

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
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	0 NM	2500 NM
Disposition Summary						
Animals Initially In Study	23	23	23	23	22	19
Early Deaths						
Unscheduled Sacrifice			3	2		
Scheduled Deaths						
Scheduled sacrifice, terminal (SD 15 - 178)	23	23	20	21	22	19
Number of Animals Examined	23	23	23	23	22	19
ALIMENTARY SYSTEM						
LIVER	(23)	(23)	(23)	(23)	(22)	(19)
CAUDATE PROCESS; LEFT; DEFORMITY; MARKED				1 (4.3%)		
ACCESSORY LOBE; DISCOLORATION; DARK, MODERATE			1 (4.3%)			
CAUDATE PROCESS; DISCOLORATION; BROWN, MODERATE			1 (4.3%)			
CARDIOVASCULAR SYSTEM						
None						
ENDOCRINE SYSTEM						
ADRENAL GLANDS	(23)	(23)	(23)	(23)	(22)	(19)
PITUITARY GLAND	(23)	(23)	(23)	(23)	(22)	(19)
THYROID GLANDS	(23)	(23)	(23)	(23)	(22)	(19)
GENERAL BODY SYSTEM						
None						

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F0 Male

Treatment Groups (ppm)

	0	750	2500	5000	0 NM	2500 NM
GENITAL SYSTEM						
COAGULATING GLANDS	(23)	(23)	(23)	(23)	(22)	(19)
COWPERS GLANDS	(23)	(23)	(23)	(23)	(22)	(19)
RIGHT; REDUCED IN SIZE; MILD	1 (4.3%)					
DORSAL PROSTATE	(23)	(23)	(23)	(23)	(22)	(19)
EPIDIDYMIDES	(23)	(23)	(23)	(23)	(22)	(19)
RIGHT; CYST; MILD, SOFT	1 (4.3%)					
CAUDA; RIGHT; REDUCED IN SIZE; MINIMAL			1 (4.3%)			
LEFT; REDUCED IN SIZE; MODERATE					1 (4.5%)	
LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE	(23)	(23)	(23)	(23)	(22)	(19)
PREPUTIAL GLANDS	(23)	(23)	(23)	(23)	(22)	(19)
BILATERAL; DISCOLORATION; BROWN, MILD		1 (4.3%)	1 (4.3%)	1 (4.3%)		
BILATERAL; DISCOLORATION; BROWN, MODERATE		1 (4.3%)				
BILATERAL; DISCOLORATION; GREEN, MILD	3 (13.0%)	1 (4.3%)		1 (4.3%)		
BILATERAL; DISCOLORATION; GREEN, MINIMAL	1 (4.3%)	1 (4.3%)				
BILATERAL; DISCOLORATION; GREEN, MODERATE		1 (4.3%)		2 (8.7%)		
LEFT; DISCOLORATION; GREEN, MILD	2 (8.7%)					
LEFT; DISCOLORATION; GREEN, MINIMAL	1 (4.3%)					
DISCOLORATION; GREEN, MILD		1 (4.3%)				
DISCOLORATION; GREEN, MINIMAL					1 (4.5%)	
LEFT; ENLARGED; MILD	1 (4.3%)					
LEFT; ENLARGED; MODERATE	1 (4.3%)					
SEMINAL VESICLES	(23)	(23)	(23)	(23)	(22)	(19)
TESTES	(23)	(23)	(23)	(23)	(22)	(19)
LEFT; REDUCED IN SIZE; MARKED					1 (4.5%)	
RIGHT; REDUCED IN SIZE; MODERATE					1 (4.5%)	

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	F0 Male					
	Treatment Groups (ppm)					
	0	750	2500	5000	0 NM	2500 NM
VENTRAL PROSTATE REDUCED IN SIZE; MODERATE	(23)	(23)	(23)	(23) 1 (4.3%)	(22)	(19)
HEMATOPOIETIC SYSTEM						
THYMUS	(23)	(23)	(23)	(23)	(22)	(19)
INTEGUMENTARY SYSTEM						
None						
LYMPHOID SYSTEM						
None						
MUSCULOSKELETAL SYSTEM						
DIAPHRAGM MEDIAN LOBE; HERNIA; MILD MEDIAN LOBE; HERNIA; MODERATE	(23)	(23)	(23)	(23) 1 (4.3%)	(22) 1 (4.5%)	(19)
NERVOUS SYSTEM						
None						
RESPIRATORY SYSTEM						
None						
SPECIAL SENSES SYSTEM						
None						
URINARY SYSTEM						
KIDNEYS	(23)	(23)	(23)	(23)	(22)	(19)

