

Experiment Number: 00058 - 04
Test Type: CHRONIC
Route: GAVAGE
Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
Time Report Requested: 11:32:38
First Dose M/F: NA / 04/09/12
Lab: BAT

2-year Core Mice_Final 1

NTP Study Number:	C00058B		
Lock Date:	10/02/2018		
Cage Range:	ALL		
Date Range:	ALL		
Reasons For Removal:	25022 ACCK 25019 MSAC	25021 TSAC	25020 NATD
Removal Date Range:	ALL		
Treatment Groups:	Include ALL		
Study Gender:	Female		
TDMSE Version:	3.0.2.3_002		
PWG Approval Date:	NONE		

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Lab: BAT

B6C3F1/N MICE FEMALE 0 mg/kg	DAY ON TEST	0729	0732	0729	0731	0770	0773	0773	0773	0773	0676	0773	0773	0773	0773	0773	0773	0773	0766	0776	0777	0777	0774	0779	0773	0773	0749	0777	0774	females (cont...)	
	ANIMAL ID	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000		0000
		2	3	4	5	6	7	9	0	1	2	5	6	8	9	0	1	3	4	5	6	7	9	0	1	3	3	3	3	2	

ALIMENTARY SYSTEM

Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine Large, Cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine Large, Colon Inflammation, Acute Ulcer	+	+	+	+	+	+	+	+	+	+	2	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine Large, Rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine Small, Duodenum Polyarteritis Nodosa	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine Small, Ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine Small, Jejunum Epithelium, Hyperplasia Peyer's Patch, Hyperplasia, Lymphocyte	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Angiectasis																													1
Basophilic Focus					X														X										
Clear Cell Focus										X																			
Eosinophilic Focus					X	X				X																			
Fatty Change										1																			
Intrahepatocellular Erythrocytes																												X	
Necrosis																													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

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Species/Strain: MICE/B6C3F1/N

Lab: BAT

B6C3F1/N MICE FEMALE 0 mg/kg	DAY ON TEST																							females (cont...)					
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0						
	7	7	7	7	7	7	7	7	7	6	7	7	7	7	7	7	7	6	7	6	7	7	4						
	2	3	2	3	3	3	3	3	3	9	3	3	3	3	3	3	4	3	9	2	3	3	9						
	9	2	9	1	0	1	3	0	2	1	1	3	1	1	3	1	2	2	9	2	1	9	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	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0						
	0	0	0	0	0	0	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	2	2	2	2	2	2	3	3						
	2	3	4	5	6	7	9	0	1	2	5	6	8	9	0	1	3	4	5	6	7	9	2						
Pigment	1																												
Tension Lipidosis												1																	
Bile Duct, Cyst																													
Hepatocyte, Atrophy	2																												
Mesentery								+						+					+		+								
Inflammation, Granulomatous																													
Fat, Necrosis												3																	
Pancreas																													
Acinar Cell, Vacuolation, Cytoplasmic																													
Acinus, Atrophy												2																	
Salivary Glands																													
Polyarteritis Nodosa																													
Stomach, Forestomach																													
Diverticulum																													
Stomach, Glandular																													
Mineral																													
Polyarteritis Nodosa																													
CARDIOVASCULAR SYSTEM																													
Aorta																													
Polyarteritis Nodosa																													
Blood Vessel																													
Heart																													

* .. 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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Test Type: CHRONIC

Black Cohosh

Time Report Requested: 11:32:38

Route: GAVAGE

CAS Number: 84776-26-1

First Dose M/F: NA / 04/09/12

Species/Strain: MICE/B6C3F1/N

Lab: BAT

B6C3F1/N MICE FEMALE 0 mg/kg	DAY ON TEST	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		7	7	7	7	7	7	7	7	6	7	7	7	7	7	7	7	7	6	7	6	7	7	7	4
		2	3	2	3	3	3	3	3	9	3	3	3	3	3	3	3	4	3	9	2	3	3	9	
		9	2	9	1	0	1	3	0	2	1	3	1	1	3	1	2	2	9	2	1	9	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	1	1	1	1	1	1	1	2	2	2	2	2	2	3	3	
		2	3	4	5	6	7	9	0	1	2	5	6	8	9	0	1	3	4	5	6	7	9	2	

females
(cont...)

Cardiomyopathy																														
Mineral																														
Polyarteritis Nodosa																														
Valve, Degeneration, Myxomatous																														
Valve, Inflammation, Acute																														

ENDOCRINE SYSTEM

Adrenal Cortex																																
Hyperplasia, Focal																																
Hypertrophy, Focal																																
Bilateral, Vacuolation, Cytoplasmic, Focal																																
Adrenal Medulla																																
Hyperplasia, Focal																																
Islets, Pancreatic																																
Hyperplasia																																
Parathyroid Gland																																
Pituitary Gland																																
Pars Distalis, Atypia Cellular																																
Pars Distalis, Hyperplasia, Focal																																
Pars Distalis, Hypertrophy																																
Pars Intermedia, Hyperplasia, Focal																																
Thyroid Gland																																

GENERAL BODY SYSTEM

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I .. Insufficient tissue BLANK .. Not examined microscopically 2) Mild 4) Marked

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 First Dose M/F: NA / 04/09/12
 Lab: BAT

B6C3F1/N MICE 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	ANIMAL ID	females (cont...)
	0 mg/kg	7	7	7	7	7	7	7	7	6	7	7	7	7	7	7	7	6	7	6	7	7	7	7	4	7		
		2	3	2	3	3	3	3	3	9	3	3	3	3	3	3	4	3	9	2	3	3	3	9	9	0		
		9	2	9	1	0	1	3	0	2	1	1	3	1	1	3	1	2	2	9	2	1	9	2	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	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
		2	3	4	5	6	7	9	0	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	3	0		
Lymph Node																												
Lymph Node, Mandibular Atrophy																												
Lymph Node, Mesenteric Atrophy																												
Extramedullary Hematopoiesis																												
Hemorrhage																												
Hyperplasia, Lymphocyte Infiltration Cellular, Plasma Cell																												
Spleen																												
Extramedullary Hematopoiesis, Increased																												
Hyperplasia, Lymphocyte Pigment																												
White Pulp, Atrophy																												
Thymus																												
INTEGUMENTARY SYSTEM																												
Mammary Gland																												
Skin																												
Subcutaneous Tissue, Fibrosis																												
MUSCULOSKELETAL SYSTEM																												
Bone																												

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 First Dose M/F: NA / 04/09/12
 Lab: BAT

B6C3F1/N MICE FEMALE	DAY ON TEST																								
	0729	0732	0729	0731	0733	0735	0737	0739	0741	0743	0745	0747	0749	0751	0753	0755	0757	0759	0801	0803	0805	0807	0809	0811	
0 mg/kg	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	females (cont...)

Fibro-Osseous Lesion

1 1 2

Skeletal Muscle

NERVOUS SYSTEM

Brain	+																							
Inflammation, Chronic Active Polyarteritis Nodosa	1																							
Medulla, Necrosis																								
Peripheral Nerve																								
Spinal Cord																								
Axon, Degeneration																								

RESPIRATORY SYSTEM

Lung	+																							
Hemorrhage																								
Infiltration Cellular, Histiocyte																								
Alveolus, Epithelium, Hyperplasia	4																							
Nose	+																							
Olfactory Epithelium, Atrophy																								
Olfactory Epithelium, Metaplasia, Respiratory																								
Respiratory Epithelium, Accumulation, Hyaline Droplet	2 1 1																							
Respiratory Epithelium, Hyperplasia	1 1 1 1																							
Respiratory Epithelium, Inflammation, Acute	1 1 1																							

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B6C3F1/N MICE FEMALE	DAY ON TEST																							females (cont...)
		0 7 2 9	0 7 3 2	0 7 2 9	0 7 3 1	0 7 3 3	0 7 3 3	0 7 3 3	0 7 3 3	0 7 3 0	0 7 2 2	0 6 1 1	0 7 3 3	0 7 3 3	0 7 3 3	0 7 3 1	0 7 3 3	0 6 4 3	0 7 3 2	0 6 9 1	0 7 2 2	0 7 3 3	0 7 3 4	
0 mg/kg	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 1	0 0 0 1	0 0 0 1	0 0 0 1	0 0 0 1	0 0 0 1	0 0 0 2	0 0 0 2	0 0 0 2	0 0 0 2	0 0 0 2	0 0 0 2	0 0 0 3	0 0 0 3	

Respiratory Epithelium, Inflammation, Chronic Active

Trachea

+ +

SPECIAL SENSES SYSTEM

Eye

Phthisis Bulbi

Cornea, Inflammation, Chronic Active

Lens, Cataract

+
X
1 2

Harderian Gland

Fibrosis

Hyperplasia

+
4
4

URINARY SYSTEM

Kidney

Infarct, Chronic

Infiltration Cellular, Lymphocyte

Nephropathy, Chronic Progressive

Polyarteritis Nodosa

Renal Tubule, Cyst

+
1
1 1 1 2
1
X X

Urinary Bladder

Infiltration Cellular, Lymphocyte

Polyarteritis Nodosa

+ +

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| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS |
|----------------------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
| | 0729 | 0730 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | |
| 0 mg/kg | 00033 | 00033 | 00033 | 00033 | 00044 | 00044 | 00044 | 00044 | 00044 | 00044 | 00055 | 00055 | 00055 | 00055 | 00055 | 00066 | 00066 | 00066 | 00066 | 00066 | 00066 | 00066 | 00066 | 00066 | 50 |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|-------|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | M | M | M | + | + | 46 | |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Intestine Large, Colon
Inflammation, Acute
Ulcer | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 2.0 |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Intestine Small, Duodenum
Polyarteritis Nodosa | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 2.0 |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Intestine Small, Jejunum
Epithelium, Hyperplasia
Peyer's Patch, Hyperplasia, Lymphocyte | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 2.0 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | |
| Basophilic Focus | | | | | X | X | | | | | X | X | | | | | | | | | | | | | 6 | |
| Clear Cell Focus | | X | | | | | | | | | | | | | | | | | | | | | X | | 3 | |
| Eosinophilic Focus | | | | | | | | | | X | X | X | | | | | | | | | | X | | | 7 | |
| Fatty Change | | | | | | | | | | | | | | | | | | | | | | 1 | | | 2 1.0 | |
| Intrahepatocellular Erythrocytes | | | | | | | | | | | | | | | | | | | | X | | | | | 2 | |
| Necrosis | | | | | | | | | | | | | | | | 1 | | | | | | | | | 2 1.0 | |

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Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS | | |
|---------------------------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|-----|-----|
| | 0729 | 0730 | 0731 | 0732 | 0733 | 0734 | 0735 | 0736 | 0737 | 0738 | 0739 | 0740 | 0741 | 0742 | 0743 | 0744 | 0745 | 0746 | 0747 | 0748 | 0749 | 0750 | 0751 | 0752 | | | |
| 0 mg/kg | 0033 | 0033 | 0033 | 0033 | 0044 | 0044 | 0044 | 0044 | 0044 | 0044 | 0055 | 0055 | 0055 | 0055 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 1 | 1.0 | |
| Pigment | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 1.5 |
| Tension Lipidosis | | | | | | | | | | | | | | | | | | | | | | | | | | X | 1 |
| Bile Duct, Cyst | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocyte, Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | | | 2.0 |
| Mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | 6 | |
| Inflammation, Granulomatous | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| Fat, Necrosis | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 3.0 |
| Pancreas | | | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Acinar Cell, Vacuolation, Cytoplasmic | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Acinus, Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | | 3 | 2.3 |
| Salivary Glands | | | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| Stomach, Forestomach | | | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Diverticulum | | | | | | | | | | | | | | | | | | | | | | | | | | X | 1 |
| Stomach, Glandular | | | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Mineral | | | | | | | | | | | | | | | | | | | | | | | | | | X | 1 |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |

CARDIOVASCULAR SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|-----|
| Aorta | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| Blood Vessel | | | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Heart | | | | | | | | | | | | | | | | | | | | | | | | | | 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 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|
| | 0729 | 0730 | 0731 | 0732 | 0733 | 0734 | 0735 | 0736 | 0737 | 0738 | 0739 | 0740 | 0741 | 0742 | 0743 | 0744 | 0745 | 0746 | 0747 | 0748 | 0749 | 0750 | 0751 | 0752 | |
| 0 mg/kg | 0033 | 0033 | 0033 | 0033 | 0044 | 0044 | 0044 | 0044 | 0044 | 0044 | 0055 | 0055 | 0055 | 0055 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 8 |
| ANIMAL ID | 0003 | 0003 | 0003 | 0003 | 0004 | 0004 | 0004 | 0004 | 0004 | 0004 | 0005 | 0005 | 0005 | 0005 | 0006 | 0006 | 0006 | 0006 | 0006 | 0006 | 0006 | 0006 | 0006 | 0006 | 1.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------------------|---|---|--|---|--|--|--|--|--|--|--|--|--|--|---|--|--|--|--|--|--|--|--|--|---|-----|-----|
| Cardiomyopathy | 1 | 1 | | | | | | | | | | | | | | | | | | | | | | | 8 | 1.0 | |
| Mineral | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Polyarteritis Nodosa | | | | 2 | | | | | | | | | | | | | | | | | | | | | | 2 | 1.5 |
| Valve, Degeneration, Myxomatous | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Valve, Inflammation, Acute | | | | | | | | | | | | | | | 4 | | | | | | | | | | | 1 | 4.0 |

