 0647  | 0677  | 0666  | 0677  | 0666  | 0700  | 0707  | 0755  | 0776  | 0766  | 0755  | 0766  | 0777  | 0777  | 0744  | 0755  | 0755  | 0744  | 0755  | females<br>(cont...) |
|  | ANIMAL ID   | 00351 | 00352 | 00353 | 00354 | 00355 | 00356 | 00357 | 00358 | 00359 | 00360 | 00361 | 00362 | 00363 | 00364 | 00365 | 00366 | 00367 | 00368 | 00369 | 00370 | 00371 | 00372 |                      |
|  |             | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |                      |

CARDIOVASCULAR SYSTEM

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Blood Vessel                           | + | + | + | + | + | + |   | + | + | + | M | + |   | + | + | + | + | + |   | + | + | + | + | + |
| Mineral                                |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Carotid Artery, Polyarteritis Nodosa   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Heart                                  | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cardiomyopathy                         |   |   | 1 |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   | 1 |   | 1 |
| Polyarteritis Nodosa                   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Endocardium, Hyperplasia, Schwann Cell |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |

ENDOCRINE SYSTEM

|                               |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | + | + | + | + |   |
| Angiectasis                   |   |   |   |   |   |   |   |   |   | 1 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Degeneration, Cystic          |   |   | 2 |   |   | 1 |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   | 1 |   |   |
| Hyperplasia, Focal            |   |   |   |   |   | 1 |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   | 1 |   |   |   |   |
| Necrosis                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Thrombus                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |
| Adrenal Medulla               | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | + | + | + | + | + | + | + | + | + |   |
| Hyperplasia, Focal            |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Bilateral, Hyperplasia, Focal |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Islets, Pancreatic            | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + |   |
| Hyperplasia                   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Parathyroid Gland             | M | M | + | + | M | + | + | + | M | + | + | M | + | + | + | + | + | + | + | M | + | I | + | + | 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



Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

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

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | females<br>(cont...) |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------------------|
|  | 0729        | 0600  | 0602  | 0605  | 0607  | 0607  | 0606  | 0606  | 0607  | 0600  | 0607  | 0605  | 0607  | 0606  | 0606  | 0605  | 0606  | 0607  | 0607  | 0607  | 0604  | 0605  | 0605  | 0604  |                      |
| ANIMAL ID  | 00351       | 00332 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333 | 00333                |
| Pituitary Gland  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +                    |
| Polyarteritis Nodosa                                     |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |
| Pars Distalis, Hyperplasia                               | 3           | 1     |       |       | 4     |       |       | 2     | 3     | 3     |       |       | 2     | 2     |       | 2     |       |       | 3     | 3     |       |       | 1     | 2     | 3                    |
| Thyroid Gland  | +           | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | M     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +     | +                    |
| C-cell, Hyperplasia                                      |             |       |       |       |       |       |       | 4     | 1     |       |       |       |       |       | 2     |       |       |       |       |       |       |       | 3     |       |                      |
| Follicular Cell, Hyperplasia                             | 2           |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |                      |

**GENERAL BODY SYSTEM**

NONE

**GENITAL SYSTEM**

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clitoral Gland        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Squamous Metaplasia   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Ovary                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Atrophy               | 2 | 2 | 3 | 2 | 3 | 2 | 1 | 2 | 2 |   | 2 | 2 | 2 | 2 |   | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 |   |
| Cyst                  |   |   |   |   |   |   | X |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |
| Polyarteritis Nodosa  |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Follicle, Cyst        |   |   |   |   |   |   |   |   |   |   | X |   |   | X | X | X |   |   |   |   |   |   |   |   |   |
| Uterus                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenomyosis           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3 |   |   |   |
| Angiectasis           |   |   |   |   |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Cyst, Squamous        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Dilation              |   | 4 |   | 3 |   | 4 | 4 |   |   |   | 3 |   |   |   |   |   |   |   | 4 |   | 4 | 4 | 4 | 2 | 4 |
| Hemorrhage            |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1 | 3 | 4 |
| Hyperplasia, Atypical |   |   |   |   | 2 |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

