Experiment Number: 20725 - 04

Species/Strain: MICE/B6C3F1

Test Type: CHRONIC

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH Date Report Requested: 04/15/2016 AVERAGE SEVERITY GRADES[b]

RAGE SEVERITY GRADES[b]

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

Lab: BNW

F1_Mice

NTP Study Number: C20725

Lock Date: 10/11/2012

Cage Range: ALL

Route: RESPIRATORY EXPOSURE WHOLE BODY

Date Range: ALL

Reasons For Removal: ALL

Removal Date Range: ALL

Treatment Groups: Include ALL

Study Gender: Both

TDMSE Version: 3.0.2.3_002

PWG Approval Date: 01/25/2016

Test Type: CHRONIC Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione **CAS Number:** 431-03-8 Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
Disposition Summary					
Animals Initially In Study	50	50	50	50	
Early Deaths					
Accidentally Killed		1			
Moribund Sacrifice	6	5	4	14	
Natural Death	9	5	9	11	
Survivors					
Terminal Sacrifice	35	39	37	25	
Animals Examined Microscopically	50	50	50	50	
ALIMENTARY SYSTEM					
Esophagus	(50)	(50)	(50)	(50)	
Epithelium, Hyperplasia		1 [2.0]			
Periesophageal Tissue, Inflammation, Chronic Active				3 [1.7]	
Submucosa, Inflammation, Chronic Active				1 [1.0]	
Gallbladder	(45)	(42)	(43)	(43)	
Inflammation				1 [2.0]	
Intestine Large, Cecum	(46)	(48)	(47)	(48)	
Inflammation	7 [1.6]		2 [1.0]		
Intestine Large, Colon	(46)	(47)	(48)	(47)	
Intestine Large, Rectum	(46)	(46)	(45)	(49)	
Inflammation				1 [1.0]	
Intestine Small, Duodenum	(45)	(47)	(44)	(44)	
Inflammation	1 [3.0]				
Necrosis	1 [2.0]				
Intestine Small, Ileum	(45)	(47)	(44)	(46)	
Hemorrhage				1 [2.0]	
Hyperplasia, Lymphoid	1 [1.0]	1 [2.0]	2 [2.0]		
Inflammation	3 [1.0]		1 [1.0]		
Intestine Small, Jejunum	(44)	(46)	(43)	(43)	
Hyperplasia, Lymphoid	1 [1.0]		1 [2.0]	1 [1.0]	
Inflammation	1 [1.0]	1 [2.0]			
Liver	(50)	(50)	(50)	(50)	

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

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
Basophilic Focus	7	5	7	6	
Clear Cell Focus	2	5	5		
Cyst	1	1			
Eosinophilic Focus	4	6	4	4	
Hematopoietic Cell Proliferation				1 [1.0]	
Hepatodiaphragmatic Nodule	1				
Mixed Cell Focus	4	7	2	1	
Pigmentation, Ceroid	1 [2.0]				
Syncytial Alteration		1 [1.0]			
Tension Lipidosis		2 [1.0]		1 [1.0]	
Thrombosis		1 [4.0]			
Hepatocyte, Degeneration	2 [2.5]				
Hepatocyte, Necrosis	4 [2.0]	5 [2.4]	1 [2.0]	3 [1.7]	
Mesentery	(4)	(1)	(5)	(0)	
Hemorrhage	1 [2.0]		, ,	. ,	
Artery, Thrombosis	1 [2.0]				
Fat, Necrosis	1 [2.0]	1 [1.0]	2 [1.5]		
Pancreas	(48)	(48)	(50)	(50)	
Necrosis	, ,	, ,	1 [1.0]	, ,	
Acinus, Atrophy	2 [2.5]		1 [1.0]		
Salivary Glands	(50)	(49)	(50)	(50)	
Stomach, Forestomach	(48)	(48)	(49)	(50)	
Inflammation	2 [1.0]	1 [1.0]	1 [2.0]	, ,	
Necrosis			1 [1.0]		
Epithelium, Hyperplasia	3 [1.3]	2 [1.0]	1 [3.0]	1 [1.0]	
Stomach, Glandular	(47)	(48)	(49)	(49)	
Inflammation	3 [1.0]	4 [1.0]	2 [1.0]		
Mineralization			1 [1.0]		
Epithelium, Hyperplasia	1 [1.0]				
Tooth	(2)	(2)	(1)	(0)	
Dysplasia	2 [1.5]	2 [1.5]	1 [1.0]	. ,	
CARDIOVASCULAR SYSTEM					
Blood Vessel	(50)	(50)	(50)	(50)	

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)

Experiment Number: 20725 - 04

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH Date Report Requested: 04/15/2016 AVERAGE SEVERITY GRADES[b]

Test Type: CHRONIC

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
Inflammation	2 [1.0]			1 [1.0]	
Heart	(50)	(50)	(50)	(49)	
Cardiomyopathy	4 [1.0]	1 [2.0]	8 [1.3]	3 [1.0]	
Inflammation, Acute	1 [1.0]		1 [3.0]	3 [3.0]	
Inflammation, Chronic Active			1 [1.0]	5 [1.0]	
Mineralization		1 [2.0]			
Necrosis	1 [4.0]			3 [2.7]	
Polyarteritis	3 [2.0]			1 [2.0]	
Thrombosis	1 [2.0]				
Valve, Inflammation, Chronic Active	1 [1.0]				
ENDOCRINE SYSTEM					
Adrenal Cortex	(50)	(49)	(50)	(50)	
Hyperplasia	1 [2.0]				
Inflammation, Suppurative				1 [1.0]	
Vacuolization Cytoplasmic	1 [2.0]				
Zona Fasciculata, Hypertrophy, Focal	23 [1.1]	26 [1.1]	35 [1.1]	9 [1.0]	
Adrenal Medulla	(50)	(48)	(50)	(50)	
Hyperplasia			3 [1.0]		
Islets, Pancreatic	(48)	(48)	(49)	(50)	
Hyperplasia	1 [1.0]	1 [1.0]	4 [1.5]		
Parathyroid Gland	(40)	(39)	(44)	(37)	
Pituitary Gland	(50)	(49)	(50)	(50)	
Pars Distalis, Hyperplasia	1 [1.0]	2 [1.5]			
Thyroid Gland	(50)	(49)	(50)	(50)	
Cyst	1				
Inflammation, Chronic Active	1 [1.0]			2 [1.5]	
Follicular Cell, Hyperplasia		1 [1.0]		1 [1.0]	
GENERAL BODY SYSTEM					
Tissue NOS	(0)	(0)	(0)	(1)	
Inflammation, Chronic Active	(0)	(0)	(5)	1 [2.0]	

