

TDMS No. 20007 - 05
Test Type: CHRONIC
Route: GAVAGE
Species/Strain: RATS/F 344/N

P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Kava kava extract
CAS Number: 9000-38-8

Date Report Requested: 09/21/2010
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

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| | | | | |
|------------------------------|-----------------|-----------------|-----------------|-----------------|
| 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 (2%) | | | |
| Epithelium, Necrosis | 1 (2%) | | | |
| Muscularis, Degeneration | 1 (2%) | | | |
| Intestine Large, Cecum | (49) | (50) | (50) | (50) |
| Inflammation | | 1 (2%) | | |
| Intestine Large, Colon | (49) | (50) | (50) | (50) |
| Parasite Metazoan | 7 (14%) | 2 (4%) | 5 (10%) | 2 (4%) |
| Intestine Small, Duodenum | (49) | (50) | (50) | (50) |
| Ectopic Tissue | 1 (2%) | | | |
| Intestine Small, Ileum | (49) | (50) | (50) | (50) |
| Necrosis | 1 (2%) | | | |
| Liver | (49) | (50) | (50) | (50) |
| Angiectasis | | 1 (2%) | 2 (4%) | 1 (2%) |
| Basophilic Focus | 21 (43%) | 30 (60%) | 18 (36%) | 13 (26%) |
| Clear Cell Focus | 18 (37%) | 25 (50%) | 25 (50%) | 11 (22%) |
| Degeneration, Cystic | | 4 (8%) | 3 (6%) | 5 (10%) |
| Eosinophilic Focus | 15 (31%) | 18 (36%) | 14 (28%) | 13 (26%) |
| Fatty Change, Diffuse | 11 (22%) | 8 (16%) | 12 (24%) | 8 (16%) |
| Fibrosis | | | | 1 (2%) |
| Hematopoietic Cell Proliferation | 3 (6%) | 3 (6%) | 1 (2%) | |
| Hepatodiaphragmatic Nodule | 2 (4%) | 7 (14%) | 4 (8%) | 1 (2%) |

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| FISCHER 344 RATS MALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|--------------------------------|----------|----------|----------|----------|
| Inflammation, Chronic Active | 36 (73%) | 39 (78%) | 32 (64%) | 34 (68%) |
| Mixed Cell Focus | 4 (8%) | 5 (10%) | 4 (8%) | |
| Necrosis | 1 (2%) | 2 (4%) | | 1 (2%) |
| Pigmentation, Hemosiderin | 1 (2%) | | 2 (4%) | 2 (4%) |
| Tension Lipidosis | | | | 1 (2%) |
| Bile Duct, Cyst | | 1 (2%) | | |
| Bile Duct, Hyperplasia | 32 (65%) | 39 (78%) | 40 (80%) | 34 (68%) |
| Centrilobular, Degeneration | | | 1 (2%) | |
| Centrilobular, Fatty Change | 1 (2%) | 7 (14%) | 4 (8%) | 21 (42%) |
| Centrilobular, Necrosis | | 2 (4%) | | 1 (2%) |
| Hepatocyte, Hyperplasia | | | 1 (2%) | |
| Hepatocyte, Hypertrophy | | 2 (4%) | 2 (4%) | 22 (44%) |
| Oval Cell, Hyperplasia | | 2 (4%) | 1 (2%) | 1 (2%) |
| Mesentery | (6) | (8) | (7) | (6) |
| Hemorrhage | 1 (17%) | | | |
| Thrombosis | | | 1 (14%) | |
| Fat, Necrosis | 4 (67%) | 7 (88%) | 6 (86%) | 5 (83%) |
| Oral Mucosa | (1) | (1) | (0) | (1) |
| Hyperplasia, Squamous | | 1 (100%) | | |
| Pancreas | (49) | (50) | (50) | (50) |
| Atrophy | 16 (33%) | 13 (26%) | 18 (36%) | 18 (36%) |
| Basophilic Focus | | 1 (2%) | | |
| Inflammation | | | 2 (4%) | 1 (2%) |
| Acinus, Hyperplasia | 6 (12%) | 9 (18%) | 9 (18%) | 2 (4%) |
| Acinus, Metaplasia, Hepatocyte | | | | 6 (12%) |
| Salivary Glands | (49) | (50) | (50) | (50) |
| Atrophy | | 1 (2%) | 1 (2%) | |
| Stomach, Forestomach | (49) | (50) | (50) | (50) |
| Erosion | | | 1 (2%) | 4 (8%) |
| Inflammation | 8 (16%) | 4 (8%) | 9 (18%) | 22 (44%) |
| Mineralization | | 2 (4%) | 1 (2%) | 3 (6%) |
| Ulcer | 4 (8%) | | 6 (12%) | 13 (26%) |
| Epithelium, Dysplasia | 1 (2%) | | 2 (4%) | 1 (2%) |
| Epithelium, Hyperplasia | 6 (12%) | 4 (8%) | 11 (22%) | 27 (54%) |
| Stomach, Glandular | (49) | (50) | (50) | (50) |
| Hyperplasia | | | | 1 (2%) |