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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
Scheduled Deaths				
Scheduled sacrifice, terminal (LD 4, SD 28 - 220)	22	22	19	12
Number of Animals Examined	23	23	23	23
ALIMENTARY SYSTEM				
LIVER	(23)	(23)	(23)	(23)
MEDIAL LOBE; DEFORMITY; MINIMAL DISCOLORATION; MILD, MOTTLED		1 (4.3%)		
DISCOLORATION; MILD, PALE				1 (4.3%)
DISCOLORATION; MODERATE, MOTTLED	1 (4.3%)			1 (4.3%)
CARDIOVASCULAR SYSTEM				
None				
ENDOCRINE SYSTEM				
ADRENAL GLANDS	(23)	(23)	(23)	(23)
BILATERAL; DISCOLORATION; MINIMAL, PALE LEFT; DISCOLORATION; MILD, PALE			1 (4.3%)	1 (4.3%)
BILATERAL; ENLARGED; MINIMAL				1 (4.3%)
PITUITARY GLAND	(23)	(23)	(23)	(23)
THYROID GLANDS	(23)	(23)	(23)	(23)

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
GENERAL BODY SYSTEM				
WHOLE BODY	(23)	(23)	(23)	(23)
DISCOLORATION; MODERATE, PALE				1 (4.3%)
GENITAL SYSTEM				
CERVIX	(23)	(23)	(23)	(23)
CLITORAL GLANDS	(23)	(23)	(23)	(23)
BILATERAL; DISCOLORATION; GREEN, MILD				1 (4.3%)
BILATERAL; DISCOLORATION; MILD, TAN		1 (4.3%)		
LEFT; DISCOLORATION; BROWN, MODERATE		1 (4.3%)		
LEFT; DISCOLORATION; DARK, MILD	1 (4.3%)			
LEFT; DISCOLORATION; GREEN, MINIMAL		1 (4.3%)		
RIGHT; DISCOLORATION; GREEN, MODERATE			1 (4.3%)	
RIGHT; DISCOLORATION; MILD, PALE		1 (4.3%)		
BILATERAL; ENLARGED; MILD		1 (4.3%)		
LEFT; ENLARGED; MILD	1 (4.3%)			
LEFT; ENLARGED; MODERATE		1 (4.3%)		
RIGHT; ENLARGED; MILD		1 (4.3%)		
OVARIES	(23)	(23)	(23)	(23)
BILATERAL; DISCOLORATION; MODERATE, RED	1 (4.3%)			
BILATERAL; ENLARGED; MILD	1 (4.3%)			
PLACENTA	(23)	(23)	(23)	(23)
ENLARGED; MODERATE	0 **		1 (4.3%)	5 (21.7%) *
UTERUS	(23)	(23)	(23)	(23)
BILATERAL; DILATION; FLUID-FILLED, MODERATE		1 (4.3%)		
LUMEN; LEFT; NODULE; RED		1 (4.3%)		
VAGINA	(23)	(23)	(23)	(23)