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Test Type: CHRONIC Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione **CAS Number:** 431-03-8 Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
GENITAL SYSTEM					
Epididymis	(49)	(49)	(50)	(49)	
Exfoliated Germ Cell	32	23	25	26	
Granuloma Sperm	1 [2.0]	2 [1.5]		1 [4.0]	
Infiltration Cellular, Lymphoid	1 [1.0]				
Inflammation	3 [1.7]	2 [2.0]	1 [1.0]	1 [1.0]	
Preputial Gland	(50)	(49)	(50)	(49)	
Ectasia		2 [1.0]	2 [1.5]	1 [1.0]	
Inflammation	1 [2.0]	3 [1.3]	5 [2.0]	3 [2.0]	
Prostate	(49)	(49)	(49)	(50)	
Inflammation		2 [1.0]		1 [2.0]	
Seminal Vesicle	(49)	(49)	(50)	(50)	
Dilatation	2 [1.0]				
Testes	(49)	(49)	(50)	(49)	
Interstitial Cell, Hyperplasia			1 [2.0]	1 [2.0]	
Seminiferous Tubule, Degeneration	14 [1.3]	6 [1.2]	13 [1.4]	6 [1.2]	
HEMATOPOIETIC SYSTEM					
Bone Marrow	(48)	(47)	(50)	(49)	
Infiltration Cellular, Mast Cell	(10)	(. ,)	1 [1.0]	(13)	
Necrosis	1 [1.0]		. [•]		
Myeloid Cell, Hyperplasia	9 [2.1]	8 [1.4]	20 [1.3]	39 [2.5]	
Lymph Node	(5)	(1)	(3)	(8)	
Deep Cervical, Ectasia	()	()	()	1 [2.0]	
Deep Cervical, Hematopoietic Cell Proliferation				1 [3.0]	
Deep Cervical, Hyperplasia, Lymphoid				4 [2.8]	
Deep Cervical, Infiltration Cellular, Plasma Cell				1 [3.0]	
Pancreatic, Ectasia			1 [3.0]		
Pancreatic, Hyperplasia, Lymphoid				1 [4.0]	
Renal, Ectasia	1 [1.0]		1 [2.0]		
Renal, Hematopoietic Cell Proliferation				1 [2.0]	
Lymph Node, Bronchial	(34)	(43)	(38)	(31)	

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

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
Ectasia				1 [2.0]	
Hematopoietic Cell Proliferation			1 [2.0]	• •	
Hyperplasia, Lymphoid		1 [1.0]	3 [1.0]	2 [1.0]	
Infiltration Cellular, Plasma Cell				1 [2.0]	
Inflammation, Chronic Active				2 [1.5]	
Pigmentation				3 [1.0]	
Lymph Node, Mandibular	(36)	(33)	(30)	(32)	
Ectasia	(()	,	4 [2.0]	
Hematopoietic Cell Proliferation				3 [2.7]	
Hyperplasia, Lymphoid	2 [1.0]	5 [1.2]	11 [1.3]	10 [1.7]	
Infiltration Cellular, Plasma Cell	1 [1.0]		2 [1.0]	14 [2.0]	
Lymph Node, Mediastinal	(37)	(33)	(38)	(32)	
Hematopoietic Cell Proliferation	(()	1 [1.0]	1 [2.0]	
Hyperplasia, Lymphoid				2 [1.0]	
Infiltration Cellular, Plasma Cell			1 [2.0]	2 [1.5]	
Inflammation, Chronic Active				2 [3.0]	
Lymph Node, Mesenteric	(47)	(47)	(49)	(47)	
Ectasia	1 [2.0]	,	1 [2.0]	,	
Hematopoietic Cell Proliferation	4 [1.5]	1 [1.0]		2 [1.5]	
Hyperplasia, Lymphoid	7 [1.7]	1 [3.0]	2 [1.0]		
Inflammation			1 [2.0]		
Spleen	(48)	(49)	(50)	(50)	
Angiectasis	(1 [1.0]	,	,	
Congestion		,		1 [2.0]	
Hematopoietic Cell Proliferation	11 [2.2]	12 [1.7]	15 [1.8]	25 [2.0]	
Hyperplasia, Lymphoid		4 [1.3]	1 [1.0]	3 [1.7]	
Inflammation	1 [1.0]	,	1	2 [1.5]	
Necrosis				2 [1.5]	
Lymphoid Follicle, Atrophy				2 [2.0]	
Thymus	(43)	(42)	(44)	(30)	
Atrophy	10 [1.4]	5 [1.2]	2 [1.5]	5 [1.6]	
Cyst	1		r -1	1	
Ectopic Parathyroid Gland	6 [1.0]	4 [1.0]	11 [1.0]	4 [1.0]	
Inflammation, Chronic Active	1 [1.0]	r - 3	1	3 [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)