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

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 Lab: BAT

| FISCHER 344 RATS MALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|-----------------------|-----------|----------|----------|-----------|
| Inflammation | 2 (4%) | 3 (6%) | 3 (6%) | 3 (6%) |
| Epithelium, Necrosis | 2 (4%) | 1 (2%) | 2 (4%) | 3 (6%) |
| Tooth | (10) | (6) | (9) | (11) |
| Malformation | 10 (100%) | 6 (100%) | 9 (100%) | 11 (100%) |

CARDIOVASCULAR SYSTEM

| | | | | |
|--|----------|----------|----------|----------|
| Blood Vessel | (49) | (50) | (50) | (50) |
| Mineralization | | | | 1 (2%) |
| Pulmonary Artery, Inflammation, Chronic Active | | | 1 (2%) | |
| Heart | (49) | (50) | (50) | (50) |
| Cardiomyopathy | 48 (98%) | 49 (98%) | 48 (96%) | 46 (92%) |
| Inflammation, Suppurative | | | | 1 (2%) |
| Mineralization | | | 1 (2%) | |
| Atrium, Thrombosis | 2 (4%) | 2 (4%) | 3 (6%) | 1 (2%) |
| Coronary Artery, Degeneration | | | 1 (2%) | |
| Epicardium, Inflammation | | | 1 (2%) | |

ENDOCRINE SYSTEM

| | | | | |
|----------------------------------|---------|----------|----------|----------|
| Adrenal Cortex | (49) | (50) | (50) | (50) |
| Degeneration, Cystic | 1 (2%) | | | |
| Hematopoietic Cell Proliferation | | 1 (2%) | 1 (2%) | |
| Hypertrophy | 2 (4%) | 5 (10%) | 3 (6%) | 3 (6%) |
| Necrosis | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Vacuolization Cytoplasmic | 1 (2%) | | | |
| Zona Fasciculata, Hyperplasia | 8 (16%) | 6 (12%) | 9 (18%) | 13 (26%) |
| Adrenal Medulla | (49) | (50) | (50) | (50) |
| Hemorrhage | | | | 1 (2%) |
| Hyperplasia | 9 (18%) | 11 (22%) | 10 (20%) | 10 (20%) |
| Thrombosis | | | | 1 (2%) |
| Islets, Pancreatic | (49) | (50) | (50) | (50) |
| Hyperplasia | 2 (4%) | 2 (4%) | 2 (4%) | 3 (6%) |
| Parathyroid Gland | (49) | (50) | (48) | (50) |
| Hyperplasia | 1 (2%) | | 1 (2%) | 10 (20%) |

