TDMS No. 20007 - 05

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH Date Report Requested: 09/21/2010 AVERAGE SEVERITY GRADES[b]

Test Type: CHRONIC Route: GAVAGE Species/Strain: RATS/F 344/N Kava kava extract CAS Number: 9000-38-8 Time Report Requested: 09:10:56 First Dose M/F: 08/18/04 / 08/19/04 Lab: BAT

F2\_R2

C Number:	C20007
Lock Date:	03/27/2007
Cage Range:	ALL
Date Range:	ALL
Reasons For Removal:	ALL
Removal Date Range:	ALL
Treatment Groups:	Include ALL
Study Gender:	Both
TDMSE Version:	2.2.0

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATE	Date Report Requested: 09/21/2010				
Test Type: CHRONIC		Kava kava extract				
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04	
Species/Strain: RATS/F 344/N					Lab: BAT	
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG		
Disposition Summary						
Animals Initially In Study	50	50	50	50		
Early Deaths		••	•••	••		
Dosing Accident		1	1	3		
Moribund Sacrifice	10	10	13	13		
Natural Death	5	4	2	3		
Survivors	-	•	-	-		
Natural Death			1			
Terminal Sacrifice	34	35	33	31		
Animals Examined Microscopically	49	50	50	50		
ALIMENTARY SYSTEM						
Esophagus	(49)	(50)	(50)	(50)		
Epithelium, Hyperplasia	1 [1.0]					
Epithelium, Necrosis	1 [1.0]					
Muscularis, Degeneration	1 [2.0]					
Intestine Large, Cecum	(49)	(50)	(50)	(50)		
Inflammation		1 [1.0]	( )			
Intestine Large, Colon	(49)	(50)	(50)	(50)		
Parasite Metazoan	7	2	5	2		
Intestine Small, Duodenum	(49)	(50)	(50)	(50)		
Ectopic Tissue	1 [2.0]	x - /	x - /			
Intestine Small, Ileum	(49)	(50)	(50)	(50)		
Necrosis	1 [1.0]	()		<u>\ /</u>		
Liver	(49)	(50)	(50)	(50)		
Angiectasis	()	1 [1.0]	2 [1.0]	1 [1.0]		
Basophilic Focus	21	30	18	13		
Clear Cell Focus	18	25	25	11		
Degeneration, Cystic	-	4 [1.0]	3 [1.3]	5 [1.2]		
Eosinophilic Focus	15	18	14	13		
Fatty Change, Diffuse	11 [1.8]	8 [1.1]	12 [1.6]	8 [1.5]		
Fibrosis	L - J		L - J	1 [2.0]		
Hematopoietic Cell Proliferation	3 [1.0]	3 [1.0]	1 [2.0]	· ·-1		
Hepatodiaphragmatic Nodule	2	7	4	1		

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATI	Date Report Requested: 09/21/2010						
Test Type: CHRONIC		AVERAGE SEVERITY GRADES[b] Kava kava extract						
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04			
Species/Strain: RATS/F 344/N				,	Lab: BAT			
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG				
Inflammation, Chronic Active	36 [1.0]	39 [1.0]	32 [1.0]	34 [1.1]				
Mixed Cell Focus	30 [1.0] 4	5 [1.0]	32 [1.0] 4	54[1.1]				
Necrosis	1 [2.0]	2 [1.5]	4	1 [3.0]				
Pigmentation, Hemosiderin		2 [1.5]	2 [1.5]	2 [1.0]				
-	1 [3.0]		2 [1.5]					
Tension Lipidosis		1 [1 0]		1 [2.0]				
Bile Duct, Cyst	22 [4 2]	1 [1.0]	40 [4 4]	24 [4 4]				
Bile Duct, Hyperplasia	32 [1.3]	39 [1.3]	40 [1.4]	34 [1.4]				
Centrilobular, Degeneration	4 [2 0]	7 [4 0]	1 [2.0]	04 [4 7]				
Centrilobular, Fatty Change	1 [2.0]	7 [1.3]	4 [1.3]	21 [1.7]				
Centrilobular, Necrosis		2 [2.0]	4 [0 0]	1 [3.0]				
Hepatocyte, Hyperplasia		0.[4.0]	1 [2.0]	00 [4 4]				
Hepatocyte, Hypertrophy		2 [1.0]	2 [1.0]	22 [1.4]				
Oval Cell, Hyperplasia		2 [2.0]	1 [1.0]	1 [1.0]				
Mesentery	(6)	(8)	(7)	(6)				
Hemorrhage	1 [3.0]							
Thrombosis			1 [3.0]	<b>5</b> ( 4 o)				
Fat, Necrosis	4 [2.5]	7 [1.4]	6 [1.7]	5 [1.6]				
Oral Mucosa	(1)	(1)	(0)	(1)				
Hyperplasia, Squamous	<i></i>	1 [3.0]	()	()				
Pancreas	(49)	(50)	(50)	(50)				
Atrophy	16 [1.3]	13 [1.0]	18 [1.3]	18 [1.3]				
Basophilic Focus		1						
Inflammation			2 [1.0]	1 [2.0]				
Acinus, Hyperplasia	6 [1.5]	9 [1.2]	9 [1.6]	2 [2.0]				
Acinus, Metaplasia, Hepatocyte				6 [1.5]				
Salivary Glands	(49)	(50)	(50)	(50)				
Atrophy		1 [2.0]	1 [2.0]					
Stomach, Forestomach	(49)	(50)	(50)	(50)				
Erosion			1 [2.0]	4 [1.0]				
Inflammation	8 [2.3]	4 [1.5]	9 [2.8]	22 [2.0]				
Mineralization		2 [1.0]	1 [1.0]	3 [1.7]				
Ulcer	4 [2.5]		6 [3.0]	13 [1.6]				
Epithelium, Dysplasia	1 [1.0]		2 [1.0]	1 [4.0]				
Epithelium, Hyperplasia	6 [2.2]	4 [1.5]	11 [2.5]	27 [2.3]				
Stomach, Glandular	(49)	(50)	(50)	(50)				
Hyperplasia				1 [2.0]				

