

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence

Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

C Number:

R92025B

Study Gender:

Both

PWG Approval Date

See web page for date of PWG Approval

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	F0 Male			
	Treatment Groups (ppm)			
	0	750	2500	5000
Disposition Summary				
Animals Initially In Study	23	23	23	23
Early Deaths				
Unscheduled Sacrifice			3	2
Survivors				
Scheduled sacrifice, terminal (SD 15 - 178)	23	23	20	21
Animals Examined Microscopically	23	23	23	23
ALIMENTARY SYSTEM				
LIVER	(23)	(0)	(23)	(23)
BASOPHILIC FOCUS			1 (4%)	
CLEAR CELL FOCUS			3 (13%)	
HEPATODIAPHRAGMATIC NODULE			1 (4%)	
PERIPORTAL; LYMPHOCYTE; INFILTRATION; FOCAL INFLAMMATION, CHRONIC; ACTIVE, FOCAL			2 (9%)	
CENTRIOBULAR; NECROSIS; DIFFUSE			1 (4%)	
CENTRIOBULAR; NECROSIS; FOCAL			1 (4%)	
CENTRIOBULAR; HEPATOCYTE; VACUOLATION; CYTOPLASMIC				19 (83%)
CARDIOVASCULAR SYSTEM				
No Tissues/Organs Examined				

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	F0 Male			
	Treatment Groups (ppm)			
	0	750	2500	5000
<hr/>				
ENDOCRINE SYSTEM				
ADRENAL GLANDS	(23)	(0)	(23)	(23)
CORTEX; HYPERTROPHY; FOCAL				3 (13%)
CORTEX; BILATERAL; VACUOLATION; DIFFUSE	3 (13%)		3 (13%)	
CORTEX; VACUOLATION; FOCAL	1 (4%)		1 (4%)	5 (22%)
PITUITARY GLAND	(23)	(0)	(23)	(23)
PARS DISTALIS; CYST				1 (4%)
THYROID GLANDS	(23)	(0)	(23)	(23)
C-CELL; HYPERPLASIA; FOCAL	1 (4%)			
<hr/>				
GENERAL BODY SYSTEM				
No Tissues/Organs Examined				

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Species/Strain: Rat/Sprague-Dawley

F0 Male

Treatment Groups (ppm)

	0	750	2500	5000
GENITAL SYSTEM				
COAGULATING GLANDS	(23)	(0)	(23)	(23)
COWPERS GLANDS	(23)	(0)	(20)	(21)
UNILATERAL; ATROPHY	1 (4%)			
EPIDIDYMIS	(22)	(23)	(23)	(23)
DUCT; RIGHT; EXFOLIATED GERM CELL			1 (4%)	
DUCT; EXFOLIATED GERM CELL	1 (5%)		2 (9%)	7 (30%)
DUCT; EXFOLIATED GERM CELL (TOTAL)	1 (5%)		3 (13%)	7 (30%)
HYOSPERMIA			1 (4%)	
LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE	(23)	(0)	(20)	(21)
PREPUTIAL GLANDS	(9)	(6)	(1)	(4)
UNILATERAL; ABSCESS	1 (11%)			
DUCT; ECTASIA	5 (56%)	5 (83%)	1 (100%)	4 (100%)
INFILTRATION; MONONUCLEAR CELL	1 (11%)			
INFLAMMATION		1 (17%)		
UNILATERAL; INFLAMMATION, CHRONIC; ACTIVE	1 (11%)			
INFLAMMATION, CHRONIC; ACTIVE	6 (67%)	5 (83%)		2 (50%)
INFLAMMATION, CHRONIC; ACTIVE (TOTAL)	7 (78%)	5 (83%)		2 (50%)
PROSTATE	(23)	(23)	(23)	(23)
VENTRAL LOBE; ATROPHY		9 (39%)	20 (87%)	23 (100%)
VENTRAL LOBE, INTERSTITIUM; LYMPHOCYTE; INFILTRATION	5 (22%)	5 (22%)	1 (4%)	
VENTRAL LOBE; INFLAMMATION; CHRONIC ACTIVE		1 (4%)		
SEMINAL VESICLES	(23)	(0)	(23)	(23)
TESTIS	(22)	(23)	(23)	(23)
GERMINAL EPITHELIUM; ATROPHY				1 (4%)
GERM CELL; DEGENERATION	1 (5%)		4 (17%)	8 (35%)
SEMINIFEROUS TUBULE; BILATERAL; SPERMATID RETENTION				1 (4%)
SEMINIFEROUS TUBULE; SPERMATID RETENTION	2 (9%)	3 (13%)	1 (4%)	7 (30%)

