

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
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	
CLEAR CELL FOCUS			3	
HEPATODIAPHRAGMATIC NODULE			1 [3.0]	
PERIPORTAL; LYMPHOCYTE; INFILTRATION; FOCAL			2 [1.0]	
INFLAMMATION, CHRONIC; ACTIVE, FOCAL			1 [1.0]	
CENTRIOBULAR; NECROSIS; DIFFUSE			1 [3.0]	
CENTRIOBULAR; NECROSIS; FOCAL			1 [3.0]	
CENTRIOBULAR; HEPATOCYTE; VACUOLATION; CYTOPLASMIC				19 [1.9]
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 [2.0]
CORTEX; BILATERAL; VACUOLATION; DIFFUSE	3 [1.7]		3 [1.3]	
CORTEX; VACUOLATION; FOCAL	1 [2.0]		1 [1.0]	5 [1.0]
PITUITARY GLAND	(23)	(0)	(23)	(23)
PARS DISTALIS; CYST				1
THYROID GLANDS	(23)	(0)	(23)	(23)
C-CELL; HYPERPLASIA; FOCAL	1 [1.0]			
<hr/>				
GENERAL BODY SYSTEM				
No Tissues/Organs Examined				

Experiment Number: R92025B

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:50

Route: Dosing in Feed

CAS Number: 822-36-6

Lab: RTI

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 [2.0]			
EPIDIDYMIS	(22)	(23)	(23)	(23)
DUCT; RIGHT; EXFOLIATED GERM CELL			1 [2.0]	
DUCT; EXFOLIATED GERM CELL	1 [1.0]		2 [1.5]	7 [1.3]
DUCT; EXFOLIATED GERM CELL (TOTAL)	1 [1.0]		3 [1.7]	7 [1.3]
HYOSPERMIA			1 [2.0]	
LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE	(23)	(0)	(20)	(21)
PREPUTIAL GLANDS	(9)	(6)	(1)	(4)
UNILATERAL; ABSCESS	1 [3.0]			
DUCT; ECTASIA	5 [2.0]	5 [2.8]	1 [3.0]	4 [2.3]
INFILTRATION; MONONUCLEAR CELL	1 [1.0]			
INFLAMMATION		1 [1.0]		
UNILATERAL; INFLAMMATION, CHRONIC; ACTIVE	1 [2.0]			
INFLAMMATION, CHRONIC; ACTIVE	6 [2.0]	5 [2.2]		2 [2.5]
INFLAMMATION, CHRONIC; ACTIVE (TOTAL)	7 [2.0]	5 [2.2]		2 [2.5]
PROSTATE	(23)	(23)	(23)	(23)
VENTRAL LOBE; ATROPHY		9 [1.0]	20 [1.1]	23 [2.4]
VENTRAL LOBE, INTERSTITIUM; LYMPHOCYTE; INFILTRATION	5 [1.2]	5 [1.0]	1 [1.0]	
VENTRAL LOBE; INFLAMMATION; CHRONIC ACTIVE		1 [1.0]		
SEMINAL VESICLES	(23)	(0)	(23)	(23)
TESTIS	(22)	(23)	(23)	(23)
GERMINAL EPITHELIUM; ATROPHY				1 [1.0]
GERM CELL; DEGENERATION	1 [1.0]		4 [1.8]	8 [1.6]
SEMINIFEROUS TUBULE; BILATERAL; SPERMATID RETENTION				1 [2.0]
SEMINIFEROUS TUBULE; SPERMATID RETENTION	2 [1.0]	3 [1.0]	1 [1.0]	7 [1.1]

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	F0 Male			
	Treatment Groups (ppm)			
	0	750	2500	5000
SEMINIFEROUS TUBULE; SPERMATID RETENTION (TOTAL)	2 [1.0]	3 [1.0]	1 [1.0]	8 [1.3]
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 [1.0]	
NEPHROPATHY, CHRONIC PROGRESSIVE	22 [1.9]		19 [1.1]	22 [1.1]