Test Type: CHRONIC Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione **CAS Number:** 431-03-8 Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

INTEGUMENTARY SYSTEM Mammary Gland (1) Skin (50) Hyperkeratosis Inflammation, Chronic Active 1 [3.0] Pigmentation, Melanin Epidermis, Hyperplasia Epidermis, Necrosis Epidermis, Ulcer 1 [3.0] Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	(0) (49) 1 [3.0] 1 [2.0] 2 [2.0] 1 [3.0]	(0) (50) 1 [2.0] 2 [3.5] 1 [1.0] 1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0] 1 [3.0]	(1) (49) 1 [3.0]	
Skin (50) Hyperkeratosis Inflammation, Chronic Active 1 [3.0] Pigmentation, Melanin Epidermis, Hyperplasia Epidermis, Necrosis Epidermis, Ulcer 1 [3.0] Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	(49) 1 [3.0] 1 [2.0] 2 [2.0] 1 [3.0]	(50) 1 [2.0] 2 [3.5] 1 [1.0] 1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0] 1 [3.0]	(49) 1 [3.0]	
Hyperkeratosis Inflammation, Chronic Active 1 [3.0] Pigmentation, Melanin Epidermis, Hyperplasia Epidermis, Necrosis Epidermis, Ulcer 1 [3.0] Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	1 [3.0] 1 [2.0] 2 [2.0] 1 [3.0]	1 [2.0] 2 [3.5] 1 [1.0] 1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0] 1 [3.0]	1 [3.0]	
Inflammation, Chronic Active Pigmentation, Melanin Epidermis, Hyperplasia Epidermis, Necrosis Epidermis, Ulcer Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion Maxilla, Osteomalacia Skeletal Muscle Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	1 [2.0] 2 [2.0] 1 [3.0]	2 [3.5] 1 [1.0] 1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0] 1 [3.0]		
Pigmentation, Melanin Epidermis, Hyperplasia Epidermis, Necrosis Epidermis, Ulcer 1 [3.0] Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	1 [2.0] 2 [2.0] 1 [3.0]	1 [1.0] 1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0]		
Pigmentation, Melanin Epidermis, Hyperplasia Epidermis, Necrosis Epidermis, Ulcer 1 [3.0] Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	1 [2.0] 2 [2.0] 1 [3.0]	1 [1.0] 1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0]	(50)	
Epidermis, Necrosis Epidermis, Ulcer 1 [3.0] Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	1 [3.0]	1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0] 1 [3.0]	(50)	
Epidermis, Necrosis Epidermis, Ulcer 1 [3.0] Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	1 [3.0]	1 [3.0] 1 [2.0] 1 [3.0] 1 [4.0] 1 [3.0]	(50)	
Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute		1 [2.0] 1 [3.0] 1 [4.0] 1 [3.0]	(50)	
Subcutaneous Tissue, Cyst Epithelial Inclusion Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute		1 [3.0] 1 [4.0] 1 [3.0]	(50)	
Subcutaneous Tissue, Inflammation, Suppurative Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	(50)	1 [4.0] 1 [3.0]	(50)	
Subcutaneous Tissue, Necrosis MUSCULOSKELETAL SYSTEM Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	(50)		(50)	
Bone (50) Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	(50)	(50)	(50)	
Fibro-Osseous Lesion 1 [1.0] Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	(50)	(50)	(50)	
Maxilla, Osteomalacia Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute				
Skeletal Muscle (2) Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	1 [1.0]	3 [2.0]	2 [1.5]	
Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute			1 [2.0]	
Degeneration Hemorrhage, Acute Inflammation Necrosis, Acute	(4)	(5)	(2)	
Inflammation Necrosis, Acute	1 [1.0]		1 [1.0]	
Necrosis, Acute	2 [3.5]			
· · · · · · · · · · · · · · · · · · ·	1 [1.0]		1 [2.0]	
NERVOUS SYSTEM	1 [3.0]			
Brain (50)	(50)	(50)	(50)	
Infiltration Cellular, Lymphocyte	(30)	(50) 2 [1.0]	(30)	
Inflammation, Acute 1 [2.0]		2 [1.0] 1 [1.0]		
Inflammation, Active		1 [1.0]	1 [2.0]	
Necrosis, Chronic Active 1 [2.0]			1 [2.0]	
			(1)	
Peripheral Nerve (0) Degeneration	(2)	(1)	/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)

Test Type: CHRONIC

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43
First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
Spinal Cord	(0)	(2)	(1)	(1)	
RESPIRATORY SYSTEM					
Larynx	(49)	(49)	(49)	(50)	
Inflammation, Suppurative	2 [1.0]				
Inflammation, Chronic Active	4 [1.0]	2 [1.0]	11 [1.2]	42 [1.6]	
Artery, Inflammation, Chronic Active				1 [2.0]	
Lumen, Exudate				2 [3.5]	
Respiratory Epithelium, Hyperplasia	1 [1.0]			11 [1.3]	
Respiratory Epithelium, Metaplasia, Squamous	3 [1.0]		6 [1.2]	50 [3.1]	
Respiratory Epithelium, Necrosis	2 [1.0]	1 [1.0]	9 [1.0]	34 [1.2]	
Respiratory Epithelium, Regeneration				32 [1.8]	
Squamous Epithelium, Hyperplasia	3 [1.3]	7 [1.3]	15 [1.4]	42 [1.8]	
Lung	(50)	(49)	(50)	(50)	
Foreign Body				1	
Inflammation, Suppurative				3 [2.3]	
Inflammation, Chronic Active	1 [1.0]		2 [1.5]		
Mineralization	1 [1.0]				
Thrombosis	2 [1.0]	1		2	
Alveolar Epithelium, Hyperplasia	1 [1.0]	1 [1.0]			
Alveolar Epithelium, Hyperplasia, Focal	3 [2.0]	3 [1.3]	4 [2.8]		
Alveolus, Infiltration Cellular, Histiocyte	7 [2.0]	2 [2.0]	3 [1.3]	9 [1.4]	
Bronchiole, Epithelium, Hyperplasia	1 [1.0]		1 [2.0]	2 [2.0]	
Bronchus, Inflammation, Suppurative				1 [1.0]	
Bronchus, Epithelium, Necrosis				2 [1.5]	
Bronchus, Epithelium, Regeneration				34 [1.9]	
Interstitium, Fibrosis	1 [1.0]		1 [1.0]		
Mediastinum, Inflammation, Suppurative				3 [1.3]	
Mediastinum, Inflammation, Chronic Active	1 [1.0]			8 [1.1]	
Mediastinum, Necrosis				1 [2.0]	
Pleura, Inflammation, Suppurative				2 [1.5]	
Pleura, Inflammation, Chronic Active			1 [2.0]		
Nose	(49)	(48)	(50)	(50)	
Foreign Body	, ,	, ,	`3	, ,	