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	F0 Male			
	Treatment Groups (ppm)			
	0	750	2500	5000
SEMINIFEROUS TUBULE; SPERMATID RETENTION (TOTAL)	2 (9%)	3 (13%)	1 (4%)	8 (35%)
HEMATOPOIETIC SYSTEM				
THYMUS	(23)	(0)	(23)	(23)
INTEGUMENTARY SYSTEM				
No Tissues/Organs Examined				
LYMPHOID SYSTEM				
No Tissues/Organs Examined				
MUSCULOSKELETAL SYSTEM				
No Tissues/Organs Examined				
NERVOUS SYSTEM				
No Tissues/Organs Examined				
RESPIRATORY SYSTEM				
No Tissues/Organs Examined				
SPECIAL SENSES SYSTEM				
No Tissues/Organs Examined				
URINARY SYSTEM				
KIDNEYS	(23)	(0)	(23)	(23)
PELVIS; CONCRETION; FOCAL			1 (4%)	
NEPHROPATHY, CHRONIC PROGRESSIVE	22 (96%)		19 (83%)	22 (96%)

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
Disposition Summary				
Animals Initially In Study	23	23	23	23
Early Deaths				
Euthanized, moribund	1	1	3	8
Found Dead			1	1
Unscheduled Sacrifice				2
Survivors				
Scheduled sacrifice, terminal (LD 4, SD 28 - 220)	22	22	19	12
Animals Examined Microscopically	23	10	23	23
ALIMENTARY SYSTEM				
LIVER	(23)	(3)	(23)	(23)
ATROPHY; DIFFUSE				2 (9%)
CONGESTION; DIFFUSE	1 (4%)			1 (4%)
DEFORMITY		1 (33%)		
HEMATOPOIESIS; EXTRAMEDULLARY, FOCAL			1 (4%)	2 (9%)
HEPATODIAPHRAGMATIC NODULE		1 (33%)		
PERIportal; LYMPHOCYTE; INFILTRATION; FOCAL	2 (9%)		1 (4%)	2 (9%)
CENTRIOBULAR; NECROSIS; DIFFUSE				1 (4%)
CENTRIOBULAR; NECROSIS; FOCAL			1 (4%)	
CARDIOVASCULAR SYSTEM				
No Tissues/Organs Examined				

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
ENDOCRINE SYSTEM				
ADRENAL GLANDS	(23)	(1)	(23)	(23)
CONGESTION; DIFFUSE			1 (4%)	
CORTEX; HYPERTROPHY; FOCAL				2 (9%)
CORTEX; VACUOLATION; FOCAL	3 (13%)			3 (13%)
PITUITARY GLAND	(23)	(1)	(23)	(23)
PARS DISTALIS; CYST				2 (9%)
THYROID GLANDS	(23)	(1)	(23)	(23)
C-CELL; HYPERPLASIA; FOCAL				3 (13%)
GENERAL BODY SYSTEM				
WHOLE BODY	(0)	(0)	(0)	(1)

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Lab: RTI

Species/Strain: Rat/Sprague-Dawley

	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
GENITAL SYSTEM				
CERVIX	(23)	(1)	(23)	(21)
INFLAMMATION; ACUTE			1 (4%)	
CLITORAL GLANDS	(3)	(4)	(1)	(1)
UNILATERAL; ABSCESS; CHRONIC			1 (100%)	
DUCT; UNILATERAL; ECTASIA	1 (33%)	3 (75%)		
DUCT; ECTASIA	1 (33%)	1 (25%)		1 (100%)
DUCT; ECTASIA (TOTAL)	2 (67%)	4 (100%)		1 (100%)
INFILTRATION; MONONUCLEAR CELL	1 (33%)			1 (100%)
DUCT; LUMEN; INFLAMMATION, ACUTE				1 (100%)
UNILATERAL; INFLAMMATION, CHRONIC; ACTIVE		2 (50%)		
INFLAMMATION, CHRONIC; ACTIVE		1 (25%)		
INFLAMMATION, CHRONIC; ACTIVE (TOTAL)		3 (75%)		
OVARIES	(23)	(1)	(23)	(23)
CONGESTION	1 (4%)			
CORPUS LUTEUM; CYST				2 (9%)
FOLLICLE; CYST				1 (4%)
PLACENTA	(0)	(0)	(1)	(5)
BILATERAL; EDEMA				1 (20%)
EDEMA; DIFFUSE				3 (60%)
EDEMA				1 (20%)
INFLAMMATION; ACUTE				1 (20%)
INFLAMMATION; SUPPURATIVE				1 (20%)
BILATERAL; NECROSIS; DIFFUSE				1 (20%)
NECROSIS; DIFFUSE				1 (20%)
NECROSIS				1 (20%)
UTERUS	(23)	(3)	(23)	(23)
ENDOMETRIUM; CYST				1 (4%)