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

		Date Report Requested: 09/21/2010			
Test Type: CHRONIC		Kava kav	Time Report Requested: 09:10:56		
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04
Species/Strain: RATS/F 344/N					Lab: BAT
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
Inflammation	2 [2.0]	3 [1.0]	3 [1.7]	3 [1.7]	
Epithelium, Necrosis	2 [1.5]	1 [2.0]	2 [2.0]	3 [2.3]	
Tooth	(10)	(6)	(9)	(11)	
Malformation	10 [1.0]	6 [1.0]	9 [1.0]	11 [1.1]	
CARDIOVASCULAR SYSTEM					
Blood Vessel	(49)	(50)	(50)	(50)	
Mineralization				1 [1.0]	
Pulmonary Artery, Inflammation, Chronic Active			1 [2.0]		
Heart	(49)	(50)	(50)	(50)	
Cardiomyopathy	48 [2.4]	49 [2.4]	48 [2.3]	46 [2.3]	
Inflammation, Suppurative				1 [2.0]	
Mineralization			1 [1.0]		
Atrium, Thrombosis	2 [2.0]	2 [1.5]	3 [1.7]	1 [2.0]	
Coronary Artery, Degeneration			1 [1.0]		
Epicardium, Inflammation			1 [1.0]		
ENDOCRINE SYSTEM					
Adrenal Cortex	(49)	(50)	(50)	(50)	
Degeneration, Cystic	1 [3.0]				
Hematopoietic Cell Proliferation		1 [2.0]	1 [1.0]		
Hypertrophy	2 [1.5]	5 [1.4]	3 [1.0]	3 [1.0]	
Necrosis	1 [1.0]	1 [1.0]	1 [1.0]	1 [2.0]	
Vacuolization Cytoplasmic	1 [3.0]				
Zona Fasciculata, Hyperplasia	8 [1.0]	6 [1.2]	9 [1.0]	13 [1.1]	
Adrenal Medulla	(49)	(50)	(50)	(50)	
Hemorrhage	. /	· /	. /	1 [3.0]	
Hyperplasia	9 [1.7]	11 [1.9]	10 [1.8]	10 [1.9]	
Thrombosis				1 [2.0]	
Islets, Pancreatic	(49)	(50)	(50)	(50)	
Hyperplasia	2 [2.5]	2 [1.0]	2 [1.0]	3 [2.7]	
Parathyroid Gland	(49)	(50)	(48)	(50)	
Hyperplasia	1 [2.0]	<u> </u>	1 [1.0]	10 [1.8]	

