

TDMS No. 20007 - 06

**P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH
AVERAGE SEVERITY GRADES[b]**

Date Report Requested: 04/13/2009

Test Type: CHRONIC

Kava kava extract

Time Report Requested: 10:57:30

Route: GAVAGE

CAS Number: 9000-38-8

First Dose M/F: 08/24/04 / 08/23/04

Species/Strain: MICE/B6C3F1

Lab: BAT

F_M3

C Number: C20007
Lock Date: 05/10/2007
Cage Range: ALL
Date Range: ALL
Reasons For Removal: ALL
Removal Date Range: ALL
Treatment Groups: Include ALL
Study Gender: Both
TDMSE Version: 2.1.0

Test Type: CHRONIC

Kava kava extract

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Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE MALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Disposition Summary				
Animals Initially in Study	50	50	50	50
Early Deaths				
Moribund Sacrifice	3	10	10	7
Natural Death	13	7	5	7
Survivors				
Moribund Sacrifice			1	
Natural Death	1			
Terminal Sacrifice	33	33	34	36
Animals Examined Microscopically	50	50	50	50

ALIMENTARY SYSTEM

Gallbladder	(49)	(50)	(49)	(47)
Infiltration Cellular, Mononuclear Cell	1 [1.0]		1 [1.0]	1 [1.0]
Inflammation, Granulomatous			1 [2.0]	
Intestine Large, Cecum	(50)	(50)	(50)	(50)
Amyloid Deposition	1 [2.0]			
Serosa, Inflammation, Granulomatous	1 [2.0]			
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Intestine Small, Ileum	(50)	(50)	(50)	(50)
Inflammation, Chronic	1 [2.0]		1 [2.0]	
Epithelium, Hyperplasia	1 [2.0]			
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Epithelium, Hyperplasia		2 [3.0]		
Peyer's Patch, Hyperplasia, Lymphoid			1 [3.0]	1 [4.0]
Liver	(50)	(50)	(50)	(50)
Amyloid Deposition			1 [3.0]	1 [3.0]
Angiectasis	3 [1.0]	6 [1.0]	7 [1.1]	10 [1.7]
Basophilic Focus	2	3	3	1
Clear Cell Focus	18	18	19	21
Degeneration, Cystic	1 [1.0]		1 [1.0]	1 [1.0]
Eosinophilic Focus	28	32	42	43
Fatty Change	32 [1.3]	34 [1.3]	27 [1.2]	24 [1.3]
Fibrosis	1 [2.0]			
Hematopoietic Cell Proliferation	1 [2.0]	2 [2.5]		1 [2.0]
Hepatodiaphragmatic Nodule			1	

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

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Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE MALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Infarct		1 [3.0]	2 [2.5]	
Infiltration Cellular, Mononuclear Cell	49 [1.0]	47 [1.1]	47 [1.0]	48 [1.1]
Inflammation, Suppurative				1 [3.0]
Mineralization	1 [1.0]	2 [1.5]	2 [1.5]	1 [2.0]
Mixed Cell Focus	15	28	15	12
Necrosis	3 [1.7]	10 [2.0]	7 [2.0]	13 [2.0]
Tension Lipidosis	5	2	3	2
Vacuolization Cytoplasmic		1 [2.0]		1 [2.0]
Bile Duct, Cyst				1 [2.0]
Centrilobular, Fatty Change		1 [3.0]		1 [4.0]
Centrilobular, Hypertrophy		34 [1.0]	30 [2.0]	39 [2.0]
Mesentery	(3)	(6)	(2)	(3)
Inflammation, Chronic	1 [3.0]			
Fat, Necrosis	2 [2.0]	6 [2.2]	2 [2.0]	3 [2.7]
Pancreas	(50)	(50)	(50)	(50)
Inflammation, Granulomatous			1 [1.0]	
Inflammation, Chronic			1 [2.0]	
Acinus, Atrophy	1 [4.0]		1 [3.0]	
Acinus, Hypertrophy	2 [1.5]			
Duct, Cyst				1
Salivary Glands	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	43 [1.1]	36 [1.1]	40 [1.0]	36 [1.1]
Parotid Gland, Atrophy	1 [2.0]			
Parotid Gland, Hyperplasia			1 [2.0]	
Parotid Gland, Mineralization		1 [1.0]		
Submandibular Gland, Atrophy		1 [2.0]		
Stomach, Forestomach	(50)	(50)	(50)	(50)
Inflammation, Chronic	19 [1.7]	22 [1.6]	24 [1.6]	24 [1.5]
Mineralization			1 [1.0]	
Necrosis	8 [2.0]	11 [1.9]	12 [2.3]	10 [1.8]
Epithelium, Hyperplasia	18 [2.3]	22 [1.6]	25 [2.0]	22 [1.8]
Stomach, Glandular	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	2 [1.0]		2 [1.0]	1 [1.0]
Mineralization		1 [1.0]		
Ulcer	1 [2.0]			
Epithelium, Hyperplasia	2 [2.0]			
Glands, Ectasia	2 [1.0]	1 [1.0]	2 [1.0]	2 [1.5]
Tooth	(33)	(32)	(27)	(21)
Dysplasia	33 [2.3]	32 [2.1]	27 [2.4]	21 [1.5]
Inflammation, Suppurative		1 [3.0]		