ENDOCRINE SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|
| Adrenal Cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Hyperplasia, Focal | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Hypertrophy, Focal | | | | | 1 | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Bilateral, Vacuolation, Cytoplasmic, Focal | | | | | | | | | | | 2 | | | | | | | | | | | | | | | 2 | 2.5 |
| Adrenal Medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Hyperplasia, Focal | | | | | | | | | | | | | | | | | | | | | | | | 1 | | 1 | 1.0 |
| Islets, Pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Hyperplasia | | | | | | 3 | | | | 1 | | | | | | | | | | | | | 1 | 3 | | 7 | 1.6 |
| Parathyroid Gland | + | + | + | M | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | M | + | + | 41 | | |
| Pituitary Gland | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | | |
| Pars Distalis, Atypia Cellular | | | | | | | | | | | | 1 | | | | | | | | | | | | | 1 | 1.0 | |
| Pars Distalis, Hyperplasia, Focal | | | 1 | | | 2 | | | | | | | 1 | | | | | | | | | 1 | | 1 | 8 | 1.4 | |
| Pars Distalis, Hypertrophy | | | | | 1 | | | | | | | | 1 | | | | | | | | | | | | 2 | 1.0 | |
| Pars Intermedia, Hyperplasia, Focal | | | | | | | | | | | | | | | | | | | | | | | 1 | | 1 | 1.0 | |
| Thyroid Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |

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
2) Mild 4) Marked

Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| DAY ON TEST | B6C3F1/N MICE FEMALE | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS |
|-------------|----------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|
| | 0729 | 0730 | 0731 | 0732 | 0733 | 0734 | 0735 | 0736 | 0737 | 0738 | 0739 | 0740 | 0741 | 0742 | 0743 | 0744 | 0745 | 0746 | 0747 | 0748 | 0749 | 0750 | 0751 | 0752 | |
| ANIMAL ID | 0033 | 0034 | 0038 | 0039 | 0041 | 0042 | 0043 | 0044 | 0045 | 0046 | 0048 | 0051 | 0053 | 0055 | 0056 | 0058 | 0060 | 0062 | 0063 | 0064 | 0065 | 0066 | 0067 | 0068 | 50 |

NONE

GENITAL SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|--|---|---|---|---|---|---|---|---|---|---|----|-----|-----|
| Clitoral Gland | + | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Ovary | + | | | | | | | | | | | | | | | | | | | | | | | | 49 | |
| Atrophy | 3 | | 3 | | 4 | 4 | 2 | 1 | 3 | 3 | | 2 | | 4 | | 3 | 2 | 3 | 4 | M | 3 | | 4 | 3 | 35 | 3.1 |
| Cyst, Epithelial | | X | | | | | | | X | | | | | | | | | | | | | | | | 3 | |
| Infiltration Cellular, Lymphocyte | | | | 3 | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| Thrombus | | | | | | | | | | | | | | X | | | | | | | | | | | 1 | |
| Follicle, Cyst | | | | | | | | | | | | | | | | | | | | | | | | | 10 | |
| Germinal Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | 2 | | 1 | 2.0 |
| Rete Ovarii, Cyst | | | | | | | X | | | | | | | | | | | | | | | | | | 1 | |
| Uterus | + | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| Inflammation, Acute | | | | 2 | | | | | 1 | | | 1 | | | | | | | | | 2 | | | | 5 | 1.8 |
| Endometrium, Hyperplasia, Cystic | | 1 | 2 | | 2 | 2 | 1 | 1 | 4 | 2 | 1 | 4 | | 4 | 1 | 4 | 1 | 4 | | 2 | | 1 | 2 | 41 | 2.2 | |
| Endometrium, Metaplasia, Squamous | | | 1 | | | | | 1 | | | | | | | | | | | | | | | | 2 | 1.0 | |
| Vagina | + | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Inflammation, Acute | | 1 | | 1 | 1 | 1 | | 1 | | 2 | 1 | 1 | | | | 1 | 1 | | 2 | | | | | 21 | 1.2 | |
| Epithelium, Hyperplasia, Squamous | 1 | 2 | 2 | 2 | 2 | 2 | | 3 | | 3 | 1 | | | 1 | 1 | 3 | | 2 | 2 | 2 | 1 | | 2 | 3 | 31 | 2.1 |

HEMATOPOIETIC SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------|---|--|--|--|--|--|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|-----|
| Bone Marrow | + | | | | | | | | | | | | | | | | | | | | | | | | 50 | |
| Hypercellularity | | | | | | | 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:

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Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS | | | |
|--|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|----|-------|-----|
| | 0729 | 0730 | 0732 | 0733 | 0734 | 0735 | 0737 | 0738 | 0739 | 0740 | 0741 | 0742 | 0743 | 0744 | 0745 | 0746 | 0747 | 0748 | 0749 | 0750 | 0751 | 0752 | 0753 | 0754 | | | | |
| 0 mg/kg | ANIMAL ID | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 00033 | 00034 | 00038 | 00039 | 00041 | 00042 | 00043 | 00044 | 00045 | 00046 | 00048 | 00051 | 00053 | 00055 | 00056 | 00058 | 00060 | 00062 | 00063 | 00064 | 00065 | 00066 | 00067 | 00068 | 00070 | | | |
| Lymph Node | | | | | | | | | | | | | | | | | | | | | | | | | | 6 | | |
| Lymph Node, Mandibular Atrophy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 2.0 | |
| Lymph Node, Mesenteric Atrophy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 2.0 | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 | |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 | |
| Hyperplasia, Lymphocyte Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | 2 | | | | | | | | | | | 2 | 11 | 2.5 | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 17 | |
| Extramedullary Hematopoiesis, Increased | | | | X | X | X | X | | X | | X | X | | X | X | | X | X | | X | X | | X | X | | 10 | 1.9 | |
| Hyperplasia, Lymphocyte | | | | | | | | | 1 | | | | | | | | | | | | | | | | 3 | 2 | 2 | 1.0 |
| Pigment | | | 1 | | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| White Pulp, Atrophy | | | | | | | | | | | | | | 1 | | | | | | | | | | | | | 2 | 2.0 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 | | |
| INTEGUMENTARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Subcutaneous Tissue, Fibrosis | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 2.0 |
| MUSCULOSKELETAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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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Experiment Number: 00058 - 04

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P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|
| | 0729 | 0730 | 0731 | 0732 | 0733 | 0734 | 0735 | 0736 | 0737 | 0738 | 0739 | 0740 | 0741 | 0742 | 0743 | 0744 | 0745 | 0746 | 0747 | 0748 | 0749 | 0750 | 0751 | 0752 | |
| 0 mg/kg | 0033 | 0033 | 0033 | 0033 | 0044 | 0044 | 0044 | 0044 | 0044 | 0044 | 0055 | 0055 | 0055 | 0055 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 0066 | 8 1.3 |

Fibro-Osseous Lesion

1

1

1 2

1

8 1.3

Skeletal Muscle

+

1

NERVOUS SYSTEM

Brain

+ 50

Inflammation, Chronic Active

1

1 1.0

Polyarteritis Nodosa

2

2 1.5

Medulla, Necrosis

1

1 1.0

Peripheral Nerve

+

2

Spinal Cord

+

2

Axon, Degeneration

1

1 1.0

RESPIRATORY SYSTEM

Lung

+ 50

Hemorrhage

2

1 2.0

Infiltration Cellular, Histiocyte

2

1 2.0

Alveolus, Epithelium, Hyperplasia

1

2 2.5

Nose

+ 50

Olfactory Epithelium, Atrophy

1

1 1.0

Olfactory Epithelium, Metaplasia, Respiratory

1

1

4 1.0

Respiratory Epithelium, Accumulation, Hyaline Droplet

1

1

2

1

1

1

1

13 1.2

Respiratory Epithelium, Hyperplasia

1

1

1

1

1

1

1

17 1.0

Respiratory Epithelium, Inflammation, Acute

1

1

2 1.0

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

+ .. Tissue examined microscopically

M .. Missing tissue

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| | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B6C3F1/N MICE 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 |
| | | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
| 30 mg/kg | 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 |
| | | 7 | 7 | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 0 | 0 | 0 | 0 |
| | | 1 | 2 | 3 | 4 | 5 | 7 | 9 | 0 | 1 | 2 | 3 | 4 | 6 | 7 | 8 | 0 | 3 | 5 | 8 | 0 | 3 | 4 |
| | | | | | | | | | | | | | | | | | | | | | | | |

females (cont...)

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | | | | 2 | | | | | | | | | | | | 2 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Basophilic Focus | | | | | | | | | | | X | | | | | | | | | | | |
| Clear Cell Focus | | | | | | | | | | | | | | | | | | | | | | |
| Eosinophilic Focus | | | | | | | | | | | X | | | | | | X | | X | | X | |
| Inflammation, Chronic Active | | | | | | | | 1 | | | | | | | | | | | | | | |
| Intrahepatocellular Erythrocytes | | | | | | | | | | | | | X | | | | | | | | | |
| Tension Lipidosis | | | | | | | | | 1 | | | | | | | | | | | | | |
| Mesentery | | | | | | | | | | | | | | | | | | | | | | |
| Fat, Necrosis | | | | | | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

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 Black Cohosh
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Date Report Requested: 12/10/2020
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 First Dose M/F: NA / 04/09/12
 Lab: BAT

| DAY ON TEST | 0 | | | | | | | | | | | | | | | | | | | | | | | | ANIMAL ID | females
(cont...) |
|--|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-----------|----------------------|
| | 6 7 7 6 7 7 7 7 7 7 7 7 7 7 7 7 7 5 7 7 7 7 7 7 | | | | | | | | | | | | | | | | | | | | | | | | | |
| B6C3F1/N MICE FEMALE

30 mg/kg | 0 2 2 2 3 3 3 3 3 3 3 3 3 3 2 3 2 3 7 3 3 3 3 3 | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 0 7 9 4 1 1 2 2 0 0 3 0 1 3 9 0 9 1 0 7 8 3 3 2 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 | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 7 7 7 7 7 7 8 8 8 8 8 8 8 8 9 9 9 9 0 0 0 0 0 0 | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 1 2 3 4 5 7 9 0 1 2 3 4 6 7 8 0 3 5 8 0 3 4 6 7 8 | | | | | | | | | | | | | | | | | | | | | | | | | |

Infiltration Cellular, Adipocyte
 Acinus, Atrophy
 Acinus, Hypertrophy

2
 2
 1

Salivary Glands
 Atrophy

+
 3

Stomach, Forestomach
 Ulcer
 Epithelium, Hyperplasia, Focal

+
 2
 1

Stomach, Glandular
 Mineral
 Epithelium, Hyperplasia

+
 3

Tooth
 Necrosis

CARDIOVASCULAR SYSTEM

Blood Vessel
 Infiltration Cellular, Lymphocyte

+ M + M +
 2

Heart
 Cardiomyopathy

+
 1
 1

ENDOCRINE SYSTEM

Adrenal Cortex
 Infiltration Cellular, Lymphocyte

+
 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 - 04
Test Type: CHRONIC
Route: GAVAGE
Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
Time Report Requested: 11:32:38
First Dose M/F: NA / 04/09/12
Lab: BAT

| B6C3F1/N MICE FEMALE
30 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|----------------------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----|----------------------|
| | 0600 | 0702 | 0707 | 0622 | 0703 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | 0707 | | |
| | 000 | 007 | 007 | 002 | 003 | 003 | 003 | 003 | 003 | 003 | 003 | 003 | 003 | 003 | 003 | 002 | 003 | 002 | 003 | 003 | 007 | 008 | 003 | 003 | 003 | |
| ANIMAL ID | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | |
| | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 000 | 001 | 001 | 001 | 001 | 001 | |
| | 771 | 772 | 773 | 774 | 775 | 777 | 779 | 880 | 881 | 882 | 883 | 884 | 886 | 887 | 888 | 888 | 889 | 889 | 889 | 889 | 990 | 990 | 990 | 990 | 990 | |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Islets, Pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid Gland | + | + | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary Gland
Pars Distalis, Hyperplasia, Focal
Pars Distalis, Hypertrophy | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + |
| Thyroid Gland
Infiltration Cellular, Lymphocyte
Follicle, Dilation | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

GENERAL BODY SYSTEM
NONE

GENITAL SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clitoral Gland | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Atrophy | 4 | 4 | 4 | 3 | | 3 | 3 | | 3 | 3 | 4 | 4 | | 4 | 4 | | | 3 | 2 | 4 | | 4 | 4 | 2 | 4 |
| Cyst, Epithelial, Multiple | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Cyst, Epithelial | | | | | | | X | | | | | | | | | | X | | | | | | | | |
| Thrombus | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Follicle, Cyst | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Follicle, Cyst, Multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| Interstitial Cell, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | |

* .. 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 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