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| 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%) | | 1 (2%) | |
| Pars Distalis, Angiectasis | | | 1 (2%) | |
| Pars Distalis, Hyperplasia | 17 (35%) | 20 (40%) | 21 (42%) | 11 (22%) |
| Thyroid Gland | (49) | (50) | (50) | (50) |
| Infiltration Cellular, Lymphocyte | | 1 (2%) | | |
| C-cell, Hyperplasia | 8 (16%) | 12 (24%) | 12 (24%) | 7 (14%) |
| Follicular Cell, Hyperplasia | | 2 (4%) | | 1 (2%) |
| Follicular Cell, Hypertrophy | | | | 1 (2%) |
| GENERAL BODY SYSTEM | | | | |
| Peritoneum | (0) | (0) | (1) | (0) |
| Tissue NOS | (0) | (1) | (0) | (0) |
| GENITAL SYSTEM | | | | |
| Coagulating Gland | (2) | (2) | (0) | (0) |
| Fibrosis | 1 (50%) | | | |
| Inflammation | 1 (50%) | 2 (100%) | | |
| Epididymis | (49) | (50) | (50) | (50) |
| Inflammation | 1 (2%) | 4 (8%) | 3 (6%) | 2 (4%) |
| Preputial Gland | (49) | (50) | (49) | (50) |
| Inflammation | | | 1 (2%) | 2 (4%) |
| Duct, Hyperplasia, Atypical | | | | 1 (2%) |
| Prostate | (49) | (50) | (50) | (50) |
| Atrophy | | | | 1 (2%) |
| Inflammation | 28 (57%) | 24 (48%) | 21 (42%) | 16 (32%) |
| Epithelium, Hyperplasia | 9 (18%) | 8 (16%) | 2 (4%) | 3 (6%) |
| Seminal Vesicle | (49) | (50) | (50) | (50) |
| Atrophy | | | | 1 (2%) |
| Inflammation | | | 1 (2%) | 2 (4%) |
| Testes | (49) | (50) | (50) | (50) |
| Cyst | | | | 1 (2%) |
| Arteriole, Necrosis | 1 (2%) | | | |

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| FISCHER 344 RATS MALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|-----------------------------------|----------|----------|----------|----------|
| Germinal Epithelium, Degeneration | 3 (6%) | | | |
| Interstitial Cell, Hyperplasia | 17 (35%) | 15 (30%) | 10 (20%) | 4 (8%) |

HEMATOPOIETIC SYSTEM

| | | | | |
|---|----------|----------|----------|----------|
| Bone Marrow | (49) | (50) | (50) | (50) |
| Hemorrhage | | 1 (2%) | | |
| Hyperplasia | 16 (33%) | 17 (34%) | 24 (48%) | 29 (58%) |
| Necrosis | | 1 (2%) | | 1 (2%) |
| Lymph Node | (4) | (3) | (2) | (5) |
| Mediastinal, Ectasia | | | 1 (50%) | |
| Mediastinal, Hyperplasia, Lymphoid | 3 (75%) | | | 1 (20%) |
| Mediastinal, Infiltration Cellular, Plasma Cell | | 1 (33%) | 1 (50%) | |
| Lymph Node, Mesenteric | (49) | (50) | (50) | (50) |
| Atrophy | 2 (4%) | 2 (4%) | | 5 (10%) |
| Spleen | (49) | (50) | (50) | (50) |
| Accessory Spleen | 1 (2%) | | | 1 (2%) |
| Amyloid Deposition | | 1 (2%) | | |
| Fibrosis | | | | 2 (4%) |
| Hematopoietic Cell Proliferation | 10 (20%) | 10 (20%) | 7 (14%) | 5 (10%) |
| Hemorrhage | 1 (2%) | | | |
| Hyperplasia, Histiocytic | | | | 1 (2%) |
| Inflammation | 1 (2%) | | | |
| Necrosis | 1 (2%) | | | |
| Pigmentation, Hemosiderin | 31 (63%) | 32 (64%) | 35 (70%) | 32 (64%) |
| Thrombosis | | | | 2 (4%) |
| Lymphoid Follicle, Atrophy | 2 (4%) | 2 (4%) | 2 (4%) | 1 (2%) |
| Lymphoid Follicle, Hyperplasia | | | 1 (2%) | |
| Thymus | (48) | (50) | (50) | (50) |
| Atrophy | 47 (98%) | 49 (98%) | 49 (98%) | 46 (92%) |

INTEGUMENTARY SYSTEM

| | | | | |
|---------------|--------|------|------|------|
| Mammary Gland | (48) | (50) | (50) | (50) |
| Hyperplasia | 1 (2%) | | | |