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATI	P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH AVERAGE SEVERITY GRADES[b]					
Test Type: CHRONIC		Kava kav	va extract		Time Report Requested: 09:10:56		
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04		
Species/Strain: RATS/F 344/N				,	Lab: BAT		
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG			
Pituitary Gland	(49)	(50)	(50)	(50)			
Hemorrhage	1 [2.0]	()	1 [2.0]	()			
Pars Distalis, Angiectasis	. []		1 [2.0]				
Pars Distalis, Hyperplasia	17 [1.5]	20 [1.9]	21 [1.4]	11 [1.5]			
Thyroid Gland	(49)	(50)	(50)	(50)			
Infiltration Cellular, Lymphocyte	(10)	1 [2.0]	(00)				
C-cell, Hyperplasia	8 [1.9]	12 [1.9]	12 [1.8]	7 [1.4]			
Follicular Cell, Hyperplasia	0 [0]	2 [1.5]	[]	1 [2.0]			
Follicular Cell, Hypertrophy		_[]		1 [1.0]			
GENERAL BODY SYSTEM							
Peritoneum	(0)	(0)	(1)	(0)			
Tissue NOS	(0)	(1)	(0)	(0)			
GENITAL SYSTEM							
Coagulating Gland	(2)	(2)	(0)	(0)			
Fibrosis	1 [3.0]						
Inflammation	1 [2.0]	2 [3.0]					
Epididymis	(49)	(50)	(50)	(50)			
Inflammation	1 [1.0]	4 [1.3]	3 [1.7]	2 [1.5]			
Preputial Gland	(49)	(50)	(49)	(50)			
Inflammation			1 [2.0]	2 [4.0]			
Duct, Hyperplasia, Atypical				1 [1.0]			
Prostate	(49)	(50)	(50)	(50)			
Atrophy				1 [2.0]			
Inflammation	28 [2.0]	24 [1.8]	21 [1.8]	16 [1.9]			
Epithelium, Hyperplasia	9 [1.1]	8 [1.8]	2 [1.0]	3 [1.0]			
Seminal Vesicle	(49)	(50)	(50)	(50)			
Atrophy		. ,	. ,	1 [2.0]			
Inflammation			1 [2.0]	2 [2.0]			
Testes	(49)	(50)	(50)	(50)			
Cyst	· · ·			1 [4.0]			
Arteriole, Necrosis	1 [1.0]						

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATE	Date Report Requested: 09/21/2010			
Test Type: CHRONIC		AVERAGE SEVE Kava kav	Time Report Requested: 09:10:56		
Route: GAVAGE			er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04
Species/Strain: RATS/F 344/N					Lab: BAT
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
	· · · · · · · · · · · · · · · · · · ·				
Germinal Epithelium, Degeneration	3 [1.7]				
Interstitial Cell, Hyperplasia	17 [1.9]	15 [2.1]	10 [2.4]	4 [2.5]	
HEMATOPOIETIC SYSTEM					
Bone Marrow	(49)	(50)	(50)	(50)	
Hemorrhage		1 [4.0]			
Hyperplasia	16 [2.4]	17 [2.9]	24 [2.1]	29 [2.4]	
Necrosis		1 [1.0]		1 [2.0]	
Lymph Node	(4)	(3)	(2)	(5)	
Mediastinal, Ectasia			1 [2.0]		
Mediastinal, Hyperplasia, Lymphoid	3 [2.0]			1 [2.0]	
Mediastinal, Infiltration Cellular, Plasma Cell	0 [=.0]	1 [2.0]	1 [3.0]	. [=.0]	
Lymph Node, Mesenteric	(49)	(50)	(50)	(50)	
Atrophy	2 [2.0]	2 [1.0]	(00)	5 [1.8]	
Spleen	(49)	(50)	(50)	(50)	
Accessory Spleen	(43)	(50)	(30)	(50)	
	I	1 [2 0]		I	
Amyloid Deposition		1 [2.0]			
Fibrosis		40 [0 0]	7 [4 7]	2 [1.5]	
Hematopoietic Cell Proliferation	10 [1.7]	10 [2.2]	7 [1.7]	5 [1.6]	
Hemorrhage	1 [3.0]				
Hyperplasia, Histiocytic				1 [2.0]	
Inflammation	1 [2.0]				
Necrosis	1 [2.0]				
Pigmentation, Hemosiderin	31 [1.1]	32 [1.0]	35 [1.1]	32 [1.1]	
Thrombosis				2 [2.5]	
Lymphoid Follicle, Atrophy	2 [3.5]	2 [2.5]	2 [3.0]	1 [2.0]	
Lymphoid Follicle, Hyperplasia			1 [3.0]		
Thymus	(48)	(50)	(50)	(50)	
Atrophy	47 [3.3]	49 [3.2]	49 [3.3]	46 [3.2]	
INTEGUMENTARY SYSTEM					
Mammary Gland	(48)	(50)	(50)	(50)	
Hyperplasia	1 [2.0]	-	-	-	