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	Treatment Groups (ppm)			
	0	750	2500	5000
HEMATOPOIETIC SYSTEM				
LYMPH NODE, BRONCHIAL	(23)	(23)	(23)	(23)
DISCOLORATION; MODERATE, RED	1 (4.3%)			
ENLARGED; MODERATE	1 (4.3%)			
THYMUS	(23)	(23)	(23)	(23)
INTEGUMENTARY SYSTEM				
MAMMARY GLANDS	(23)	(23)	(23)	(23)
AXILLARY; LEFT; MASS; FIRM	1 (4.3%)			
INGUINAL; RIGHT; MASS; FIRM	1 (4.3%)	1 (4.3%)		
RIGHT; THORACIC; MASS; SOFT		1 (4.3%)		
SKIN	(23)	(23)	(23)	(23)
THORACIC; ALOPECIA; MODERATE			1 (4.3%)	
TAIL; MISSHAPEN; MINIMAL	1 (4.3%)			
LYMPHOID SYSTEM				
None				
MUSCULOSKELETAL SYSTEM				
DIAPHRAGM	(23)	(23)	(23)	(23)
MEDIAN LOBE; HERNIA; MINIMAL		1 (4.3%)		
LIMB	(23)	(23)	(23)	(23)
BILATERAL; FORELIMB; ALOPECIA; MINIMAL		1 (4.3%)		
BILATERAL; FORELIMB; ALOPECIA; MODERATE			1 (4.3%)	
LEFT; FORELIMB; ALOPECIA; MODERATE			1 (4.3%)	
FORELIMB; RIGHT; LACERATION; MARKED			1 (4.3%)	
NERVOUS SYSTEM				
BRAIN	(23)	(23)	(23)	(23)

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	F0 Female			
	Treatment Groups (ppm)			
	0	750	2500	5000
RESPIRATORY SYSTEM				
NOSE	(23)	(23)	(23)	(23)
SWELLING; MODERATE			1 (4.3%)	
SPECIAL SENSES SYSTEM				
None				
URINARY SYSTEM				
KIDNEYS	(23)	(23)	(23)	(23)
BILATERAL; DISCOLORATION; MODERATE, PALE	2 (8.7%)			

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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			
Scheduled Deaths			
Scheduled sacrifice, terminal (PND 91 - 93)	49	56	20
Number of Animals Examined	49	56	20
Total number litters	18	22	8
ALIMENTARY SYSTEM			
LIVER	(49)	(56)	(20)
MEDIAL LOBE; DEFORMITY; MILD			1 (5.0%) [1]
ACCESSORY LOBE; DISCOLORATION; MODERATE, MOTTLED		1 (1.8%) [1]	
CARDIOVASCULAR SYSTEM			
None			
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(49)	(56)	(20)
RIGHT; REDUCED IN SIZE; MODERATE		1 (1.8%) [1]	
PITUITARY GLAND	(49)	(56)	(20)
THYROID GLANDS	(49)	(56)	(20)
GENERAL BODY SYSTEM			
None			

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F1 Male: F1 NonParental Male

	Treatment Groups (ppm)		
	0	750	2500
GENITAL SYSTEM			
COAGULATING GLANDS	(49)	(56)	(20)
COWPERS GLANDS	(49)	(56)	(20)
LEFT; DISCOLORATION; MINIMAL, PINK		1 (1.8%) [1]	
RIGHT; DISCOLORATION; MILD, PINK		1 (1.8%) [1]	
RIGHT; MISSING		1 (1.8%) [1]	
DORSAL PROSTATE	(49)	(56)	(20)
EPIDIDYMIDES	(49)	(56)	(20)
LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE	(49)	(56)	(20)
SEMINAL VESICLES	(49)	(56)	(20)
RIGHT; ADHESION; MILD		1 (1.8%) [1]	
LEFT; REDUCED IN SIZE; MODERATE	1 (2.0%) [1]		
REDUCED IN SIZE; MILD			1 (5.0%) [1]
REDUCED IN SIZE; MINIMAL			1 (5.0%) [1]
TESTES	(49)	(56)	(20)
VENTRAL PROSTATE	(49)	(56)	(20)
HEMATOPOIETIC SYSTEM			
THYMUS	(49)	(56)	(20)
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS	(49)	(56)	(20)
SKIN	(49)	(56)	(20)
TAIL; ABRASION; MINIMAL		1 (1.8%) [1]	
TAIL; MISSHAPEN; MINIMAL	1 (2.0%) [1]	1 (1.8%) [1]	
TAIL; REDUCED IN SIZE			1 (5.0%) [1]
LYMPHOID SYSTEM			
None			

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F1 Male: F1 NonParental Male