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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 [1.0]
CONGESTION; DIFFUSE	1 [2.0]			1 [2.0]
DEFORMITY		1 [1.0]		
HEMATOPOIESIS; EXTRAMEDULLARY, FOCAL			1 [1.0]	2 [1.5]
HEPATODIAPHRAGMATIC NODULE		1 [1.0]		
PERIportal; LYMPHOCYTE; INFILTRATION; FOCAL	2 [1.0]		1 [1.0]	2 [1.0]
CENTRIOBULAR; NECROSIS; DIFFUSE				1 [2.0]
CENTRIOBULAR; NECROSIS; FOCAL			1 [2.0]	
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 [3.0]	
CORTEX; HYPERTROPHY; FOCAL				2 [1.5]
CORTEX; VACUOLATION; FOCAL	3 [1.0]			3 [1.0]
PITUITARY GLAND	(23)	(1)	(23)	(23)
PARS DISTALIS; CYST				2
THYROID GLANDS	(23)	(1)	(23)	(23)
C-CELL; HYPERPLASIA; FOCAL				3 [1.0]
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 [2.0]	
CLITORAL GLANDS	(3)	(4)	(1)	(1)
UNILATERAL; ABSCESS; CHRONIC			1 [4.0]	
DUCT; UNILATERAL; ECTASIA	1 [3.0]	3 [2.3]		
DUCT; ECTASIA	1 [4.0]	1 [2.0]		1 [2.0]
DUCT; ECTASIA (TOTAL)	2 [3.5]	4 [2.3]		1 [2.0]
INFILTRATION; MONONUCLEAR CELL	1 [2.0]			1 [2.0]
DUCT; LUMEN; INFLAMMATION, ACUTE				1 [2.0]
UNILATERAL; INFLAMMATION, CHRONIC; ACTIVE		2 [2.0]		
INFLAMMATION, CHRONIC; ACTIVE		1 [2.0]		
INFLAMMATION, CHRONIC; ACTIVE (TOTAL)		3 [2.0]		
OVARIES	(23)	(1)	(23)	(23)
CONGESTION	1 [2.0]			
CORPUS LUTEUM; CYST				2
FOLLICLE; CYST				1
PLACENTA	(0)	(0)	(1)	(5)
BILATERAL; EDEMA				1 [2.0]
EDEMA; DIFFUSE				3 [2.3]
EDEMA				1 [3.0]
INFLAMMATION; ACUTE				1 [2.0]
INFLAMMATION; SUPPURATIVE				1 [2.0]
BILATERAL; NECROSIS; DIFFUSE				1 [3.0]
NECROSIS; DIFFUSE				1 [2.0]
NECROSIS				1 [2.0]
UTERUS	(23)	(3)	(23)	(23)
ENDOMETRIUM; CYST				1

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Lab: RTI

Species/Strain: Rat/Sprague-Dawley

	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
OVIDUCT; CYST			1	
HORN; LUMEN; DILATION			1 [3.0]	
DILATION		1 [2.0]		
DILATION (TOTAL)		1 [2.0]	1 [3.0]	
ENDOMETRIUM; HYPERPLASIA; CYSTIC	2 [2.0]			4 [1.5]
INFLAMMATION; CHRONIC-ACTIVE			1 [3.0]	
INFLAMMATION; SUPPURATIVE				2 [2.5]
ENDOMETRIUM; METAPLASIA; SQUAMOUS	2 [2.0]			
ENDOMETRIUM; METAPLASIA; SQUAMOUS (TOTAL)	2 [2.0]	1 [1.0]		
METAPLASIA; SQUAMOUS		1 [1.0]		
NECROSIS				1 [2.0]
ULCER; MULTIFOCAL			1 [2.0]	
VAGINA	(23)	(1)	(23)	(23)
CYST			1	
SUBMUCOSA; LYMPHOCYTE; INFILTRATION; FOCAL	1 [1.0]			
INFLAMMATION; ACUTE			1 [2.0]	
MUCIFICATION	7 [3.0]		5 [3.0]	
ULCER; FOCAL			1 [2.0]	
HEMATOPOIETIC SYSTEM				
LYMPH NODE, MEDIASTINAL	(3)	(0)	(0)	(0)
CONGESTION	1 [2.0]			
THYMUS	(23)	(1)	(22)	(23)
CORTEX; DECREASED LYMPHOCYTE; DIFFUSE			2 [3.5]	6 [2.5]

