

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

PA11: Statistical Analysis of Survival Data
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 01/09/2019
Time Report Requested: 08:56:21
Lab: RTI

C Number: R92025B
Study Gender: Both
PWG Approval Date: See web page for date of PWG Approval

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F0 Males
First Terminal Sacrifice at 177 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 23 Uncensored Deaths: 0 Censored Deaths: 0 Terminal: 23

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 23 Uncensored Deaths: 0 Censored Deaths: 0 Terminal: 23

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 23 Uncensored Deaths: 3 Censored Deaths: 0 Terminal: 20

UNCENSORED DEATH DAYS

14 56 56

CENSORED DEATH DAYS

None

Dose = 5000 ppm

Total: 23 Uncensored Deaths: 2 Censored Deaths: 0 Terminal: 21

UNCENSORED DEATH DAYS

56 56

CENSORED DEATH DAYS

None

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F0 Males
First Terminal Sacrifice at 177 Days

Dose (ppm)	Kaplan-Meier Survival Probability Estimates (%)		
	Time (Days)		
	14	56	177(A)
0	100.0	100.0	100.0
750	100.0	100.0	100.0
2500	95.7	87.0	87.0
5000	100.0	91.3	91.3

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F0 Males
First Terminal Sacrifice at 177 Days

Survival Summary Statistics				
Dose	0 ppm	750 ppm	2500 ppm	5000 ppm
Survival At End Of Study (Kaplan-Meier)	100.0%	100.0%	87.0%	91.3%
Significance (B) (Life Table)	P=0.162	-----	P=0.703	P=0.949
Mean Day Of Natural Deaths (C) (Standard Error)	. (.)	. (.)	42.0 (14.0)	56.0 (.)
Mean Life Span (D) (Standard Error)	177.0 (0.0)	177.0 (0.0)	159.4 (9.8)	166.5 (7.3)

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F0 Females
First Terminal Sacrifice at 219 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 23 Uncensored Deaths: 1 Censored Deaths: 0 Terminal: 22

UNCENSORED DEATH DAYS

87

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 23 Uncensored Deaths: 1 Censored Deaths: 0 Terminal: 22

UNCENSORED DEATH DAYS

192

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 23 Uncensored Deaths: 4 Censored Deaths: 0 Terminal: 19

UNCENSORED DEATH DAYS

10 41 42 120

CENSORED DEATH DAYS

None

Dose = 5000 ppm

Total: 23 Uncensored Deaths: 11 Censored Deaths: 0 Terminal: 12

UNCENSORED DEATH DAYS

41 45 62 69 80 81 82 82 85 126 168

CENSORED DEATH DAYS

None

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F0 Females
First Terminal Sacrifice at 219 Days

Kaplan-Meier Survival Probability Estimates (%)																
Dose (ppm)	Time (Days)															
	10	41	42	45	62	69	80	81	82	85	87	120	126	168	192	219(A)
0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	95.7	95.7	95.7	95.7	95.7	95.7
750	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	95.7	95.7
2500	95.7	91.3	87.0	87.0	87.0	87.0	87.0	87.0	87.0	87.0	87.0	82.6	82.6	82.6	82.6	82.6
5000	100.0	95.7	95.7	91.3	87.0	82.6	78.3	73.9	65.2	60.9	60.9	60.9	56.5	52.2	52.2	52.2

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F0 Females
First Terminal Sacrifice at 219 Days

Survival Summary Statistics

Dose	0 ppm	750 ppm	2500 ppm	5000 ppm
Survival At End Of Study (Kaplan-Meier)	95.7%	95.7%	82.6%	52.2%
Significance (B) (Life Table)	P<0.001	P=1.000N	P=0.656	P=0.006
Mean Day Of Natural Deaths (C) (Standard Error)	87.0 (.)	192.0 (.)	53.3 (23.5)	83.7 (10.8)
Mean Life Span (D) (Standard Error)	213.3 (5.7)	217.8 (1.2)	190.2 (13.9)	154.3 (15.3)

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F1 Males: F1 NonParental Male
First Terminal Sacrifice at 91 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 49