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

+ .. Tissue examined microscopically

X .. Lesion present

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|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----------|----------------------|
|  | 0729        | 0600 | 0602 | 0607 | 0607 | 0607 | 0606 | 0606 | 0607 | 0600 | 0607 | 0605 | 0607 | 0606 | 0606 | 0605 | 0606 | 0607 | 0607 | 0607 | 0604 | 0605 | 0605 | 0604 | 0605 |           |                      |
| Inflammation, Acute                                      | 4           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | 2    |      |      |      |      |      | 2    | 3    |      |           |                      |
| Inflammation, Chronic Active                             |             |      |      | 4    |      |      |      |      |      |      |      |      | 2    |      |      |      |      |      |      | 3    |      |      |      |      | 2    |           |                      |
| Polyarteritis Nodosa                                     |             |      |      |      |      |      |      | 2    |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Squamous Metaplasia                                      | 3           | 1    |      | 2    | 2    |      | 4    |      | 1    |      | 1    | 2    | 1    |      | 1    |      | 2    | 2    | 4    | 4    | 2    | 4    | 4    | 1    | 3    |           |                      |
| Thrombus   |             |      |      |      |      |      |      | X    |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | X    |      |           |                      |
| Ulcer  |             | 3    |      | 4    |      | 4    | 3    |      |      |      |      |      |      |      |      |      |      |      |      |      |      | 2    | 3    |      | 1    |           |                      |
| Cervix, Hyperplasia, Squamous                            |             |      |      |      | 2    |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Endometrium, Hyperplasia, Cystic                         |             |      |      |      | 1    |      |      |      |      |      | 3    | 2    |      | 1    |      |      |      | 2    |      |      |      |      |      |      |      |           |                      |
| Vagina   | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    |           |                      |
| Hyperplasia, Squamous                                    |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Inflammation, Chronic                                    |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | 1    |      |      |      |           |                      |
| <b>HEMATOPOIETIC SYSTEM</b>                              |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Bone Marrow  | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +         |                      |
| Hemorrhage   |             |      |      | 1    |      |      |      |      |      |      |      |      | 1    |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Hypercellularity   | 2           | 3    | 2    | 3    | 2    | 4    | 3    | 3    | 2    |      | 2    | 4    | 2    |      | 4    | 4    | 4    |      | 3    | 2    | 3    | 4    | 4    | 4    | 4    |           |                      |
| Lymph Node   |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Lumbar, Infiltration Cellular, Plasma Cell               |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Mediastinal, Hemorrhage                                  |             |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | 2         |                      |
| Lymph Node, Mandibular                                   | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +         |                      |
| Atrophy  |             |      |      |      |      |      |      |      |      |      |      |      | 3    |      |      |      |      |      |      |      |      |      |      |      |      |           |                      |
| Lymph Node, Mesenteric                                   | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +         |                      |
| Spleen   | +           | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | M    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +         |                      |
| Extramedullary Hematopoiesis                             | 2           | 3    | 2    |      | 2    | 3    | 3    | 3    | 2    | 2    | 2    |      | 2    | 1    |      | 3    | 3    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3         |                      |

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|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------|----------------------|
|  | 0<br>7<br>2<br>9      | 0<br>6<br>0<br>0      | 0<br>6<br>2<br>9      | 0<br>4<br>7<br>5      | 0<br>7<br>2<br>9      | 0<br>7<br>2<br>9      | 0<br>6<br>5<br>0      | 0<br>6<br>7<br>5      | 0<br>7<br>2<br>9      | 0<br>0<br>0<br>4      | 0<br>7<br>0<br>9      | 0<br>5<br>2<br>1      | 0<br>7<br>0<br>9      | 0<br>6<br>3<br>7      | 0<br>6<br>1<br>7      | 0<br>5<br>3<br>8      | 0<br>6<br>3<br>5      | 0<br>7<br>3<br>0      | 0<br>7<br>3<br>0      | 0<br>4<br>3<br>0      | 0<br>5<br>5<br>1      | 0<br>5<br>7<br>0      | 0<br>4<br>7<br>8      | 0<br>5<br>7<br>2      |                       |           |                      |
|  | 0<br>0<br>3<br>5<br>1 | 0<br>0<br>3<br>5<br>2 | 0<br>0<br>3<br>5<br>3 | 0<br>0<br>3<br>5<br>4 | 0<br>0<br>3<br>5<br>5 | 0<br>0<br>3<br>5<br>6 | 0<br>0<br>3<br>5<br>7 | 0<br>0<br>3<br>5<br>8 | 0<br>0<br>3<br>5<br>9 | 0<br>0<br>3<br>6<br>0 | 0<br>0<br>3<br>6<br>1 | 0<br>0<br>3<br>6<br>2 | 0<br>0<br>3<br>6<br>3 | 0<br>0<br>3<br>6<br>4 | 0<br>0<br>3<br>6<br>5 | 0<br>0<br>3<br>6<br>6 | 0<br>0<br>3<br>6<br>7 | 0<br>0<br>3<br>6<br>8 | 0<br>0<br>3<br>6<br>9 | 0<br>0<br>3<br>7<br>0 | 0<br>0<br>3<br>7<br>1 | 0<br>0<br>3<br>7<br>2 | 0<br>0<br>3<br>7<br>3 | 0<br>0<br>3<br>7<br>4 | 0<br>0<br>3<br>7<br>5 |           |                      |