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| 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 (2%) | | 1 (2%) |
| Inflammation | | 2 (4%) | | 1 (2%) |
| Epidermis, Hyperplasia, Basal Cell | | | 1 (2%) | |
| Subcutaneous Tissue, Fibrosis | 1 (2%) | | | |
| MUSCULOSKELETAL SYSTEM | | | | |
| Bone | (49) | (50) | (50) | (50) |
| Osteopetrosis | | | | 1 (2%) |
| Ligament, Mineralization | | | | 1 (2%) |
| Skeletal Muscle | (1) | (0) | (1) | (1) |
| NERVOUS SYSTEM | | | | |
| Brain | (49) | (50) | (50) | (50) |
| Hemorrhage | 1 (2%) | 1 (2%) | | 2 (4%) |
| Hydrocephalus | | 1 (2%) | | 1 (2%) |
| Necrosis | 2 (4%) | | 2 (4%) | 2 (4%) |
| Choroid Plexus, Infiltration Cellular, Lymphocyte | | | 1 (2%) | |
| Spinal Cord | (2) | (0) | (0) | (0) |
| RESPIRATORY SYSTEM | | | | |
| Lung | (49) | (50) | (50) | (50) |
| Congestion | | 1 (2%) | 1 (2%) | 1 (2%) |
| Foreign Body | | | | 1 (2%) |
| Hemorrhage | | | | 1 (2%) |
| Inflammation, Granulomatous | | | | 3 (6%) |
| Inflammation, Chronic Active | 6 (12%) | 3 (6%) | 9 (18%) | 9 (18%) |
| Necrosis | 2 (4%) | | | |
| Thrombosis | 1 (2%) | | 1 (2%) | |
| Alveolar Epithelium, Hyperplasia | 19 (39%) | 13 (26%) | 20 (40%) | 15 (30%) |

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| FISCHER 344 RATS MALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|---|----------|----------|----------|----------|
| Alveolar Epithelium, Hypertrophy | 2 (4%) | | 2 (4%) | 1 (2%) |
| Alveolar Epithelium, Metaplasia | | | 1 (2%) | |
| Alveolar Epithelium, Metaplasia, Squamous | 1 (2%) | 1 (2%) | 1 (2%) | |
| Alveolus, Infiltration Cellular, Histiocyte | 8 (16%) | 3 (6%) | 11 (22%) | 9 (18%) |
| Arteriole, Hyperplasia | | | | 1 (2%) |
| Serosa, Inflammation, Acute | | | | 1 (2%) |
| Nose | (49) | (50) | (50) | (50) |
| Foreign Body | 1 (2%) | 4 (8%) | 1 (2%) | 2 (4%) |
| Inflammation | 18 (37%) | 14 (28%) | 10 (20%) | 18 (36%) |
| Olfactory Epithelium, Metaplasia | 2 (4%) | 1 (2%) | 3 (6%) | 5 (10%) |
| Respiratory Epithelium, Hyperplasia | 1 (2%) | 3 (6%) | 1 (2%) | 4 (8%) |

SPECIAL SENSES SYSTEM

| | | | | |
|--------------------------------|---------|---------|----------|----------|
| Ear | (0) | (2) | (1) | (0) |
| Eye | (49) | (50) | (50) | (50) |
| Anterior Chamber, Inflammation | | | | 1 (2%) |
| Cornea, Fibrosis | 1 (2%) | | | |
| Cornea, Inflammation | | | 1 (2%) | |
| Iris, Inflammation | | | | 2 (4%) |
| Iris, Synechia | 1 (2%) | | | |
| Lens, Cataract | 2 (4%) | 1 (2%) | 2 (4%) | |
| Retina, Degeneration | 6 (12%) | 6 (12%) | 10 (20%) | 16 (32%) |
| Retina, Retinal Detachment | 1 (2%) | | | |
| Harderian Gland | (49) | (50) | (50) | (50) |
| Zymbal's Gland | (0) | (0) | (1) | (0) |