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
OVIDUCT; CYST			1 (4%)	
HORN; LUMEN; DILATION			1 (4%)	
DILATION		1 (33%)		
DILATION (TOTAL)		1 (33%)	1 (4%)	
ENDOMETRIUM; HYPERPLASIA; CYSTIC	2 (9%)			4 (17%)
INFLAMMATION; CHRONIC-ACTIVE			1 (4%)	
INFLAMMATION; SUPPURATIVE				2 (9%)
ENDOMETRIUM; METAPLASIA; SQUAMOUS	2 (9%)			
ENDOMETRIUM; METAPLASIA; SQUAMOUS (TOTAL)	2 (9%)	1 (33%)		
METAPLASIA; SQUAMOUS		1 (33%)		
NECROSIS				1 (4%)
ULCER; MULTIFOCAL			1 (4%)	
VAGINA	(23)	(1)	(23)	(23)
CYST			1 (4%)	
SUBMUCOSA; LYMPHOCYTE; INFILTRATION; FOCAL	1 (4%)			
INFLAMMATION; ACUTE			1 (4%)	
MUCIFICATION	7 (30%)		5 (22%)	
ULCER; FOCAL			1 (4%)	
HEMATOPOIETIC SYSTEM				
LYMPH NODE, MEDIASTINAL	(3)	(0)	(0)	(0)
CONGESTION	1 (33%)			
THYMUS	(23)	(1)	(22)	(23)
CORTEX; DECREASED LYMPHOCYTE; DIFFUSE			2 (9%)	6 (26%)

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
INTEGUMENTARY SYSTEM				
MAMMARY GLANDS	(1)	(2)	(0)	(0)
INFILTRATION; BACTERIA	1 (100%)			
INFLAMMATION; SUPPURATIVE	1 (100%)			
SKIN	(2)	(0)	(1)	(0)
ALOPECIA			1 (100%)	
LYMPHOID SYSTEM				
No Tissues/Organs Examined				
MUSCULOSKELETAL SYSTEM				
BONE	(1)	(0)	(0)	(0)
INTERVERTEBRAL DISK; RUPTURE; FOCAL	1 (100%)			
LIMB	(2)	(1)	(2)	(0)
ALOPECIA		1 (100%)	1 (50%)	
EPIDERMIS; HYPERPLASIA; FOCAL		1 (100%)		
EPIDERMIS; PARAKERATOSIS; FOCAL		1 (100%)		
RIGHT; ULCER; DIFFUSE			1 (50%)	
NERVOUS SYSTEM				
BRAIN	(0)	(0)	(0)	(2)
RESPIRATORY SYSTEM				
NOSE	(0)	(0)	(1)	(0)
SUBCUTANEOUS; CYST			1 (100%)	
SPECIAL SENSES SYSTEM				
No Tissues/Organs Examined				

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
URINARY SYSTEM				
KIDNEYS	(23)	(1)	(23)	(23)
PELVIS; CONCRETION; FOCAL PAPILLA; COLLECTING DUCT; DILATION INFLAMMATION, ACUTE; FOCAL	1 (4%)			1 (4%)
MINERAL	1 (4%)		2 (9%)	1 (4%)
RENAL TUBULE; NECROSIS; ACUTE, MULTIFOCAL				3 (13%)
NEPHROPATHY, CHRONIC PROGRESSIVE	17 (74%)	1 (100%)	11 (48%)	11 (48%)

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F1 Male: F1 NonParental Male

	Treatment Groups (ppm)		
	0	750	2500
Disposition Summary			
Animals Initially In Study	49	56	20
Early Deaths			
Survivors			
Scheduled sacrifice, terminal (PND 91 - 93)	49	56	20
Animals Examined Microscopically	49	56	20
Total number litters	18	22	8
ALIMENTARY SYSTEM			
LIVER	(49)	(1)	(20)
DEFORMITY			1 (5%) [1]
HEMATOPOIETIC CELL PROLIFERATION; EXTRAMEDULLARY			1 (5%) [1]
HYPERTROPHY; HEPATOCELLULAR	3 (6%) [2]		
ACCESSORY LOBE; INFARCTION		1 (100%) [1]	
LYMPHOCYTE; INFILTRATION; MULTIFOCAL	1 (2%) [1]		
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(49)	(1)	(20)
ATROPHY; DIFFUSE		1 (100%) [1]	
CORTEX; HYPERTROPHY; FOCAL	2 (4%) [1]		
METAPLASIA; OSSEOUS			1 (5%) [1]
CORTEX; VACUOLATION; FOCAL	1 (2%) [1]		
PITUITARY GLAND	(49)	(0)	(20)
PARS DISTALIS; CYST	4 (8%) [3]		
THYROID GLANDS	(49)	(0)	(20)