TDMS No. 20007 - 05	P18: INCIDENCE RATI	Date Report Requested: 09/21/2010			
Test Type: CHRONIC		Kava kav	/a extract		Time Report Requested: 09:10:56
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04
Species/Strain: RATS/F 344/N					Lab: BAT
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
Skin	(49)	(50)	(50)	(50)	
Cyst Epithelial Inclusion		1		1 [3.0]	
Inflammation		2 [1.0]		1 [2.0]	
Epidermis, Hyperplasia, Basal Cell			1 [3.0]		
Subcutaneous Tissue, Fibrosis	1 [4.0]				
MUSCULOSKELETAL SYSTEM					
Bone	(49)	(50)	(50)	(50)	
Osteopetrosis				1 [2.0]	
Ligament, Mineralization		(-)		1 [2.0]	
Skeletal Muscle	(1)	(0)	(1)	(1)	
NERVOUS SYSTEM					
Brain	(49)	(50)	(50)	(50)	
Hemorrhage	1 [1.0]	1 [1.0]		2 [2.0]	
Hydrocephalus		1 [1.0]		1 [1.0]	
Necrosis	2 [2.0]		2 [3.0]	2 [1.5]	
Choroid Plexus, Infiltration Cellular, Lymphocyte			1 [2.0]		
Spinal Cord	(2)	(0)	(0)	(0)	
RESPIRATORY SYSTEM					
Lung	(49)	(50)	(50)	(50)	
Congestion	. ,	1 [2.0]	1 [3.0]	1 [2.0]	
Foreign Body				1	
Hemorrhage				1 [1.0]	
Inflammation, Granulomatous		_	_	3 [1.7]	
Inflammation, Chronic Active	6 [1.5]	3 [1.0]	9 [1.1]	9 [1.0]	
Necrosis	2 [1.5]				
Thrombosis	1 [1.0]		1 [1.0]	46 [4 0]	
Alveolar Epithelium, Hyperplasia	19 [1.4]	13 [1.7]	20 [1.4]	15 [1.3]	

<b>TDMS No</b> . 20007 - 05	P18: INCIDENCE RATI	Date Report Requested: 09/21/2010					
Test Type: CHRONIC		AVERAGE SEVERITY GRADES[b] Kava kava extract					
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04		
Species/Strain: RATS/F 344/N					Lab: BAT		
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG			
Alveolar Epithelium, Hypertrophy	2 [1.0]		2 [1.5]	1 [1.0]			
Alveolar Epithelium, Metaplasia			1 [2.0]				
Alveolar Epithelium, Metaplasia, Squamous	1 [1.0]	1 [2.0]	1 [2.0]				
Alveolus, Infiltration Cellular, Histiocyte	8 [1.0]	3 [1.0]	11 [1.1]	9 [1.6]			
Arteriole, Hyperplasia	• [ · · • ]	• []	[]	1 [1.0]			
Serosa, Inflammation, Acute				1 [2.0]			
Nose	(49)	(50)	(50)	(50)			
Foreign Body	1	4	1	2			
Inflammation	18 [1.7]	14 [1.8]	10 [1.6]				
Olfactory Epithelium, Metaplasia	2 [2.0]	1 [2.0]	3 [1.3]	5 [1.6]			
Respiratory Epithelium, Hyperplasia	1 [2.0]	3 [2.3]	1 [1.0]	4 [1.0]			
SPECIAL SENSES SYSTEM Ear Eye Anterior Chamber, Inflammation	(0) (49)	(2) (50)	(1) (50)	(0) (50) 1 [2.0]			
Cornea, Fibrosis	1 [2.0]						
Cornea, Inflammation			1 [3.0]				
Iris, Inflammation				2 [1.0]			
Iris, Synechia	1 [4.0]						
Lens, Cataract	2 [1.5]	1 [1.0]	2 [2.0]				
Retina, Degeneration	6 [1.5]	6 [1.0]	10 [1.5]	16 [1.6]			
Retina, Retinal Detachment	1 [4.0]						
Harderian Gland	(49)	(50)	(50)	(50)			
Zymbal's Gland	(0)	(0)	(1)	(0)			
URINARY SYSTEM				· · · · · · · · · · · · · · · · · · ·			
Kidney	(49)	(50)	(50)	(50)			
Accumulation, Hyaline Droplet Hyperplasia, Oncocytic	1 [1.0]		1 [1.0]	2 [1.0] 1 [1.0]			
Infarct	1 [2 0]		1 [1 0]	1[1.0]			
	1 [2.0]		1 [1.0]				
Inflammation, Acute	20 [4 0]	10 11 01	1 [2.0]	24 [4 0]			
Mineralization	38 [1.0]	43 [1.0]	41 [1.0]	34 [1.0]			