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 | females
(cont...) |
|----------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|
| B6C3F1/N MICE FEMALE | DAY ON TEST | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | |
| | 30 mg/kg | 0 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 3 | 3 | 7 | 2 | 3 | 3 | 3 | 3 | |
| 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 | 1 | 1 | 1 | 1 | 1 | |
| | | 7 | 7 | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 0 | 0 | 0 | 0 | 0 | |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | |
| Adenomyosis | | | | | 2 | | | | | | | | | | | | | | | | | | | | | | |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dilation | | | | | | | | | | | | | | | | | | | | 2 | | | | | | | |
| Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Endometrium, Hyperplasia, Cystic | | 1 | | | 4 | 3 | 1 | | | 1 | 2 | 2 | 1 | | 4 | 4 | 3 | 1 | 2 | | 1 | 2 | | 1 | | | |
| Vagina | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | | | |
| Inflammation, Acute | | 1 | | | | | | | | | | | | | | | | | 1 | | 1 | | 1 | | | | |
| Epithelium, Hyperplasia, Cystic | | | | | | | | | | | 2 | | | | | | | | | | | | | | | | |
| Epithelium, Hyperplasia, Squamous | | 1 | 1 | | | 3 | 2 | 3 | 1 | 4 | 2 | | | | 2 | 3 | 3 | 2 | 1 | 3 | | 1 | 1 | 1 | 2 | 3 | 3 |

HEMATOPOIETIC SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | |
| Hypercellularity | | | | | 2 | | | | | | | | | | | | | | | | | | | | |
| Lymph Node | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph Node, Mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 3 | + | + | + | + | |
| Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hyperplasia, Lymphocyte | | | | | | | | | 2 | | | | | | 4 | | 4 | | | | | | | | |
| Pigment | | | | | | | | | | | | | | | 1 | | | | | | | | | | 1 |
| Lymph Node, Mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | 2 | 3 | | | | | | | | | 2 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | |
| Extramedullary Hematopoiesis, Increased | | X | X | | | | | X | | | | X | | | X | X | | | | X | | | | 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
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Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 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 | |
|---|--|-------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B6C3F1/N MICE FEMALE | | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | |
| 30 mg/kg | | 0 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 3 | 3 | 7 | 2 | 3 | 3 | 3 | 3 | 3 | |
| 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 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| | | 7 | 7 | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | 1 | 2 | 3 | 4 | 5 | 7 | 9 | 0 | 1 | 2 | 3 | 4 | 6 | 7 | 8 | 0 | 3 | 5 | 8 | 0 | 3 | 4 | 6 | 7 | 8 |
| | | females (cont...) | | | | | | | | | | | | | | | | | | | | | | | | |
| Pigment | | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Alveolus, Epithelium, Hyperplasia | | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Olfactory Epithelium, Metaplasia, Respiratory | | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Respiratory Epithelium, Accumulation, Hyaline Droplet | | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Respiratory Epithelium, Hyperplasia | | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Respiratory Epithelium, Inflammation, Acute | | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Trachea | | + | | | | | | | | | | | | | | | | | | | | | | | | |
| SPECIAL SENSES SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Phthisis Bulbi | | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Anterior Chamber, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ciliary Body, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cornea, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Harderian Gland | | + | | | | | | | | | | | | | | | | | | | | | | | | |
| URINARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Infarct, Chronic | | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Infiltration Cellular, Lymphocyte | | 2 | | | | | | | | | | | | | | | | | | | | | | | | |
| Nephropathy, Chronic Progressive | | 2 | | | | | | | | | | | | | | | | | | | | | | | | |
| Glomerulus, Cyst | | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Renal Tubule, Accumulation, Hyaline Droplet | | 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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 1) Minimal 3) Moderate
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Experiment Number: 00058 - 04

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Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| | | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) | | | | | | | | | | | |
|----------------------|-----------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|---|---|---|---|---|---|---|---|---|---|---|
| B6C3F1/N MICE FEMALE | 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 | | |
| | | 6 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
| | | 0 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 3 | 2 | 3 | 7 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | | |
| 30 mg/kg | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | |
| | | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| | | 1 | 2 | 3 | 4 | 5 | 7 | 9 | 0 | 1 | 2 | 3 | 4 | 6 | 7 | 8 | 0 | 3 | 5 | 8 | 0 | 3 | 4 | 6 | 7 | 8 | | | | | | | | | | | |
| | 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

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 1) Minimal 3) Moderate
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Experiment Number: 00058 - 04
 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: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|------|
| | 0733 | 0734 | 0752 | 0771 | 0772 | 0773 | 0774 | 0775 | 0776 | 0777 | 0778 | 0779 | 0780 | 0781 | 0782 | 0783 | 0784 | 0785 | 0786 | 0787 | | 0788 | 0789 | 0790 |
| 30 mg/kg | 0010 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 50 |
| 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 | 50 |
| | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 50 |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|---|-----|-----|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | 3 | | | | | | | 3 | | | | | | | | 1 | | 50 | 5 | 2.2 | |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Basophilic Focus | | | | | | | | | | | | | | | | | | | | | | | | | 1 | | |
| Clear Cell Focus | | | | | | | | | X | | | | | | | | | | | | | | | | 1 | | |
| Eosinophilic Focus | | | | | | | | | | | | | | | | | X | | | | | | | | 5 | | |
| Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 | |
| Intrahepatocellular Erythrocytes | | | | | | | | | | | | | | | | | | | | | | | | | 1 | | |
| Tension Lipidosis | | | | | | | | | | 1 | | | | | | | | | | | | | | | 2 | 1.0 | |
| Mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fat, Necrosis | | | | + | | | | | | | | | | | | | | | | | | | + | 2 | 2 | | |
| | | | | | | | | | | | | | | | | | | | | | | | + | | 2 | 1 | 2.0 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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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 Black Cohosh
 CAS Number: 84776-26-1

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| B6C3F1/N MICE FEMALE
30 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | |
|---|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|-------------------------|
| | 0733 | 0734 | 0750 | 0772 | 0773 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | 0777 | 0777 |
| ANIMAL ID | 0010 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | |
| Infiltration Cellular, Adipocyte Acinus, Atrophy
Acinus, Hypertrophy | | | | | | | | | | | | | | | | | | | | | | | 1 2.0
1 2.0
1 1.0 |
| Salivary Glands
Atrophy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
1 3.0 |
| Stomach, Forestomach
Ulcer
Epithelium, Hyperplasia, Focal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
1 2.0
2 2.5 |
| Stomach, Glandular
Mineral
Epithelium, Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
1
1 3.0 |
| Tooth
Necrosis | | | + | + | | | | | | | | | | | | + | | | | | | | 3
1 1.0 |
| CARDIOVASCULAR SYSTEM | | | | | | | | | | | | | | | | | | | | | | | |
| Blood Vessel
Infiltration Cellular, Lymphocyte | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48
1 2.0 |
| Heart
Cardiomyopathy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
2
1 1
5 1.2 |
| ENDOCRINE SYSTEM | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal Cortex
Infiltration Cellular, Lymphocyte | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
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 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE
30 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|---|---|-------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | | | | | | | | | | | | | | | | | | | | | |
| | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | | 7 | 7 | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | 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 | 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 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 4 | | |
| | | | | | | | | | | | | | | | | | | | | | 9 | 1 | 4 | 5 | 6 | 7 | 8 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 3 | 4 | 7 | 8 | 9 | 0 |
| Adrenal Medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | | | | | | | | | | | | | | | | | | |
| Islets, Pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | | | | | | | | | | | | | | | | | | |
| Parathyroid Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | M | M | + | + | + | 45 | | | | | | | | | | | | | | | | | | | | |
| Pituitary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | | | | | | | | | | | | | | | | | | | | |
| Pars Distalis, Hyperplasia, Focal | | 2 | | | | | | | | | | | | | | | | 4 | 1 | | 1 | 1 | | | 8 1.9 | | | | | | | | | | | | | | | | | | | | |
| Pars Distalis, Hypertrophy | | | | | | | | | | 1 | | | | | | | | | | | | | | | 1 1.0 | | | | | | | | | | | | | | | | | | | | |
| Thyroid Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | | | | | | | | | | | | | | | | | | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | | | | | | | | | | | | | | | | | | | | |
| Follicle, Dilation | | | | | 2 | | | | | | | | | | | | | | | | | | | | 1 2.0 | | | | | | | | | | | | | | | | | | | | |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Clitoral Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Atrophy | | 2 | | | 4 | 4 | 4 | 4 | 3 | 4 | 1 | 3 | | 2 | 3 | 4 | 4 | 3 | 4 | | 4 | 4 | 4 | 4 | 38 3.4 |
| Cyst, Epithelial, Multiple | | | | | | | | | | | | | | | | | | | | X | | | | | 2 |
| Cyst, Epithelial | | | | | | | | | | | | | | | | | X | | | | | X | | | 4 |
| Thrombus | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Follicle, Cyst | X | | | | | | | | | | | | | | X | | | | | | | | | | 3 |
| Follicle, Cyst, Multiple | | | | | | | | | | | | | | | | | | | | | X | | | | 1 |
| Interstitial Cell, 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

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
30 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | |
|---|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|--------|--------|--------|
| | 0733 | 0734 | 0752 | 0772 | 0773 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | | 0777 | |
| ANIMAL ID | 0010 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Adenomyosis | | | | | | | | | | | | | | | | | | | | | | 1 2.0 | | |
| Angiectasis | | | | | | | | | | 2 | | | | | 2 | | | | | | | 2 2.0 | | |
| Dilation | | | | | | | | | | | | | | | | | | | | | | 1 2.0 | | |
| Inflammation, Acute | | | | | | | | | | | | | | | | | | | 2 | | | 1 2.0 | | |
| Endometrium, Hyperplasia, Cystic | 1 | | | | | 1 | 1 | | 3 | 1 | 4 | | 1 | 3 | 1 | 1 | | 1 | 2 | | 2 | 31 1.9 | | |
| Vagina | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Inflammation, Acute | | 1 | | | | | | | | | 1 | | | | | | | | | | | 6 1.0 | | |
| Epithelium, Hyperplasia, Cystic | | | | | | | | | | | | | | | | | | | | | | 1 2.0 | | |
| Epithelium, Hyperplasia, Squamous | 2 | 1 | | | 2 | 2 | 1 | 1 | 2 | 3 | | | 1 | 2 | 2 | 2 | 1 | | 3 | 1 | | 2 | 38 1.9 | |
| HEMATOPOIETIC SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone Marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Hypercellularity | | | | | | | | | | | | | | | | | | | 1 | | | | 2 1.5 | |
| Lymph Node | | | | + | | | | | | | | | | | | | | | | | | 1 | | |
| Lymph Node, Mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | 49 | | |
| Atrophy | | | | | | | | | | | | | | | | | | | | | | 1 3.0 | | |
| Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | 3 | | 4 3.3 | | |
| Pigment | | | | | | | | | | | | | | | | | | | | | | 2 1.0 | | |
| Lymph Node, Mesenteric | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | 2 | 1 2.0 | |
| Hyperplasia, Lymphocyte | | | | | | | 2 | | | | | | 3 | | 2 | | | | 2 | | 1 | 2 | 4 | 10 2.3 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Extramedullary Hematopoiesis, Increased | | | X | X | X | X | | | | X | | | | X | X | | X | | | X | X | | 21 | |

* .. 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 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
30 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | | | | | | |
|---|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|-----|---|----|----|---|-----|-----|
| | 0733 | 0732 | 0540 | 0721 | 0772 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | | 0773 | 0773 | | | | | | | |
| ANIMAL ID | 0010 | 0001 | 0001 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | | | | | | | | |
| Hyperplasia, Lymphocyte Pigment | 2 | | | 2 | 3 | 2 | | 2 | | | 4 | 3 | 3 | | 3 | | | 2 | | | | 4 | 18 | 2.5 | | | | | | |
| White Pulp, Atrophy | | | 4 | 4 | | | | | | | | | | | | | | | | 1 | | | 4 | 3.8 | | | | | | |
| Thymus | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | M | + | + | + | + | M | + | + | 46 | | | | |
| INTEGUMENTARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary Gland Epithelium, Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 | 2.0 | |
| Skin Infiltration Cellular, Lymphocyte | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 | 2.0 | |
| MUSCULOSKELETAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone Fibro-Osseous Lesion | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 3 | 2.0 | |
| Skeletal Muscle | | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | | | |
| NERVOUS SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain Infiltration Cellular, Lymphocyte | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 2 | 1.5 | |
| RESPIRATORY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lung Hemorrhage | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 | 3.0 | |
| Lung Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | | | | 3 | 2 | 3 | 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
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Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
30 mg/kg | DAY ON TEST | | ANIMAL ID | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | |
|----------------------------------|-------------|------|-----------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|-----------|------|--|
| | 0733 | 0573 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | | 0773 | 0773 | 0773 | |
| | 0 | 0 | 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 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | |
| | 3 | 3 | 4 | 2 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 2 | 8 | 3 | 3 | 5 | 2 | 3 | 3 | 2 | 9 | |
| | 3 | 2 | 0 | 1 | 2 | 3 | 0 | 1 | 3 | 9 | 9 | 0 | 0 | 2 | 3 | 0 | 9 | 8 | 2 | 1 | 8 | 4 | 3 | 0 | 9 | | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 0 | 0 | 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 | |
| | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | | |
| | 9 | 1 | 4 | 5 | 6 | 7 | 8 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 3 | 4 | 7 | 8 | 9 | 0 | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | 50 | | |
| 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
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1-4 .. Lesion qualified as:
 1) Minimal 3) Moderate
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Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------------------|
| | 0730 | 0732 | 0735 | 0737 | 0739 | 0741 | 0743 | 0745 | 0747 | 0749 | 0751 | 0753 | 0755 | 0757 | 0759 | 0761 | 0763 | 0765 | 0767 | 0769 | |
| 100 mg/kg | 0041 | 0043 | 0045 | 0047 | 0049 | 0051 | 0053 | 0055 | 0057 | 0059 | 0061 | 0063 | 0065 | 0067 | 0069 | 0071 | 0073 | 0075 | 0077 | 0079 | 0081 |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Perforation | | | | | | | | | | | | | | | | | | | | | | |
| Ulcer | | | | | | | | | | | | | | | | | | | | | | |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Amyloid | | | | | | | | | | | | | | | | | | | | | | |
| Clear Cell Focus | X | | | | | | | | | | | | | | | | | | | | | |
| Eosinophilic Focus | | | | | | | | | | | | | | | | | | | | | | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | |
| Fatty Change | | | | | | | | | | | | | | | | | | | | | | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | |
| Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | |
| Intrahepatocellular Erythrocytes | | | | | | | | | | | | | | | | | | | | | | |