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b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

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Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE MALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	14 [1.2]	16 [1.1]	11 [1.3]	14 [1.1]
Inflammation, Suppurative		1 [2.0]		1 [2.0]
Inflammation, Chronic		1 [3.0]		
Artery, Infiltration Cellular, Mononuclear Cell	2 [1.0]	1 [1.0]	1 [1.0]	1 [1.0]
Myocardium, Mineralization	1 [2.0]	4 [1.0]		1 [2.0]
Valve, Inflammation				1 [4.0]
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Hypertrophy	1 [1.0]	2 [1.0]		2 [1.0]
Infiltration Cellular, Mononuclear Cell	1 [1.0]			
Vacuolization Cytoplasmic	2 [1.5]	2 [1.0]	2 [1.5]	3 [1.0]
Subcapsular, Hyperplasia	44 [1.3]	45 [1.3]	48 [1.3]	49 [1.3]
Zona Reticularis, Hyperplasia	5 [2.0]	3 [1.7]	2 [1.5]	4 [2.3]
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia	1 [2.0]		1 [2.0]	
Islets, Pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	37 [1.9]	35 [1.7]	36 [1.8]	33 [1.3]
Parathyroid Gland	(47)	(44)	(46)	(44)
Cyst	1 [1.0]	1 [2.0]		1 [1.0]
Infiltration Cellular, Mononuclear Cell	1 [2.0]			
Pituitary Gland	(49)	(50)	(50)	(50)
Cyst	1 [1.0]		1 [1.0]	2 [1.0]
Pars Distalis, Hyperplasia	1 [2.0]		1 [2.0]	
Thyroid Gland	(50)	(50)	(49)	(50)
Atrophy	1 [3.0]			
Cyst	4 [1.8]		1 [1.0]	
Follicle, Hyperplasia	1 [2.0]		1 [1.0]	
GENERAL BODY SYSTEM				
Peritoneum	(0)	(0)	(0)	(2)

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Lab: BAT

B6C3F1 MICE MALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Inflammation, Chronic				2 [2.5]
GENITAL SYSTEM				
Coagulating Gland	(0)	(1)	(1)	(0)
Hyperplasia		1 [2.0]		
Epididymis	(50)	(50)	(50)	(50)
Granuloma Sperm	2 [2.5]		3 [2.3]	1 [2.0]
Infiltration Cellular, Mononuclear Cell	29 [1.0]	22 [1.2]	33 [1.0]	28 [1.0]
Inflammation, Chronic		1 [2.0]		
Penis	(0)	(1)	(0)	(0)
Infiltration Cellular, Polymorphonuclear		1 [1.0]		
Preputial Gland	(50)	(50)	(50)	(50)
Cyst	4 [2.0]	5 [2.0]	5 [2.2]	3 [2.3]
Inflammation	10 [2.1]	4 [1.0]	9 [1.7]	13 [1.3]
Prostate	(50)	(50)	(50)	(50)
Atrophy				1 [3.0]
Fibrosis			1 [1.0]	
Hyperplasia	1 [1.0]			1 [2.0]
Infiltration Cellular, Mononuclear Cell	29 [1.0]	31 [1.0]	38 [1.0]	29 [1.0]
Inflammation	4 [2.0]	9 [2.1]	4 [1.8]	2 [2.5]
Mineralization		1 [1.0]		
Seminal Vesicle	(50)	(50)	(50)	(50)
Atrophy				1 [3.0]
Fibrosis	2 [1.5]			
Hyperplasia				1 [2.0]
Infiltration Cellular, Mononuclear Cell	4 [1.0]	4 [1.0]	6 [1.0]	
Inflammation	6 [1.0]	5 [1.4]		2 [1.5]
Testes	(50)	(50)	(50)	(50)
Inflammation	1 [2.0]			
Mineralization	1 [1.0]			
Germinal Epithelium, Atrophy	2 [2.0]	4 [2.0]	1 [2.0]	1 [2.0]
HEMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(50)
Lymph Node	(0)	(1)	(3)	(3)
Renal, Hyperplasia, Lymphoid			1 [4.0]	
Lymph Node, Mandibular	(50)	(50)	(50)	(49)