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

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
Inflammation, Suppurative	2 [1.0]	4 [1.0]	47 [1.4]	50 [3.2]	
Glands, Olfactory Epithelium, Inflammation, Acute		1 [1.0]			
Glands, Respiratory Epithelium, Cyst		1 [3.0]		5	
Glands, Sinus, Metaplasia, Respiratory			1 [2.0]	13 [1.0]	
Lamina Propria, Fibrosis			44 [1.0]	50 [2.0]	
Lateral Wall, Inflammation, Chronic Active	5 [2.2]	8 [1.9]	5 [2.0]	2 [2.5]	
Mucosa, Regeneration			47 [1.2]	47 [1.6]	
Nasopharyngeal Duct, Polyp, Inflammatory				1	
Olfactory Epithelium, Accumulation, Hyaline Droplet	1 [1.0]		1 [1.0]	2 [1.5]	
Olfactory Epithelium, Atrophy		14 [1.1]	48 [2.1]	38 [1.8]	
Olfactory Epithelium, Metaplasia, Respiratory	1 [1.0]		39 [1.6]	45 [2.7]	
Olfactory Epithelium, Metaplasia, Squamous	1 [1.0]				
Olfactory Epithelium, Necrosis				19 [2.2]	
Respiratory Epithelium, Accumulation, Hyaline Droplet	3 [1.0]	1 [1.0]	6 [1.0]	7 [1.0]	
Respiratory Epithelium, Cyst		1 [3.0]			
Respiratory Epithelium, Hyperplasia	1 [1.0]			8 [1.0]	
Respiratory Epithelium, Metaplasia, Squamous		6 [1.0]	47 [1.5]	50 [2.4]	
Respiratory Epithelium, Necrosis			34 [1.1]	50 [1.6]	
Respiratory Epithelium, Regeneration			2 [2.0]		
Septum, Perforation			3	11	
Turbinate, Atrophy		8 [1.1]	49 [1.2]	50 [2.3]	
Turbinate, Necrosis			4 [1.0]	27 [1.0]	
Trachea	(48)	(49)	(49)	(49)	
Inflammation, Chronic Active			2 [1.0]	45 [1.6]	
Necrosis				47 [1.5]	
Carina, Epithelium, Hyperplasia				1 [1.0]	
Carina, Epithelium, Necrosis				1 [1.0]	
Carina, Submucosa, Fibrosis				16 [1.7]	
Carina, Submucosa, Inflammation, Chronic Active				4 [1.8]	
Carina, Submucosa, Mineralization				15 [1.9]	
Epithelium, Hyperplasia				6 [2.0]	
Epithelium, Metaplasia, Squamous				5 [1.0]	
Epithelium, Regeneration				45 [2.9]	

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

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43
First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm	
Lumen, Exudate				4 [3.0]	
Submucosa, Fibrosis				46 [2.3]	
SPECIAL SENSES SYSTEM					
Eye	(49)	(49)	(50)	(50)	
Phthisis Bulbi				1	
Anterior Chamber, Inflammation, Suppurative				5 [2.0]	
Cornea, Edema				1 [1.0]	
Cornea, Inflammation, Acute	2 [1.5]		1 [1.0]	17 [1.4]	
Cornea, Mineralization				5 [1.4]	
Cornea, Neovascularization				1 [3.0]	
Cornea, Epithelium, Hyperplasia	1 [1.0]			9 [1.2]	
Cornea, Epithelium, Ulcer				3 [2.0]	
Lens, Cataract	1 [2.0]	1 [1.0]		2 [2.0]	
Harderian Gland	(50)	(49)	(50)	(50)	
Hyperplasia	2 [1.5]	3 [2.0]	1 [2.0]	2 [1.0]	
URINARY SYSTEM					
Kidney	(49)	(50)	(50)	(50)	
Cyst	1	2	1		
Infarct	2 [2.0]	1 [1.0]	2 [2.0]	1 [1.0]	
Infiltration Cellular, Lymphocyte		1 [1.0]			
Inflammation	1 [2.0]		2 [3.5]	1 [2.0]	
Metaplasia, Osseous	2 [1.0]	2 [1.0]	4 [1.3]	2 [1.0]	
Mineralization	-	1 [1.0]	-		
Nephropathy	34 [1.1]	26 [1.1]	25 [1.3]	10 [1.0]	
Pigmentation, Hemosiderin			1 [2.0]		
Papilla, Necrosis				1 [2.0]	
Pelvis, Dilatation		1 [1.0]	1 [4.0]		
Urinary Bladder	(49)	(48)	(50)	(49)	
Angiectasis	1 [1.0]	. ,	. ,		
Hyperplasia, Lymphoid			1 [2.0]		
Inflammation		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)