Pigment  
White Pulp, Atrophy

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

Thymus  
Atrophy  
Ectopic Parathyroid Gland  
Polyarteritis Nodosa

+ + + + + + + + + M + + + + + + + + + + + + + +  
3 2 1 3 2 3 3 1 2 3 3 1 3 2 3 2 2 2 2 2 4 1 1

INTEGUMENTARY SYSTEM

Mammary Gland  
Galactoceles  
Hyperplasia

+ + + + + + + + M + + + + + + + + + + + + + +  
1 2

Skin

+ +

MUSCULOSKELETAL SYSTEM

Bone

+ +

Skeletal Muscle

NERVOUS SYSTEM

Brain  
Gliosis

+  
3 1

RESPIRATORY SYSTEM

Lung  
Infiltration Cellular, Histiocyte

+ + + + + + + + + + M + + + + + + + + + + + + + +  
3 2 2 2 3 1 3 2 3 3 4 2 3 2 3 4 2 2 2 2 2 2 2

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|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|----------------------|---|
|  | 07<br>29    | 06<br>00 | 06<br>02 | 04<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 06<br>07 | 07<br>02 | 07<br>02 | 00<br>02 | 07<br>02 | 05<br>02 | 07<br>03 | 06<br>06 | 05<br>07 | 06<br>03 | 07<br>03 | 07<br>03 | 04<br>03 | 05<br>05 | 05<br>07 | 04<br>08 | 05<br>05 |           |                      |   |
|  | 0           | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0        | 0         | 000351               |   |
| Inflammation, Granulomatous                              |             |          |          |          |          |          |          |          |          | 1        |          | 2        |          |          | 1        |          |          |          |          | 1        |          |          |          |          |          |           |                      |   |
| Inflammation, Acute                                      |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Inflammation, Chronic Active                             |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |           |                      |   |
| Polyarteritis Nodosa                                     |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Squamous Metaplasia                                      |             |          |          | 2        |          |          |          | 2        |          |          |          | 1        |          |          | 1        |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Thrombus   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Alveolar Epithelium, Hyperplasia                         |             |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Bronchiole, Foreign Body                                 |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Nose   | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        |           |                      |   |
| Foreign Body   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Inflammation, Suppurative                                |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Inflammation, Acute                                      | 3           |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |           |                      |   |
| Inflammation, Chronic                                    |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Inflammation, Chronic Active                             |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Nasolacrimal Duct, Inflammation, Chronic                 |             |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Respiratory Epithelium, Hyperplasia                      |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Turbinate, Atrophy                                       |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      | 1 |
| Trachea  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | M        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        |           |                      |   |
| <b>SPECIAL SENSES SYSTEM</b>                             |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Eye  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +         |                      |   |
| Cornea, Inflammation, Acute                              |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           |                      |   |
| Harderian Gland  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +         |                      |   |
| <b>URINARY SYSTEM</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:  
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Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | DAY ON TEST |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |       | females<br>(cont...) |
|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-------|----------------------|
|  | 07<br>29    | 06<br>00 | 06<br>02 | 04<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 07<br>02 | 07<br>02 | 06<br>05 | 06<br>07 | 07<br>02 | 07<br>02 | 04<br>05 | 05<br>05 | 05<br>07 | 04<br>07 | 05<br>04 | 05<br>05 |       |                      |
| ANIMAL ID  | 00351       | 00352    | 00353    | 00354    | 00355    | 00356    | 00357    | 00358    | 00359    | 00360    | 00361    | 00362    | 00363    | 00364    | 00365    | 00366    | 00367    | 00368    | 00369    | 00370    | 00371    | 00372    | 00373    | 00374    | 00375 |                      |
| Kidney   | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +     |                      |
| Edema, Focal   |             |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |       |                      |
| Infarct  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2     |                      |
| Inflammation, Chronic                                    |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2     |                      |
| Inflammation, Chronic Active                             |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 4        |          |          |          |          |          |          |          |          |       |                      |
| Nephropathy, Chronic Progressive                         | 1           | 2        | 1        | 1        | 2        | 1        | 3        | 1        | 3        |          | 3        | 1        | 2        | 3        | 1        | 3        | 1        | 1        | 1        | 4        | 1        | 2        | 2        | 2        | 2     |                      |
| Polyarteritis Nodosa                                     |             |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |       |                      |
| Capsule, Inflammation, Chronic                           |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |       |                      |
| Pelvis, Dilation   |             |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |       |                      |
| Pelvis, Inflammation, Chronic                            |             |          |          |          |          |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |       |                      |
| Renal Tubule, Accumulation, Hyaline Droplet              |             |          |          |          |          |          |          |          |          |          |          | 2        |          |          |          | 1        |          |          |          |          |          |          |          |          |       |                      |
| Renal Tubule, Apoptosis                                  |             | 2        |          | 3        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          | 2        | 2        |          |       |                      |
| Renal Tubule, Dilation                                   |             |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |       |                      |
| Urinary Bladder  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +     |                      |

