

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

R03: Summary of Litter Data
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 05/16/2018
Time Report Requested: 10:14:13
Lab: RTI

C Number:	R92025B
Cage Range:	All
Date Range:	All
Reasons For Removal:	All
Removal Date Range:	All
Treatment Groups:	All
Study Gender:	Both

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F1 Pups

Treatment Groups (ppm)

Litter ID		0	750	2500	5000
A	Total Litter Size ^a				
	PND 0	14.6 ± 0.4 (22) **	13.3 ± 0.6 (22)	9.9 ± 0.7 (17) **	5.7 ± 1.9 (6) **
	Live Litter Size ^a				
	PND 0	14.0 ± 0.4 (22) **	12.7 ± 0.6 (22)	7.8 ± 1.0 (17) **	1.8 ± 1.6 (6) **
	PND 1	13.5 ± 0.5 (22) **	12.7 ± 0.6 (22)	7.1 ± 1.0 (17) **	0.7 ± 0.7 (6) **
	PND 4	13.5 ± 0.5 (22) **	12.5 ± 0.6 (22)	7.0 ± 0.9 (17) **	0.3 ± 0.3 (6) **
	Total Dead ^a				
	PND 0	0.68 ± 0.17 (22) *	0.55 ± 0.28 (22)	2.06 ± 0.76 (17)	3.83 ± 1.22 (6) *
	PND 1 - 4	0.50 ± 0.22 (22)	0.23 ± 0.09 (22)	0.93 ± 0.38 (15)	4.50 ± 3.50 (2)
	Survival Ratio ^a				
	PND 0	0.95 ± 0.01 (22) **	0.96 ± 0.02 (22)	0.77 ± 0.08 (17)	0.17 ± 0.13 (6) **
	PND 1 - 4	0.96 ± 0.02 (22)	0.98 ± 0.01 (22)	0.91 ± 0.04 (15)	0.10 ± 0.10 (2)

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F1 Pups

Treatment Groups (ppm)

Litter ID		0	750	2500	5000
B	Total Litter Size ^a				
	PND 0	14.2 ± 0.5 (19) **	13.5 ± 0.6 (23)	9.2 ± 0.7 (17) **	4.7 ± 0.9 (6) **
	Live Litter Size ^a				
	PND 0	13.7 ± 0.5 (19) **	12.7 ± 0.5 (23)	8.5 ± 0.6 (17) **	0.5 ± 0.5 (6) **
	PND 1	13.4 ± 0.6 (19) **	12.6 ± 0.5 (23)	7.9 ± 0.7 (17) **	0.3 ± 0.3 (6) **
	PND 4	13.3 ± 0.6 (19) **	12.5 ± 0.5 (23)	7.8 ± 0.7 (17) **	0.3 ± 0.3 (6) **
	Total Dead ^a				
	PND 0	0.47 ± 0.19 (19) **	0.78 ± 0.23 (23)	0.76 ± 0.25 (17)	4.17 ± 0.87 (6) **
	PND 1 - 4	0.42 ± 0.32 (19)	0.22 ± 0.09 (23)	0.65 ± 0.32 (17)	1.00 (1)
	Survival Ratio ^a				
	PND 0	0.97 ± 0.01 (19) **	0.95 ± 0.01 (23)	0.92 ± 0.02 (17)	0.08 ± 0.08 (6) **
	PND 1 - 4	0.97 ± 0.02 (19)	0.98 ± 0.01 (23)	0.93 ± 0.03 (17)	0.67 (1)