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
INTEGUMENTARY SYSTEM				
MAMMARY GLANDS	(1)	(2)	(0)	(0)
INFILTRATION; BACTERIA	1 [3.0]			
INFLAMMATION; SUPPURATIVE	1 [3.0]			
SKIN	(2)	(0)	(1)	(0)
ALOPECIA			1 [3.0]	
LYMPHOID SYSTEM				
No Tissues/Organs Examined				
MUSCULOSKELETAL SYSTEM				
BONE	(1)	(0)	(0)	(0)
INTERVERTEBRAL DISK; RUPTURE; FOCAL	1 [4.0]			
LIMB	(2)	(1)	(2)	(0)
ALOPECIA		1 [1.0]	1 [3.0]	
EPIDERMIS; HYPERPLASIA; FOCAL		1 [2.0]		
EPIDERMIS; PARAKERATOSIS; FOCAL		1 [1.0]		
RIGHT; ULCER; DIFFUSE			1 [3.0]	
NERVOUS SYSTEM				
BRAIN	(0)	(0)	(0)	(2)
RESPIRATORY SYSTEM				
NOSE	(0)	(0)	(1)	(0)
SUBCUTANEOUS; CYST			1	
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				1 [1.0]
PAPILLA; COLLECTING DUCT; DILATION	1 [1.0]			
INFLAMMATION, ACUTE; FOCAL				1 [1.0]
MINERAL	1 [1.0]		2 [1.0]	1 [2.0]
RENAL TUBULE; NECROSIS; ACUTE, MULTIFOCAL				3 [1.3]
NEPHROPATHY, CHRONIC PROGRESSIVE	17 [1.2]	1 [1.0]	11 [1.0]	11 [1.1]

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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 [2.0] (1)
HEMATOPOIETIC CELL PROLIFERATION; EXTRAMEDULLARY			1 [1.0] (1)
HYPERTROPHY; HEPATOCELLULAR	3 [1.0] (2)		
ACCESSORY LOBE; INFARCTION		1 [3.0] (1)	
LYMPHOCYTE; INFILTRATION; MULTIFOCAL	1 [1.0] (1)		
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(49)	(1)	(20)
ATROPHY; DIFFUSE		1 [3.0] (1)	
CORTEX; HYPERTROPHY; FOCAL	2 [1.0] (1)		
METAPLASIA; OSSEOUS			1 [1.0] (1)
CORTEX; VACUOLATION; FOCAL	1 [2.0] (1)		
PITUITARY GLAND	(49)	(0)	(20)
PARS DISTALIS; CYST	4 (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 [1.3] (2)

5 [1.2] (4)

4 [1.3] (4)

LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE

(49)

(0)

(20)

PROSTATE

(49)

(56)

(20)

VENTRAL LOBE; ATROPHY

4 [1.0] (3)

25 [1.0] (17)

17 [1.2] (7)

VENTRAL LOBE, INTERSTITIUM; LYMPHOCYTE; INFILTRATION

25 [1.1] (13)

33 [1.4] (18)

6 [1.0] (5)

VENTRAL LOBE; INFLAMMATION; CHRONIC ACTIVE

1 [2.0] (1)

INFLAMMATION; CHRONIC ACTIVE

1 [3.0] (1)

SEMINAL VESICLES

(49)

(1)

(20)

ATROPHY

1 [3.0] (1)

1 [1.0] (1)

RUPTURE

1 [3.0] (1)

TESTIS

(49)

(56)

(20)

GERM CELL; DEGENERATION

4 [1.3] (3)

6 [1.0] (4)

1 [2.0] (1)

SEMIFEROUS TUBULE; SPERMATID RETENTION

3 [1.0] (2)

4 [1.0] (3)

HEMATOPOIETIC SYSTEM

THYMUS

(49)

(0)

(20)

INTEGUMENTARY SYSTEM

SKIN

(1)