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Black Cohosh

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|  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | DAY ON TEST | 079   | 079   | 050   | 051   | 079   | 070   | 070   | 070   | 061   | 070   | 079   | 065   | 060   | 070   | 054   | 055   | 055   | 070   | 074   | 047   | 060   | 076   | 071   | * TOTALS |
|  | ANIMAL ID   | 00376 | 00377 | 00378 | 00379 | 00380 | 00381 | 00382 | 00383 | 00384 | 00385 | 00386 | 00387 | 00388 | 00389 | 00390 | 00391 | 00392 | 00393 | 00394 | 00395 | 00396 | 00397 | 00398 |          |
|  |             | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |          |

ALIMENTARY SYSTEM

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |       |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-------|
| Esophagus                    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | 49 |       |
| Intestine Large, Cecum       | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |       |
| Erosion                      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 2.0 |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 1.0 |
| Intestine Large, Colon       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Parasite Metazoan            |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1     |
| Intestine Large, Rectum      | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Parasite Metazoan            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3     |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3 2.3 |
| Intestine Small, Duodenum    | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Intestine Small, Ileum       | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Intestine Small, Jejunum     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |       |
| Polyarteritis Nodosa         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1 2.0 |
| Liver                        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | 48 |       |
| Angiectasis                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3 1.0 |
| Clear Cell Focus             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 4     |
| Degeneration, Cystic         |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 2 1.0 |
| Eosinophilic Focus           | X |   |   | X | X | X |   |   |   | X | X | X |   |   | X |   |   |   |   |   |   |   |   |   |    | 13    |
| Extramedullary Hematopoiesis |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 5 1.4 |
| Hepatodiaphragmatic Nodule   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1     |
| Necrosis                     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 9 1.9 |

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

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Black Cohosh

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| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | DAY ON TEST |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|  | 0729        | 0729  | 0750  | 0751  | 0772  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  | 0773  |          |
| ANIMAL ID  | 00376       | 00377 | 00378 | 00379 | 00380 | 00381 | 00382 | 00383 | 00384 | 00385 | 00386 | 00387 | 00388 | 00389 | 00390 | 00391 | 00392 | 00393 | 00394 | 00395 | 00396 | 00397 | 00398 | 00399 | 00400    |
| Bile Duct, Cyst  |             |       |       |       | X     | X     |       |       |       | X     |       |       |       |       | X     |       |       |       | X     |       |       |       |       |       |          |
| Bile Duct, Dilation                                      |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Bile Duct, Hyperplasia                                   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Mesentery  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Pancreas   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Inflammation, Chronic                                    |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Polyarteritis Nodosa                                     |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Acinus, Atrophy  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Salivary Glands  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Stomach, Forestomach                                     |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Cyst, Squamous   |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Inflammation, Chronic                                    |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Inflammation, Chronic Active                             |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Mineral  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Polyarteritis Nodosa                                     |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Ulcer  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Epithelium, Hyperplasia                                  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Stomach, Glandular                                       |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Erosion  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Mineral  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Polyarteritis Nodosa                                     |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Tooth  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Dysplasia  |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |
| Inflammation, Chronic                                    |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |          |