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Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Male: F1 NonParental Male

Treatment Groups (ppm)

0

750

2500

GENERAL BODY SYSTEM

No Tissues/Organs Examined

GENITAL SYSTEM

COAGULATING GLANDS

(49)

(0)

(20)

COWPERS GLANDS

(48)

(3)

(20)

EPIDIDYMIS

(49)

(56)

(20)

DUCT; EXFOLIATED GERM CELL

3 (6%) [2]

5 (9%) [4]

4 (20%) [4]

LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE

(49)

(0)

(20)

PROSTATE

(49)

(56)

(20)

VENTRAL LOBE; ATROPHY

4 (8%) [3]

25 (45%) [17]

17 (85%) [7]

VENTRAL LOBE, INTERSTITIUM; LYMPHOCYTE; INFILTRATION

25 (51%) [13]

33 (59%) [18]

6 (30%) [5]

VENTRAL LOBE; INFLAMMATION; CHRONIC ACTIVE

1 (2%) [1]

INFLAMMATION; CHRONIC ACTIVE

1 (2%) [1]

SEMINAL VESICLES

(49)

(1)

(20)

ATROPHY

1 (2%) [1]

1 (100%) [1]

RUPTURE

1 (100%) [1]

TESTIS

(49)

(56)

(20)

GERM CELL; DEGENERATION

4 (8%) [3]

6 (11%) [4]

1 (5%) [1]

SEMIFEROUS TUBULE; SPERMATID RETENTION

3 (5%) [2]

4 (20%) [3]

HEMATOPOIETIC SYSTEM

THYMUS

(49)

(0)

(20)

INTEGUMENTARY SYSTEM

SKIN

(1)

(1)

(1)

DERMIS; FIBROSIS; FOCAL

1 (100%) [1]

EPIDERMIS; HYPERPLASIA; FOCAL

1 (100%) [1]

LYMPHOID SYSTEM

No Tissues/Organs Examined

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F1 Male: F1 NonParental Male

	Treatment Groups (ppm)		
	0	750	2500
MUSCULOSKELETAL SYSTEM			
LIMB	(5)	(1)	(0)
BONE; DEFORMITY	4 (80%) [4]	1 (100%) [1]	
NERVOUS SYSTEM			
No Tissues/Organs Examined			
RESPIRATORY SYSTEM			
LUNGS	(1)	(1)	(0)
CONGESTION; DIFFUSE		1 (100%) [1]	
SPECIAL SENSES SYSTEM			
No Tissues/Organs Examined			
URINARY SYSTEM			
KIDNEYS	(49)	(1)	(20)
PAPILLA; COLLECTING DUCT; DILATION			1 (5%) [1]
PELVIS; RIGHT; DILATION	7 (14%) [6]	1 (100%) [1]	3 (15%) [3]
TRANSITIONAL CELL; EPITHELIUM; HYPERPLASIA; FOCAL MINERAL		1 (100%) [1]	1 (5%) [1]
NEPHROPATHY, CHRONIC PROGRESSIVE	45 (92%) [17]	1 (100%) [1]	20 (100%) [8]

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F1 Female: F1 NonParent Female

	Treatment Groups (ppm)		
	0	750	2500
Disposition Summary			
Animals Initially In Study	47	58	27
Early Deaths			
Survivors			
Scheduled sacrifice, terminal (PND 91 - 93)	47	58	27
Animals Examined Microscopically	47	58	27
Total number litters	17	22	12
ALIMENTARY SYSTEM			
LIVER	(47)	(2)	(27)
HEPATODIAPHRAGMATIC NODULE	1 (2%) [1]	1 (50%) [1]	1 (4%) [1]
LYMPHOCYTE; INFILTRATION; MULTIFOCAL	5 (11%) [5]		
INFLAMMATION, CHRONIC; ACTIVE, FOCAL	1 (2%) [1]		
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(47)	(0)	(27)
PITUITARY GLAND	(47)	(0)	(27)
PARS DISTALIS; CYST	1 (2%) [1]		1 (4%) [1]
THYROID GLANDS	(47)	(0)	(25)
FOLLICULAR CELL; MINERAL			1 (4%) [1]
GENERAL BODY SYSTEM			
No Tissues/Organs Examined			

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Species/Strain: Rat/Sprague-Dawley