Experiment Number: 20725 - 04

Species/Strain: MICE/B6C3F1

Route: RESPIRATORY EXPOSURE WHOLE BODY

Test Type: CHRONIC

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH Date Report Requested: 04/15/2016 AVERAGE SEVERITY GRADES[b]

2,3-Butanedione

CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

Lab: BNW

B6C3F1 MICE MALE	Control	12.5 ppm	25 ppm	50 ppm
Mineralization				1 [1.0]

*** END OF MALE ***

Test Type: CHRONIC Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione **CAS Number:** 431-03-8 Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Disposition Summary					
Animals Initially In Study	50	50	50	50	
Early Deaths					
Moribund Sacrifice	10	6	4	15	
Natural Death	4	4	4	17	
Survivors					
Moribund Sacrifice				1	
Terminal Sacrifice	36	40	42	17	
Animals Examined Microscopically	50	50	50	50	
ALIMENTARY SYSTEM					
Esophagus	(50)	(50)	(50)	(50)	
Epithelium, Hyperplasia	(-3)	1 [1.0]	(-0)	(/	
Periesophageal Tissue, Inflammation, Chronic		. []		9 [1.6]	
Active					
Gallbladder	(42)	(45)	(45)	(37)	
Hyperplasia		1 [1.0]			
Inflammation				3 [1.0]	
Ulcer		1 [1.0]			
Intestine Large, Cecum	(47)	(49)	(50)	(41)	
Inflammation	2 [1.5]		2 [1.5]		
Inflammation, Granulomatous	1 [4.0]				
Necrosis		1 [1.0]			
Intestine Large, Colon	(47)	(49)	(50)	(46)	
Intestine Large, Rectum	(49)	(49)	(46)	(43)	
Inflammation		1 [1.0]			
Intestine Small, Duodenum	(47)	(48)	(49)	(38)	
Inflammation	1 [4.0]	2 [1.0]			
Necrosis	1 [4.0]				
Intestine Small, Ileum	(47)	(48)	(49)	(39)	
Hyperplasia, Lymphoid		1 [1.0]	1 [1.0]		
Inflammation	1 [4.0]				
Necrosis	1 [4.0]	1 [1.0]			
Ulcer	1 [4.0]				

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Test Type: CHRONIC

Experiment Number: 20725 - 04

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43

First Dose M/F: 08/31/09 / 08/31/09

6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Intestine Small, Jejunum	(46)	(49)	(49)	(39)	
Liver	(50)	(50)	(50)	(50)	
Amyloid Deposition			1 [4.0]		
Angiectasis	1 [2.0]			1 [2.0]	
Basophilic Focus	1	3	3	1	
Clear Cell Focus	1	7	3		
Cyst	1		1	2	
Eosinophilic Focus	4	4		1	
Fatty Change		1 [3.0]	2 [1.5]		
Fibrosis, Focal		1 [2.0]			
Hematopoietic Cell Proliferation		1 [2.0]	1 [1.0]	1 [2.0]	
Hepatodiaphragmatic Nodule				1 [2.0]	
Hyperplasia, Lymphoid		2 [1.0]	4 [1.3]		
Infiltration Cellular, Lymphocyte				1 [2.0]	
Inflammation			1 [4.0]	• •	
Mixed Cell Focus	2				
Tension Lipidosis				1 [1.0]	
Centrilobular, Hepatocyte, Hypertrophy				1 [1.0]	
Hepatocyte, Degeneration		1 [3.0]			
Hepatocyte, Necrosis	3 [1.7]	4 [2.0]	1 [4.0]	1 [1.0]	
Kupffer Cell, Hypertrophy				1 [1.0]	
Mesentery	(6)	(10)	(4)	(1)	
Fat, Necrosis	4 [1.3]	9 [1.6]	4 [1.5]		
Pancreas	(50)	(50)	(50)	(47)	
Cyst	1			1	
Inflammation, Chronic Active	1 [2.0]	1 [3.0]	1 [1.0]		
Necrosis		1 [3.0]			
Acinus, Atrophy	1 [1.0]	2 [2.0]	1 [1.0]		
Salivary Glands	(49)	(50)	(50)	(50)	
Inflammation, Chronic Active	. ,	. ,	. ,	3 [2.0]	
Stomach, Forestomach	(50)	(50)	(50)	(49)	
Infiltration Cellular, Lymphoid	, ,	, ,	1 [1.0]	. ,	
Inflammation	3 [1.3]	1 [1.0]	3 [1.0]		
Mineralization	1 [1.0]				
Epithelium, Hyperplasia	3 [1.7]	2 [1.5]	2 [1.0]	1 [1.0]	
Stomach, Glandular	(49)	(50)	(50)	(46)	

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Test Type: CHRONIC

Experiment Number: 20725 - 04

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Cyst	1				
Degeneration		1 [1.0]			
Infiltration Cellular, Lymphoid	1 [1.0]		1 [1.0]		
Inflammation	5 [1.6]		1 [1.0]	2 [1.0]	
Mineralization	3 [1.3]			1 [1.0]	
Necrosis	1 [1.0]				
Tooth	(1)	(0)	(0)	(0)	
CARDIOVASCULAR SYSTEM					
Blood Vessel	(50)	(50)	(50)	(50)	
Inflammation	1 [2.0]	1 [2.0]		3 [1.7]	
Heart	(50)	(50)	(50)	(50)	
Cardiomyopathy	4 [1.0]	1 [1.0]	2 [1.0]	4 [1.0]	
Inflammation, Acute	2 [1.5]			2 [1.5]	
Inflammation, Chronic Active		2 [1.0]	1 [2.0]	7 [1.7]	
Mineralization		1 [1.0]		1 [1.0]	
Necrosis	1 [1.0]			2 [1.5]	
Polyarteritis	1 [3.0]			3 [1.7]	
Valve, Inflammation, Chronic Active				1 [1.0]	
Valve, Thrombosis	1 [2.0]				
ENDOCRINE SYSTEM					
Adrenal Cortex	(50)	(50)	(50)	(50)	
Accessory Adrenal Cortical Nodule	1 [1.0]				
Angiectasis				2 [1.0]	
Hematopoietic Cell Proliferation				1 [2.0]	
Hemorrhage				1 [2.0]	
Hyperplasia			1 [1.0]	1 [1.0]	
Hypertrophy				2 [1.0]	
Inflammation, Chronic Active			1 [4.0]		
Necrosis	1 [1.0]		1 [4.0]		
Vacuolization Cytoplasmic	1 [3.0]	1 [2.0]			
Zona Fasciculata, Hyperplasia, Focal		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