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Lab: BAT

B6C3F1 MICE MALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Hyperplasia, Lymphoid Lymph Node, Mesenteric Atrophy	(50) 1 [3.0]	3 [3.3] (50)	2 [3.0] (50)	1 [3.0] (49)
Hyperplasia, Lymphoid Spleen	(50)	1 [3.0] (50)	2 [3.0] (49)	(50)
Angiectasis Hematopoietic Cell Proliferation	16 [2.4]	19 [1.9]	21 [2.0]	15 [2.1]
Hyperplasia, Lymphoid Lymphoid Follicle, Atrophy	3 [2.0] 6 [2.7]	3 [2.0] 5 [2.4]	2 [3.0] 3 [1.3]	3 [1.3] 6 [3.0]
Thymus Atrophy	(48) 41 [2.7]	(47) 41 [2.8]	(47) 46 [3.1]	(49) 43 [2.8]
Ectopic Thyroid Hyperplasia, Histiocytic Infiltration Cellular, Histiocyte	1 [3.0]	1 [2.0]	2 [2.0]	
Inflammation, Chronic Active Epithelial Cell, Hyperplasia		1 [2.0]		1 [3.0] 1 [2.0]
INTEGUMENTARY SYSTEM				
Skin	(50)	(50)	(50)	(50)
Cyst Epithelial Inclusion Hemorrhage			2 [1.5]	1 [3.0]
Inflammation, Chronic Ulcer	1 [2.0] 1 [3.0]	1 [3.0] 1 [4.0]		1 [2.0] 4 [3.0]
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Cranium, Hyperostosis Skeletal Muscle	1 [2.0] (2)	(0)	(1)	(0)
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Hemorrhage Hypothalamus, Compression		1 [3.0]	1 [4.0]	
RESPIRATORY SYSTEM				

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Lab: BAT

B6C3F1 MICE MALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Lung	(50)	(50)	(50)	(50)
Inflammation		2 [1.5]	3 [1.3]	2 [1.0]
Metaplasia, Osseous			1 [1.0]	
Mineralization			2 [1.0]	
Alveolar Epithelium, Hyperplasia	2 [1.5]	3 [1.0]	1 [1.0]	2 [1.5]
Alveolus, Infiltration Cellular, Histiocyte	2 [1.5]	6 [1.8]	5 [2.2]	1 [3.0]
Bronchus, Hyperplasia	2 [2.0]	2 [1.0]		1 [2.0]
Bronchus, Infiltration Cellular, Histiocyte			1 [1.0]	
Nose	(50)	(50)	(50)	(50)
Inflammation, Suppurative	1 [2.0]	1 [1.0]	4 [1.5]	1 [2.0]
Inflammation, Chronic	9 [1.0]	8 [1.0]	7 [1.0]	5 [1.2]
Polyp, Inflammatory		2 [2.0]		1 [2.0]
Nasolacrimal Duct, Inflammation, Suppurative	1 [2.0]	2 [2.0]	2 [1.5]	3 [1.7]
Respiratory Epithelium, Hyperplasia	1 [2.0]		1 [1.0]	
Trachea	(50)	(50)	(50)	(50)
Inflammation, Chronic		1 [2.0]	1 [2.0]	
Epithelium, Cytoplasmic Alteration			1 [2.0]	
SPECIAL SENSES SYSTEM				
Eye	(50)	(50)	(50)	(50)
Degeneration		1 [4.0]		
Anterior Chamber, Inflammation, Suppurative				1 [3.0]
Cornea, Inflammation, Chronic		1 [3.0]	1 [2.0]	2 [1.5]
Retrolbulbar, Inflammation, Chronic				1 [2.0]
Harderian Gland	(50)	(50)	(50)	(50)
Fibrosis	1 [2.0]			
Hyperplasia	4 [2.0]	3 [2.3]	1 [4.0]	8 [1.9]
Infiltration Cellular, Mononuclear Cell	36 [1.1]	30 [1.0]	34 [1.0]	39 [1.0]
Inflammation, Granulomatous			1 [2.0]	
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Amyloid Deposition			1 [1.0]	
Hydronephrosis	6 [2.2]	1 [3.0]		1 [3.0]
Inflammation	2 [3.0]	2 [2.0]	1 [3.0]	1 [3.0]