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATE	Date Report Requested: 09/21/2010			
Test Type: CHRONIC		Kava kav	va extract		Time Report Requested: 09:10:56
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04
Species/Strain: RATS/F 344/N					Lab: BAT
FISCHER 344 RATS MALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
Nephropathy	46 [1.4]	47 [1.2]	48 [1.8]	48 [3.1]	
Cortex, Cyst	1 [2.0]			1 [2.0]	
Papilla, Necrosis	1 [4.0]				
Pelvis, Dilatation		1 [2.0]			
Pelvis, Inflammation	1 [3.0]			1 [1.0]	
Pelvis, Transitional Epithelium, Hyperplasia		1 [1.0]	1 [2.0]	15 [1.3]	
Ureter	(1)	(1)	(0)	(0)	
Inflammation	1 [4.0]				
Urethra	(1)	(0)	(0)	(0)	
Inflammation	1 [4.0]				
Urinary Bladder	(49)	(50)	(50)	(50)	
Inflammation	2 [2.5]		1 [2.0]	2 [2.5]	
Transitional Epithelium, Hyperplasia	1 [2.0]				

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

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)

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATI	Date Report Requested: 09/21/2010			
Test Type: CHRONIC		Kava kav	/a extract		Time Report Requested: 09:10:56
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04
Species/Strain: RATS/F 344/N					Lab: BAT
FISCHER 344 RATS FEMALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
Disposition Summary					
Animals Initially In Study	50	50	50	50	
Early Deaths					
Dosing Accident	1	1	2	2	
Moribund Sacrifice	12	12	13	6	
Natural Death	3	2	11	8	
Survivors	-				
Natural Death		1			
Terminal Sacrifice	34	34	24	34	
Animals Examined Microscopically	50	50	50	50	
ALIMENTARY SYSTEM					
Esophagus	(50)	(50)	(50)	(50)	
Hyperplasia		1 [1.0]			
Inflammation		1 [2.0]	1 [3.0]		
Perforation			1 [4.0]		
Intestine Large, Cecum	(50)	(50)	(50)	(50)	
Inflammation			1 [4.0]		
Necrosis			1 [4.0]		
Intestine Large, Colon	(50)	(50)	(50)	(50)	
Parasite Metazoan	3	1	8	6	
Liver	(50)	(50)	(50)	(50)	
Angiectasis	1 [2.0]	2 [1.5]		3 [1.3]	
Basophilic Focus	44	42	41	11	
Clear Cell Focus	12	14	11	8	
Degeneration, Cystic				1 [1.0]	
Eosinophilic Focus	23	31	24	23	
Fatty Change, Focal	1 [1.0]				
Fatty Change, Diffuse	9 [1.3]	10 [1.4]	10 [1.5]	11 [1.1]	
Hematopoietic Cell Proliferation	1 [1.0]	3 [1.0]			
Hepatodiaphragmatic Nodule	5	6	1	2	
Inflammation, Chronic Active	43 [1.0]	40 [1.0]	38 [1.0]	35 [1.0]	
Mixed Cell Focus	15	10	9	3	
Necrosis	2 [3.0]	1 [1.0]			