F1 Female: F1 NonParent Female

	Treatment Groups (ppm)		
	0	750	2500
GENITAL SYSTEM			
CERVIX	(47)	(0)	(26)
ENDOMETRIUM; CYST	1 (2%) [1]		
OVARIES	(47)	(2)	(27)
CORPUS LUTEUM; CYST	1 (2%) [1]		1 (4%) [1]
FOLLICLE; UNILATERAL; CYST		1 (50%) [1]	
UTERUS	(47)	(2)	(27)
OVIDUCT; CYST			1 (4%) [1]
SUBSEROVA; CYST	4 (9%) [4]		
ENDOMETRIUM; HYPERPLASIA; CYSTIC	4 (9%) [4]		
VAGINA	(47)	(0)	(27)
MUCIFICATION	5 (11%) [3]		
HEMATOPOIETIC SYSTEM			
LYMPH NODE	(1)	(0)	(0)
NO MICROSCOPIC FINDING RECORDED	1 (100%) [1]		
LYMPH NODE, MEDIASTINAL	(1)	(0)	(1)
CONGESTION			1 (100%) [1]
DECREASED LYMPHOCYTE			1 (100%) [1]
SPLEEN	(2)	(1)	(0)
THYMUS	(47)	(0)	(27)
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS	(47)	(0)	(27)
SKIN	(1)	(1)	(0)
ALOPECIA; DIFFUSE		1 (100%) [1]	
NO MICROSCOPIC FINDING RECORDED		1 (100%) [1]	
LYMPHOID SYSTEM			
No Tissues/Organs Examined			

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F1 Female: F1 NonParent Female

	Treatment Groups (ppm)		
	0	750	2500
MUSCULOSKELETAL SYSTEM			
LIMB	(4)	(4)	(1)
BONE; DEFORMITY	3 (75%) [3]	4 (100%) [3]	1 (100%) [1]
PAW	(1)	(0)	(0)
NO MICROSCOPIC FINDING RECORDED	1 (100%) [1]		
NERVOUS SYSTEM			
No Tissues/Organs Examined			
RESPIRATORY SYSTEM			
No Tissues/Organs Examined			
SPECIAL SENSES SYSTEM			
No Tissues/Organs Examined			
URINARY SYSTEM			
KIDNEYS	(47)	(58)	(27)
MINERAL	9 (19%) [7]	44 (76%) [19]	20 (74%) [11]
NEPHROPATHY, CHRONIC PROGRESSIVE	27 (57%) [14]		21 (78%) [12]

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
Disposition Summary			
Animals Initially In Study	40	44	40
Early Deaths			
Euthanized, moribund			1
Survivors			
Scheduled sacrifice, terminal (PND 218 - 224)	40	44	39
Animals Examined Microscopically	40	44	40
Total number litters	18	22	15
ALIMENTARY SYSTEM			
LIVER	(40)	(0)	(40)
CLEAR CELL FOCUS	1 (3%) [1]		4 (10%) [3]
HEPATODIAPHRAGMATIC NODULE	3 (8%) [3]		5 (13%) [4]
BILE DUCT; HYPERPLASIA; FOCAL	1 (3%) [1]		1 (3%) [1]
HYPERTROPHY; DIFFUSE, HEPATOCELLULAR			1 (3%) [1]
LYMPHOCYTE; PERIportal; INFILTRATION; MULTIFOCAL	1 (3%) [1]		7 (18%) [6]
INFLAMMATION, CHRONIC; ACTIVE, FOCAL	3 (8%) [3]		
HEPATOCYTE; NECROSIS; FOCAL	1 (3%) [1]		2 (5%) [2]
HEPATOCYTE; CENTRIOBULAR; VACUOLATION; CYTOPLASMIC, DIFFUSE			1 (3%) [1]
HEPATOCYTE; VACUOLATION; CYTOPLASMIC, FOCAL			1 (3%) [1]
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(40)	(0)	(40)
CORTEX; HYPERTROPHY; FOCAL	1 (3%) [1]		1 (3%) [1]
CORTEX; VACUOLATION; FOCAL			3 (8%) [3]
CORTEX; VACUOLATION, CYTOPLASMIC; DIFFUSE	1 (3%) [1]		1 (3%) [1]
PITUITARY GLAND	(40)	(0)	(40)
PARS DISTALIS; CYST	3 (8%) [3]		1 (3%) [1]
THYROID GLANDS	(40)	(0)	(40)
C-CELL; HYPERPLASIA; FOCAL	1 (3%) [1]		1 (3%) [1]
GENERAL BODY SYSTEM			
FAT	(2)	(0)	(0)