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Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE MALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Metaplasia, Osseous Mineralization	3 [1.0]	2 [2.0]		2 [1.5]
Nephropathy	32 [1.4]	40 [1.3]	37 [1.3]	38 [1.3]
Thrombosis		1 [2.0]		
Cortex, Medulla, Necrosis	6 [3.2]			
Papilla, Necrosis	3 [2.0]			3 [1.0]
Renal Tubule, Cyst			3 [1.7]	
Renal Tubule, Dilatation		1 [2.0]		
Renal Tubule, Hyperplasia	6 [1.3]	20 [1.1]	13 [1.3]	10 [1.1]
Renal Tubule, Mineralization	31 [1.1]	42 [1.0]	38 [1.0]	31 [1.0]
Renal Tubule, Pigmentation, Lipofuscin	1 [2.0]		1 [2.0]	2 [2.5]
Urethra	(2)	(4)	(0)	(1)
Cyst		1 [3.0]		
Inflammation	2 [2.5]	4 [2.3]		1 [3.0]
Necrosis				1 [3.0]
Urinary Bladder	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	20 [1.0]	25 [1.1]	26 [1.0]	20 [1.0]
Inflammation	4 [2.0]	2 [2.5]		
Transitional Epithelium, Cytoplasmic Alteration				1 [2.0]
Transitional Epithelium, Hyperplasia		1 [4.0]		

*** END OF MALE ***

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B6C3F1 MICE FEMALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Disposition Summary				
Animals Initially in Study	50	50	50	50
Early Deaths				
Accidently Killed	1			1
Moribund Sacrifice	4	4	1	7
Natural Death	7	12	4	5
Survivors				
Terminal Sacrifice	38	34	45	37
Animals Examined Microscopically	50	50	50	50
ALIMENTARY SYSTEM				
Esophagus	(50)	(50)	(50)	(50)
Inflammation, Chronic		1 [2.0]		
Gallbladder	(50)	(48)	(49)	(50)
Cyst	1 [1.0]	1 [1.0]		1 [1.0]
Epithelium, Cytoplasmic Alteration				1 [2.0]
Intestine Large, Cecum	(50)	(50)	(50)	(50)
Inflammation, Chronic	1 [1.0]			
Intestine Small, Duodenum	(50)	(50)	(50)	(50)
Metaplasia, Squamous				1 [1.0]
Epithelium, Hyperplasia			1 [2.0]	
Intestine Small, Ileum	(50)	(50)	(50)	(50)
Inflammation, Chronic Active			1 [2.0]	
Ulcer			1 [1.0]	
Intestine Small, Jejunum	(50)	(50)	(50)	(50)
Epithelium, Hyperplasia				1 [3.0]
Peyer's Patch, Hyperplasia			1 [4.0]	
Liver	(50)	(50)	(50)	(50)
Angiectasis	3 [1.0]		2 [1.0]	
Basophilic Focus		1	4	1
Clear Cell Focus	3		1	5
Cyst			1 [1.0]	
Eosinophilic Focus	9	7	16	26
Fatty Change	39 [1.6]	33 [1.5]	42 [1.3]	23 [1.3]
Hematopoietic Cell Proliferation	1 [2.0]	4 [1.3]	4 [1.3]	1 [2.0]
Infiltration Cellular, Mononuclear Cell	45 [1.1]	47 [1.1]	49 [1.1]	44 [1.1]