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

Lab: BNW

B6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm
Zona Fasciculata, Hypertrophy, Focal	2 [1.0]		2 [1.0]	3 [1.0]
Adrenal Medulla	(50)	(50)	(49)	(50)
Hyperplasia	2 [1.5]	4 [1.0]	1 [1.0]	2 [1.0]
Islets, Pancreatic	(49)	(50)	(49)	(48)
Hyperplasia		1 [2.0]		
Parathyroid Gland	(38)	(39)	(46)	(46)
Hyperplasia			1 [1.0]	
Pituitary Gland	(49)	(49)	(50)	(48)
Pars Distalis, Angiectasis	3 [1.3]	1 [1.0]	1 [2.0]	
Pars Distalis, Hyperplasia	15 [1.5]	7 [1.1]	6 [1.7]	1 [1.0]
Pars Distalis, Inflammation, Suppurative			1 [1.0]	
Pars Intermedia, Angiectasis			1 [1.0]	
Thyroid Gland	(50)	(49)	(48)	(50)
Inflammation, Chronic Active				9 [1.2]
Mineralization				1 [1.0]
Follicular Cell, Hyperplasia		2 [1.0]	1 [1.0]	

GENERAL BODY SYSTEM

None

GENITAL SYSTEM				
Clitoral Gland	(47)	(49)	(48)	(44)
Ovary	(49)	(50)	(49)	(50)
Angiectasis			1 [1.0]	
Cyst	15	17	12	12
Hemorrhage		1 [2.0]	1 [4.0]	
Hyperplasia, Tubular		1 [1.0]		
Inflammation	2 [4.0]	1 [1.0]	3 [2.0]	6 [2.2]
Mineralization		1 [2.0]	1 [2.0]	
Necrosis		1 [3.0]	1 [2.0]	
Uterus	(50)	(50)	(50)	(50)
Angiectasis	1 [3.0]	4 [1.8]	2 [2.5]	
Hemorrhage	1 [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)

Test Type: CHRONIC Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione **CAS Number:** 431-03-8 Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

Inflammation	4 [2.5] 1 [3.0]	2 [2.0]		
	1 [3.0]			
Thrombosis		3 [1.7]	1 [2.0]	
Artery, Necrosis	1 [4.0]			
Endometrium, Hyperplasia, Cystic	42 [2.4]	43 [2.3]	47 [2.1]	30 [1.9]
EMATOPOIETIC SYSTEM				
Bone Marrow	(50)	(50)	(50)	(49)
Myeloid Cell, Hyperplasia	3 [2.3]	2 [1.0]	7 [2.1]	33 [2.2]
Lymph Node	(11)	(10)	(11)	(7)
Deep Cervical, Hyperplasia, Lymphoid			1 [3.0]	4 [2.5]
Deep Cervical, Infiltration Cellular, Plasma Cell				1 [3.0]
Iliac, Ectasia		1 [2.0]		
Lumbar, Ectasia	1 [2.0]	1 [2.0]	1 [3.0]	
Lumbar, Hyperplasia	1 [2.0]			
Lumbar, Hyperplasia, Lymphoid	1 [1.0]		1 [3.0]	
Renal, Amyloid Deposition	1 [2.0]			
Renal, Ectasia			1 [2.0]	
Renal, Hyperplasia, Lymphoid	2 [2.5]	1 [2.0]		
Renal, Necrosis	1 [2.0]			
Lymph Node, Bronchial	(40)	(42)	(43)	(43)
Ectasia	1 [1.0]			
Hematopoietic Cell Proliferation		1 [2.0]		1 [1.0]
Hyperplasia, Lymphoid	5 [1.6]	7 [1.1]	4 [1.3]	1 [1.0]
Inflammation, Chronic Active				5 [2.6]
Necrosis, Lymphoid		1 [1.0]		1 [1.0]
Lymph Node, Mandibular	(39)	(47)	(45)	(39)
Amyloid Deposition	1 [2.0]			
Ectasia		1 [2.0]		3 [2.0]
Hematopoietic Cell Proliferation			2 [2.0]	1 [3.0]
Hyperplasia, Lymphoid	4 [1.3]	5 [1.0]	12 [1.3]	12 [1.6]
Hyperplasia, Plasma Cell				2 [2.5]
Infiltration Cellular, Plasma Cell	1 [1.0]			5 [2.6]
Infiltration Cellular, Polymorphonuclear				1 [1.0]
Inflammation, Suppurative				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)