URINARY SYSTEM

| | | | | |
|-------------------------------|----------|----------|----------|----------|
| Kidney | (49) | (50) | (50) | (50) |
| Accumulation, Hyaline Droplet | 1 (2%) | | 1 (2%) | 2 (4%) |
| Hyperplasia, Oncocytic | | | | 1 (2%) |
| Infarct | 1 (2%) | | 1 (2%) | |
| Inflammation, Acute | | | 1 (2%) | |
| Mineralization | 38 (78%) | 43 (86%) | 41 (82%) | 34 (68%) |

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| FISCHER 344 RATS MALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|--|----------|----------|----------|----------|
| Nephropathy | 46 (94%) | 47 (94%) | 48 (96%) | 48 (96%) |
| Cortex, Cyst | 1 (2%) | | | 1 (2%) |
| Papilla, Necrosis | 1 (2%) | | | |
| Pelvis, Dilatation | | 1 (2%) | | |
| Pelvis, Inflammation | 1 (2%) | | | 1 (2%) |
| Pelvis, Transitional Epithelium, Hyperplasia | | 1 (2%) | 1 (2%) | 15 (30%) |
| Ureter | (1) | (1) | (0) | (0) |
| Inflammation | 1 (100%) | | | |
| Urethra | (1) | (0) | (0) | (0) |
| Inflammation | 1 (100%) | | | |
| Urinary Bladder | (49) | (50) | (50) | (50) |
| Inflammation | 2 (4%) | | 1 (2%) | 2 (4%) |
| Transitional Epithelium, Hyperplasia | 1 (2%) | | | |

*** END OF MALE ***

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| FISCHER 344 RATS FEMALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|---------------------------------|-----------|----------|----------|----------|
| Pigmentation, Hemosiderin | 1 (2%) | | 1 (2%) | 1 (2%) |
| Artery, Necrosis | 1 (2%) | | | |
| Bile Duct, Cyst | | 1 (2%) | | |
| Bile Duct, Hyperplasia | 12 (24%) | 15 (30%) | 10 (20%) | 10 (20%) |
| Centrilobular, Fatty Change | | | | 2 (4%) |
| Centrilobular, Necrosis | | 1 (2%) | | 1 (2%) |
| Hepatocyte, Hypertrophy | 5 (10%) | 2 (4%) | 3 (6%) | 33 (66%) |
| Oval Cell, Hyperplasia | | 2 (4%) | 2 (4%) | |
| Serosa, Fibrosis | 1 (2%) | 1 (2%) | | |
| Mesentery | (10) | (9) | (7) | (9) |
| Fat, Necrosis | 10 (100%) | 9 (100%) | 7 (100%) | 9 (100%) |
| Oral Mucosa | (0) | (1) | (2) | (0) |
| Hyperplasia, Squamous | | | 1 (50%) | |
| Pancreas | (50) | (50) | (50) | (50) |
| Atrophy | 13 (26%) | 10 (20%) | 16 (32%) | 17 (34%) |
| Basophilic Focus | 1 (2%) | | | |
| Inflammation | | | | 1 (2%) |
| Acinus, Hyperplasia | 1 (2%) | 3 (6%) | | |
| Acinus, Metaplasia, Hepatocyte | | 1 (2%) | | 4 (8%) |
| Salivary Glands | (50) | (50) | (50) | (50) |
| Atrophy | | | | 1 (2%) |
| Stomach, Forestomach | (50) | (50) | (50) | (50) |
| Erosion | | 1 (2%) | 2 (4%) | |
| Hyperplasia, Atypical | 1 (2%) | | | |
| Inflammation | 5 (10%) | 7 (14%) | 7 (14%) | 13 (26%) |
| Ulcer | 1 (2%) | 1 (2%) | 3 (6%) | 7 (14%) |
| Epithelium, Hyperplasia | 5 (10%) | 6 (12%) | 8 (16%) | 19 (38%) |
| Stomach, Glandular | (50) | (50) | (50) | (50) |
| Amyloid Deposition | | | 1 (2%) | |
| Inflammation | | 2 (4%) | | |
| Epithelium, Hyperplasia | | | 1 (2%) | |
| Epithelium, Necrosis | 1 (2%) | 1 (2%) | | |
| Tooth | (5) | (3) | (4) | (2) |
| Malformation | 5 (100%) | 3 (100%) | 4 (100%) | 2 (100%) |
| Peridontal Tissue, Inflammation | | | | 1 (50%) |