Experiment Number: R92025B

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:43

Route: Dosing in Feed

CAS Number: 822-36-6

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
GENITAL SYSTEM			
COAGULATING GLANDS	(40)	(0)	(40)
COWPERS GLANDS	(40)	(0)	(40)
EPIDIDYMIS	(40)	(44)	(40)
DUCT; LEFT; EXFOLIATED GERM CELL			1 (3%) [1]
DUCT; RIGHT; EXFOLIATED GERM CELL			2 (5%) [2]
DUCT; EXFOLIATED GERM CELL		5 (11%) [5]	1 (3%) [1]
DUCT; EXFOLIATED GERM CELL (TOTAL)		5 (11%) [5]	4 (10%) [4]
LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE	(40)	(0)	(40)
PREPUTIAL GLANDS	(3)	(1)	(0)
DUCT; UNILATERAL; ABSCESS	1 (33%) [1]		
UNILATERAL; INFLAMMATION, CHRONIC; ACTIVE		1 (100%) [1]	
PROSTATE	(40)	(44)	(40)
DORSAL LOBE; EPITHELIUM; ATROPHY			1 (3%) [1]
VENTRAL LOBE; ATROPHY	4 (10%) [3]	10 (23%) [8]	35 (88%) [15]
VENTRAL LOBE, INTERSTITIUM; LYMPHOCYTE; INFILTRATION	5 (13%) [4]	1 (2%) [1]	
SEMINAL VESICLES	(40)	(1)	(40)
ATROPHY			2 (5%) [2]
TESTIS	(40)	(44)	(40)
GERMINAL EPITHELIUM; LEFT; ATROPHY	1 (3%) [1]		1 (3%) [1]
GERMINAL EPITHELIUM; ATROPHY			1 (3%) [1]
GERMINAL EPITHELIUM; ATROPHY (TOTAL)	1 (3%) [1]		2 (5%) [2]
GERM CELL; LEFT; DEGENERATION	1 (3%) [1]		1 (3%) [1]
GERM CELL; DEGENERATION	1 (3%) [1]	5 (11%) [5]	4 (10%) [4]
GERM CELL; DEGENERATION (TOTAL)	2 (5%) [2]	5 (11%) [5]	5 (13%) [4]
SEMINIFEROUS TUBULE; SPERMATID RETENTION		5 (11%) [5]	4 (10%) [3]

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
HEMATOPOIETIC SYSTEM			
LYMPH NODE, MEDIASTINAL	(1)	(0)	(0)
LYMPH NODE, RENAL	(1)	(0)	(0)
SPLEEN	(3)	(0)	(1)
HEMATOPOIETIC CELL PROLIFERATION; EXTRAMEDULLARY PIGMENTED MACROPHAGE; INCREASED NUMBER; DIFFUSE	1 (33%) [1]		1 (100%) [1]
THYMUS	(40)	(0)	(40)
INTEGUMENTARY SYSTEM			
SKIN	(0)	(2)	(0)
SKIN, ABDOMINAL	(3)	(0)	(0)
LYMPHOID SYSTEM			
No Tissues/Organs Examined			
MUSCULOSKELETAL SYSTEM			
DIAPHRAGM	(0)	(0)	(1)
LIMB	(1)	(0)	(1)
BONE; DEFORMITY	1 (100%) [1]		
NERVOUS SYSTEM			
No Tissues/Organs Examined			
RESPIRATORY SYSTEM			
No Tissues/Organs Examined			
SPECIAL SENSES SYSTEM			
No Tissues/Organs Examined			

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
URINARY SYSTEM			
KIDNEYS	(40)	(6)	(40)
PELVIS; CONCRETION; FOCAL	6 (15%) [5]		1 (3%) [1]
PAPILLA; CYST			1 (3%) [1]
PELVIS; LEFT; DILATION	1 (3%) [1]		
PELVIS; RIGHT; DILATION	8 (20%) [7]	4 (67%) [3]	1 (3%) [1]
PELVIS; DILATION (TOTAL)	9 (23%) [8]	4 (67%) [3]	1 (3%) [1]
EPITHELIUM; TRANSITIONAL CELL; HYPERPLASIA; FOCAL (TOTAL)	5 (13%) [4]	1 (17%) [1]	1 (3%) [1]
EPITHELIUM; TRANSITIONAL CELL; HYPERPLASIA; FOCAL, LEFT	1 (3%) [1]		
EPITHELIUM; TRANSITIONAL CELL; HYPERPLASIA; FOCAL, RIGHT	4 (10%) [3]	1 (17%) [1]	1 (3%) [1]
TRANSITIONAL CELL; EPITHELIUM; INFLAMMATION, CHRONIC; ACTIVE, FOCAL	2 (5%) [2]	1 (17%) [1]	
MINERAL	3 (8%) [3]		5 (13%) [2]
NEPHROPATHY, CHRONIC PROGRESSIVE	40 (100%) [18]	6 (100%) [4]	40 (100%) [15]