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

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Experiment Number: 00058 - 03

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | 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 | * TOTALS |   |
|--|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|---|
|  |             | 7 | 7 | 5 | 5 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 5 | 6 | 7 | 5 | 5 | 5 | 7 | 7 | 4 | 7 | 6 |          | 7 |
|  | ANIMAL ID   | 2 | 2 | 7 | 7 | 2 | 3 | 3 | 3 | 4 | 3 | 2 | 2 | 2 | 0 | 6 | 0 | 4 | 8 | 4 | 0 | 3 | 9 | 3 | 0 |          | 1 |
|  |             | 9 | 9 | 0 | 1 | 9 | 0 | 0 | 0 | 1 | 0 | 9 | 9 | 5 | 9 | 1 | 2 | 8 | 6 | 0 | 2 | 0 | 8 | 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 |          |   |
|  |             | 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 | 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 |          |   |

|                              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |
|------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|
| Pituitary Gland              | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>50</b>     |
| Polyarteritis Nodosa         |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 2.0</b>  |
| Pars Distalis, Hyperplasia   | 1 |   | 3 |   | 4 | 1 |   |   |   | 3 |   | 2 |   | 1 |   |   | 1 |   |   |   |   | 2 |   |   | <b>24 2.3</b> |
| Thyroid Gland                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | <b>49</b>     |
| C-cell, Hyperplasia          |   |   | 4 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   | <b>6 2.5</b>  |
| Follicular Cell, Hyperplasia |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | <b>1 2.0</b>  |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

|                       |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               |               |
|-----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---------------|
| Clitoral Gland        | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | <b>49</b>     |               |
| Squamous Metaplasia   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 1.0</b>  |
| Ovary                 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | <b>49</b>     |               |
| Atrophy               | 2 | 2 | 2 | 2 | 2 | 2 | 4 | 3 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 4 | 2 | 2 | 2 | 2 |   | <b>47 2.1</b> |               |
| Cyst                  |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   | <b>4</b>      |               |
| Polyarteritis Nodosa  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 2.0</b>  |
| Follicle, Cyst        | X |   |   |   |   | X |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>6</b>      |
| Uterus                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | <b>49</b>     |               |
| Adenomyosis           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 3.0</b>  |
| Angiectasis           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |               | <b>1 4.0</b>  |
| Cyst, Squamous        |   |   |   |   |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   |   |               | <b>1</b>      |
| Dilation              |   |   | 4 | 4 | 4 |   |   | 4 |   |   | 4 | 4 |   |   |   | 4 |   | 4 | 4 | 4 |   |   |   |               | <b>22 3.8</b> |
| Hemorrhage            |   |   | 4 |   | 2 |   |   |   |   |   |   | 3 |   |   |   | 4 |   | 4 | 4 | 4 |   |   |   |               | <b>8 3.1</b>  |
| Hyperplasia, Atypical |   | 1 |   |   |   |   |   |   |   | 1 |   |   |   |   |   |   |   |   |   |   |   | 1 |   |               | <b>5 1.2</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

Experiment Number: 00058 - 03

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: RATS/HSD

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 10/07/2020

Time Report Requested: 11:17:00

First Dose M/F: 07/03/12 / 07/02/12

Lab: BAT

| DAY ON TEST<br>HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | ANIMAL ID |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       | * TOTALS |
|---|-----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
|   | 079       | 079   | 050   | 051   | 079   | 077   | 077   | 077   | 067   | 077   | 077   | 066   | 055   | 066   | 077   | 055   | 055   | 077   | 077   | 044   | 077   | 066   | 077   |       |          |
|   | 00376     | 00377 | 00378 | 00379 | 00380 | 00381 | 00382 | 00383 | 00384 | 00385 | 00386 | 00387 | 00388 | 00389 | 00390 | 00391 | 00392 | 00393 | 00394 | 00395 | 00396 | 00397 | 00398 | 00399 |          |