	Treatment Groups (ppm)		
	0	750	2500
MUSCULOSKELETAL SYSTEM			
LIMB	(49)	(56)	(20)
HINDLIMB; RIGHT; DEFORMITY; MILD	1 (2.0%) [1]		
PAW	(49)	(56)	(20)
HINDFOOT; LEFT; DEFORMITY; MILD	1 (2.0%) [1]		
HINDFOOT; RIGHT; DEFORMITY; MILD	1 (2.0%) [1]		
HINDFOOT; RIGHT; DEFORMITY; MODERATE	1 (2.0%) [1]		
NERVOUS SYSTEM			
None			
RESPIRATORY SYSTEM			
LUNGS	(49)	(56)	(20)
DISCOLORATION; MINIMAL, MOTTLED		1 (1.8%) [1]	
SPECIAL SENSES SYSTEM			
None			
URINARY SYSTEM			
KIDNEYS	(49)	(56)	(20)
PELVIS; BILATERAL; DILATION; MINIMAL	1 (2.0%) [1]		
PELVIS; RIGHT; DILATION; MILD	1 (2.0%) [1]	1 (1.8%) [1]	
PELVIS; RIGHT; DILATION; MODERATE	2 (4.1%) [2]		1 (5.0%) [1]

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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			
Scheduled Deaths			
Scheduled sacrifice, terminal (PND 91 - 93)	47	58	27
Number of Animals Examined	47	58	27
Total number litters	17	22	12

ALIMENTARY SYSTEM

LIVER	(47)	(58)	(27)
NODULE; PALE		1 (1.7%) [1]	

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

ADRENAL GLANDS	(47)	(58)	(27)
PITUITARY GLAND	(47)	(58)	(27)
THYROID GLANDS	(47)	(58)	(27)

GENERAL BODY SYSTEM

None

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F1 Female: F1 NonParent Female

	Treatment Groups (ppm)		
	0	750	2500
GENITAL SYSTEM			
CERVIX	(47)	(58)	(27)
OVARIES	(47)	(58)	(27)
LEFT; CYST; CLEAR, MODERATE		1 (1.7%) [1]	
RIGHT; CYST; 2, PALE		1 (1.7%) [1]	
RIGHT; CYST; DARK			1 (3.7%) [1]
UTERUS	(47)	(58)	(27)
LEFT; CYST; CLEAR	1 (2.1%) [1]		
CYST	1 (2.1%) [1]		
BILATERAL; DILATION; MILD		1 (1.7%) [1]	
DILATION; MILD		1 (1.7%) [1]	
BILATERAL; DISCOLORATION; MILD, RED		1 (1.7%) [1]	
LEFT; NODULE; PALE	1 (2.1%) [1]		
VAGINA	(47)	(58)	(27)
HEMATOPOIETIC SYSTEM			
LYMPH NODE, BRONCHIAL	(47)	(58)	(27)
LEFT; DISCOLORATION; MILD, RED			1 (3.7%) [1]
LYMPH NODE, INGUINAL	(47)	(58)	(27)
DISCOLORATION; DARK, MODERATE	1 (2.1%) [1]		
SPLEEN	(47)	(58)	(27)
NODULE; PALE		1 (1.7%) [1]	
THYMUS	(47)	(58)	(27)
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS	(47)	(58)	(27)
SKIN	(47)	(58)	(27)
FORELIMB; BILATERAL; ALOPECIA; MINIMAL		1 (1.7%) [1]	
TAIL; REDUCED IN SIZE	1 (2.1%) [1]		

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F1 Female: F1 NonParent Female

Treatment Groups (ppm)

0

750

2500

LYMPHOID SYSTEM

None

MUSCULOSKELETAL SYSTEM

DIAPHRAGM

(47)

(58)

(27)

MEDIAN LOBE; HERNIA; MILD

1 (2.1%) [1]

HERNIA; MILD

1 (1.7%) [1]

1 (3.7%) [1]

LIMB

(47)

(58)

(27)

HINDLIMB; LEFT; DEFORMITY; MILD

1 (1.7%) [1]

HINDLIMB; RIGHT; DEFORMITY; MILD

1 (1.7%) [1]

LEFT; DEFORMITY; MILD

1 (2.1%) [1]

PAW

(47)

(58)

(27)

HINDFOOT; LEFT; DEFORMITY; MILD

2 (4.3%) [2]

1 (1.7%) [1]

HINDFOOT; LEFT; DEFORMITY; MODERATE

1 (1.7%) [1]

HINDFOOT; RIGHT; DEFORMITY; MILD

1 (2.1%) [1]