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| 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 (2%) | | | |
| Heart | (50) | (50) | (50) | (50) |
| Cardiomyopathy | 42 (84%) | 45 (90%) | 45 (90%) | 47 (94%) |
| Atrium, Thrombosis | | 1 (2%) | | 1 (2%) |
| Valve, Thrombosis | | 1 (2%) | | |

ENDOCRINE SYSTEM

| | | | | |
|-------------------------------|----------|----------|----------|----------|
| Adrenal Cortex | (50) | (50) | (50) | (50) |
| Amyloid Deposition | | 1 (2%) | | |
| Degeneration, Cystic | 3 (6%) | 6 (12%) | 7 (14%) | 6 (12%) |
| Hemorrhage | | | | 1 (2%) |
| Hypertrophy | 2 (4%) | 3 (6%) | 1 (2%) | 3 (6%) |
| Metaplasia, Osseous | | | 1 (2%) | |
| Necrosis | 2 (4%) | | 1 (2%) | 2 (4%) |
| Zona Fasciculata, Hyperplasia | 6 (12%) | 6 (12%) | 4 (8%) | 9 (18%) |
| Adrenal Medulla | (50) | (50) | (50) | (50) |
| Hyperplasia | 3 (6%) | | 1 (2%) | 1 (2%) |
| Necrosis | | 1 (2%) | | |
| Islets, Pancreatic | (50) | (50) | (50) | (50) |
| Hyperplasia | 1 (2%) | | 3 (6%) | 1 (2%) |
| Parathyroid Gland | (44) | (47) | (44) | (47) |
| Pituitary Gland | (50) | (50) | (50) | (50) |
| Cyst | | | 1 (2%) | |
| Pars Distalis, Angiectasis | 1 (2%) | 1 (2%) | 1 (2%) | 2 (4%) |
| Pars Distalis, Hyperplasia | 11 (22%) | 20 (40%) | 16 (32%) | 23 (46%) |
| Thyroid Gland | (50) | (50) | (50) | (50) |
| C-cell, Hyperplasia | 15 (30%) | 15 (30%) | 6 (12%) | 4 (8%) |
| Follicle, Cyst | | | | 2 (4%) |
| Follicular Cell, Hyperplasia | 1 (2%) | 1 (2%) | 4 (8%) | 4 (8%) |

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

TDMS No. 20007 - 05
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: RATS/F 344/N

P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Kava kava extract
 CAS Number: 9000-38-8

Date Report Requested: 09/21/2010
 Time Report Requested: 09:10:56
 First Dose M/F: 08/18/04 / 08/19/04
 Lab: BAT

| FISCHER 344 RATS FEMALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|-------------------------|----------|----------|----------|----------|
|-------------------------|----------|----------|----------|----------|

GENERAL BODY SYSTEM

None

GENITAL SYSTEM

| | | | | |
|---------------------------------------|---------|---------|---------|----------|
| Clitoral Gland | (50) | (49) | (50) | (49) |
| Hyperplasia | | 3 (6%) | 5 (10%) | 1 (2%) |
| Inflammation | 1 (2%) | 2 (4%) | | |
| Ovary | (50) | (50) | (50) | (50) |
| Cyst | 7 (14%) | 9 (18%) | 6 (12%) | 5 (10%) |
| Cyst, Multiple | 1 (2%) | | | |
| Uterus | (50) | (50) | (50) | (50) |
| Congestion | | 1 (2%) | | |
| Hemorrhage | | 2 (4%) | | 1 (2%) |
| Necrosis | | 1 (2%) | | |
| Endometrium, Hyperplasia, Adenomatous | | | 1 (2%) | |
| Endometrium, Hyperplasia, Cystic | 5 (10%) | 5 (10%) | 6 (12%) | 10 (20%) |
| Stroma, Hyperplasia | | | 1 (2%) | |