* .. 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 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

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 | 0 | 0 | 0 | 0 | | | |
|----------------------|--|-------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
| DAY ON TEST | | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | |
| B6C3F1/N MICE FEMALE | | 3 | 2 | 7 | 3 | 3 | 3 | 9 | 3 | 3 | 3 | 2 | 3 | 2 | 7 | 3 | 3 | 3 | 8 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | | |
| 100 mg/kg | | 0 | 9 | 5 | 2 | 2 | 1 | 0 | 2 | 2 | 0 | 9 | 3 | 9 | 3 | 1 | 1 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 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 | 0 | 0 | 0 | 0 | 0 | |
| ANIMAL ID | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| | | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | |
| | | 1 | 3 | 5 | 6 | 7 | 8 | 9 | 2 | 3 | 4 | 5 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 6 | 7 | 0 | 1 | 4 | 5 | | | | | | | |
| | | females (cont...) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

Adrenal Medulla +

Islets, Pancreatic Hyperplasia + + + + + + + + + + 1 + + + + + + + + + + + + + + +

Parathyroid Gland M + + M +

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

Thyroid Gland Follicle, Dilatation Follicular Cell, Hyperplasia + 1 2

GENERAL BODY SYSTEM

Tissue NOS Fat, Necrosis

GENITAL SYSTEM

Clitoral Gland +

Ovary
Angiectasis + + + + + + + + + + + + + + 4 + + + + + + + + + +
Atrophy 2 4 4 2 2 2 3 3 1 2 3 2 4 3 2 3 1
Cyst, Epithelial, Multiple
Cyst, Epithelial X
Fatty Change
Hemorrhage 3
Infiltration Cellular, Lymphocyte 2

* .. 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

| B6C3F1/N MICE FEMALE

100 mg/kg | DAY ON TEST | 0
7
3
0 | 0
7
2
9 | 0
6
7
5 | 0
7
3
2 | 0
7
3
2 | 0
7
3
1 | 0
6
9
0 | 0
7
3
2 | 0
7
3
0 | 0
7
3
9 | 0
7
3
2 | 0
7
3
3 | 0
7
3
2 | 0
6
7
3 | 0
7
3
1 | 0
7
3
1 | 0
7
3
3 | 0
6
8
3 | 0
7
3
2 | 0
7
3
1 | 0
7
3
3 | 0
7
3
3 | 0
7
3
0 | 0
7
3
1 | females
(cont...) |
|---------------------------------------|-------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|----------------------|
| | ANIMAL ID | 0
0
1
4
1 | 0
0
1
4
3 | 0
0
1
4
5 | 0
0
1
4
6 | 0
0
1
4
7 | 0
0
1
4
8 | 0
0
1
4
9 | 0
0
1
5
2 | 0
0
1
5
3 | 0
0
1
5
4 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
6
0 | 0
0
1
6
1 | 0
0
1
6
2 | 0
0
1
6
3 | 0
0
1
6
4 | 0
0
1
6
6 | 0
0
1
7
7 | 0
0
1
7
7 | 0
0
1
7
7 | |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|---|
| Pigment | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Thrombus | | | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Bilateral, Follicle, Cyst | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bursa, Cyst | | | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Follicle, Cyst | | | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Germinal Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Interstitial Cell, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Endometrium, Hyperplasia, Cystic | 1 | 4 | | 4 | 4 | 1 | 1 | 4 | | 2 | 2 | 1 | 2 | 1 | 1 | | 1 | | 2 | 1 | 2 | 2 | 2 | 3 | 2 | |

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Vagina | + | + | l | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Epithelium, Hyperplasia, Squamous | 3 | 2 | | | 2 | 2 | | 2 | 2 | 2 | 3 | 2 | 3 | | 2 | 1 | 4 | | 2 | 1 | 1 | 3 | 2 | 2 | | |

HEMATOPOIETIC SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone Marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Hypercellularity | | | | | | | | | | | | | | | | | | | | | | | | | | 4 |
| Necrosis | | | | | | | | | | | | | | | | | | | | | | | | | | 4 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|
| Lymph Node | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lumbar, Angiectasis | | | | | | | | | | | | | | | | | | | | | | | | | | 3 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lymph Node, Mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Sinus, Infiltration Cellular, Neutrophil | | | | | | | | | | | | | | | | | | | | | | | | | | |

* .. 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
l .. Insufficient tissue BLANK .. Not examined microscopically 2) Mild 4) Marked

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
100 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|---|-------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|----------------------|
| | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | 0730 | |
| ANIMAL ID | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | 001414 | |
| Lymph Node, Mesenteric
Angiectasis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hyperplasia, Lymphocyte
Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Extramedullary Hematopoiesis, Increased | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Hyperplasia, Lymphocyte
White Pulp, Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Hyperplasia, Epithelial | | | | | | | | | | | | | | | | | | | | | | | | | |
| INTEGUMENTARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Duct, Hyperplasia
Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Ulcer | | | | | | | | | | | | | | | | | | | | | | | | | |
| MUSCULOSKELETAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Fibro-Osseous Lesion
Increased Bone
Joint, Degeneration | | | | | | | | | | | | | | | | | | | | | | | | | |

* .. 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 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------|-------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|------------------------------|
| B6C3F1/N MICE FEMALE | DAY ON TEST | 0
7
3
0 | 0
7
2
9 | 0
6
7
5 | 0
7
3
2 | 0
7
3
2 | 0
7
3
1 | 0
6
9
0 | 0
7
3
2 | 0
7
3
0 | 0
7
3
9 | 0
7
2
3 | 0
7
3
2 | 0
7
3
9 | 0
6
7
3 | 0
7
3
1 | 0
7
3
1 | 0
7
3
2 | 0
6
8
1 | 0
7
3
2 | 0
7
3
3 | 0
7
3
3 | 0
7
3
3 | 0
7
3
0 | 0
7
3
3 | 0
7
3
1 | females
(cont...) |
| | ANIMAL ID | 0
0
1
4
1 | 0
0
1
4
3 | 0
0
1
4
5 | 0
0
1
4
6 | 0
0
1
4
7 | 0
0
1
4
8 | 0
0
1
4
9 | 0
0
1
5
2 | 0
0
1
5
3 | 0
0
1
5
4 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
7 | 0
0
1
5
8 | 0
0
1
6
0 | 0
0
1
6
1 | 0
0
1
6
2 | 0
0
1
6
3 | 0
0
1
6
4 | 0
0
1
6
6 | 0
0
1
6
7 | 0
0
1
7
0 | 0
0
1
7
1 | 0
0
1
7
4 | |

NERVOUS SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hydrocephalus | | | | X | | | | | | | | | | X | | | | | | | | | | | |
| Necrosis | | | | | | | | | | | | | | | | | | | | | | | | | |

RESPIRATORY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage | | | | | | | | | | | | | | | | | | | 1 | | | | | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | |
| Alveolus, Epithelium, Hyperplasia | | | | 1 | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Olfactory Epithelium, Accumulation, Hyaline Droplet | | | | | | | | | | | | | | | 2 | | | | | | | | | |
| Olfactory Epithelium, Atrophy | | | | | | | | | | | | | | 3 | | | | | | | | | | |
| Olfactory Epithelium, Metaplasia, Respiratory | | | | | | | | | | | | 1 | | | | | 1 | | | | | 1 | | |
| Respiratory Epithelium, Accumulation, Hyaline Droplet | 1 | | | 2 | | | | | 1 | | 1 | | | | | | | | | | 1 | 1 | 2 | |
| Respiratory Epithelium, Hyperplasia | 1 | 1 | | | | | | | | | 1 | | | | | | | | | 1 | | | | |
| Respiratory Epithelium, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | |
| Respiratory Epithelium, Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

SPECIAL SENSES SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

* .. 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 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------|------------------|--------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|------------------------------|
| B6C3F1/N MICE FEMALE | 100 mg/kg | DAY ON TEST | 0
7
3
0 | 0
7
2
9 | 0
6
7
5 | 0
7
3
2 | 0
7
3
2 | 0
7
3
1 | 0
6
9
0 | 0
7
3
2 | 0
7
3
2 | 0
7
3
0 | 0
7
3
9 | 0
7
3
2 | 0
7
3
9 | 0
6
7
3 | 0
7
3
1 | 0
7
3
1 | 0
7
3
2 | 0
6
8
1 | 0
7
3
2 | 0
7
3
1 | 0
7
3
3 | 0
7
3
3 | 0
7
3
0 | 0
7
3
1 | females
(cont...) |
| | | ANIMAL ID | 0
0
1
4
1 | 0
0
1
4
3 | 0
0
1
4
5 | 0
0
1
4
6 | 0
0
1
4
7 | 0
0
1
4
8 | 0
0
1
4
9 | 0
0
1
5
2 | 0
0
1
5
3 | 0
0
1
5
4 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
5
5 | 0
0
1
6
0 | 0
0
1
6
1 | 0
0
1
6
1 | 0
0
1
6
2 | 0
0
1
6
3 | 0
0
1
6
4 | 0
0
1
6
6 | 0
0
1
6
7 | 0
0
1
7
0 | |

Harderian Gland
 Hyperplasia

+
 2 2

URINARY SYSTEM

Kidney
 Infiltration Cellular, Lymphocyte
 Nephropathy, Chronic Progressive
 Renal Tubule, Accumulation, Hyaline Droplet

Urinary Bladder
 Infiltration Cellular, Lymphocyte

+
 1 1 2 1 1
 +

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

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|------|
| | 0733 | 0651 | 0730 | 0731 | 0771 | 0772 | 0773 | 0774 | 0775 | 0776 | 0777 | 0778 | 0779 | 0780 | 0781 | 0782 | 0783 | 0784 | 0785 | 0786 | | 0787 | 0788 | 0789 |
| 100 mg/kg | 0076 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 50 |
| ANIMAL ID | 0176 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 1 |
| | 7881 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 1 |
| | 6013 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 0003 | 3 |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Perforation | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Ulcer | | | | | | | | | | | | | | | | | | | | | | | | 1 4.0 |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | 2 1.5 |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | 4 | | 3 3.3 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Amyloid | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Clear Cell Focus | | | | X | | | | | | | | | X | | | | | | | | | | | 3 |
| Eosinophilic Focus | | | | | | | | | | | | | | | X | | | | | | | | | 2 |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Fatty Change | | | | | | | | | | | | | | | | | | | 1 | | | | | 1 1.0 |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | 1 | | | 3 1.7 |
| Inflammation, Chronic Active | 1 | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Intrahepatocellular Erythrocytes | | | | | | 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 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE
100 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|------------|
| | 0
7
3
3 | 0
6
5
1 | 0
7
3
0 | 0
7
3
1 | 0
7
3
1 | 0
7
2
9 | 0
7
3
1 | 0
7
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0 | 0
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3 | 0
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2 | 0
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3 | 0
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7
3
3 | 0
7
2
9 | 0
7
2
9 | 0
7
3
2 | 0
7
3
9 | 0
5
9
9 | | 0
7
3
2 | 0
7
3
3 | |
| ANIMAL ID | 0
0
1
7
6 | 0
0
1
8
0 | 0
0
1
8
1 | 0
0
1
8
3 | 0
0
1
8
4 | 0
0
1
8
5 | 0
0
1
8
8 | 0
0
1
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9 | 0
0
1
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9
1 | 0
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1
9
3 | 0
0
1
9
4 | 0
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1
9
6 | 0
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1
9
7 | 0
0
2
9
9 | 0
0
2
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9 | 0
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9 | 0
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9 | 0
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2
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9 | 0
0
2
9
9 | 0
0
2
9
9 | 0
0
2
9
9 | |
| Mixed Cell Focus
Necrosis | | | | | | | | X | | | | | | | | | | | | | X | | | 3
1 1.0 |
| Tension Lipidosis
Hepatocyte, Atrophy | | | | | | | | | 1 | 1 | | | | | | | | | | | | | | 4
1 2.0 |
| Pancreas
Acinus, Atrophy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
1 1.0 | |
| Salivary Glands
Infiltration Cellular, Lymphocyte | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 2 | + | + | + | + | 50
1 2.0 | |
| Stomach, Forestomach
Epithelium, Hyperplasia, Focal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
1 1.0 | |
| Stomach, Glandular
Mineral | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | X | 50
1 | |
| Tongue | | | | | | | | | | | | | | | | | | | | | | + | 1 | |
| CARDIOVASCULAR SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood Vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | 49 | |
| Heart
Cardiomyopathy | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | 1 | 1 | 1 | 50
8 1.0 | |
| ENDOCRINE SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal Cortex
Subcapsular, Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 1 | 50
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 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
100 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------------|----------|
| | 0733 | 0651 | 0730 | 0731 | 0771 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | |
| ANIMAL ID | 001766 | 00001 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | 00000 | |
| Adrenal Medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Islets, Pancreatic Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
3 1.0 | |
| Parathyroid Gland | + | M | + | + | M | + | M | M | + | + | + | + | + | + | M | + | + | + | + | + | M | + | + | 42 | |
| Pituitary Gland Pars Distalis, Hyperplasia, Focal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
10 1.4 | |
| Thyroid Gland Follicle, Dilation | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49
1 1.0 | |
| Thyroid Gland Follicular Cell, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 | |
| GENERAL BODY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tissue NOS Fat, Necrosis | | | | | | | | | | | | | | | | | | | | | | | | 1
4 4.0 | |
| GENITAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Ovary Angiectasis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
2 2.5 | |
| Ovary Atrophy | 4 | 4 | 3 | 3 | 2 | 2 | 1 | | 3 | | 2 | 2 | | | 3 | 3 | 1 | 3 | | | 1 | 4 | 4 | 34 2.6 | |
| Ovary Cyst, Epithelial, Multiple | | | | | | | | | | | | | | | X | | | | | | | | | 1 | |
| Ovary Cyst, Epithelial | | | | | | | X | | | | | | | | | | | | | | | | | 2 | |
| Ovary Fatty Change | | | | | | | | | | | | | | | | | | | | | 2 | | | 1 2.0 | |
| Ovary Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | 1 3.0 | |
| Ovary 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
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Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|
| | 0733 | 0651 | 0730 | 0771 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | 0777 |
| 100 mg/kg | 0017 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 0008 | 36 |
| ANIMAL ID | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 0011 | 9 |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|--|---|-----|
| Pigment | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Thrombus | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Bilateral, Follicle, Cyst | | | | | | | | | | | | | | | | | | | | | X | | 1 | |
| Bursa, Cyst | | | | | | | | | | | | | | | | | | | | | | | 2 | |
| Follicle, Cyst | | | | | | | | | | | | | | | | | | | | | | | 4 | |
| Germinal Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| Interstitial Cell, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | 1 | 1 | 1.0 |
| Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | 2 | 1.5 |
| Endometrium, Hyperplasia, Cystic | 1 | 1 | 4 | 2 | 2 | 1 | 3 | 4 | 1 | 1 | 1 | 3 | | 2 | 3 | 1 | 1 | 3 | 1 | 1 | 1 | 1 | 45 | 1.9 |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Vagina | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | |
| Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | 1 | 1 |
| Epithelium, Hyperplasia, Squamous | 3 | | 2 | 2 | 3 | 2 | 3 | 2 | 2 | 2 | 3 | 1 | 1 | 3 | 1 | 2 | 2 | 3 | | 2 | 1 | 2 | 41 | 2.1 |