1 (3.7%) [1]

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

KIDNEYS

(47)

(58)

(27)

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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
Scheduled Deaths			
Scheduled sacrifice, terminal (PND 218 - 224)	40	44	39
Number of Animals Examined	40	44	40
Total number litters	18	22	15
ALIMENTARY SYSTEM			
LIVER	(40)	(44)	(40)
CARDIOVASCULAR SYSTEM			
None			
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(40)	(44)	(40)
PITUITARY GLAND	(40)	(44)	(40)
THYROID GLANDS	(40)	(44)	(40)
GENERAL BODY SYSTEM			
FAT	(40)	(44)	(40)
PERINEUM; ANUS; DISCOLORATION; MODERATE, YELLOW		1 (2.3%) [1]	

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F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
GENITAL SYSTEM			
COAGULATING GLANDS	(40)	(44)	(40)
COWPERS GLANDS	(40)	(44)	(40)
RIGHT; MISSING		1 (2.3%) [1]	
DORSAL PROSTATE	(40)	(44)	(40)
EPIDIDYMIDES	(40)	(44)	(40)
LEFT; REDUCED IN SIZE; MILD	1 (2.5%) [1]		1 (2.5%) [1]
LEFT; REDUCED IN SIZE; MINIMAL	1 (2.5%) [1]		
LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE	(40)	(44)	(40)
PREPUTIAL GLANDS	(40)	(44)	(40)
LEFT; DISCOLORATION; GREEN, MILD		1 (2.3%) [1]	
RIGHT; DISCOLORATION; GREEN, MODERATE	1 (2.5%) [1]		
SEMINAL VESICLES	(40)	(44)	(40)
BILATERAL; REDUCED IN SIZE; MILD			1 (2.5%) [1]
RIGHT; REDUCED IN SIZE; MINIMAL		1 (2.3%) [1]	
TESTES	(40)	(44)	(40)
LEFT; MISSHAPEN; MINIMAL	1 (2.5%) [1]		
LEFT; REDUCED IN SIZE; FLACCID, MINIMAL	1 (2.5%) [1]		
LEFT; REDUCED IN SIZE; MILD			1 (2.5%) [1]
LEFT; REDUCED IN SIZE; MINIMAL	1 (2.5%) [1]		
LEFT; UNDESCENDED; FLACCID, MINIMAL		1 (2.3%) [1]	
VENTRAL PROSTATE	(40)	(44)	(40)

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F1 Male: F1 Parental Males

	Treatment Groups (ppm)		
	0	750	2500
HEMATOPOIETIC SYSTEM			
LYMPH NODE, BRONCHIAL	(40)	(44)	(40)
BILATERAL; DISCOLORATION; GREEN, MODERATE	1 (2.5%) [1]		
LYMPH NODE, RENAL	(40)	(44)	(40)
BILATERAL; DISCOLORATION; GREEN, MODERATE	1 (2.5%) [1]		
SPLEEN	(40)	(44)	(40)
ENLARGED; MILD			1 (2.5%) [1]
ENLARGED; MODERATE	1 (2.5%) [1]		
THYMUS	(40)	(44)	(40)
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS	(40)	(44)	(40)
SKIN	(40)	(44)	(40)
AXILLARY; RIGHT; MASS; DORSAL		1 (2.3%) [1]	
SKIN, ABDOMINAL	(40)	(44)	(40)
LEFT; MASS; FIRM	1 (2.5%) [1]		
LYMPHOID SYSTEM			
None			
MUSCULOSKELETAL SYSTEM			
DIAPHRAGM	(40)	(44)	(40)
MEDIAN LOBE; HERNIA; MILD	2 (5.0%) [2]		3 (7.5%) [3]
MEDIAN LOBE; HERNIA; MODERATE	1 (2.5%) [1]		2 (5.0%) [2]
LIMB	(40)	(44)	(40)
RIGHT; ALOPECIA; MILD			1 (2.5%) [1]
HINDLIMB; RIGHT; DEFORMITY; MILD	1 (2.5%) [1]		

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F1 Male: F1 Parental Males

Treatment Groups (ppm)

0

750

2500

NERVOUS SYSTEM

BRAIN

(40)

(44)

(40)

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

KIDNEYS

(40)