HEMATOPOIETIC SYSTEM

| | | | | |
|---------------------------|----------|----------|----------|----------|
| Bone Marrow | (50) | (50) | (50) | (50) |
| Hemorrhage | 1 (2%) | | | |
| Hyperplasia | 26 (52%) | 27 (54%) | 19 (38%) | 23 (46%) |
| Inflammation, Histiocytic | | | 1 (2%) | |
| Myelofibrosis | 2 (4%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Necrosis | 1 (2%) | | | |
| Lymph Node | (1) | (3) | (3) | (2) |
| Lymph Node, Mesenteric | (50) | (50) | (50) | (50) |
| Atrophy | 1 (2%) | 1 (2%) | 1 (2%) | |
| Inflammation | 2 (4%) | | | |
| Spleen | (50) | (50) | (50) | (50) |

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TDMS No. 20007 - 05
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: RATS/F 344/N

P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Kava kava extract
 CAS Number: 9000-38-8

Date Report Requested: 09/21/2010
 Time Report Requested: 09:10:56
 First Dose M/F: 08/18/04 / 08/19/04
 Lab: BAT

| FISCHER 344 RATS FEMALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|------------------------------------|----------|----------|----------|----------|
| Accessory Spleen | | | 1 (2%) | |
| Fibrosis | | 3 (6%) | | 2 (4%) |
| Hematopoietic Cell Proliferation | 19 (38%) | 18 (36%) | 17 (34%) | 7 (14%) |
| Hyperplasia, Histiocytic | 1 (2%) | | 1 (2%) | |
| Pigmentation, Hemosiderin | 37 (74%) | 37 (74%) | 41 (82%) | 42 (84%) |
| Lymphoid Follicle, Atrophy | 1 (2%) | 1 (2%) | 4 (8%) | 2 (4%) |
| Lymphoid Follicle, Necrosis | 1 (2%) | | | |
| Thymus | (50) | (50) | (49) | (48) |
| Atrophy | 48 (96%) | 43 (86%) | 47 (96%) | 45 (94%) |
| Infiltration Cellular, Plasma Cell | 1 (2%) | | | |
| Inflammation | | | 1 (2%) | |
| INTEGUMENTARY SYSTEM | | | | |
| Mammary Gland | (50) | (50) | (50) | (50) |
| Galactocele | | | 1 (2%) | |
| Hyperplasia | | | 2 (4%) | |
| Skin | (50) | (50) | (50) | (50) |
| Epidermis, Hyperkeratosis | | | 1 (2%) | |
| Epidermis, Hyperplasia, Basal Cell | | 1 (2%) | | |
| MUSCULOSKELETAL SYSTEM | | | | |
| Bone | (50) | (50) | (50) | (50) |
| Osteopetrosis | 1 (2%) | | | |
| Skeletal Muscle | (1) | (0) | (1) | (0) |
| Inflammation | 1 (100%) | | | |
| NERVOUS SYSTEM | | | | |
| Brain | (50) | (50) | (50) | (50) |
| Hemorrhage | | 2 (4%) | 2 (4%) | |
| Infiltration Cellular, Mixed Cell | | | 1 (2%) | |
| Necrosis | | 3 (6%) | 2 (4%) | |

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TDMS No. 20007 - 05
 Test Type: CHRONIC
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P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Kava kava extract
 CAS Number: 9000-38-8

Date Report Requested: 09/21/2010
 Time Report Requested: 09:10:56
 First Dose M/F: 08/18/04 / 08/19/04
 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 (100%) | |
| Necrosis | | | 1 (100%) | |