(1)

(1)

DERMIS; FIBROSIS; FOCAL

1 [2.0] (1)

EPIDERMIS; HYPERPLASIA; FOCAL

1 [1.0] (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 [2.0] (4)	1 [2.0] (1)	
NERVOUS SYSTEM			
No Tissues/Organs Examined			
RESPIRATORY SYSTEM			
LUNGS	(1)	(1)	(0)
CONGESTION; DIFFUSE		1 [1.0] (1)	
SPECIAL SENSES SYSTEM			
No Tissues/Organs Examined			
URINARY SYSTEM			
KIDNEYS	(49)	(1)	(20)
PAPILLA; COLLECTING DUCT; DILATION			1 [1.0] (1)
PELVIS; RIGHT; DILATION	7 [2.0] (6)	1 [2.0] (1)	3 [2.0] (3)
TRANSITIONAL CELL; EPITHELIUM; HYPERPLASIA; FOCAL MINERAL		1 [1.0] (1)	1 [1.0] (1)
NEPHROPATHY, CHRONIC PROGRESSIVE	45 [1.2] (17)	1 [1.0] (1)	20 [1.0] (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 [2.0] (1)	1 [2.0] (1)	1 [2.0] (1)
LYMPHOCYTE; INFILTRATION; MULTIFOCAL	5 [1.0] (5)		
INFLAMMATION, CHRONIC; ACTIVE, FOCAL	1 [1.0] (1)		
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(47)	(0)	(27)
PITUITARY GLAND	(47)	(0)	(27)
PARS DISTALIS; CYST	1 (1)		1 (1)
THYROID GLANDS	(47)	(0)	(25)
FOLLICULAR CELL; MINERAL			1 [1.0] (1)
GENERAL BODY SYSTEM			
No Tissues/Organs Examined			

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F1 Female: F1 NonParent Female

	Treatment Groups (ppm)		
	0	750	2500
GENITAL SYSTEM			
CERVIX	(47)	(0)	(26)
ENDOMETRIUM; CYST	1 (1)		
OVARIES	(47)	(2)	(27)
CORPUS LUTEUM; CYST	1 (1)		1 (1)
FOLLICLE; UNILATERAL; CYST		1 (1)	
UTERUS	(47)	(2)	(27)
OVIDUCT; CYST			1 (1)
SUBSEROVA; CYST	4 (4)		
ENDOMETRIUM; HYPERPLASIA; CYSTIC	4 [1.3] (4)		
VAGINA	(47)	(0)	(27)
MUCIFICATION	5 [3.0] (3)		
HEMATOPOIETIC SYSTEM			
LYMPH NODE	(1)	(0)	(0)
NO MICROSCOPIC FINDING RECORDED	1 (1)		
LYMPH NODE, MEDIASTINAL	(1)	(0)	(1)
CONGESTION			1 [2.0] (1)
DECREASED LYMPHOCYTE			1 [2.0] (1)
SPLEEN	(2)	(1)	(0)
THYMUS	(47)	(0)	(27)
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS	(47)	(0)	(27)
SKIN	(1)	(1)	(0)
ALOPECIA; DIFFUSE		1 [1.0] (1)	
NO MICROSCOPIC FINDING RECORDED		1 (1)	
LYMPHOID SYSTEM			
No Tissues/Organs Examined			

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
Lab: RTI

F1 Female: F1 NonParent Female

	Treatment Groups (ppm)		
	0	750	2500
MUSCULOSKELETAL SYSTEM			
LIMB	(4)	(4)	(1)
BONE; DEFORMITY	3 [2.0] (3)	4 [2.3] (3)	1 [2.0] (1)
PAW	(1)	(0)	(0)
NO MICROSCOPIC FINDING RECORDED	1 (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 [1.0] (7)	44 [1.3] (19)	20 [1.2] (11)
NEPHROPATHY, CHRONIC PROGRESSIVE	27 [1.1] (14)		21 [1.0] (12)

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
 Test Compound: 4-Methylimidazole
 CAS Number: 822-36-6