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Lab: BAT

B6C3F1 MICE FEMALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Mixed Cell Focus	12	13	14	7
Necrosis	5 [1.6]	4 [1.3]	5 [1.2]	1 [1.0]
Tension Lipidosis	3	8	7	4
Vacuolization Cytoplasmic				1 [2.0]
Centrilobular, Hypertrophy		20 [1.0]	48 [1.9]	49 [2.0]
Mesentery	(8)	(10)	(5)	(6)
Fat, Necrosis	8 [2.6]	10 [2.9]	5 [2.6]	6 [2.3]
Pancreas	(49)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell				1 [1.0]
Inflammation, Chronic	2 [1.0]			
Acinus, Atrophy			1 [2.0]	
Acinus, Hypertrophy				1 [1.0]
Acinus, Vacuolization Cytoplasmic			1 [2.0]	
Duct, Cyst		1 [4.0]	1 [4.0]	1 [3.0]
Salivary Glands	(49)	(49)	(50)	(50)
Atrophy		1 [1.0]		
Infiltration Cellular, Mononuclear Cell	34 [1.1]	33 [1.1]	31 [1.1]	26 [1.0]
Duct, Submandibular Gland, Hyperplasia			1 [2.0]	
Parotid Gland, Hyperplasia				1 [2.0]
Stomach, Forestomach	(50)	(50)	(50)	(50)
Erosion		1 [2.0]	14 [3.1]	11 [2.7]
Inflammation, Chronic	3 [1.7]	6 [1.5]	21 [2.6]	22 [2.5]
Ulcer		2 [2.5]	3 [3.0]	6 [2.3]
Epithelium, Hyperplasia	3 [1.3]	6 [1.3]	23 [2.8]	24 [2.3]
Stomach, Glandular	(50)	(50)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	2 [1.0]	1 [1.0]		1 [2.0]
Mineralization	1 [1.0]			
Ulcer				2 [2.0]
Epithelium, Hyperplasia			1 [1.0]	2 [2.0]
Glands, Ectasia	1 [1.0]	1 [1.0]	2 [1.0]	
Tooth	(1)	(1)	(2)	(2)
Dysplasia	1 [1.0]	1 [1.0]	2 [1.0]	2 [1.0]

CARDIOVASCULAR SYSTEM

Blood Vessel	(50)	(50)	(50)	(50)
Mineralization		1 [2.0]		
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	2 [1.0]	1 [2.0]	4 [1.0]	1 [1.0]

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Lab: BAT

B6C3F1 MICE FEMALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Thrombosis		1 [4.0]		
Artery, Infiltration Cellular, Mononuclear Cell	1 [1.0]	4 [1.0]	3 [1.0]	
Myocardium, Mineralization		2 [2.0]		1 [2.0]
Valve, Inflammation		2 [4.0]		
ENDOCRINE SYSTEM				
Adrenal Cortex	(50)	(50)	(50)	(50)
Atrophy	1 [1.0]			
Mineralization	1 [1.0]			
Vacuolization Cytoplasmic	1 [1.0]		4 [1.8]	
Subcapsular, Hyperplasia	49 [1.9]	50 [2.0]	50 [2.0]	50 [1.9]
Zona Reticularis, Hyperplasia				1 [1.0]
Adrenal Medulla	(50)	(50)	(50)	(50)
Hyperplasia	1 [1.0]		2 [2.0]	2 [1.5]
Vacuolization Cytoplasmic				1 [1.0]
Islets, Pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	4 [1.3]	4 [1.0]	1 [2.0]	
Parathyroid Gland	(48)	(44)	(48)	(48)
Cyst		1 [1.0]		
Pituitary Gland	(50)	(50)	(49)	(50)
Angiectasis			1 [2.0]	
Cyst	1 [1.0]	1 [1.0]	2 [1.0]	1 [1.0]
Pars Distalis, Hyperplasia	4 [2.8]	4 [1.3]	7 [1.3]	5 [1.8]
Thyroid Gland	(50)	(50)	(50)	(50)
Cyst		1 [1.0]		
Ectopic Thymus	1 [1.0]			
Infiltration Cellular, Mononuclear Cell	1 [1.0]			
Follicle, Hyperplasia	1 [2.0]			
GENERAL BODY SYSTEM				
Tissue NOS	(0)	(0)	(0)	(1)
Inflammation, Chronic				1 [3.0]
GENITAL SYSTEM				