|                                  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |     |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|
| Inflammation, Acute              |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 4   | 2.8 |
| Inflammation, Chronic Active     |   |   |   | 2 | 2 |   |   |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |    | 7   | 2.4 |
| Polyarteritis Nodosa             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1   | 2.0 |
| Squamous Metaplasia              | 1 | 1 | 4 | 4 | 1 | 2 | 1 | 4 |   | 1 | 1 | 3 |   | 4 | 2 | 2 |   | 1 | 3 | 3 |   | 4 | 2  | 38  | 2.3 |
| Thrombus                         |   |   | X |   |   |   |   |   |   |   |   |   |   | X |   |   |   |   |   |   |   | X |    | 5   |     |
| Ulcer                            |   |   |   |   |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   | 1 |    | 9   | 2.7 |
| Cervix, Hyperplasia, Squamous    |   |   |   |   |   | 1 |   | 4 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 3   | 2.3 |
| Endometrium, Hyperplasia, Cystic | 1 | 1 |   |   |   | 1 |   |   |   |   | 2 | 1 |   |   |   |   | 2 |   | 1 |   | 3 |   | 13 | 1.6 |     |
| Vagina                           | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +  | 50  |     |
| Hyperplasia, Squamous            |   |   |   |   |   |   |   | 2 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1   | 2.0 |
| Inflammation, Chronic            |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    | 1   | 1.0 |

HEMATOPOIETIC SYSTEM

|  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |    |     |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Bone Marrow                                | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |     |
| Hemorrhage                                 |   | 1 |   |   |   |   |   |   | 3 |   | 2 |   |   |   |   |   | 1 | 1 |   |   | 1 |   | 1 | 9  | 1.3 |
| Hypercellularity                           |   | 2 | 4 | 4 | 3 |   | 2 | 2 | 2 |   |   |   |   | 4 | 4 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 42 | 3.2 |
| Lymph Node                                 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 3  |     |
| Lumbar, Infiltration Cellular, Plasma Cell |   |   |   |   |   | 3 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |
| Mediastinal, Hemorrhage                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 2.0 |
| Lymph Node, Mandibular                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | 49 |     |
| Atrophy                                    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 1  | 3.0 |
| Lymph Node, Mesenteric                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | 49 |     |
| Spleen                                     | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |     |
| Extramedullary Hematopoiesis               | 2 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 2 | 4 | 2 | 4 | 3 | 3 | 3 | 3 | 2 | 47 | 2.5 |

\* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade  
+ .. Tissue examined microscopically M .. Missing tissue  
X .. Lesion present A .. Autolysis precludes evaluation  
I .. Insufficient tissue BLANK .. Not examined microscopically  
1-4 .. Lesion qualified as:  
1) Minimal 3) Moderate  
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Experiment Number: 00058 - 03