HEMATOPOIETIC SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Bone Marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Hypercellularity | | | | | | | | | | | | | | | | | | | | | | 3 | 5 | 2.8 |
| Necrosis | | | | | | | | | | | | | | | | | | | | | | | 1 | 4.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|-----|
| Lymph Node | | | | | | | | | | | | | | | | | | | | | | | 2 | |
| Lumbar, Angiectasis | | | | | | | | | | | | | | | | | | | | | | | 1 | 3.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Lymph Node, Mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | 2 | 2.0 |
| Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | | | | | | | | | | 1 | 2.0 |
| Sinus, Infiltration Cellular, Neutrophil | | | | | | | | | | | | | | | | | | | | | | 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:

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Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

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Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE
100 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | |
|-----------------------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|---|---|
| | 0733 | 0651 | 0730 | 0771 | 0771 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | 0577 | 0777 | | |
| ANIMAL ID | 0017 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | | | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 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 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | |
| | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | |
| | 6 | 0 | 1 | 3 | 4 | 5 | 8 | 9 | 0 | 1 | 3 | 4 | 6 | 7 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Lymph Node, Mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Hyperplasia, Lymphocyte | 2 | | | | | 3 | | 2 | 1 | | | 4 | | 2 | | | | | | | | | | | 11 2.4 |
| Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | | 2 | | | | | | | | | | 1 2.0 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Extramedullary Hematopoiesis, Increased | | X | | X | X | | X | X | | | X | | X | | X | X | | | | | X | X | X | | 22 |
| Hyperplasia, Lymphocyte | | | | | 2 | 2 | | | | | | 3 | | | 2 | | | 2 | | | | | | | 10 2.0 |
| White Pulp, Atrophy | | 4 | | | | | | | | | | | | | | | | | | | | 3 | | | 3 3.3 |
| Thymus | + | + | + | + | + | + | + | + | + | M | + | + | + | I | + | + | + | + | + | + | + | + | + | + | 48 |
| Hyperplasia, Epithelial | | | | | | | | | | | | | | | | | | | | | | | | | 1 4.0 |

INTEGUMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|-------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Mammary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Duct, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Ulcer | | 4 | | | | | | | | | | | | | | | | | | | | | | | 2 3.0 |

MUSCULOSKELETAL SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Fibro-Osseous Lesion | | | | | | | | | | | | | | | | | | | | | | | | | 2 2.5 |
| Increased Bone | | | | X | | | | | | | | | | | | | | | | | | | | | 1 |
| Joint, Degeneration | | | | | | | | | | | | | | | | | | | | | | | | | 1 3.0 |

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

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 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 | |
| B6C3F1/N MICE FEMALE | | 7 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 7 | 7 | |
| | | 3 | 5 | 3 | 3 | 3 | 2 | 3 | 3 | 3 | 3 | 2 | 3 | 3 | 3 | 2 | 3 | 3 | 2 | 2 | 3 | 9 | 3 | 3 |
| 100 mg/kg | | 3 | 1 | 0 | 1 | 1 | 9 | 1 | 0 | 3 | 9 | 3 | 3 | 2 | 0 | 0 | 0 | 9 | 9 | 2 | 9 | 0 | 3 | |
| | | 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 | |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | |
| | | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | 6 | 0 | 1 | 3 | 4 | 5 | 8 | 9 | 0 | 1 | 3 | 4 | 6 | 7 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | |
| | | | | | | | | | | | | | | | | | | | | | | * TOTALS | | |

NERVOUS SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|--------------|
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Hydrocephalus | | | | | | | | | | | | | | | | | | | | | | | | 2 | |
| Necrosis | | | | | | | | | | | | | | | | | | | | | | | | 2 | 1 2.0 |

RESPIRATORY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|--------------|
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | 2 | 1 2.0 |
| Alveolus, Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | 2 | 1.5 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Olfactory Epithelium, Accumulation, Hyaline Droplet | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 | |
| Olfactory Epithelium, Atrophy | | | | | | | | | | | | | | | | | | | | | | | | 1 3.0 | |
| Olfactory Epithelium, Metaplasia, Respiratory | | | | | | | | | | | | | | | | | | | | | | | | 5 1.0 | |
| Respiratory Epithelium, Accumulation, Hyaline Droplet | | | | | | | | | | | | | | | | | | | | | | | | 15 1.3 | |
| Respiratory Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | 9 1.0 | |
| Respiratory Epithelium, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | |
| Respiratory Epithelium, Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |

SPECIAL SENSES SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------|
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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
 I .. Insufficient tissue BLANK .. Not examined microscopically 2) Mild 4) Marked

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS | |
|---|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|--|
| | 0733 | 0651 | 0730 | 0731 | 0731 | 0779 | 0771 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | | |
| 100 mg/kg | ANIMAL ID | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 0017 | 0011 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | 0018 | |
| Harderian Gland Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | 3 2.7 | |
| URINARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | 2 | | | | | | | | | | | | | 1 2.0 | |
| Nephropathy, Chronic Progressive | 1 | | | | | 2 | | | | | 1 | | | | 2 | | | | | | | | | | 1 | 10 1.3 | |
| Renal Tubule, Accumulation, Hyaline Droplet | | | | | | | | | | | | | | | | | | | | | | | | 2 | | 1 2.0 | |
| Urinary Bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | 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

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | 300 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | females (cont...) | | | |
|----------------------|-----------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------------------|---|---|---|
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | |
| | | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 4 | 7 | 6 | 7 | 5 | 7 | 7 | 6 | 7 | | 6 | 7 | |
| | | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 7 | 5 | 2 | 6 | 3 | 7 | 3 | 3 | 5 | 3 | 3 | 6 | 7 | |
| | | 1 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 3 | 9 | 7 | 5 | 9 | 5 | 3 | 2 | 2 | 9 | 3 | 3 | 0 | 6 | 3 | |
| | | ANIMAL ID | | | | | | | | | | | | | | | | | | | | | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | |
| | | 1 | 2 | 3 | 4 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 0 | 2 | 4 | 7 | 8 | 9 | 2 | 3 |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Clear Cell Focus | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eosinophilic Focus | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Intrahepatocellular Erythrocytes | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Necrosis | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tension Lipidosis | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Acinus, Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | | |

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

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

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

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------------------|
| | 0731 | 0733 | 0732 | 0732 | 0732 | 0731 | 0731 | 0731 | 0733 | 0733 | 0733 | 0732 | 0739 | 0647 | 0472 | 0665 | 0733 | 0572 | 0773 | 0665 | 0733 | 0730 | 0662 | 0730 | |
| 300 mg/kg | 0011 | 0012 | 0013 | 0014 | 0017 | 0018 | 0019 | 0020 | 0021 | 0022 | 0023 | 0024 | 0025 | 0026 | 0027 | 0028 | 0029 | 0030 | 0031 | 0032 | 0033 | 0034 | 0035 | 0036 | |

Duct, Cyst

X

Salivary Glands

+ +

Stomach, Forestomach

+ +

Stomach, Glandular
Mineral

+ + + + + + + + + + + + X + + + + + + + + + + + +

Tooth
Inflammation, Acute
Necrosis

CARDIOVASCULAR SYSTEM

Blood Vessel

+ +

Heart
Cardiomyopathy

+
 1 1 1

ENDOCRINE SYSTEM

Adrenal Cortex
Hypertrophy, Focal
Vacuolation, Cytoplasmic, Focal

+
 1

Adrenal Medulla

+ +

Islets, Pancreatic
Atrophy

+ +

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

1-4 .. Lesion qualified as:
 1) Minimal 3) Moderate
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Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE
300 mg/kg | 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 | females
(cont...) | | | | |
|-----------------------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------------------|---|---|---|--|
| | | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 4 | 7 | 6 | 7 | 5 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | | 7 | | | |
| | ANIMAL ID | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 7 | 5 | 2 | 6 | 3 | 7 | 3 | 2 | 9 | 3 | 5 | 3 | | 3 | 6 | 7 | |
| | | 1 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 3 | 9 | 7 | 5 | 9 | 5 | 3 | 2 | 2 | 9 | 3 | 3 | 5 | 3 | 3 | 6 | 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 | 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 | |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | |
| | | 1 | 2 | 3 | 4 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 0 | 2 | 4 | 7 | 8 | 9 | 1 | 2 | 3 | 3 | |
| Parathyroid Gland | | + | + | M | + | + | + | + | + | M | + | + | + | + | + | + | M | + | M | M | + | + | + | + | + | + | | |
| Pituitary Gland | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Pars Distalis, Hyperplasia, Focal | | | | 1 | 1 | | | 1 | | | | | | | | | | | | | | | | | | | 1 | |
| Pars Distalis, Hypertrophy | | | | | | | | | 1 | | | | | | | | | | | | | | | | | | | |
| Thyroid Gland | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | |
| Follicle, Dilation | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| GENERAL BODY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| GENITAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral Gland | + | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ovary | + | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Atrophy | 3 | | 2 | 3 | 3 | 3 | | 2 | 4 | 4 | 4 | 3 | 4 | 3 | | 3 | 2 | | 3 | | | | 3 | 3 | 3 | 2 | | |
| Cyst, Epithelial | | | | | | | X | | | | | | | | | | | | | | | | | | | | X | |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Follicle, Cyst | | X | | | | | | | | | | | | | | | | | | X | | | | | | | X | |
| Interstitial Cell, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | | |
| Paraovarian Tissue, Cyst | | | | | | | | | | | | | | | | | | | | | | X | | | | | | |
| Rete Ovarii, Cyst | | | | | | | | | | | | | | | | | | | | | X | | | | | | | |
| Uterus | + | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thrombus | X | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Endometrium, Hyperplasia, Cystic | 1 | 1 | | 2 | 2 | 1 | 2 | 4 | | 3 | 1 | 2 | | 1 | 3 | 2 | | 2 | 1 | 2 | 1 | 3 | 3 | 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:

1) Minimal 3) Moderate

2) Mild 4) Marked

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B6C3F1/N MICE 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 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 4 | 7 | 6 | 7 | 5 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | 7 | 6 | 7 | |
| | 300 mg/kg | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 7 | 5 | 2 | 6 | 3 | 7 | 3 | 2 | 3 | 5 | 3 | 3 | 5 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | |
| | ANIMAL ID | 1 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 3 | 9 | 7 | 5 | 9 | 5 | 3 | 2 | 2 | 9 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 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 | |
| | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 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 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 0 | 2 | 4 | 7 | 8 | 9 | 1 | 2 | 3 | 4 | 7 | 8 | 9 | 1 | 2 | 3 | 4 | 7 | 8 | 9 | 1 | |

females (cont...)