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Kava kava extract

Time Report Requested: 10:57:30

Route: GAVAGE

CAS Number: 9000-38-8

First Dose M/F: 08/24/04 / 08/23/04

Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE FEMALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Clitoral Gland	(49)	(48)	(50)	(50)
Inflammation	1 [1.0]			
Ovary	(49)	(50)	(50)	(50)
Angiectasis	1 [2.0]	1 [3.0]	2 [2.0]	1 [1.0]
Cyst	4 [1.7]	10 [1.0]	6 [1.3]	4 [1.0]
Hemorrhage	1 [3.0]			
Thrombosis		1 [4.0]	2 [3.5]	
Uterus	(50)	(50)	(50)	(50)
Inflammation, Suppurative	3 [1.3]	1 [2.0]		
Metaplasia, Squamous	1 [2.0]	2 [2.5]		
Endometrium, Hyperplasia, Cystic	42 [2.1]	44 [2.0]	42 [2.1]	36 [1.8]
Vagina	(0)	(0)	(0)	(1)
Vacuolization Cytoplasmic				1 [2.0]

HEMATOPOIETIC SYSTEM

Bone Marrow	(50)	(50)	(50)	(50)
Fibrosis		2 [2.0]	1 [2.0]	1 [1.0]
Necrosis				1 [2.0]
Lymph Node	(3)	(3)	(0)	(0)
Mediastinal, Hyperplasia, Lymphoid	1 [4.0]			
Mediastinal, Hyperplasia, Plasma Cell		1 [3.0]		
Lymph Node, Mandibular	(48)	(49)	(50)	(50)
Hyperplasia, Lymphoid	4 [3.3]	4 [2.0]	4 [2.0]	2 [2.5]
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)
Hyperplasia, Lymphoid				1 [2.0]
Hyperplasia, Plasma Cell		1 [3.0]		
Inflammation, Granulomatous				1 [3.0]
Spleen	(49)	(48)	(50)	(49)
Hematopoietic Cell Proliferation	26 [1.8]	24 [1.8]	20 [1.5]	10 [1.8]
Hyperplasia, Lymphoid	7 [1.6]	6 [1.8]	6 [2.0]	5 [2.0]
Lymphoid Follicle, Atrophy	4 [2.8]	2 [2.0]	4 [2.5]	2 [3.5]
Thymus	(50)	(50)	(49)	(47)
Atrophy	39 [2.6]	44 [2.1]	46 [1.7]	40 [2.1]
Hyperplasia, Histiocytic	1 [3.0]		2 [2.0]	1 [2.0]
Infiltration Cellular, Histiocyte	5 [2.4]			2 [2.5]
Epithelial Cell, Hyperplasia	1 [1.0]			