(44)

(40)

PELVIS; RIGHT; DILATION; MILD

2 (5.0%) [2]

3 (6.8%) [2]

PELVIS; RIGHT; DILATION; MINIMAL

2 (5.0%) [2]

1 (2.3%) [1]

BILATERAL; IRREGULAR; MILD, ROUGHENED

1 (2.3%) [1]

RIGHT; IRREGULAR; MILD, ROUGHENED

1 (2.3%) [1]

RIGHT; MASS; PALE

1 (2.5%) [1]

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
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
Scheduled Deaths			
Scheduled sacrifice, terminal (LD 26 - 28, PND 246 - 251)	37	39	32
Number of Animals Examined	40	44	40
Total number litters	19	22	15
ALIMENTARY SYSTEM			
LIVER	(40)	(44)	(40)
DISCOLORATION; MINIMAL, PALE			1 (2.5%) [1]
DISCOLORATION; MODERATE, PALE		1 (2.3%) [1]	
ENLARGED; MODERATE		1 (2.3%) [1]	
MEDIAL LOBE; RIGHT; MASS; PALE		1 (2.3%) [1]	
ACCESSORY LOBE; TORSION; DARK, MODERATE			1 (2.5%) [1]
CARDIOVASCULAR SYSTEM			
None			

Study Number: R92025B

Test Type: RACB

Route: Dosing in Feed

Species/Strain: Rat/Sprague-Dawley

PA46R: Summary of Gross Pathology with Litter Incidence

Test Compound: 4-Methylimidazole

CAS Number: 822-36-6

Date Report Requested: 10/16/2018

Time Report Requested: 08:36:55

Lab: RTI

F1 Female: F1 Parental Females

	Treatment Groups (ppm)		
	0	750	2500
ENDOCRINE SYSTEM			
ADRENAL GLANDS	(40)	(44)	(40)
BILATERAL; DISCOLORATION; MODERATE, PALE		1 (2.3%) [1]	
BILATERAL; ENLARGED; MODERATE		1 (2.3%) [1]	
LEFT; MISSING	1 (2.5%) [1]		
PITUITARY GLAND	(40)	(44)	(40)
THYROID GLANDS	(40)	(44)	(40)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
CERVIX	(40)	(44)	(40)
CLITORAL GLANDS	(40)	(44)	(40)
LEFT; DISCOLORATION; GREEN, MILD	1 (2.5%) [1]		
OVARIES	(40)	(44)	(40)
LEFT; CYST; CLEAR, MILD			1 (2.5%) [1]
LEFT; CYST; CLEAR, MINIMAL		1 (2.3%) [1]	
LEFT; CYST; CLEAR, MODERATE	1 (2.5%) [1]		
LEFT; CYST; MODERATE		1 (2.3%) [1]	
OVIDUCTS	(40)	(44)	(40)
RIGHT; CYST			1 (2.5%) [1]
UTERUS	(40)	(44)	(40)
LEFT; CYST; MILD			1 (2.5%) [1]
RIGHT; CYST; MILD		1 (2.3%) [1]	
RIGHT; CYST; MINIMAL	1 (2.5%) [1]		
RIGHT; CYST; RED		1 (2.3%) [1]	
VAGINA	(40)	(44)	(40)

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F1 Female: F1 Parental Females

Treatment Groups (ppm)

	0	750	2500
HEMATOPOIETIC SYSTEM			
LYMPH NODE, BRONCHIAL	(40)	(44)	(40)
DISCOLORATION; MODERATE, RED	1 (2.5%) [1]		
ENLARGED; MODERATE	1 (2.5%) [1]		
LYMPH NODE, MESENTERIC	(40)	(44)	(40)
DISCOLORATION; MODERATE, MOTTLED		1 (2.3%) [1]	
MASS		1 (2.3%) [1]	
SPLEEN	(40)	(44)	(40)
ENLARGED; MARKED		1 (2.3%) [1]	
MASS		1 (2.3%) [1]	
THYMUS	(40)	(44)	(40)
DISCOLORATION; DARK, MODERATE		1 (2.3%) [1]	
DISCOLORATION; MODERATE, MOTTLED		1 (2.3%) [1]	

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F1 Female: F1 Parental Females