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---------------------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Endometrium, Metaplasia, Squamous | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Vagina | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Inflammation, Acute | 1 1 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Epithelium, Hyperplasia, Squamous | 1 2 1 1 4 1 2 2 2 1 1 3 2 2 3 3 2 2 3 | | | | | | | | | | | | | | | | | | | | | | | | |

HEMATOPOIETIC SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|-----------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| Bone Marrow | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Fibrosis | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Hypercellularity | 2 | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph Node | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph Node, Mandibular | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Atrophy | 3 | | | | | | | | | | | | | | | | | | | | | | | | |
| Infiltration Cellular, Plasma Cell | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph Node, Mesenteric | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Atrophy | M | | | | | | | | | | | | | | | | | | | | | | | | |
| Extramedullary Hematopoiesis | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Hyperplasia, Lymphocyte | 3 | | | | | | | | | | | | | | | | | | | | | | | | |
| Infiltration Cellular, Histiocyte | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Infiltration Cellular, Plasma Cell | 2 3 | | | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | + | | | | | | | | | | | | | | | | | | | | | | | | |
| Extramedullary Hematopoiesis, Increased | X X X X X | | | | | | | | | | | | | | | | | | | | | | | | |
| Hyperplasia, Lymphocyte | 2 2 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| White Pulp, Atrophy | 2 4 | | | | | | | | | | | | | | | | | | | | | | | | |

* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade
+ .. Tissue examined microscopically
X .. Lesion present
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Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

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First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE
300 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| | 0
7
3
1 | 0
7
3
3 | 0
7
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2 | 0
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2 | 0
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1 | 0
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3 | 0
7
3
2 | 0
7
5
7 | 0
6
2
5 | 0
4
7
9 | 0
7
6
5 | 0
5
3
2 | 0
7
3
2 | 0
7
2
9 | 0
7
3
3 | 0
6
5
3 | 0
7
3
3 | 0
7
3
0 | 0
6
6
2 | 0
7
3
3 | |
| ANIMAL ID | 0
0
2
1
1 | 0
0
2
1
2 | 0
0
2
1
3 | 0
0
2
1
4 | 0
0
2
1
7 | 0
0
2
1
8 | 0
0
2
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9 | 0
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2
2
0 | 0
0
2
2
1 | 0
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3 | 0
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2
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4 | 0
0
2
2
5 | 0
0
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6 | 0
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7 | 0
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8 | 0
0
2
3
0 | 0
0
2
3
2 | 0
0
2
3
4 | 0
0
2
3
7 | 0
0
2
3
8 | 0
0
2
3
9 | 0
0
2
4
1 | 0
0
2
4
2 | 0
0
2
4
3 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

INTEGUMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mammary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Erosion | | | | | | | | | | | | | | | | | | | | | | | | |
| Epidermis, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | |

MUSCULOSKELETAL SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Fibro-Osseous Lesion | | | 1 | | | | | | 2 | | | | | | | | | | | | | | | |
| Joint, Degeneration | | 2 | | | | | | | | | | | | | | | | | | | | | | 2 |
| Skeletal Muscle | | | | | | | | | | | | | | | | | | | | | | | | |

NERVOUS SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | |
| Peripheral Nerve | | | | | | | | | | | | | | | | | | | | | | | | |
| Spinal Cord | | | | | | | | | | | | | | | | | | | | | | | | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | |
| Axon, Degeneration | | | | | | | | | | | | | | | | | | | | | | | | |

RESPIRATORY 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 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------------------|
| | 0731 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | 0733 | |
| 300 mg/kg | 0011 | 0012 | 0013 | 0014 | 0017 | 0018 | 0019 | 0020 | 0021 | 0022 | 0023 | 0024 | 0025 | 0026 | 0027 | 0028 | 0029 | 0030 | 0031 | 0032 | 0033 | 0034 | 0037 | 0038 | |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Infiltration Cellular, Histiocyte | | | | | | | | | | | | | | | | | | | | | | | | |
| Polyarteritis Nodosa | | | | | | 1 | | | | | | | | | | | | | | | | | | |
| Alveolus, Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Olfactory Epithelium, Metaplasia, Respiratory | | | | | | | | | | 1 | | 1 | | | | | | 1 | 1 | | | 1 | | |
| Respiratory Epithelium, Accumulation, Hyaline Droplet | | | | | | | 2 | | | 1 | 1 | 1 | | | 1 | 2 | | | 1 | 2 | | | | |
| Respiratory Epithelium, Hyperplasia | | | 1 | | | 1 | 1 | | | | | 1 | | 1 | | | | | | 1 | | | | |
| Respiratory Epithelium, Inflammation, Chronic | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Respiratory Epithelium, Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

SPECIAL SENSES SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Anterior Chamber, Inflammation, Acute | | | | | | | | | | 2 | | | | | | | | | | | | | | |
| Ciliary Body, Inflammation, Acute | | | | | | | | | | 2 | | | | | | | | | | | | | | |
| Cornea, Inflammation, Acute | | | | | | | | | | 2 | | | | | | | | | | | | | | |
| Harderian Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hyperplasia | | | | | | | | | | 1 | 1 | | 3 | | | | | | | | | | | |

URINARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | 2 | | | | | |
| Nephropathy, Chronic Progressive | | | | | 1 | | | 1 | 1 | 1 | 1 | 1 | | | 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 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

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 | 0 |
|-----------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B6C3F1/N MICE FEMALE | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 4 | 7 | 6 | 7 | 5 | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 7 |
| 300 mg/kg | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 7 | 5 | 2 | 6 | 3 | 7 | 3 | 2 | 3 | 2 | 3 | 5 | 3 | 3 | 6 | 3 |
| | 1 | 3 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 3 | 9 | 7 | 5 | 5 | 3 | 2 | 2 | 9 | 3 | 3 | 3 | 3 | 0 | 2 | 0 | |
| 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 | 0 | 0 | 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 |
| | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 |
| | 1 | 2 | 3 | 4 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 0 | 2 | 4 | 7 | 8 | 9 | 1 | 2 | 3 | 3 |
| Glomerulus, Amyloid | | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Renal Tubule, Cyst | | | | | X | | | | | | | | | | | | | | | | | | | | | |
| Urinary Bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Fibrosis | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ulcer | | | | | | | | | | | | | | | | | | | | | | | | | | |

females
(cont...)

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

+ .. Tissue examined microscopically

X .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|------|------|
| | 0732 | 0732 | 0730 | 0730 | 0672 | 0676 | 0666 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | | 0677 | | | |
| 300 mg/kg | 0044 | 0045 | 0046 | 0047 | 0049 | 0040 | 0041 | 0042 | 0044 | 0045 | 0046 | 0048 | 0040 | 0041 | 0043 | 0044 | 0040 | 0041 | 0042 | 0043 | 0044 | 0045 | 0047 | 0049 | 0040 |
| | 4 | 5 | 6 | 7 | 9 | 0 | 1 | 2 | 4 | 5 | 6 | 8 | 0 | 1 | 3 | 4 | 0 | 1 | 2 | 3 | 4 | 5 | 7 | 9 | 0 |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | 49 |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | | | | | | | 2 | | | | | | | | | | | | 2 2.0 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Clear Cell Focus | | | | | | | | | | | | | | | | X | | | | | | | | | 1 |
| Eosinophilic Focus | | | | | | | X | | | | | | | | | | | | | | | | | | 1 |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Intrahepatocellular Erythrocytes | | | | | | | | | | | | X | | | | | | | | | | | | | 2 |
| Necrosis | | | | | | | | | | | | 1 | | | | | | | | | | | | | 1 1.0 |
| Tension Lipidosis | | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Mesentery | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Acinus, Atrophy | | | | | | | 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

Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|
| | 0732 | 0732 | 0730 | 0730 | 0672 | 0676 | 0666 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | 0677 | |
| 300 mg/kg | 0044 | 0045 | 0046 | 0047 | 0049 | 0050 | 0051 | 0052 | 0054 | 0055 | 0056 | 0058 | 0059 | 0060 | 0061 | 0063 | 0064 | 0066 | 0067 | 0068 | 0069 | 0071 | 0072 | 0073 | 50 |
| ANIMAL ID | 0044 | 0045 | 0046 | 0047 | 0049 | 0050 | 0051 | 0052 | 0054 | 0055 | 0056 | 0058 | 0059 | 0060 | 0061 | 0063 | 0064 | 0066 | 0067 | 0068 | 0069 | 0071 | 0072 | 0073 | |

Duct, Cyst 1

Salivary Glands + 50

Stomach, Forestomach + 50

Stomach, Glandular Mineral + 50 1

Tooth Inflammation, Acute Necrosis + 2 1 2 1 1.0 1 1.0

CARDIOVASCULAR SYSTEM

Blood Vessel + M 49

Heart Cardiomyopathy + 50 11 1.1

ENDOCRINE SYSTEM

Adrenal Cortex Hypertrophy, Focal Vacuolation, Cytoplasmic, Focal + 50 1 1.0 1 1.0

Adrenal Medulla + 50

Islets, Pancreatic Atrophy + 50 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:
1) Minimal 3) Moderate
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 Black Cohosh
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Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
300 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | | | | | | | | | | | | |
|-----------------------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|---|---|---|----|----|---|-----|-----|----|-----|-----|-----|--|
| | 0732 | 0732 | 0730 | 0730 | 0672 | 0672 | 0666 | 0666 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | 0779 | | | 0779 | | | | | | | | | | | | | |
| ANIMAL ID | 0044 | 0044 | 0044 | 0044 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | 0045 | | | | | | | | | | | | | | |
| Parathyroid Gland | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | M | M | + | + | + | + | + | + | + | + | + | 41 | | | | | | | | | |
| Pituitary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | | | | | | |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pars Distalis, Hyperplasia, Focal | | | | | 1 | 1 | | | | | 1 | | | | | | | | | | | | | | | | | | 7 | 1.0 | | | | | | |
| Pars Distalis, Hypertrophy | | | | | | 1 | 1 | | | | | | | | | | | | | | | | | | | | | | | 3 | 1.0 | | | | | |
| Thyroid Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | | | | | |
| Follicle, Dilatation | | | | | | | 1 | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 | | | |
| GENERAL BODY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | + | | | | | | | | | | | | | | | | | | | | | | 1 | | | | | |
| GENITAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | | |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Atrophy | 2 | | 3 | 3 | | 3 | 3 | 4 | | 4 | 3 | 4 | 3 | 3 | 4 | 2 | 4 | 4 | 3 | 4 | | 4 | | 4 | | 4 | 4 | | | | | | 39 | 3.2 | | |
| Cyst, Epithelial | | | | | | | | | | | | | X | | | | | | | | | | | | | | | | | | | | 3 | | | |
| Hemorrhage | | | | | | | | | | | | | | | 3 | | | | | | | | | | | | | | | | | | 1 | 3.0 | | |
| Follicle, Cyst | | | | | | X | | | | | | | | | | | | | | | | | | | X | | | | | | | | 5 | | | |
| Interstitial Cell, Hyperplasia | | | | | | | | | | | | | | | 1 | | | | | | | | | | | | | | | | | | 2 | 1.5 | | |
| Paraovarian Tissue, Cyst | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | | | |
| Rete Ovarii, Cyst | | | | | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Inflammation, Acute | | | | | | 1 | | | | 1 | | | | | 1 | | 2 | | | | | | | | | | | | | | | | | 5 | 1.4 | |
| Thrombus | | | | | | | | | X | | | | | | | | | | | | | | | | | | | | | | | | | 2 | | |
| Endometrium, Hyperplasia, Cystic | 1 | 3 | 1 | 2 | 3 | 3 | | 2 | 1 | 3 | 3 | | 2 | 4 | 4 | 3 | 1 | 2 | 1 | 3 | 2 | | | | | | 1 | 1 | | | | | 41 | 2.1 | | |

* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade
 + .. Tissue examined microscopically
 X .. Lesion present
 I .. Insufficient tissue
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 A .. Autolysis precludes evaluation
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 1-4 .. Lesion qualified as:
 1) Minimal 3) Moderate
 2) Mild 4) Marked

Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE
300 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | | | |
|---|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|------|------|--------|--|
| | 0732 | 0733 | 0730 | 0730 | 0762 | 0769 | 0766 | 0766 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | 0777 | | | | | |
| ANIMAL ID | 0044 | 0045 | 0046 | 0047 | 0049 | 0050 | 0051 | 0052 | 0053 | 0054 | 0055 | 0056 | 0057 | 0058 | 0059 | 0060 | 0061 | 0062 | 0063 | 0064 | 0065 | 0066 | 0067 | 0068 | 0069 | 0070 | |
| Endometrium, Metaplasia, Squamous | | | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | |
| Vagina | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | |
| Inflammation, Acute | | | | | | 1 | | | | | | | | | | | | | | | | | | | | 6 1.0 | |
| Epithelium, Hyperplasia, Squamous | | 1 | | | | 3 | | 1 | 1 | 2 | 2 | 3 | 2 | 3 | 2 | 2 | | 2 | 3 | 3 | 3 | | 1 | 1 | 1 | 37 2.0 | |
| HEMATOPOIETIC SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone Marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Fibrosis | | | | | | | | | | | | | | | | | | | | | | 1 | | | | 1 1.0 | |
| Hypercellularity | | | | | 1 | | 2 | | | | | | | 1 | | | | | | | | | | | 3 | 5 1.8 | |
| Lymph Node | | | | | | | + | | | | | | | | | | | | | | | | + | | | 5 | |
| Lymph Node, Mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | | 1 3.0 | |
| Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | | | | | | | | | | | | 3 | 1 3.0 | |
| Lymph Node, Mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | |
| Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | 1 | | | | | | | | | | 1 1.0 | |
| Hyperplasia, Lymphocyte | | | | | | | | 3 | | | 2 | | | | | | | | | | | | 4 | | | 4 3.0 | |
| Infiltration Cellular, Histiocyte | | | | | | | | | | | 2 | | | | | | | | | | | | | | | 1 2.0 | |
| Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | 2 | | | | | | | | | | | | 3 2.3 | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Extramedullary Hematopoiesis, Increased | | | | | | | X | X | | X | X | | X | | X | | | | | | | | X | X | | 14 | |
| Hyperplasia, Lymphocyte | | | | | | | | | 3 | 2 | | | 2 | | | | | | 2 | 3 | | | | | | 14 2.3 | |
| White Pulp, Atrophy | | | | | | | 3 | 3 | | | | | | | | | | | | | | | | 4 | | 5 3.2 | |