INTEGUMENTARY SYSTEM

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Kava kava extract

Time Report Requested: 10:57:30

Route: GAVAGE

CAS Number: 9000-38-8

First Dose M/F: 08/24/04 / 08/23/04

Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE FEMALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Mammary Gland	(50)	(49)	(50)	(50)
Hyperplasia	1 [2.0]			
Inflammation, Chronic Active	1 [2.0]			
Metaplasia, Squamous	1 [2.0]			
Skin	(50)	(50)	(50)	(50)
Fibrosis			1 [3.0]	
Inflammation, Chronic	1 [3.0]		1 [3.0]	
Ulcer	1 [4.0]	1 [4.0]		
Subcutaneous Tissue, Fibrosis		1 [2.0]		
Subcutaneous Tissue, Necrosis			1 [3.0]	
MUSCULOSKELETAL SYSTEM				
Bone	(50)	(50)	(50)	(50)
Fibrosis	15 [1.6]	8 [1.9]	7 [1.6]	9 [1.8]
Joint, Inflammation, Chronic		1 [1.0]		
Skeletal Muscle	(3)	(1)	(0)	(0)
NERVOUS SYSTEM				
Brain	(50)	(50)	(50)	(50)
Choroid Plexus, Infiltration Cellular, Mononuclear Cell	1 [1.0]			
Hypothalamus, Compression	2 [4.0]			
Peripheral Nerve	(1)	(0)	(0)	(1)
Infiltration Cellular, Mononuclear Cell	1 [2.0]			
Axon, Degeneration	1 [3.0]			1 [4.0]
Spinal Cord	(1)	(0)	(0)	(1)
Axon, Degeneration	1 [3.0]			
RESPIRATORY SYSTEM				
Lung	(50)	(50)	(50)	(50)
Hemorrhage	1 [3.0]			
Inflammation	1 [1.0]		2 [1.0]	
Inflammation, Acute		1 [2.0]		
Metaplasia, Osseous		1 [1.0]		
Mineralization		1 [1.0]		

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

Kava kava extract

Time Report Requested: 10:57:30

Route: GAVAGE

CAS Number: 9000-38-8

First Dose M/F: 08/24/04 / 08/23/04

Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE FEMALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
Alveolar Epithelium, Hyperplasia	3 [1.0]	1 [1.0]		1 [2.0]
Alveolus, Infiltration Cellular, Histiocyte		1 [2.0]		1 [1.0]
Serosa, Fibrosis		1 [1.0]		
Nose	(50)	(50)	(50)	(50)
Inflammation, Suppurative				1 [2.0]
Inflammation, Chronic	4 [1.3]	2 [1.0]		
Glands, Dilatation			1 [2.0]	
Nasolacrimal Duct, Inflammation, Suppurative			1 [2.0]	
Olfactory Epithelium, Degeneration	1 [2.0]			
Trachea	(50)	(50)	(50)	(50)
Inflammation, Chronic		1 [1.0]		
SPECIAL SENSES SYSTEM				
Eye	(50)	(50)	(50)	(50)
Anterior Chamber, Inflammation, Suppurative	1 [3.0]			
Harderian Gland	(50)	(49)	(50)	(50)
Atrophy	1 [1.0]		1 [1.0]	
Hyperplasia	3 [1.7]	4 [1.5]	5 [1.6]	5 [2.0]
Infiltration Cellular, Mononuclear Cell	38 [1.0]	42 [1.0]	42 [1.0]	38 [1.0]
URINARY SYSTEM				
Kidney	(50)	(50)	(50)	(50)
Amyloid Deposition	1 [1.0]	2 [1.0]	2 [1.0]	1 [2.0]
Hydronephrosis		1 [4.0]		
Inflammation	1 [1.0]	1 [2.0]		1 [3.0]
Metaplasia, Osseous	3 [1.3]	1 [1.0]	1 [1.0]	5 [1.2]
Mineralization	12 [1.0]	20 [1.2]	7 [1.0]	13 [1.1]
Nephropathy	21 [1.4]	25 [1.2]	26 [1.3]	20 [1.9]
Papilla, Necrosis	1 [2.0]	3 [2.0]	1 [2.0]	3 [2.0]
Pelvis, Cyst			1 [2.0]	
Renal Tubule, Hyperplasia	3 [1.0]	1 [1.0]	2 [1.0]	
Urinary Bladder	(50)	(48)	(50)	(50)
Infiltration Cellular, Mononuclear Cell	34 [1.1]	34 [1.1]	40 [1.0]	34 [1.0]
Inflammation		1 [4.0]		

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TDMS No. 20007 - 06

**P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH
AVERAGE SEVERITY GRADES[b]**

Date Report Requested: 04/13/2009

Test Type: CHRONIC

Kava kava extract

Time Report Requested: 10:57:30

Route: GAVAGE

CAS Number: 9000-38-8

First Dose M/F: 08/24/04 / 08/23/04

Species/Strain: MICE/B6C3F1

Lab: BAT

B6C3F1 MICE FEMALE	0 G/KG	0.25 G/KG	0.5 G/KG	1.0 G/KG
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*** END OF REPORT ***

a - Number of animals examined microscopically at site and number of animals with lesion
b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)