TDMS No. 20007 - 05

## P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH Date Report Requested: 09/21/2010 AVERAGE SEVERITY GRADES[b]

<b>Fest Type:</b> CHRONIC Route: GAVAGE Species/Strain: RATS/F 344/N		Time Report Requested: 09:10:5 First Dose M/F: 08/18/04 / 08/19/0 Lab: BAT			
FISCHER 344 RATS FEMALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
Pigmentation, Hemosiderin	1 [2.0]		1 [1.0]	1 [2.0]	
Artery, Necrosis	1 [2.0]				
Bile Duct, Cyst		1 [1.0]			
Bile Duct, Hyperplasia	12 [1.0]	15 [1.5]	10 [1.3]	10 [1.1]	
Centrilobular, Fatty Change				2 [2.0]	
Centrilobular, Necrosis		1 [3.0]		1 [2.0]	
Hepatocyte, Hypertrophy	5 [1.6]	2 [1.0]	3 [1.3]	33 [1.8]	
Oval Cell, Hyperplasia		2 [2.0]	2 [1.0]		
Serosa, Fibrosis	1 [3.0]	1 [2.0]			
Mesentery	(10)	(9)	(7)	(9)	
Fat, Necrosis	10 [1.5]	9 [1.9]	7 [1.9]	9 [1.7]	
Oral Mucosa	(0)	(1)	(2)	(0)	
Hyperplasia, Squamous			1 [4.0]		
Pancreas	(50)	(50)	(50)	(50)	
Atrophy	13 [1.0]	10 [1.4]	16 [1.3]	17 [1.4]	
Basophilic Focus	1				
Inflammation				1 [1.0]	
Acinus, Hyperplasia	1 [1.0]	3 [1.3]			
Acinus, Metaplasia, Hepatocyte		1 [1.0]		4 [1.3]	
Salivary Glands	(50)	(50)	(50)	(50)	
Atrophy		( )	( )	1 [2.0]	
Stomach, Forestomach	(50)	(50)	(50)	(50)	
Erosion	· · · ·	1 [1.0]	2 [1.0]		
Hyperplasia, Atypical	1 [4.0]				
Inflammation	5 [2.0]	7 [1.7]	7 [2.1]	13 [1.8]	
Ulcer	1 [3.0]	1 [4.0]	3 [2.3]	7 [2.3]	
Epithelium, Hyperplasia	5 [2.2]	6 [2.3]	8 [1.8]	19 [1.9]	
Stomach, Glandular	(50)	(50)	(50)	(50)	
Amyloid Deposition	(/	()	1 [2.0]	(/	
Inflammation		2 [2.0]	[]		
Epithelium, Hyperplasia		[]	1 [3.0]		
Epithelium, Necrosis	1 [1.0]	1 [2.0]	. []		
Tooth	(5)	(3)	(4)	(2)	
Malformation	5 [1.0]	3 [1.3]	4 [1.0]	2 [2.0]	
Peridontal Tissue, Inflammation	0[110]	0 [ 110]	. [ ]	1 [3.0]	

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)

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATI	Date Report Requested: 09/21/2010 Time Report Requested: 09:10:56 First Dose M/F: 08/18/04 / 08/19/04 Lab: BAT			
Test Type: CHRONIC Route: GAVAGE Species/Strain: RATS/F 344/N					
FISCHER 344 RATS FEMALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
CARDIOVASCULAR SYSTEM					
Blood Vessel	(50)	(50)	(50)	(50)	
Inflammation	1 [3.0]	( )	( ),	( )	
Heart	(50)	(50)	(50)	(50)	
Cardiomyopathy	42 [1.9]	45 [1.9]	45 [1.9]	47 [1.7]	
Atrium, Thrombosis		1 [2.0]		1 [2.0]	
Valve, Thrombosis		1 [2.0]			
ENDOCRINE SYSTEM					
Adrenal Cortex	(50)	(50)	(50)	(50)	
Amyloid Deposition		1 [2.0]			
Degeneration, Cystic	3 [1.3]	6 [1.2]	7 [1.6]	6 [1.2]	
Hemorrhage				1 [4.0]	
Hypertrophy	2 [2.5]	3 [1.0]	1 [2.0]	3 [1.0]	
Metaplasia, Osseous			1 [2.0]		
Necrosis	2 [3.0]		1 [1.0]	2 [2.0]	
Zona Fasciculata, Hyperplasia	6 [1.0]	6 [1.2]	4 [1.3]	9 [1.1]	
Adrenal Medulla	(50)	(50)	(50)	(50)	
Hyperplasia	3 [1.3]		1 [1.0]	1 [1.0]	
Necrosis		1 [4.0]			
Islets, Pancreatic	(50)	(50)	(50)	(50)	
Hyperplasia	1 [1.0]		3 [1.3]	1 [1.0]	
Parathyroid Gland	(44)	(47)	(44)	(47)	
Pituitary Gland	(50)	(50)	(50)	(50)	
Cyst			1 [1.0]		
Pars Distalis, Angiectasis	1 [2.0]	1 [1.0]	1 [2.0]	2 [2.5]	
Pars Distalis, Hyperplasia	11 [1.7]	20 [2.2]	16 [2.3]	23 [2.0]	
Thyroid Gland	(50)	(50)	(50)	(50)	
C-cell, Hyperplasia	15 [2.1]	15 [1.9]	6 [2.3]	4 [1.3]	
Follicle, Cyst				2 [1.5]	
Follicular Cell, Hyperplasia	1 [3.0]	1 [1.0]	4 [2.5]	4 [2.0]	

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)