Date Report Requested: 08/23/2018
 Time Report Requested: 14:02:50
 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 (1)		4 (3)
HEPATODIAPHRAGMATIC NODULE	3 [2.0] (3)		5 [2.8] (4)
BILE DUCT; HYPERPLASIA; FOCAL	1 [1.0] (1)		1 [1.0] (1)
HYPERTROPHY; DIFFUSE, HEPATOCELLULAR			1 [2.0] (1)
LYMPHOCYTE; PERIportal; INFILTRATION; MULTIFOCAL	1 [1.0] (1)		7 [1.0] (6)
INFLAMMATION, CHRONIC; ACTIVE, FOCAL	3 [1.0] (3)		
HEPATOCYTE; NECROSIS; FOCAL	1 [1.0] (1)		2 [1.0] (2)
HEPATOCYTE; CENTRIOBULAR; VACUOLATION; CYTOPLASMIC, DIFFUSE			1 [1.0] (1)
HEPATOCYTE; VACUOLATION; CYTOPLASMIC, FOCAL			1 [1.0] (1)
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
Lab: RTI

F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(40)	(0)	(40)
CORTEX; HYPERTROPHY; FOCAL	1 [2.0] (1)		1 [1.0] (1)
CORTEX; VACUOLATION; FOCAL			3 [1.3] (3)
CORTEX; VACUOLATION, CYTOPLASMIC; DIFFUSE	1 [2.0] (1)		1 [1.0] (1)
PITUITARY GLAND	(40)	(0)	(40)
PARS DISTALIS; CYST	3 (3)		1 (1)
THYROID GLANDS	(40)	(0)	(40)
C-CELL; HYPERPLASIA; FOCAL	1 [3.0] (1)		1 [2.0] (1)
GENERAL BODY SYSTEM			
FAT	(2)	(0)	(0)

Experiment Number: R92025B

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:50

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 [1.0] (1)
DUCT; RIGHT; EXFOLIATED GERM CELL			2 [1.0] (2)
DUCT; EXFOLIATED GERM CELL		5 [1.2] (5)	1 [2.0] (1)
DUCT; EXFOLIATED GERM CELL (TOTAL)		5 [1.2] (5)	4 [1.3] (4)
LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE	(40)	(0)	(40)
PREPUTIAL GLANDS	(3)	(1)	(0)
DUCT; UNILATERAL; ABSCESS	1 (1)		
UNILATERAL; INFLAMMATION, CHRONIC; ACTIVE		1 [3.0] (1)	
PROSTATE	(40)	(44)	(40)
DORSAL LOBE; EPITHELIUM; ATROPHY			1 [1.0] (1)
VENTRAL LOBE; ATROPHY	4 [1.0] (3)	10 [1.0] (8)	35 [1.5] (15)
VENTRAL LOBE, INTERSTITIUM; LYMPHOCYTE; INFILTRATION	5 [1.0] (4)	1 [1.0] (1)	
SEMINAL VESICLES	(40)	(1)	(40)
ATROPHY			2 [1.0] (2)
TESTIS	(40)	(44)	(40)
GERMINAL EPITHELIUM; LEFT; ATROPHY	1 [1.0] (1)		1 [2.0] (1)
GERMINAL EPITHELIUM; ATROPHY			1 [2.0] (1)
GERMINAL EPITHELIUM; ATROPHY (TOTAL)	1 [1.0] (1)		2 [2.0] (2)
GERM CELL; LEFT; DEGENERATION	1 [1.0] (1)		1 [2.0] (1)
GERM CELL; DEGENERATION	1 [1.0] (1)	5 [2.0] (5)	4 [1.0] (4)
GERM CELL; DEGENERATION (TOTAL)	2 [1.0] (2)	5 [2.0] (5)	5 [1.2] (4)
SEMINIFEROUS TUBULE; SPERMATID RETENTION		5 [1.2] (5)	4 [1.0] (3)

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
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 [2.0] (1)		1 [3.0] (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 [2.0] (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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
Lab: RTI