RESPIRATORY SYSTEM

| | | | | |
|---|----------|----------|----------|----------|
| Lung | (50) | (50) | (50) | (50) |
| Atelectasis | 1 (2%) | 1 (2%) | | |
| Congestion | 1 (2%) | | | 1 (2%) |
| Hemorrhage | | | | 1 (2%) |
| Inflammation, Chronic Active | 4 (8%) | 5 (10%) | 2 (4%) | 7 (14%) |
| Alveolar Epithelium, Hyperplasia | 11 (22%) | 14 (28%) | 6 (12%) | 7 (14%) |
| Alveolar Epithelium, Hypertrophy | 1 (2%) | 1 (2%) | | |
| Alveolar Epithelium, Metaplasia | 1 (2%) | | | |
| Alveolar Epithelium, Metaplasia, Squamous | 1 (2%) | 3 (6%) | | |
| Alveolus, Infiltration Cellular, Histiocyte | 12 (24%) | 17 (34%) | 12 (24%) | 16 (32%) |
| Mediastinum, Foreign Body | 1 (2%) | | | |
| Mediastinum, Inflammation, Chronic Active | 1 (2%) | | | |
| Nose | (50) | (50) | (50) | (50) |
| Cyst | 1 (2%) | | | |
| Foreign Body | 2 (4%) | | | |
| Inflammation | 8 (16%) | 2 (4%) | 9 (18%) | 8 (16%) |
| Glands, Dilatation | | | 1 (2%) | |
| Olfactory Epithelium, Metaplasia | 1 (2%) | | 1 (2%) | |
| Respiratory Epithelium, Hyperplasia | | | 1 (2%) | |
| Pleura | (0) | (0) | (0) | (1) |
| Mesothelium, Hyperplasia | | | | 1 (100%) |
| Trachea | (50) | (50) | (50) | (50) |
| Peritracheal Tissue, Inflammation | | | 1 (2%) | |

SPECIAL SENSES SYSTEM

| | | | | |
|-----|------|------|------|------|
| Ear | (1) | (0) | (0) | (1) |
| Eye | (50) | (50) | (50) | (50) |

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TDMS No. 20007 - 05
 Test Type: CHRONIC
 Route: GAVAGE
 Species/Strain: RATS/F 344/N

P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

Kava kava extract
 CAS Number: 9000-38-8

Date Report Requested: 09/21/2010
 Time Report Requested: 09:10:56
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 Lab: BAT

| FISCHER 344 RATS FEMALE | 0.0 G/KG | 0.1 G/KG | 0.3 G/KG | 1.0 G/KG |
|--|----------|----------|----------|----------|
| Synechia | | | 1 (2%) | |
| Cornea, Fibrosis | 1 (2%) | | | 1 (2%) |
| Cornea, Inflammation | 1 (2%) | | 2 (4%) | 2 (4%) |
| Lens, Cataract | 2 (4%) | 3 (6%) | 1 (2%) | 3 (6%) |
| Posterior Chamber, Inflammation | | | | 1 (2%) |
| Retina, Degeneration | 5 (10%) | 5 (10%) | 5 (10%) | 12 (24%) |
| Retina, Dysplasia | | | 1 (2%) | |
| Retina, Gliosis | 1 (2%) | | 3 (6%) | 1 (2%) |
| Retina, Inflammation | | 1 (2%) | | |
| Zymbal's Gland | (0) | (0) | (0) | (1) |
| URINARY SYSTEM | | | | |
| Kidney | (50) | (50) | (50) | (50) |
| Accumulation, Hyaline Droplet | | 2 (4%) | 1 (2%) | 1 (2%) |
| Glomerulosclerosis | | 1 (2%) | | |
| Infarct | 2 (4%) | 3 (6%) | 4 (8%) | 3 (6%) |
| Mineralization | 43 (86%) | 43 (86%) | 45 (90%) | 46 (92%) |
| Nephropathy | 34 (68%) | 35 (70%) | 37 (74%) | 43 (86%) |
| Cortex, Cyst | 2 (4%) | | | |
| Medulla, Cyst | 1 (2%) | | | |
| Papilla, Necrosis | | | 1 (2%) | 1 (2%) |
| Pelvis, Inflammation | 1 (2%) | 1 (2%) | 5 (10%) | 4 (8%) |
| Pelvis, Transitional Epithelium, Hyperplasia | | | 4 (8%) | 6 (12%) |
| Pelvis, Transitional Epithelium, Metaplasia | | | 1 (2%) | |
| Renal Tubule, Dilatation | | | 1 (2%) | |
| Renal Tubule, Necrosis | | | 1 (2%) | 2 (4%) |
| Urinary Bladder | (50) | (50) | (50) | (50) |

*** END OF REPORT ***

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