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 49

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 56

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 56

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 20

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 20

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

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F1 Males: F1 NonParental Male
First Terminal Sacrifice at 91 Days

Kaplan-Meier Survival Probability Estimates (%)	
Dose (ppm)	Time (Days)
	91(A)
0	100.0
750	100.0
2500	100.0

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F1 Males: F1 NonParental Male
First Terminal Sacrifice at 91 Days

Survival Summary Statistics			
Dose	0 ppm	750 ppm	2500 ppm
Survival At End Of Study (Kaplan-Meier)	100.0%	100.0%	100.0%
Significance (B) (Life Table)	----	----	----
Mean Day Of Natural Deaths (C) (Standard Error)	. (.)	. (.)	. (.)
Mean Life Span (D) (Standard Error)	91.0 (0.0)	91.0 (0.0)	91.0 (0.0)

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Test Type: RACB
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Species/Strain: Rat/Sprague-Dawley

PA11: Statistical Analysis of Survival Data
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CAS Number: 822-36-6

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F1 Females: F1 NonParent Female
First Terminal Sacrifice at 91 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 47

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 47

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 58

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 58

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 27

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 27

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

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Species/Strain: Rat/Sprague-Dawley

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CAS Number: 822-36-6

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F1 Females: F1 NonParent Female
First Terminal Sacrifice at 91 Days

Kaplan-Meier Survival Probability Estimates (%)	
Dose (ppm)	Time (Days)
	91(A)
0	100.0
750	100.0
2500	100.0

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

PA11: Statistical Analysis of Survival Data
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F1 Females: F1 NonParent Female
First Terminal Sacrifice at 91 Days

Survival Summary Statistics			
Dose	0 ppm	750 ppm	2500 ppm
Survival At End Of Study (Kaplan-Meier)	100.0%	100.0%	100.0%
Significance (B) (Life Table)	----	----	----
Mean Day Of Natural Deaths (C) (Standard Error)	. (.)	. (.)	. (.)
Mean Life Span (D) (Standard Error)	91.0 (0.0)	91.0 (0.0)	91.0 (0.0)

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F1 Males: F1 Parental Males
First Terminal Sacrifice at 218 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 40

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 40

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 44

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 44

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 40

Uncensored Deaths: 1

Censored Deaths: 0

Terminal: 39

UNCENSORED DEATH DAYS

188

CENSORED DEATH DAYS

None

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F1 Males: F1 Parental Males
First Terminal Sacrifice at 218 Days

Dose (ppm)	Kaplan-Meier Survival Probability Estimates (%)	
	Time (Days)	
	188	218(A)
0	100.0	100.0
750	100.0	100.0
2500	97.5	97.5

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

PA11: Statistical Analysis of Survival Data
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F1 Males: F1 Parental Males
First Terminal Sacrifice at 218 Days

Survival Summary Statistics			
Dose	0 ppm	750 ppm	2500 ppm
Survival At End Of Study (Kaplan-Meier)	100.0%	100.0%	97.5%
Significance (B) (Life Table)	P=0.864	-----	P=1.000
Mean Day Of Natural Deaths (C) (Standard Error)	. (.)	. (.)	188.0 (.)
Mean Life Span (D) (Standard Error)	218.0 (0.0)	218.0 (0.0)	217.6 (0.4)

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F1 Females: F1 Parental Females
First Terminal Sacrifice at 241 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 40

Uncensored Deaths: 3

Censored Deaths: 0

Terminal: 37

UNCENSORED DEATH DAYS

142 223 224

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 44

Uncensored Deaths: 3

Censored Deaths: 0

Terminal: 41

UNCENSORED DEATH DAYS

132 138 144

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 40

Uncensored Deaths: 8

Censored Deaths: 0

Terminal: 32

UNCENSORED DEATH DAYS

132 134 139 153 170 208 224 225

CENSORED DEATH DAYS

None

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

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F1 Females: F1 Parental Females
First Terminal Sacrifice at 241 Days