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Black Cohosh

CAS Number: 84776-26-1

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Lab: BAT

| HARLAN SPRAGUE DAWLEY RATS<br>FEMALE<br>750 mg/kg female | DAY ON TEST |      | ANIMAL ID |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      | * TOTALS |   |      |      |      |      |      |      |     |     |     |
|--|-------------|------|-----------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|---|------|------|------|------|------|------|-----|-----|-----|
|  | 0729        | 0750 | 0751      | 0752 | 0753 | 0754 | 0755 | 0756 | 0757 | 0758 | 0759 | 0760 | 0761 | 0762 | 0763 | 0764 | 0765 | 0766 | 0767 | 0768 | 0769 | 0770 | 0771 | 0772 | 0773 | 0774 |          |   | 0775 | 0776 | 0777 | 0778 | 0779 | 0780 |     |     |     |
| Pigment  | 1           | 1    |           |      |      | 2    | 1    | 1    | 1    | 2    | 2    | 2    |      |      | 1    |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      | 21  | 1.2 |     |
| White Pulp, Atrophy                                      |             |      |           |      |      |      |      |      |      |      |      |      |      |      | 3    |      | 2    |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      | 9    | 2.4 |     |     |
| Thymus   | +           | +    | +         | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +        | + | +    | +    | +    | M    | 48   |      |     |     |     |
| Atrophy  | 2           | 2    | 3         | 3    | 3    | 2    | 3    | 2    | 2    | 2    | 1    | 1    | 3    | 2    | 3    | 2    | 3    |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      | 45  | 2.3 |     |
| Ectopic Parathyroid Gland                                | 3           | 2    |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      | 2   | 2.5 |     |
| Polyarteritis Nodosa                                     |             |      |           |      |      | 1    |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      | 1   | 1.0 |     |
| <b>INTEGUMENTARY SYSTEM</b>                              |             |      |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      |     |     |     |
| Mammary Gland  | +           | +    | +         | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +        | + | +    | +    | +    | +    | +    | +    | 49  |     |     |
| Galactoceles   | 4           |      |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      | 2   | 2.5 |     |
| Hyperplasia  |             |      |           |      |      |      |      |      |      |      |      |      |      |      | 4    |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      | 2   | 3.0 |     |
| Skin   | +           | +    | +         | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +        | + | +    | +    | +    | +    | +    | +    | 50  |     |     |
| <b>MUSCULOSKELETAL SYSTEM</b>                            |             |      |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      |     |     |     |
| Bone   | +           | +    | +         | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +        | + | +    | +    | +    | +    | +    | +    | 50  |     |     |
| Skeletal Muscle  |             |      |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      |     | 1   |     |
| <b>NERVOUS SYSTEM</b>                                    |             |      |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      |     |     |     |
| Brain  | +           | +    | +         | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +        | + | +    | +    | +    | +    | +    | +    | 50  |     |     |
| Gliosis  |             |      |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      |     | 2   | 2.0 |
| <b>RESPIRATORY SYSTEM</b>                                |             |      |           |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |          |   |      |      |      |      |      |      |     |     |     |
| Lung   | +           | +    | +         | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +    | +        | + | +    | +    | +    | +    | +    | +    | +   | 48  |     |
| Infiltration Cellular, Histiocyte                        | 3           | 2    | 2         | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 2    | 2    | 3    | 2    | 2    | 2    | 2    | 1    | 2    | 2    | 1    | 2    | 3    | 4    | 3    |      |          |   |      |      |      |      |      |      | 46  | 2.3 |     |

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I .. Insufficient tissue  
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BLANK .. Not examined microscopically  
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|--|-------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------|------------|------------|
|  | 07<br>29    | 07<br>29 | 05<br>00 | 05<br>01 | 07<br>09 | 07<br>00 | 07<br>00 | 07<br>00 | 06<br>01 | 07<br>00 | 07<br>09 | 07<br>09 | 06<br>05 | 05<br>09 | 06<br>01 | 07<br>02 | 05<br>08 | 05<br>06 | 07<br>02 | 07<br>00 | 04<br>08 | 07<br>00 | 06<br>00 | 07<br>09 |           |            |            |
| ANIMAL ID  | 00376       | 00377    | 00378    | 00379    | 00380    | 00381    | 00382    | 00383    | 00384    | 00385    | 00386    | 00387    | 00388    | 00389    | 00390    | 00391    | 00392    | 00393    | 00394    | 00395    | 00396    | 00397    | 00398    | 00399    | 00400     |            |            |
| Kidney   | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | M         | <b>49</b>  |            |
| Edema, Focal   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>2.0</b> |
| Infarct  |             |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |          |          |           | <b>2</b>   | <b>1.5</b> |
| Inflammation, Chronic                                    |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>2.0</b> |
| Inflammation, Chronic Active                             |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>4.0</b> |
| Nephropathy, Chronic Progressive                         | 3           | 2        | 1        | 1        | 2        | 3        | 4        | 3        | 1        | 1        | 2        | 1        | 1        | 1        | 3        | 2        | 1        |          | 1        | 3        | 2        | 1        | 1        | 1        | <b>47</b> | <b>1.8</b> |            |
| Polyarteritis Nodosa                                     |             |          |          |          |          |          | 2        |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>2</b>   | <b>2.0</b> |
| Capsule, Inflammation, Chronic                           |             |          |          |          |          |          |          |          |          |          |          |          |          |          | 1        |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>1.0</b> |
| Pelvis, Dilation   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>2.0</b> |
| Pelvis, Inflammation, Chronic                            |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>2.0</b> |
| Renal Tubule, Accumulation, Hyaline Droplet              |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>1.0</b> |
| Renal Tubule, Apoptosis                                  |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>4</b>   | <b>2.3</b> |
| Renal Tubule, Dilation                                   |             |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |           | <b>1</b>   | <b>2.0</b> |
| Urinary Bladder  | +           | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +        | +         | <b>50</b>  |            |

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

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+ .. 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