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATE	Date Report Requested: 09/21/2010				
Test Type: CHRONIC		AVERAGE SEVERITY GRADES[b] Kava kava extract				
Route: GAVAGE		CAS Numbe	er: 9000-38-8		Time Report Requested: 09:10:56 First Dose M/F: 08/18/04 / 08/19/04	
Species/Strain: RATS/F 344/N						
FISCHER 344 RATS FEMALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG		
GENERAL BODY SYSTEM						
None						
none						
GENITAL SYSTEM						
Clitoral Gland	(50)	(49)	(50)	(49)		
Hyperplasia	. ,	3 [2.7]	5 [2.0]	1 [1.0]		
Inflammation	1 [3.0]	2 [2.0]				
Ovary	(50)	(50)	(50)	(50)		
Cyst	7 [2.6]	9 [2.0]	6 [2.3]	5 [1.6]		
Cyst, Multiple	1 [4.0]					
Uterus	(50)	(50)	(50)	(50)		
Congestion		1 [4.0]				
Hemorrhage		2 [2.5]		1 [3.0]		
Necrosis		1 [3.0]				
Endometrium, Hyperplasia, Adenomatous			1 [2.0]			
Endometrium, Hyperplasia, Cystic	5 [1.6]	5 [1.2]	6 [2.0]	10 [1.5]		
Stroma, Hyperplasia		-	1 [3.0]	-		
HEMATOPOIETIC SYSTEM						
Bone Marrow	(50)	(50)	(50)	(50)		
Hemorrhage	1 [3.0]	. /	. ,	. ,		
Hyperplasia	26 [2.1]	27 [2.3]	19 [2.2]	23 [2.0]		
Inflammation, Histiocytic			1 [2.0]			
Myelofibrosis	2 [1.5]	1 [2.0]	1 [2.0]	1 [1.0]		
Necrosis	1 [3.0]					
Lymph Node	(1)	(3)	(3)	(2)		
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)		
Atrophy	1 [3.0]	1 [3.0]	1 [3.0]			
Inflammation	2 [2.5]					
Spleen	(50)	(50)	(50)	(50)		

TDMS No. 20007 - 05	P18: INCIDENCE RATI	Date Report Requested: 09/21/2010				
Test Type: CHRONIC		AVERAGE SEVERITY GRADES[b] Kava kava extract				
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04	
Species/Strain: RATS/F 344/N FISCHER 344 RATS FEMALE						
	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG		
Accessory Spleen			1			
Fibrosis		3 [1.7]		2 [2.5]		
Hematopoietic Cell Proliferation	19 [1.3]	18 [1.3]	17 [1.1]	7 [1.3]		
Hyperplasia, Histiocytic	1 [3.0]	[]	1 [3.0]	. []		
Pigmentation, Hemosiderin	37 [1.2]	37 [1.1]	41 [1.1]	42 [1.3]		
Lymphoid Follicle, Atrophy	1 [2.0]	1 [2.0]	4 [2.3]	2 [2.0]		
Lymphoid Follicle, Necrosis	1 [4.0]	. [=]	. [=.0]	- [-:0]		
Thymus	(50)	(50)	(49)	(48)		
Atrophy	48 [3.0]	43 [3.0]	47 [3.1]	45 [2.9]		
Infiltration Cellular, Plasma Cell	1 [2.0]	10 [0:0]	[0.1]	10 [2:0]		
Inflammation	· [2.0]		1 [2.0]			
INTEGUMENTARY SYSTEM						
Mammary Gland	(50)	(50)	(50)	(50)		
Galactocele		, , ,	1 [4.0]			
Hyperplasia			2 [3.0]			
Skin	(50)	(50)	(50)	(50)		
Epidermis, Hyperkeratosis			1 [2.0]			
Epidermis, Hyperplasia, Basal Cell		1 [2.0]				
MUSCULOSKELETAL SYSTEM						
Bone	(50)	(50)	(50)	(50)		
Osteopetrosis	1 [3.0]	. ,	. ,	. /		
Skeletal Muscle	(1)	(0)	(1)	(0)		
Inflammation	1 [3.0]	. ,	. ,	. ,		
NERVOUS SYSTEM						
Brain	(50)	(50)	(50)	(50)		
Hemorrhage	(00)	2 [3.0]	2 [1.0]	(00)		
Infiltration Cellular, Mixed Cell		2 [0.0]	1 [1.0]			
Necrosis		3 [1.7]	2 [2.0]			
		0[111]	- [2:0]			