	Treatment Groups (ppm)		
	0	750	2500
INTEGUMENTARY SYSTEM			
MAMMARY GLANDS	(40)	(44)	(40)
DISCOLORATION; MILD, WHITE		1 (2.3%) [1]	
BILATERAL; INGUINAL; ENLARGED; MILD			1 (2.5%) [1]
ABDOMINAL; RIGHT; MASS; BROWN		1 (2.3%) [1]	
AXILLARY; LEFT; MASS; SOFT	1 (2.5%) [1]		
AXILLARY; RIGHT; MASS; FIRM			1 (2.5%) [1]
AXILLARY; RIGHT; MASS; SOFT	1 (2.5%) [1]		
INGUINAL; LEFT; MASS; SOFT		1 (2.3%) [1]	
INGUINAL; RIGHT; MASS; TAN	1 (2.5%) [1]		
RIGHT; INGUINAL; MASS; SOFT			1 (2.5%) [1]
LEFT; INGUINAL; ULCERATED; TAN			1 (2.5%) [1]
SKIN	(40)	(44)	(40)
FOREFOOT; BILATERAL; ALOPECIA; MODERATE		1 (2.3%) [1]	1 (2.5%) [1]
FORELIMB; BILATERAL; ALOPECIA; MODERATE		1 (2.3%) [1]	1 (2.5%) [1]
HINDFOOT; RIGHT; DEFORMITY; MILD			1 (2.5%) [1]
TAIL; MISSING		1 (2.3%) [1]	
LYMPHOID SYSTEM			
None			

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F1 Female: F1 Parental Females

	Treatment Groups (ppm)		
	0	750	2500
MUSCULOSKELETAL SYSTEM			
DIAPHRAGM	(40)	(44)	(40)
MEDIAN LOBE; HERNIA; MILD		1 (2.3%) [1]	2 (5.0%) [2]
MEDIAN LOBE; HERNIA; MINIMAL	1 (2.5%) [1]		
LIMB	(40)	(44)	(40)
BILATERAL; ALOPECIA; MILD		1 (2.3%) [1]	
HINDLIMB; LEFT; DEFORMITY; MILD	2 (5.0%) [2]		
HINDLIMB; RIGHT; DEFORMITY; MILD	4 (10.0%) [4]		
RIGHT; HINDLIMB; DEFORMITY; MILD	2 (5.0%) [2]	1 (2.3%) [1]	
PAW	(40)	(44)	(40)
HINDFOOT; RIGHT; DEFORMITY; MILD	1 (2.5%) [1]		
HINDFOOT; RIGHT; DEFORMITY; MODERATE	1 (2.5%) [1]		
RIGHT; HINDFOOT; DEFORMITY; MILD	1 (2.5%) [1]		
NERVOUS SYSTEM			
BRAIN	(40)	(44)	(40)
RESPIRATORY SYSTEM			
None			
SPECIAL SENSES SYSTEM			
None			

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F1 Female: F1 Parental Females

Treatment Groups (ppm)

0

750

2500

URINARY SYSTEM

KIDNEYS	(40)	(44)	(40)
LEFT; ENLARGED; MARKED	1 (2.5%) [1]		
LEFT; MASS; SOFT	1 (2.5%) [1]		
LEFT; PELVIS; SUBSTANCE; MARKED, RED	1 (2.5%) [1]		
URINARY BLADDER	(40)	(44)	(40)
DISCOLORATION; BLACK, MARKED	1 (2.5%) [1]		
SUBSTANCE; MODERATE, RED	1 (2.5%) [1]		

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
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Lab: RTI

F2 Male

Treatment Groups (ppm)

0

750

2500

Disposition Summary

	0	750	2500
Animals Initially In Study	107	132	69
Early Deaths			
Scheduled Deaths			
Scheduled sacrifice, terminal (PND 28)	107	132	69
Number of Animals Examined	107	132	69
Total number litters	25	32	20

ALIMENTARY SYSTEM

None

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

COMPLETE GROSS EXAM	(107)	(132)	(69)
EXAM COMPLETE, FINDINGS LISTED	7 (6.5%) [7]	7 (5.3%) [6]	