F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
URINARY SYSTEM			
KIDNEYS	(40)	(6)	(40)
PELVIS; CONCRETION; FOCAL	6 [1.7] (5)		1 [1.0] (1)
PAPILLA; CYST			1 (1)
PELVIS; LEFT; DILATION	1 [2.0] (1)		
PELVIS; RIGHT; DILATION	8 [1.4] (7)	4 [1.8] (3)	1 [1.0] (1)
PELVIS; DILATION (TOTAL)	9 [1.4] (8)	4 [1.8] (3)	1 [1.0] (1)
EPITHELIUM; TRANSITIONAL CELL; HYPERPLASIA; FOCAL (TOTAL)	5 [1.8] (4)	1 [2.0] (1)	1 [1.0] (1)
EPITHELIUM; TRANSITIONAL CELL; HYPERPLASIA; FOCAL, LEFT	1 [1.0] (1)		
EPITHELIUM; TRANSITIONAL CELL; HYPERPLASIA; FOCAL, RIGHT	4 [2.0] (3)	1 [2.0] (1)	1 [1.0] (1)
TRANSITIONAL CELL; EPITHELIUM; INFLAMMATION, CHRONIC; ACTIVE, FOCAL	2 [1.0] (2)	1 [2.0] (1)	
MINERAL	3 [1.0] (3)		5 [1.0] (2)
NEPHROPATHY, CHRONIC PROGRESSIVE	40 [1.6] (18)	6 [1.8] (4)	40 [1.3] (15)

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
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 [1.0] (1)	
SUBCAPSULAR; HEMORRHAGE; FOCAL		1 [1.0] (1)	
HEPATODIAPHRAGMATIC NODULE	1 [2.0] (1)	1 [2.0] (1)	2 [2.0] (2)
BILE DUCT; HYPERPLASIA; DIFFUSE			1 [1.0] (1)
LYMPHOCYTE; PERIportal; INFILTRATION; MULTIFOCAL	9 [1.0] (9)	6 [1.0] (6)	5 [1.0] (3)
INFLAMMATION, CHRONIC; ACTIVE, FOCAL	1 [1.0] (1)		2 [1.0] (2)
CENTRIOBULAR; NECROSIS; FOCAL			2 [2.0] (2)
HEPATOcyTE; NECROSIS; DIFFUSE			1 [4.0] (1)
CARDIOVASCULAR SYSTEM			
No Tissues/Organs Examined			

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
Lab: RTI

F1 Female: F1 Parental Females

Treatment Groups (ppm)

	0	750	2500
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(40)	(43)	(40)
CORTEX; HYPERTROPHY; FOCAL	1 [2.0] (1)		1 [2.0] (1)
LYMPHOCYTE; INFILTRATION; MULTIFOCAL	1 [1.0] (1)		
CORTEX; VACUOLATION; FOCAL		2 [2.0] (2)	1 [1.0] (1)
PITUITARY GLAND	(39)	(43)	(40)
PARS DISTALIS; CYST		1 (1)	
THYROID GLANDS	(40)	(43)	(40)
C-CELL; HYPERPLASIA; FOCAL	5 [1.2] (5)	3 [1.0] (3)	1 [1.0] (1)
INFLAMMATION; CHRONIC ACTIVE	1 [1.0] (1)		
GENERAL BODY SYSTEM			
No Tissues/Organs Examined			

Experiment Number: R92025B

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:50

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)
SEROSEA; CYST	1 (1)		
CLITORAL GLANDS	(3)	(0)	(0)
DUCT; UNILATERAL; ECTASIA	1 [2.0] (1)		
DUCT; ECTASIA	2 [1.5] (2)		
DUCT; ECTASIA (TOTAL)	3 [1.7] (3)		
OVARIES	(40)	(43)	(40)
CORPUS LUTEUM; CYST; MULTIPLE			1 (1)
CORPUS LUTEUM; CYST		2 (2)	3 (3)
FOLLICLE; CYST		4 (4)	
CYST	1 (1)		
CORPUS LUTEUM; CYST (TOTAL)		2 (2)	4 (4)
PLACENTA	(0)	(1)	(0)
INFLAMMATION, ACUTE; MULTIFOCAL		1 [2.0] (1)	
NECROSIS; MULTIFOCAL		1 [2.0] (1)	
UTERUS	(40)	(43)	(40)
OVIDUCT; CYST			1 (1)
SUBSEROSEA; CYST	1 (1)	2 (2)	2 (2)
HORN; DECIDUAL ALTERATION		1 [2.0] (1)	
ENDOMETRIUM; HYPERPLASIA; CYSTIC	6 [1.2] (4)		
ENDOMETRIUM; INFLAMMATION; SUPPURATIVE			1 [1.0] (1)
ENDOMETRIUM; ULCER; FOCAL			1 [2.0] (1)
VAGINA	(40)	(43)	(40)
MUCIFICATION	3 [3.0] (3)		