<b>TDMS No.</b> 20007 - 05	P18: INCIDENCE RATI	Date Report Requested: 09/21/2010 Time Report Requested: 09:10:56			
Test Type: CHRONIC					
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04
Species/Strain: RATS/F 344/N			Lab: BAT		
FISCHER 344 RATS FEMALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
Peripheral Nerve	(0)	(0)	(1)	(0)	
Spinal Cord	(0)	(0)	(1)	(0)	
Hemorrhage			1 [3.0]		
Necrosis			1 [2.0]		
RESPIRATORY SYSTEM					
Lung	(50)	(50)	(50)	(50)	
Atelectasis	1 [4.0]	1 [4.0]			
Congestion	1 [2.0]			1 [2.0]	
Hemorrhage				1 [1.0]	
Inflammation, Chronic Active	4 [2.0]	5 [1.2]	2 [1.0]	7 [1.0]	
Alveolar Epithelium, Hyperplasia	11 [1.1]	14 [1.6]	6 [1.8]	7 [1.6]	
Alveolar Epithelium, Hypertrophy	1 [1.0]	1 [2.0]			
Alveolar Epithelium, Metaplasia	1 [2.0]				
Alveolar Epithelium, Metaplasia, Squamous	1 [2.0]	3 [1.7]			
Alveolus, Infiltration Cellular, Histiocyte	12 [1.0]	17 [1.0]	12 [1.1]	16 [1.0]	
Mediastinum, Foreign Body	1				
Mediastinum, Inflammation, Chronic Active	1 [4.0]				
Nose	(50)	(50)	(50)	(50)	
Cyst	1 [1.0]				
Foreign Body	2				
Inflammation	8 [1.1]	2 [1.0]	9 [1.7]	8 [1.3]	
Glands, Dilatation			1 [3.0]		
Olfactory Epithelium, Metaplasia	1 [1.0]		1 [3.0]		
Respiratory Epithelium, Hyperplasia			1 [2.0]		
Pleura	(0)	(0)	(0)	(1)	
Mesothelium, Hyperplasia				1 [2.0]	
Trachea	(50)	(50)	(50)	(50)	
Peritracheal Tissue, Inflammation			1 [3.0]		
SPECIAL SENSES SYSTEM					
Ear	(1)	(0)	(0)	(1)	
Eye	(50)	(50)	(50)	(50)	

TDMS No. 20007 - 05	P18: INCIDENCE RATE	Date Report Requested: 09/21/2010 Time Report Requested: 09:10:56			
Test Type: CHRONIC					
Route: GAVAGE		CAS Numbe	er: 9000-38-8		First Dose M/F: 08/18/04 / 08/19/04
Species/Strain: RATS/F 344/N					Lab: BAT
FISCHER 344 RATS FEMALE	0.0 G/KG	0.1 G/KG	0.3 G/KG	1.0 G/KG	
Synechia			1 [4.0]		
Cornea, Fibrosis	1 [2.0]			1 [2.0]	
Cornea, Inflammation	1 [2.0]		2 [3.0]	2 [2.0]	
Lens, Cataract	2 [3.5]	3 [3.0]	1 [4.0]	3 [2.0]	
Posterior Chamber, Inflammation				1 [1.0]	
Retina, Degeneration	5 [2.6]	5 [3.0]	5 [2.4]	12 [1.7]	
Retina, Dysplasia			1 [2.0]		
Retina, Gliosis	1 [2.0]		3 [2.0]	1 [2.0]	
Retina, Inflammation		1 [1.0]			
Zymbal's Gland	(0)	(0)	(0)	(1)	
URINARY SYSTEM					
Kidney	(50)	(50)	(50)	(50)	
Accumulation, Hyaline Droplet		2 [3.0]	1 [2.0]	1 [3.0]	
Glomerulosclerosis		1 [1.0]			
Infarct	2 [1.0]	3 [1.7]	4 [2.0]	3 [2.0]	
Mineralization	43 [1.0]	43 [1.0]	45 [1.0]	46 [1.0]	
Nephropathy	34 [1.0]	35 [1.0]	37 [1.1]	43 [1.2]	
Cortex, Cyst	2 [1.5]				
Medulla, Cyst	1 [1.0]				
Papilla, Necrosis			1 [1.0]	1 [1.0]	
Pelvis, Inflammation	1 [2.0]	1 [1.0]	5 [1.4]	4 [1.8]	
Pelvis, Transitional Epithelium, Hyperplasia			4 [1.5]	6 [1.2]	
Pelvis, Transitional Epithelium, Metaplasia			1 [2.0]		
Renal Tubule, Dilatation			1 [2.0]		
Renal Tubule, Necrosis			1 [3.0]	2 [2.0]	
Urinary Bladder	(50)	(50)	(50)	(50)	

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

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