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

+ .. Tissue examined microscopically

X .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
300 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS | | |
|-----------------------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|-------|--|
| | 0732 | 0733 | 0734 | 0735 | 0736 | 0737 | 0738 | 0739 | 0740 | 0741 | 0742 | 0743 | 0744 | 0745 | 0746 | 0747 | 0748 | 0749 | 0750 | 0751 | 0752 | 0753 | 0754 | 0755 | | 0756 | |
| ANIMAL ID | 0044 | 0045 | 0046 | 0047 | 0048 | 0049 | 0050 | 0051 | 0052 | 0053 | 0054 | 0055 | 0056 | 0057 | 0058 | 0059 | 0060 | 0061 | 0062 | 0063 | 0064 | 0065 | 0066 | 0067 | 0068 | | |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | | |
| INTEGUMENTARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary Gland | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | M | + | + | + | + | M | + | + | 47 | | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Erosion | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 1 2.0 | |
| Epidermis, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | 3 | 1 3.0 | |
| MUSCULOSKELETAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Fibro-Osseous Lesion | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 1.5 | |
| Joint, Degeneration | | | | | | | | | | | | | | | | | | | | | | | | | 3 | 2.3 | |
| Skeletal Muscle | | | | | | | | | | | | | | | | | | | | | | | | | 1 | | |
| NERVOUS SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Hemorrhage | | | | | 2 | | | | | | | | | | | | | | | | | | | | 1 | 2.0 | |
| Polyarteritis Nodosa | | | | | | | | | | | | | 2 | | | | | | | | | | | | 1 | 2.0 | |
| Peripheral Nerve | | | | | | | | | | | | | | | | | | | | | | | | | 1 | | |
| Spinal Cord | | | | | | | | | | | | | | | | | | | | | | | | | 1 | | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 | |
| Axon, Degeneration | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 | |
| RESPIRATORY 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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Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| DAY ON TEST | B6C3F1/N MICE FEMALE | | | | | | | | | | | | | | | | | | | | * TOTALS | |
|-------------|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|---|
| | 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 | 6 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 6 | 7 | 7 |
| 3 | 3 | 3 | 3 | 5 | 2 | 0 | 7 | 2 | 3 | 3 | 3 | 3 | 2 | 3 | 3 | 7 | 3 | 3 | 2 | 3 | 3 | 2 |
| 2 | 2 | 0 | 0 | 2 | 9 | 3 | 1 | 0 | 0 | 2 | 0 | 3 | 9 | 0 | 0 | 7 | 0 | 1 | 9 | 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 |
| 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 4 | 4 | 4 | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 8 |
| 4 | 5 | 6 | 7 | 9 | 0 | 1 | 2 | 4 | 5 | 6 | 8 | 0 | 1 | 3 | 4 | 0 | 1 | 2 | 3 | 4 | 5 | 7 |

| | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Infiltration Cellular, Histiocyte | | | | | | | | | | | | | | | | 2 | | | | | | | 1 2.0 |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Alveolus, Epithelium, Hyperplasia | | | | | | | | | | | | | | | | 3 | | | | | | | 1 3.0 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Olfactory Epithelium, Metaplasia, Respiratory | | | | | | | | | 1 | | | | | | | | | | 1 | | | | 7 1.0 |
| Respiratory Epithelium, Accumulation, Hyaline Droplet | | | | | 1 | | | | | | 1 | | 1 | | | | | | 1 | | 1 | | 13 1.2 |
| Respiratory Epithelium, Hyperplasia | 1 | | | | 1 | 1 | | | | | | 1 | | | 1 | | | | | | 1 | | 13 1.0 |
| Respiratory Epithelium, Inflammation, Chronic | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Respiratory Epithelium, Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

SPECIAL SENSES SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Anterior Chamber, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Ciliary Body, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Cornea, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Harderian Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hyperplasia | | | | | | | | | | | | | | | | 2 | | | | | | | 4 1.8 |

URINARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Nephropathy, Chronic Progressive | | | | | 1 | 1 | 1 | | | | | | 2 | 1 | 1 | | 1 | 1 | | | 1 | | 20 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
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Experiment Number: 00058 - 04

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Black Cohosh

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First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE

300 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | | * TOTALS |
|---------------------------------------|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|----------|
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | |
| | 7 | 7 | 7 | 7 | 6 | 7 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | 7 | 6 | 7 | 7 | 7 | | |
| ANIMAL ID | | 3 | 3 | 3 | 3 | 5 | 2 | 0 | 7 | 2 | 3 | 3 | 3 | 3 | 2 | 3 | 3 | 7 | 3 | 3 | 2 | 3 | 3 | 3 | | |
| | | 2 | 2 | 0 | 0 | 2 | 9 | 3 | 1 | 9 | 0 | 2 | 0 | 3 | 9 | 2 | 0 | 7 | 0 | 1 | 9 | 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 | | |
| | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | |
| | | 4 | 4 | 4 | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 8 | | |
| | | 4 | 5 | 6 | 7 | 9 | 0 | 1 | 2 | 4 | 5 | 6 | 8 | 0 | 1 | 3 | 4 | 0 | 1 | 2 | 3 | 4 | 5 | 9 | | |
| Glomerulus, Amyloid | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Renal Tubule, Cyst | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Urinary Bladder | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Fibrosis | | | | | | | | | 4 | | | | | | | | | | | | | | | | 1 4.0 | |
| Ulcer | | | | | | | | | 4 | | | | | | | | | | | | | | | | 1 4.0 | |

* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade
 + .. Tissue examined microscopically
 X .. Lesion present
 I .. Insufficient tissue
 M .. Missing tissue
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Experiment Number: 00058 - 04
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 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------------------|
| | 0733 | 0731 | 0382 | 0666 | 0693 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0773 | 0676 | 0776 | 0776 | 0676 | 0776 | 0776 | 0776 | 0776 | | |
| 1000 mg/kg | 0081 | 0082 | 0083 | 0084 | 0085 | 0089 | 0081 | 0082 | 0083 | 0084 | 0085 | 0087 | 0088 | 0089 | 0090 | 0091 | 0092 | 0093 | 0094 | 0095 | 0096 | 0097 | 0098 | 0099 | |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | | | 4 | | | | | | | | | | 1 | | | 2 | |
| Peyer's Patch, Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | 2 | |
| Clear Cell Focus | | X | | | | | | | | | | | | | | | | | | | | | |
| Eosinophilic Focus | | | | | | | | | | | | | | | | | | | | | | X | |
| Extramedullary Hematopoiesis | | | | | | | | | | | | 1 | 1 | | | | | | | | | | |
| Fatty Change | | | | | | | | | | | | | | | | | | | | | | | |
| Hemorrhage | | | | | | | | | | | | | | | | | | 1 | | | | | |
| Hepatodiaphragmatic Nodule | | | | | | | | | | | | | | | | | | | | | | | |
| Mixed Cell Focus | | | | | | | | | | | | | | | | | | | | | | X | |
| Necrosis | | | | | | | | | 1 | | | 1 | | 1 | 1 | | | | | 1 | | | |

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

| B6C3F1/N MICE FEMALE | DAY ON TEST | | | | | | | | | | | | | | | | | | | | ANIMAL ID | females
(cont...) | |
|----------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----------|----------------------|------|
| | 0733 | 0733 | 0738 | 0736 | 0766 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | | 0777 |
| 1000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 000281 | |

| | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mesentery | | | | | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary Glands
Polyarteritis Nodosa
Duct, Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, Forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, Glandular
Mineral | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

CARDIOVASCULAR SYSTEM

| | | | | | | | | | | | | | | | | | | | | | |
|--|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Aorta | | | | | | | | | | | | | | | | | | | | | |
| Blood Vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart
Cardiomyopathy
Valve, Inflammation, Chronic Active | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

ENDOCRINE SYSTEM

| | | | | | | | | | | | | | | | | | | | | | |
|---------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Adrenal Cortex
Hypertrophy, Focal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adrenal Medulla
Hyperplasia, Focal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

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

Experiment Number: 00058 - 04

Test Type: CHRONIC

Route: GAVAGE

Species/Strain: MICE/B6C3F1/N

P09: NON-NEOPLASTIC LESIONS BY INDIVIDUAL ANIMAL

Black Cohosh

CAS Number: 84776-26-1

Date Report Requested: 12/10/2020

Time Report Requested: 11:32:38

First Dose M/F: NA / 04/09/12

Lab: BAT

| B6C3F1/N MICE FEMALE
1000 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | | | females
(cont...) |
|--|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|--|----------------------|
| | 0733 | 0733 | 0738 | 0736 | 0766 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | |
| ANIMAL ID | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | 0000 | | |
| Islets, Pancreatic Hyperplasia | 1 | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid Gland | | | | | | | | M | | M | | | M | | | | | | | M | | | | | |
| Pituitary Gland
Pars Distalis, Hyperplasia, Focal
Pars Distalis, Hypertrophy | 3 | | | | | | | | | | | | | | | | | | | | | | | | |
| Thyroid Gland
Cyst, Congenital
Bilateral, Follicle, Dilation
Follicle, Dilation | | | | X | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clitoral Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | | |
| Atrophy | 4 | | | 3 | 4 | | 2 | 3 | | 2 | | 2 | 1 | 2 | | 1 | 4 | 2 | | 2 | 2 | | 2 |
| Cyst, Epithelial | | | | | | | | | | | | | | | | | X | | | | | | X |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | 1 | | |
| Thrombus | | | | | | | | | | | | | | | | | | | | | X | | |
| Bilateral, Follicle, Cyst | | | | X | | | | | | | | | | | | | | | | | | | |
| Bursa, Cyst | | | | | | | | | | | | | | | | | | | | | | | |
| Follicle, Cyst | | | | | | | X | X | X | | | | X | | | 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:

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Experiment Number: 00058 - 04
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 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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 Black Cohosh
 CAS Number: 84776-26-1

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
1000 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | ANIMAL ID | females
(cont...) | |
|------------------------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----------|----------------------|------|
| | 0733 | 0738 | 0736 | 0766 | 0776 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | | 0777 |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002881 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002882 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002883 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002884 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002885 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002889 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002891 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002892 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002893 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002894 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002895 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002896 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002897 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002898 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002899 | |
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0002900 | |

| | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gliosis | | | | | | | | | | | | | | | | | | | | | | 2 | |
| Hydrocephalus | | | | | | | | | | | | | | | | | | | | | | | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | 2 | | | | | | | | | | | | | | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | 2 | 2 | | |
| Peripheral Nerve | | | | | | | | | | | | | | | | | | | | | | | |
| Axon, Sciatic, Degeneration | | | | | | | | | | | | | | | | | | | | | | | |
| Spinal Cord | | | | | | | | | | | | | | | | | | | | | | | |
| Axon, Degeneration | | | | | | | | | | | | | | | | | | | | | | | |

RESPIRATORY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | |
| Alveolus, Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Olfactory Epithelium, Atrophy | | | | | | | | | | | | | | | | | | | | | | | |
| Olfactory Epithelium, Metaplasia, Respiratory | | | | | | | | | | | | | | | | | | | | | | | |
| Respiratory Epithelium, Accumulation, Hyaline Droplet | | | | | | | | | | | | | | | | | | | | | | | |
| Respiratory Epithelium, Hyperplasia | 1 | 1 | | 1 | | | | | 1 | | | 1 | | 1 | | | | | | | | 1 | |
| Respiratory Epithelium, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | | |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

SPECIAL SENSES SYSTEM

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

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| DAY ON TEST | B6C3F1/N MICE FEMALE | | | | | | | | | | | | | | | | | | | | * TOTALS | | | |
|-------------|----------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|---|---|---|
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | |
| 7 | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 1 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 6 | 5 | 7 | 7 |
| 3 | 3 | 3 | 3 | 7 | 2 | 3 | 7 | 3 | 3 | 4 | 3 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 6 | 8 | 1 | 2 |
| 0 | 3 | 2 | 3 | 0 | 9 | 0 | 1 | 0 | 2 | 8 | 2 | 9 | 2 | 9 | 0 | 3 | 2 | 1 | 9 | 3 | 6 | 9 | 6 | 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 | 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 |
| 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |
| 3 | 4 | 5 | 6 | 7 | 8 | 4 | 5 | 6 | 7 | 8 | 0 | 1 | 3 | 4 | 5 | 7 | 8 | 0 | 1 | 2 | 5 | 6 | 9 | 0 |