Experiment Number: R92025B

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence

Date Report Requested: 08/23/2018

Test Type: RACB

Test Compound: 4-Methylimidazole

Time Report Requested: 14:02:50

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	(1)	(1)	(0)
CONGESTION	1 [2.0] (1)	1 [2.0] (1)	
LYMPH NODE, MESENTERIC	(0)	(1)	(0)
SPLEEN	(0)	(1)	(0)
THYMUS	(40)	(42)	(40)
CORTEX; DECREASED LYMPHOCYTE; DIFFUSE	8 [1.3] (7)	10 [1.3] (9)	9 [2.0] (8)
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS	(40)	(43)	(40)
INFLAMMATION; SUPPURATIVE			1 [4.0] (1)
INFLAMMATION, ACUTE; FOCAL		1 [3.0] (1)	
LACTATION	1 (1)		
NECROSIS; FOCAL		1 [3.0] (1)	
SKIN	(1)	(2)	(1)
ABSCESS	1 [4.0] (1)		
ALOPECIA		2 [2.5] (2)	1 [3.0] (1)
LYMPHOID SYSTEM			
No Tissues/Organs Examined			
MUSCULOSKELETAL SYSTEM			
LIMB	(15)	(2)	(1)
BONE; DEFORMITY	11 [2.1] (7)	1 [2.0] (1)	1 [2.0] (1)
NO MICROSCOPIC FINDING RECORDED	1 (1)	1 (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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
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 [1.0] (8)	1 [1.0] (1)	2 [1.0] (2)
PAPILLA; CYST		1 (1)	
RENAL TUBULE; EPITHELIUM; HYPERPLASIA; FOCAL			1 [3.0] (1)
MINERAL	8 [1.0] (5)	21 [1.1] (14)	27 [1.1] (12)
NEPHROPATHY, CHRONIC PROGRESSIVE	34 [1.2] (17)	41 [1.1] (21)	40 [1.1] (15)
URINARY BLADDER	(1)	(0)	(0)

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
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 [1.5] (1)	1 [2.0] (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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
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 (1)		
PELVIS; LEFT; DILATION		1 [1.0] (1)	
PELVIS; RIGHT; DILATION	4 [1.8] (3)	3 [2.3] (2)	
LEFT; INFLAMMATION, CHRONIC		1 [1.0] (1)	

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
Lab: RTI

F2 Female

Treatment Groups (ppm)

0 **750** **2500**

Disposition Summary

Animals Initially In Study	98	132	76
Early Deaths			
Survivors			
Scheduled sacrifice, terminal (PND 28)	98	132	76
Animals Examined Microscopically			

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
No Tissues/Organs Examined

HEMATOPOIETIC SYSTEM
No Tissues/Organs Examined

INTEGUMENTARY SYSTEM
No Tissues/Organs Examined

LYMPHOID SYSTEM
No Tissues/Organs Examined

MUSCULOSKELETAL SYSTEM
No Tissues/Organs Examined

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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
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

PA18R: Non-Neoplastic Lesions with Mean Severity Grade and Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 08/23/2018
Time Report Requested: 14:02:50
Lab: RTI

LEGEND

[a] 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 mean severity grade in square brackets

[b] Mean severity grade denoted by 1 - minimal, 2 - mild, 3 - moderate, 4 - marked

Number of litters shown in parentheses 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 ****