Dose (ppm)	Kaplan-Meier Survival Probability Estimates (%)												
	Time (Days)												
	132	134	138	139	142	144	153	170	208	223	224	225	241(A)
0	100.0	100.0	100.0	100.0	97.5	97.5	97.5	97.5	97.5	95.0	92.5	92.5	92.5
750	97.7	97.7	95.5	95.5	95.5	93.2	93.2	93.2	93.2	93.2	93.2	93.2	93.2
2500	97.5	95.0	95.0	92.5	92.5	92.5	90.0	87.5	85.0	85.0	82.5	80.0	80.0

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F1 Females: F1 Parental Females
First Terminal Sacrifice at 241 Days

Survival Summary Statistics			
Dose	0 ppm	750 ppm	2500 ppm
Survival At End Of Study (Kaplan-Meier)	92.5%	93.2%	80.0%
Significance (B) (Life Table)	P=0.056	P=0.933N	P=0.242
Mean Day Of Natural Deaths (C) (Standard Error)	196.3 (27.2)	138.0 (3.5)	178.4 (15.2)
Mean Life Span (D) (Standard Error)	237.5 (2.6)	234.0 (3.9)	227.7 (7.0)

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F2 Males
First Terminal Sacrifice at 28 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 107

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 107

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 132

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 132

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 69

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 69

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

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Species/Strain: Rat/Sprague-Dawley

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F2 Males
First Terminal Sacrifice at 28 Days

Kaplan-Meier Survival Probability Estimates (%)	
Dose (ppm)	Time (Days)
	28(A)
0	100.0
750	100.0
2500	100.0

Study Number: R92025B
Test Type: RACB
Route: Dosing in Feed
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F2 Males
First Terminal Sacrifice at 28 Days

Survival Summary Statistics			
Dose	0 ppm	750 ppm	2500 ppm
Survival At End Of Study (Kaplan-Meier)	100.0%	100.0%	100.0%
Significance (B) (Life Table)	----	----	----
Mean Day Of Natural Deaths (C) (Standard Error)	. (.)	. (.)	. (.)
Mean Life Span (D) (Standard Error)	28.0 (0.0)	28.0 (0.0)	28.0 (0.0)

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F2 Females
First Terminal Sacrifice at 28 Days
Individual Survival Times (Days)

Dose = 0 ppm

Total: 98

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 98

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 750 ppm

Total: 132

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 132

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

Dose = 2500 ppm

Total: 76

Uncensored Deaths: 0

Censored Deaths: 0

Terminal: 76

UNCENSORED DEATH DAYS

None

CENSORED DEATH DAYS

None

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F2 Females
First Terminal Sacrifice at 28 Days

Kaplan-Meier Survival Probability Estimates (%)	
Dose (ppm)	Time (Days)
	28(A)
0	100.0
750	100.0
2500	100.0

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F2 Females
First Terminal Sacrifice at 28 Days

Survival Summary Statistics			
Dose	0 ppm	750 ppm	2500 ppm
Survival At End Of Study (Kaplan-Meier)	100.0%	100.0%	100.0%
Significance (B) (Life Table)	----	----	----
Mean Day Of Natural Deaths (C) (Standard Error)	. (.)	. (.)	. (.)
Mean Life Span (D) (Standard Error)	28.0 (0.0)	28.0 (0.0)	28.0 (0.0)

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LEGEND

(A) First Terminal Sacrifice

(B) Trend and pairwise analysis was done using Tarone, 1975 for all F0 animals and means and standard errors are calculated from the individual animal values. The F1 and F2 animals trend and pairwise analysis was done using a proportional hazards model with Dam ID as a random effect and the means and standard errors are calculated from the litter means. Pairwise tests included a Hommel adjustment for multiple comparisons. In cases where the model did not converge, Tarone's test was used. The first entry is the trend test result and subsequent entries are the results of the pairwise tests. Negative trends are indicated by "N".

(C) Mean of all uncensored deaths prior to terminal sacrifice.

(D) Mean of all deaths (uncensored, censored, terminal sacrifice).

Survival at end of study is calculated as the number of animals alive at the first terminal sacrifice day / number of animals in the dose group.

Pairwise p-values do not include corrections for multiple comparisons.

**** END OF REPORT ****