GENITAL SYSTEM

TESTES	(107)	(132)	(69)
RIGHT; DISCOLORATION; MILD, PALE	2 (1.9%) [2]		
LEFT; REDUCED IN SIZE; MODERATE		1 (0.8%) [1]	

HEMATOPOIETIC SYSTEM

None

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F2 Male

Treatment Groups (ppm)

0

750

2500

INTEGUMENTARY SYSTEM

None

LYMPHOID SYSTEM

None

MUSCULOSKELETAL SYSTEM

DIAPHRAGM

(107)

(132)

(69)

MEDIAN LOBE; HERNIA; MILD

1 (0.8%) [1]

MEDIAN LOBE; HERNIA; MINIMAL

1 (0.9%) [1]

MEDIAN LOBE; HERNIA; MODERATE

1 (0.8%) [1]

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F2 Male

Treatment Groups (ppm)

0

750

2500

URINARY SYSTEM

	0	750	2500
KIDNEYS	(107)	(132)	(69)
PELVIS; RIGHT; DILATION; MARKED	1 (0.9%) [1]		
PELVIS; RIGHT; DILATION; MINIMAL	1 (0.9%) [1]		
PELVIS; RIGHT; DILATION; MODERATE	1 (0.9%) [1]	3 (2.3%) [2]	
RIGHT; ENLARGED; MARKED	1 (0.9%) [1]		
LEFT; MALPOSITIONED; MILD		1 (0.8%) [1]	
LEFT; MISSHAPEN; MILD		1 (0.8%) [1]	
RIGHT; MISSHAPEN; MILD	1 (0.9%) [1]		
LEFT; REDUCED IN SIZE; MILD	1 (0.9%) [1]		

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F2 Female

Treatment Groups (ppm)

0

750

2500

Disposition Summary

Animals Initially In Study

98

132

76

Early Deaths

Scheduled Deaths

Scheduled sacrifice, terminal (PND 28)

98

132

76

Number of Animals Examined

98

132

76

Total number litters

27

32

22

ALIMENTARY SYSTEM

LIVER

(98)

(132)

(76)

CARDIOVASCULAR SYSTEM

None

ENDOCRINE SYSTEM

None

GENERAL BODY SYSTEM

COMPLETE GROSS EXAM

(98)

(132)

(76)

EXAM COMPLETE, FINDINGS LISTED

1 (1.0%) [1]

1 (0.8%) [1]

1 (1.3%) [1]

GENITAL SYSTEM

None

HEMATOPOIETIC SYSTEM

None

INTEGUMENTARY SYSTEM

None

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

PA46R: Summary of Gross Pathology with Litter Incidence
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 08:36:55
Lab: RTI

F2 Female

Treatment Groups (ppm)

0

750

2500

LYMPHOID SYSTEM

None

MUSCULOSKELETAL SYSTEM

DIAPHRAGM

(98)

(132)

(76)

MEDIAN LOBE; HERNIA; MILD

1 (1.0%) [1]

1 (1.3%) [1]

LIMB

(98)

(132)

(76)

FORELIMB; LEFT; ENLARGED; MILD

1 (0.8%) [1]

PAW

(98)

(132)

(76)

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

None

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

None

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

PA46R: Summary of Gross Pathology with Litter Incidence
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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. The exception to this is if statistical analysis is performed for a lesion and the control group has no animals with the lesion then a 0 is included for the control group on the table for that lesion.

Number (percent) of animals affected given for each observation

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

Statistical analysis for the F0 animals was performed by Cochran-Armitage test with poly-3 adjustment for both trend and pairwise tests.

Statistical analysis for the F1 Parental animals was performed by Cochran-Armitage test with a poly-3 adjustment for age and a Rao-Scott modification for the random effect due to litter.

Statistical analysis for the F1 NonParental and F2 animals was performed by Cochran-Armitage test with a Rao-Scott modification for the random effect due to litter.

Statistical significance for the control group indicates a significant trend test

Statistical significance for a treatment group indicates a significant pairwise test compared to the vehicle control group

* Statistically significant at $P \leq 0.05$

** Statistically significant at $P \leq 0.01$

All trend and pairwise p-values are reported as one-sided.

Non-pregnant females from the F0 and F1 generations are included in the analysis.

NM = Naive Males

**** END OF REPORT ****