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F1 Female: F1 Parental Females

	Treatment Groups (ppm)		
	0	750	2500
Disposition Summary			
Animals Initially In Study	40	44	40
Early Deaths			
Euthanized, moribund	2	3	6
Found Dead		1	1
Unscheduled Sacrifice	1	1	1
Survivors			
Scheduled sacrifice, terminal (LD 26 - 28, PND 246 - 251)	37	39	32
Animals Examined Microscopically	40	43	40
Total number litters	19	22	15
ALIMENTARY SYSTEM			
LIVER	(40)	(43)	(40)
SUBCAPSULAR; FIBROSIS; FOCAL		1 (2%) [1]	
SUBCAPSULAR; HEMORRHAGE; FOCAL		1 (2%) [1]	
HEPATODIAPHRAGMATIC NODULE	1 (3%) [1]	1 (2%) [1]	2 (5%) [2]
BILE DUCT; HYPERPLASIA; DIFFUSE			1 (3%) [1]
LYMPHOCYTE; PERIportal; INFILTRATION; MULTIFOCAL	9 (23%) [9]	6 (14%) [6]	5 (13%) [3]
INFLAMMATION, CHRONIC; ACTIVE, FOCAL	1 (3%) [1]		2 (5%) [2]
CENTRIOBULAR; NECROSIS; FOCAL			2 (5%) [2]
HEPATOcyTE; NECROSIS; DIFFUSE			1 (3%) [1]
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			

Experiment Number: R92025B

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:43

Route: Dosing in Feed

CAS Number: 822-36-6

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Female: F1 Parental Females

	Treatment Groups (ppm)		
	0	750	2500
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(40)	(43)	(40)
CORTEX; HYPERTROPHY; FOCAL	1 (3%) [1]		1 (3%) [1]
LYMPHOCYTE; INFILTRATION; MULTIFOCAL	1 (3%) [1]		
CORTEX; VACUOLATION; FOCAL		2 (5%) [2]	1 (3%) [1]
PITUITARY GLAND	(39)	(43)	(40)
PARS DISTALIS; CYST		1 (2%) [1]	
THYROID GLANDS	(40)	(43)	(40)
C-CELL; HYPERPLASIA; FOCAL	5 (13%) [5]	3 (7%) [3]	1 (3%) [1]
INFLAMMATION; CHRONIC ACTIVE	1 (3%) [1]		
GENERAL BODY SYSTEM			
No Tissues/Organs Examined			

Experiment Number: R92025B

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:43

Route: Dosing in Feed

CAS Number: 822-36-6

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Female: F1 Parental Females

	Treatment Groups (ppm)		
	0	750	2500
GENITAL SYSTEM			
CERVIX	(40)	(42)	(40)
Serosa; Cyst	1 (3%) [1]		
CLITORAL GLANDS	(3)	(0)	(0)
Duct; Unilateral; Ectasia	1 (33%) [1]		
Duct; Ectasia	2 (67%) [2]		
Duct; Ectasia (Total)	3 (100%) [3]		
OVARIES	(40)	(43)	(40)
Corpus Luteum; Cyst; Multiple			1 (3%) [1]
Corpus Luteum; Cyst		2 (5%) [2]	3 (8%) [3]
Follicle; Cyst		4 (9%) [4]	
Cyst	1 (3%) [1]		
Corpus Luteum; Cyst (Total)		2 (5%) [2]	4 (10%) [4]
PLACENTA	(0)	(1)	(0)
Inflammation, Acute; Multifocal		1 (100%) [1]	
Necrosis; Multifocal		1 (100%) [1]	
UTERUS	(40)	(43)	(40)
Oviduct; Cyst			1 (3%) [1]
Subserosa; Cyst	1 (3%) [1]	2 (5%) [2]	2 (5%) [2]
Horn; Decidual Alteration		1 (2%) [1]	
Endometrium; Hyperplasia; Cystic	6 (15%) [4]		
Endometrium; Inflammation; Suppurative			1 (3%) [1]
Endometrium; Ulcer; Focal			1 (3%) [1]
VAGINA	(40)	(43)	(40)
Mucification	3 (8%) [3]		