Test Type: CHRONIC

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Lymph Node, Mediastinal	(40)	(38)	(41)	(33)	
Hematopoietic Cell Proliferation		1 [2.0]			
Hyperplasia, Lymphoid	1 [4.0]	2 [1.5]	2 [1.5]	1 [2.0]	
Hyperplasia, Plasma Cell			1 [3.0]	1 [2.0]	
Inflammation, Acute	1 [2.0]				
Inflammation, Chronic Active				2 [1.5]	
Necrosis, Lymphoid		1 [1.0]		1 [1.0]	
Lymph Node, Mesenteric	(49)	(50)	(50)	(45)	
Ectasia		1 [2.0]	1 [2.0]		
Hematopoietic Cell Proliferation				2 [1.5]	
Hyperplasia, Lymphoid	2 [2.0]	1 [1.0]	2 [2.5]	1 [1.0]	
Infiltration Cellular, Plasma Cell	1 [4.0]				
Spleen	(50)	(50)	(50)	(48)	
Amyloid Deposition	, ,	,	1 [2.0]	,	
Angiectasis				1 [1.0]	
Hematopoietic Cell Proliferation	8 [2.3]	14 [1.9]	5 [1.4]	11 [2.3]	
Hyperplasia, Lymphoid	10 [1.6]	15 [1.3]	10 [1.4]	4 [2.3]	
Inflammation	1 [1.0]	1 [2.0]	1 [4.0]	2 [2.5]	
Necrosis		1 [3.0]	1 [4.0]	3 [1.7]	
Lymphoid Follicle, Atrophy				1 [2.0]	
Thymus	(47)	(50)	(49)	(45)	
Atrophy	4 [1.5]	5 [1.2]	2 [1.0]	12 [1.8]	
Cyst		1			
Ectopic Parathyroid Gland	4 [1.0]	8 [1.0]	4 [1.0]	3 [1.0]	
Hyperplasia, Lymphoid	3 [1.7]	4 [2.0]	2 [1.5]	1 [3.0]	
Inflammation, Chronic	2 [2.0]				
Inflammation, Chronic Active				8 [2.1]	
INTEGUMENTARY SYSTEM					
Mammary Gland	(49)	(50)	(50)	(49)	
Hyperplasia	1 [2.0]				
Inflammation, Chronic	1 [1.0]				
Skin	(50)	(50)	(50)	(50)	
Erosion	1 [1.0]				

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Test Type: CHRONIC Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione **CAS Number:** 431-03-8 Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Fibrosis				1 [2.0]	
Inflammation, Chronic Active	1 [1.0]	2 [1.0]		3 [3.7]	
Epidermis, Hyperplasia	1 [2.0]			1 [2.0]	
Subcutaneous Tissue, Necrosis				2 [2.5]	
MUSCULOSKELETAL SYSTEM					
Bone	(50)	(50)	(50)	(50)	
Fibro-Osseous Lesion	13 [1.1]	12 [1.5]	17 [1.2]	3 [1.7]	
Skeletal Muscle	(6)	(1)	(3)	(4)	
Degeneration	2 [1.0]		1 [1.0]	1 [2.0]	
Inflammation		1 [3.0]			
NERVOUS SYSTEM					
Brain	(50)	(50)	(50)	(50)	
Infiltration Cellular		1 [1.0]		1 [1.0]	
Infiltration Cellular, Lymphocyte	2 [1.0]		2 [1.5]	5 [1.2]	
Inflammation, Acute	1 [1.0]			1 [3.0]	
Inflammation, Chronic			1 [1.0]		
Peripheral Nerve	(2)	(1)	(2)	(2)	
Degeneration	1 [1.0]		2 [2.0]	1 [2.0]	
Spinal Cord	(2)	(1)	(2)	(2)	
RESPIRATORY SYSTEM					
Larynx	(49)	(50)	(50)	(49)	
Inflammation, Chronic Active	4 [1.3]	5 [1.2]	22 [1.2]	36 [2.1]	
Lumen, Exudate				4 [3.8]	
Respiratory Epithelium, Hyperplasia			4 [1.3]	1 [2.0]	
Respiratory Epithelium, Metaplasia, Atypical, Squamous		1 [3.0]		1 [3.0]	
Respiratory Epithelium, Metaplasia, Squamous	2 [1.0]		6 [1.7]	48 [3.0]	
Respiratory Epithelium, Necrosis	1 [1.0]	1 [1.0]	14 [1.1]	32 [1.5]	

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

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Experiment Number: 20725 - 04

2,3-Butanedione **CAS Number:** 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Respiratory Epithelium, Regeneration			3 [1.0]	30 [1.4]	
Squamous Epithelium, Hyperplasia	4 [1.3]	13 [1.2]	34 [1.5]	40 [2.1]	
Submucosa, Mineralization		1 [1.0]			
Lung	(50)	(50)	(50)	(50)	
Foreign Body				1	
Hematopoietic Cell Proliferation		1 [3.0]			
Hemorrhage	1 [1.0]				
Hyperplasia, Lymphoid	1 [1.0]	1 [1.0]			
Inflammation, Suppurative		1 [1.0]		5 [1.8]	
Inflammation, Chronic Active	1 [2.0]		1 [1.0]	2 [1.5]	
Necrosis				1 [3.0]	
Alveolar Epithelium, Hyperplasia, Focal	3 [1.3]				
Alveolus, Infiltration Cellular, Histiocyte	2 [2.0]	3 [1.0]	3 [1.3]	4 [1.0]	
Alveolus, Inflammation, Suppurative				1 [3.0]	
Alveolus, Epithelium, Hyperplasia			1 [2.0]		
Artery, Mediastinum, Inflammation, Chronic Active				1 [4.0]	
Bronchiole, Inflammation, Suppurative				1 [2.0]	
Bronchiole, Inflammation, Chronic				1 [1.0]	
Bronchiole, Epithelium, Hyperplasia	1 [2.0]			2 [1.0]	
Bronchus, Inflammation, Suppurative				2 [2.5]	
Bronchus, Regeneration				1 [1.0]	
Bronchus, Epithelium, Degeneration				4 [2.5]	
Bronchus, Epithelium, Necrosis	2 [1.0]			5 [1.4]	
Bronchus, Epithelium, Regeneration	2 [1.0]			38 [2.8]	
Bronchus, Smooth Muscle, Mineralization				3 [1.7]	
Bronchus, Submucosa, Fibrosis				5 [1.2]	
Interstitium, Fibrosis				1 [1.0]	
Mediastinum, Inflammation, Suppurative		1 [1.0]	1 [1.0]	8 [2.0]	
Mediastinum, Inflammation, Chronic Active			1 [1.0]	7 [1.7]	
Pleura, Inflammation, Suppurative				5 [2.0]	
Pleura, Inflammation, Chronic Active			1 [2.0]		
Nose	(50)	(50)	(50)	(50)	
Foreign Body	,	,	3	3	
Inflammation, Suppurative	3 [1.0]	20 [1.2]	50 [1.6]	50 [3.3]	
Glands, Respiratory Epithelium, Cyst				2 [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)