ALIMENTARY SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------|
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Large, Rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine Small, Jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Peyer's Patch, Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | 2 | 4 2.3 |
| Peyer's Patch, Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Clear Cell Focus | | | | X | | | | | | | | | | | | | | X | | | | | X | 4 |
| Eosinophilic Focus | | | | | | | | | | | | | X | X | | | | | | | X | | | 4 |
| Extramedullary Hematopoiesis | | | | | | | | | | | | | | | | | | | | | | | | 2 1.0 |
| Fatty Change | | | | | | | | | | | | | | | | | | | 1 | | | | | 1 1.0 |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| Hepatodiaphragmatic Nodule | | | | | | | X | | | | | | | | | | | | | | | | | 1 |
| Mixed Cell Focus | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Necrosis | | | | | | | | 2 | | | | | | | | | | | | | 1 | 1 | | 8 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
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1-4 .. Lesion qualified as:
 1) Minimal 3) Moderate
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Experiment Number: 00058 - 04
Test Type: CHRONIC
Route: GAVAGE
Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
Time Report Requested: 11:32:38
First Dose M/F: NA / 04/09/12
Lab: BAT

| B6C3F1/N MICE FEMALE
1000 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | | | | | | | | | | | | | | | | | | |
|--|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----------------|
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | |
| | 7 | 7 | 7 | 7 | 4 | 7 | 7 | 1 | 7 | 7 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | | | | | | | | | | | | | | | | | | | | | | |
| | 3 | 3 | 3 | 3 | 7 | 2 | 3 | 7 | 3 | 3 | 4 | 3 | 2 | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 2 | 3 | | | | | | | | | | | | | | | | | | | | | | |
| | 0 | 3 | 2 | 3 | 0 | 9 | 0 | 1 | 0 | 2 | 8 | 2 | 9 | 2 | 9 | 0 | 3 | 2 | 1 | 9 | 3 | 6 | | | | | | | | | | | | | | | | | | | | | | |
| | 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 | | | | | | | | | | | | | | | | | | | | | | |
| | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | | | | | | | | | | | | | | | | | | | | | | |
| | 3 | 4 | 5 | 6 | 7 | 8 | 4 | 5 | 6 | 7 | 8 | 0 | 1 | 3 | 4 | 5 | 7 | 8 | 0 | 1 | 2 | 5 | * TOTALS | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | | | | | | | | | | | | | | | | | | | | | + | 1 | | | | | | | | | | | | | | | | | | | |
| Pancreas | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Salivary Glands
Polyarteritis Nodosa
Duct, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 1.0
1 4.0 |
| Stomach, Forestomach | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Stomach, Glandular
Mineral | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 |
| CARDIOVASCULAR SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Aorta | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Blood Vessel | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | | + | + | + | + | + | + | + | + | + | + | 49 | |
| Heart
Cardiomyopathy
Valve, Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 12 1.0
1 3.0 |
| ENDOCRINE SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal Cortex
Hypertrophy, Focal | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 1.0 |
| Adrenal Medulla
Hyperplasia, Focal | | | | | | | | | | | | | | | | | | | | | | | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 1.0 |

* .. 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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| B6C3F1/N MICE FEMALE
1000 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | |
|------------------------------------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|-------|-------|------|
| | 0730 | 0733 | 0732 | 0733 | 0737 | 0732 | 0733 | 0737 | 0731 | 0737 | 0737 | 0735 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0736 | | 0735 | 0737 | 0737 |
| ANIMAL ID | 00313 | 00333 | 00302 | 00303 | 00301 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | |
| Islets, Pancreatic Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | |
| Parathyroid Gland | + | + | M | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | M | 42 |
| Pituitary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Pars Distalis, Hyperplasia, Focal | 2 | 1 | 1 | | | | | | | 2 | | | | | | | 1 | | | 1 | | | 8 1.6 | |
| Pars Distalis, Hypertrophy | | | | | | 1 | | | | | | | | | | 1 | | | | | | | 4 1.0 | |
| Thyroid Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Cyst, Congenital | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Bilateral, Follicle, Dilatation | | | | | | | | | | | | 1 | | | | | | | | | | | 1 1.0 | |
| Follicle, Dilatation | | | | | | | | | | | | | 1 | 1 | | | | | 1 | | | | 5 1.4 | |

GENERAL BODY SYSTEM

NONE

GENITAL SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------|----|
| Clitoral Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | 49 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Angiectasis | | | | | | | | | | | | | | 1 | | | | | | | | | | 1 1.0 | |
| Atrophy | 2 | | | 4 | 4 | 3 | | 2 | 3 | | | 2 | | 3 | 2 | | | | 2 | 2 | 4 | 4 | 4 | 30 2.6 | |
| Cyst, Epithelial | X | X | | | | | | | | | | X | | | | | X | | | | | | | 6 | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | 1 1.0 | |
| Thrombus | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Bilateral, Follicle, Cyst | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Bursa, Cyst | | | | | | | | | | | | | X | | | | | | | | | | | 1 | |
| Follicle, Cyst | | | | X | | | | | | | | | | | | | | | | X | | | | 8 | |

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

+ .. Tissue examined microscopically

X .. Lesion present

I .. Insufficient tissue

M .. Missing tissue

A .. Autolysis precludes evaluation

BLANK .. Not examined microscopically

1-4 .. Lesion qualified as:

1) Minimal 3) Moderate

2) Mild 4) Marked

Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
1000 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | |
|------------------------------------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|----------|------|------|
| | 0730 | 0733 | 0732 | 0733 | 0737 | 0732 | 0730 | 0731 | 0737 | 0737 | 0735 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0737 | 0736 | 0735 | | 0737 | 0737 |
| ANIMAL ID | 0001 | 0003 | 0001 | 0003 | 0001 | 0002 | 0002 | 0002 | 0002 | 0003 | 0003 | 0001 | 0001 | 0003 | 0003 | 0003 | 0001 | 0002 | 0002 | 0001 | 0002 | 0004 | |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------------------|--|--|--|--|--|--|--|--|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|-----|
| Germinal Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Interstitial Cell, Hyperplasia | | | | | | | | | 2 | | | | | | | | | | | | | | | 1 | 2.0 |
| Rete Ovarii, Cyst | | | | | | | | | | | | | | | | | | | | | | | | X | 1 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Angiectasis | | | | | 2 | | | | | | | | | | | | 2 | | | | | | | 3 | 2.0 | |
| Hemorrhage | | | | | | | | | | | | | | | | | | | | | | | | 1 | 2.0 | |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 | |
| Endometrium, Hyperplasia, Cystic | 1 | 1 | 3 | 3 | 2 | 2 | 2 | | 3 | 3 | 1 | 1 | 3 | 3 | 3 | 1 | 2 | 2 | 2 | 2 | 4 | | 2 | 1 | 45 | 2.3 |
| Endometrium, Metaplasia, Squamous | | | | | | | | | | | | | | | | | | 1 | | | | | | | 1 | 1.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Vagina | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Congestion | | | | | 3 | | | | | | | | | | | | | | | | | | | 1 | 3.0 |
| Inflammation, Acute | | | | | | | | | | | | | | | | 1 | | | | 1 | | | | 3 | 1.3 |
| Polyarteritis Nodosa | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Epithelium, Hyperplasia, Squamous | | | 1 | 1 | 2 | | | 4 | 2 | 1 | 3 | | 2 | 4 | | 3 | 2 | 1 | | 4 | 3 | 3 | 1 | 33 | 2.4 |

HEMATOPOIETIC SYSTEM

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|
| Bone Marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | |
| Angiectasis | | | | | | | | | | | | | | | | | | | | | | 3 | | 1 | 3.0 |
| Hypercellularity | | | | | | | | | | | | | | | | | | | | | | | 4 | 3 | 3.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------------------|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|---|-----|
| Lymph Node | | | | | | | | | | | | | | | | | | | | | | | | 7 | | |
| Lumbar, Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | + | 1 | 4.0 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|-----|-----|
| Lymph Node, Mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Hyperplasia, Lymphocyte | | | | | 2 | | | | | | | | | | | | | | | | | | | 3 | 7 | 2.6 |
| Infiltration Cellular, Plasma Cell | | | | | | | | | | | | | | | | | | | | | | | | 1 | 4.0 | |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|--|
| Lymph Node, Mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 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
 M .. Missing tissue
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 BLANK .. Not examined microscopically
 1-4 .. Lesion qualified as:
 1) Minimal 3) Moderate
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Experiment Number: 00058 - 04
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: MICE/B6C3F1/N

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

Date Report Requested: 12/10/2020
 Time Report Requested: 11:32:38
 First Dose M/F: NA / 04/09/12
 Lab: BAT

| B6C3F1/N MICE FEMALE
1000 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | | | | | | |
|---|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|----|-------|-------|-------|
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| ANIMAL ID | 0
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5 | 0
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6 | 0
0
3
1
7 | 0
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3
1
8 | 0
0
3
2
4 | 0
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3
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5 | 0
0
3
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6 | 0
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3
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7 | 0
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8 | 0
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9 | 0
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0 | 0
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6 | 0
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8 | 0
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9 | 0
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0 | | | | |
| Atrophy | | | | | | | | | | | | | | | | | | | | | | | | 4 | 1 4.0 | | |
| Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 7 2.4 | |
| Infiltration Cellular, Histiocyte | | | | | | | | | | | | | | | | | | | | | | | | | 3 | 1 4.0 | |
| Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 1 2.0 | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | | |
| Extramedullary Hematopoiesis, Increased | | | | | | | | | | | | | | | | | | | | | | | | | X | 11 | |
| Hyperplasia, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 7 1.7 | |
| Pigment | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1 1.0 | |
| White Pulp, Atrophy | | | | | | | | | | | | | | | | | | | | | | | | | 4 | 2 4.0 | |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 | |
| INTEGUMENTARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary Gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Galactocele | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | |
| Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1.0 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Ulcer | | | | | | | | | | | | | | | | | | | | | | | | | | 3 | 2 3.5 |
| MUSCULOSKELETAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | | |
| Fibro-Osseous Lesion | | | | | | | | | | | | | | | | | | | | | | | | | | 1 | 7 1.1 |
| Increased Bone | | | | | | | | | | | | | | | | | | | | | | | | | X | 1 | |
| Skeletal Muscle | | | | | | | | | | | | | | | | | | | | | | | | | | + | 1 |
| NERVOUS SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | |

* .. Total animals with tissue examined microscopically; Total animals with lesion and mean severity grade
 + .. Tissue examined microscopically
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Experiment Number: 00058 - 04
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 Black Cohosh
 CAS Number: 84776-26-1

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 Lab: BAT

| B6C3F1/N MICE FEMALE
1000 mg/kg | DAY ON TEST | | | | | | | | | | | | | | | | | | | | * TOTALS | |
|---|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|--------|
| | 0730 | 0733 | 0732 | 0733 | 0770 | 0779 | 0771 | 0777 | 0773 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | 0777 |
| ANIMAL ID | 00313 | 00333 | 00332 | 00333 | 00330 | 00339 | 00331 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | 00330 | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gliosis | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Hydrocephalus | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Polyarteritis Nodosa | | | | | | | | | | | | | | 1 | | | | | | | | 3 1.7 |
| Peripheral Nerve | | | | | | | | | | | | | | | | | | | | | | 1 |
| Axon, Sciatic, Degeneration | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Spinal Cord | | | | | | | | | | | | | | | | | | | | | | 1 |
| Axon, Degeneration | | | | | | | | | | | | | | | | | | | | | | 1 1.0 |
| RESPIRATORY SYSTEM | | | | | | | | | | | | | | | | | | | | | | |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Inflammation, Chronic Active | | | | | | | | | | | | | | | | | | | 1 | | | 1 1.0 |
| Alveolus, Epithelium, Hyperplasia | | | | | | | | | | | | | | | | | | | | | | 1 3.0 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Olfactory Epithelium, Atrophy | | | | | | | 1 | | | | | | | | | | | | | 2 | | 3 1.3 |
| Olfactory Epithelium, Metaplasia, Respiratory | | | | | | | | | | | | | | | | | | | | | | 3 1.0 |
| Respiratory Epithelium, Accumulation, Hyaline Droplet | | 1 | | | | 2 | | | | | | | | 1 | 1 | | 1 | 1 | | 3 | 1 | 10 1.3 |
| Respiratory Epithelium, Hyperplasia | | 1 | 1 | | | 2 | | | 1 | | | | | 1 | 1 | 1 | 1 | | | | 1 | 18 1.1 |
| Respiratory Epithelium, Inflammation, Acute | | | | | | | | | | | | | | | | | | | | | | 1 2.0 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| SPECIAL SENSES 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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|------------------------------------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|-------|-------|---------|-------|--|
| | 0730 | 0733 | 0732 | 0733 | 0740 | 0772 | 0773 | 0771 | 0777 | 0775 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | 0777 | | 0777 | 0777 | 0777 | | |
| ANIMAL ID | 00313 | 00333 | 00332 | 00333 | 00330 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | 00300 | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | 1 | | |
| Eye
Lens, Cataract | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
1 | 1 1.0 | |
| Harderian Gland
Hyperplasia | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50
2 | 3 2.3 | |
| URINARY SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney
Glomerulosclerosis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 | 1 1.0 | |
| Infiltration Cellular, Lymphocyte | | | | | | | | | | | | | | | | | | | | | | | | 1 | 1 2.0 | |
| Nephropathy, Chronic Progressive | | | | | 1 | | | 1 | | | | | | 1 | | 1 | 1 | | | 1 | | 1 | 3 | 17 | 1.4 | |
| Urinary Bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 | | |

*** END OF REPORT ***

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