Experiment Number: R92025B

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:43

Route: Dosing in Feed

CAS Number: 822-36-6

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Female: F1 Parental Females

	Treatment Groups (ppm)		
	0	750	2500
HEMATOPOIETIC SYSTEM			
LYMPH NODE, MEDIASTINAL CONGESTION	(1) 1 (100%) [1]	(1) 1 (100%) [1]	(0)
LYMPH NODE, MESENTERIC SPLEEN	(0) (0)	(1) (1)	(0) (0)
THYMUS CORTEX; DECREASED LYMPHOCYTE; DIFFUSE	(40) 8 (20%) [7]	(42) 10 (24%) [9]	(40) 9 (23%) [8]
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS INFLAMMATION; SUPPURATIVE INFLAMMATION, ACUTE; FOCAL LACTATION NECROSIS; FOCAL	(40) 1 (3%) [1]	(43) 1 (2%) [1] 1 (2%) [1]	(40) 1 (3%) [1]
SKIN ABSCCESS ALOPECIA	(1) 1 (100%) [1]	(2) 2 (100%) [2]	(1) 1 (100%) [1]
LYMPHOID SYSTEM			
No Tissues/Organs Examined			
MUSCULOSKELETAL SYSTEM			
LIMB BONE; DEFORMITY NO MICROSCOPIC FINDING RECORDED	(15) 11 (73%) [7] 1 (7%) [1]	(2) 1 (50%) [1] 1 (50%) [1]	(1) 1 (100%) [1]
NERVOUS SYSTEM			
No Tissues/Organs Examined			
RESPIRATORY SYSTEM			
No Tissues/Organs Examined			

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F1 Female: F1 Parental Females

Treatment Groups (ppm)

0

750

2500

SPECIAL SENSES SYSTEM

No Tissues/Organs Examined

URINARY SYSTEM

KIDNEYS	(40)	(43)	(40)
PELVIS; CONCRETION; FOCAL	9 (23%) [8]	1 (2%) [1]	2 (5%) [2]
PAPILLA; CYST		1 (2%) [1]	
RENAL TUBULE; EPITHELIUM; HYPERPLASIA; FOCAL			1 (3%) [1]
MINERAL	8 (20%) [5]	21 (49%) [14]	27 (68%) [12]
NEPHROPATHY, CHRONIC PROGRESSIVE	34 (85%) [17]	41 (95%) [21]	40 (100%) [15]
URINARY BLADDER	(1)	(0)	(0)

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

	F2 Male		
	Treatment Groups (ppm)		
	0	750	2500
Disposition Summary			
Animals Initially In Study	107	132	69
Early Deaths			
Survivors			
Scheduled sacrifice, terminal (PND 28)	107	132	69
Animals Examined Microscopically	10	5	
Total number litters	7	4	
ALIMENTARY SYSTEM			
No Tissues/Organs Examined			
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			
ENDOCRINE SYSTEM			
No Tissues/Organs Examined			
GENERAL BODY SYSTEM			
No Tissues/Organs Examined			
GENITAL SYSTEM			
TESTIS	(4)	(1)	(0)
SEMIFEROUS TUBULE; DEGENERATION	2 (50%) [1]	1 (100%) [1]	
HEMATOPOIETIC SYSTEM			
No Tissues/Organs Examined			
INTEGUMENTARY SYSTEM			
No Tissues/Organs Examined			
LYMPHOID SYSTEM			
No Tissues/Organs Examined			

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F2 Male

Treatment Groups (ppm)

0

750

2500

MUSCULOSKELETAL SYSTEM
No Tissues/Organs Examined

NERVOUS SYSTEM
No Tissues/Organs Examined

RESPIRATORY SYSTEM
No Tissues/Organs Examined

SPECIAL SENSES SYSTEM
No Tissues/Organs Examined

URINARY SYSTEM

KIDNEYS	(6)	(4)	(0)
RENAL TUBULE; BILATERAL; CYST	1 (17%) [1]		
PELVIS; LEFT; DILATION		1 (25%) [1]	
PELVIS; RIGHT; DILATION	4 (67%) [3]	3 (75%) [2]	
LEFT; INFLAMMATION, CHRONIC		1 (25%) [1]	

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

F2 Female

Treatment Groups (ppm)

0

750

2500

NERVOUS SYSTEM

No Tissues/Organs Examined

RESPIRATORY SYSTEM

No Tissues/Organs Examined

SPECIAL SENSES SYSTEM

No Tissues/Organs Examined

URINARY SYSTEM

No Tissues/Organs Examined

Experiment Number: R92025B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA03R: Non-Neoplastic Lesion Summary with Percent and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:43
Lab: RTI

LEGEND

Number of animals examined given for each tissue. If none of the animals examined have the specific lesion then there is a blank for that dose group for that specific lesion.

Number of animals with observation reported with percent incidence in parentheses

Number of litters shown in square brackets for F1 and F2 animals

Phase day range of terminal sacrifice shown in parentheses in disposition summary

SD – Study Day; GD – Gestation Day; LD – Lactation Day; PND – Postnatal Day, adults post-weaning

**** END OF REPORT ****