Experiment Number: 20725 - 04

P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH Date Report Requested: 04/15/2016 AVERAGE SEVERITY GRADES[b]

Test Type: CHRONIC
Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

Ear

Inflammation, Suppurative

2,3-Butanedione CAS Number: 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

Lab: BNW

C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Glands, Sinus, Metaplasia, Respiratory				12 [1.0]	
Lamina Propria, Fibrosis			47 [1.0]	49 [1.9]	
Lateral Wall, Inflammation, Chronic Active	1 [2.0]		1 [2.0]		
Mucosa, Regeneration			39 [1.2]	48 [2.1]	
Olfactory Epithelium, Accumulation, Hyaline Droplet	11 [1.0]	11 [1.1]	17 [1.2]	2 [1.0]	
Olfactory Epithelium, Atrophy		41 [1.6]	49 [2.2]	45 [1.4]	
Olfactory Epithelium, Metaplasia, Respiratory		22 [1.2]	46 [1.7]	49 [3.3]	
Olfactory Epithelium, Necrosis			1 [2.0]	20 [1.6]	
Respiratory Epithelium, Accumulation, Hyaline Droplet	18 [1.2]	28 [1.1]	28 [1.0]	3 [1.0]	
Respiratory Epithelium, Hyperplasia		1 [1.0]		2 [1.5]	
Respiratory Epithelium, Metaplasia, Squamous	1 [1.0]	9 [1.0]	48 [1.3]	50 [2.7]	
Respiratory Epithelium, Necrosis	1 [1.0]	5 [1.0]	33 [1.2]	50 [1.8]	
Septum, Perforation			6	5	
Turbinate, Atrophy		32 [1.0]	50 [1.1]	50 [2.1]	
Turbinate, Necrosis			1 [1.0]	11 [1.0]	
Pleura	(0)	(0)	(1)	(0)	
Trachea	(50)	(49)	(50)	(50)	
Inflammation, Chronic Active	1 [1.0]		4 [1.5]	42 [2.1]	
Necrosis			3 [1.0]	48 [1.9]	
Carina, Inflammation, Chronic Active				1 [1.0]	
Carina, Epithelium, Regeneration				1 [1.0]	
Carina, Submucosa, Fibrosis				6 [1.3]	
Carina, Submucosa, Mineralization				5 [1.8]	
Epithelium, Hyperplasia			1 [2.0]	1 [2.0]	
Epithelium, Metaplasia, Squamous				2 [1.5]	
Epithelium, Regeneration			9 [1.1]	45 [3.0]	
Glands, Hyperplasia			- •	1 [2.0]	
Lumen, Exudate				12 [3.4]	
Submucosa, Fibrosis				44 [2.3]	

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)

(0)

(0)

(1)

1 [1.0]

(0)

Test Type: CHRONIC Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

2,3-Butanedione **CAS Number:** 431-03-8

Time Report Requested: 10:33:43 First Dose M/F: 08/31/09 / 08/31/09

B6C3F1 MICE FEMALE	Control	12.5 ppm	25 ppm	50 ppm	
Eye	(50)	(49)	(50)	(49)	
Anterior Chamber, Inflammation, Suppurative	, ,	, ,	4 [1.8]	3 [1.0]	
Cornea, Fibrosis			1 [1.0]		
Cornea, Inflammation, Acute	1 [1.0]	2 [1.0]	20 [1.2]	23 [1.1]	
Cornea, Mineralization			13 [1.0]	16 [1.3]	
Cornea, Necrosis				6 [1.3]	
Cornea, Epithelium, Hyperplasia	2 [1.5]	2 [1.0]	10 [1.1]	9 [1.1]	
Cornea, Epithelium, Ulcer			10 [1.4]	10 [1.6]	
Lens, Cataract				2 [1.5]	
Harderian Gland	(50)	(50)	(50)	(50)	
Hyperplasia	2 [1.5]	4 [1.3]	1 [1.0]	4 [1.0]	
Inflammation				1 [2.0]	
Pigmentation, Porphyrin				1 [2.0]	
URINARY SYSTEM					
Kidney	(50)	(50)	(50)	(49)	
Amyloid Deposition	,	,	1 [4.0]	,	
Cyst	1				
Hyperplasia, Lymphoid	1 [2.0]	3 [1.7]	3 [1.3]		
Infarct		3 [1.0]	3 [1.0]	2 [1.0]	
Inflammation				1 [4.0]	
Metaplasia, Osseous	1 [1.0]	1 [1.0]	1 [1.0]		
Necrosis		1 [1.0]			
Nephropathy	14 [1.2]	15 [1.1]	6 [1.5]	6 [1.2]	
Capsule, Inflammation		1 [2.0]			
Urinary Bladder	(50)	(50)	(50)	(49)	
Hyperplasia, Lymphoid	1 [3.0]	1 [1.0]	1 [1.0]	,	

^{***} 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)