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F1 Pups

Litter ID		Treatment Groups (ppm)		
		0	750	2500
C	Total Litter Size ^a			
	PND 0	13.6 ± 0.6 (19) *	12.8 ± 0.6 (22)	10.6 ± 1.2 (16) *
	Live Litter Size ^a			
	PND 0	12.2 ± 0.8 (19)	12.4 ± 0.5 (22)	9.8 ± 1.2 (16)
	PND 1	11.9 ± 0.8 (19) *	12.4 ± 0.5 (22)	9.0 ± 1.0 (16) *
	PND 4 pre-cull	11.8 ± 0.8 (19) *	12.3 ± 0.6 (22)	8.8 ± 1.0 (16) *
	PND 4 post-cull	10.6 ± 0.6 (19) *	11.0 ± 0.4 (22)	8.4 ± 0.9 (16) *
	PND 7	10.5 ± 0.6 (19) *	10.7 ± 0.4 (22)	8.3 ± 0.9 (16) *
	PND 10	10.5 ± 0.6 (19) *	10.6 ± 0.4 (22)	8.1 ± 0.9 (16) *
	PND 13	10.4 ± 0.6 (19) *	10.5 ± 0.4 (22)	7.9 ± 0.9 (16) *
	PND 16	10.4 ± 0.6 (19) *	10.5 ± 0.4 (22)	7.9 ± 0.9 (16) *
	PND 19	10.4 ± 0.6 (19) *	10.5 ± 0.4 (22)	7.9 ± 0.9 (16) *
	PND 21	10.4 ± 0.6 (19) *	10.5 ± 0.4 (22)	7.9 ± 0.9 (16) *
	PND 25	10.4 ± 0.6 (19) *	10.5 ± 0.4 (22)	7.9 ± 0.9 (16) *
	PND 28	10.4 ± 0.6 (19) *	10.5 ± 0.4 (22)	7.9 ± 0.9 (16) *
	Total Dead ^a			
	PND 0	1.42 ± 0.54 (19)	0.41 ± 0.18 (22)	0.81 ± 0.40 (16)
	PND 1 - 4	0.42 ± 0.18 (19)	0.14 ± 0.07 (22)	1.00 ± 0.56 (15)
	PND 5 - 28	0.21 ± 0.10 (19)	0.50 ± 0.22 (22)	0.47 ± 0.19 (15)
	Survival Ratio ^a			
PND 0	0.90 ± 0.04 (19)	0.97 ± 0.01 (22)	0.91 ± 0.06 (16)	
PND 1 - 4	0.95 ± 0.03 (19)	0.98 ± 0.01 (22)	0.93 ± 0.04 (15)	
PND 5 - 28	0.98 ± 0.01 (19)	0.96 ± 0.02 (22)	0.95 ± 0.02 (15)	

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F1 Pups

Treatment Groups (ppm)

Litter ID		0	2500
D	Total Litter Size ^a		
	PND 0	11.4 ± 1.5 (12)	11.3 ± 1.7 (10)
	Live Litter Size ^a		
	PND 0	10.7 ± 1.4 (12)	11.0 ± 1.7 (10)
	PND 1	10.6 ± 1.4 (12)	9.7 ± 1.7 (10)
	PND 4	10.5 ± 1.4 (12)	9.7 ± 1.7 (10)
	Total Dead ^a		
	PND 0	0.75 ± 0.37 (12)	0.30 ± 0.21 (10)
	PND 1 - 4	0.17 ± 0.17 (12) *	1.30 ± 0.42 (10) *
	Survival Ratio ^a		
	PND 0	0.95 ± 0.02 (12)	0.97 ± 0.02 (10)
	PND 1 - 4	0.99 ± 0.01 (12) *	0.82 ± 0.10 (10) *

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F1 Pups

Litter ID		Treatment Groups (ppm)		
		0 NF	2500 NF	5000 NF
E	Total Litter Size ^a			
	PND 0	13.8 ± 0.5 (16)	11.6 ± 1.1 (15)	11.7 ± 1.8 (6)
	Live Litter Size ^a			
	PND 0	13.4 ± 0.4 (16)	10.6 ± 1.1 (15)	11.5 ± 1.9 (6)
	PND 1	13.2 ± 0.5 (16)	10.3 ± 1.1 (15)	11.3 ± 1.8 (6)
	PND 4	13.1 ± 0.5 (16)	10.1 ± 1.1 (15)	11.3 ± 1.8 (6)
	Total Dead ^a			
	PND 0	0.38 ± 0.13 (16)	1.00 ± 0.37 (15)	0.17 ± 0.17 (6)
	PND 1 - 4	0.31 ± 0.15 (16)	0.47 ± 0.24 (15)	0.17 ± 0.17 (6)
	Survival Ratio ^a			
	PND 0	0.97 ± 0.01 (16)	0.91 ± 0.04 (15)	0.98 ± 0.02 (6)
	PND 1 - 4	0.97 ± 0.01 (16)	0.96 ± 0.02 (15)	0.99 ± 0.01 (6)

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F2 Pups: F1 Parental Females

Litter ID		Treatment Groups (ppm)		
		0	750	2500
A	Total Litter Size ^a			
	PND 0	13.2 ± 0.5 (33) **	11.0 ± 0.6 (34) *	8.9 ± 0.8 (31) **
	Live Litter Size ^a			
	PND 0	11.1 ± 0.7 (33) **	9.3 ± 0.7 (34)	7.2 ± 0.8 (31) **
	PND 1	10.6 ± 0.8 (33) **	9.1 ± 0.7 (34)	6.0 ± 0.9 (31) **
	PND 4	10.2 ± 0.9 (33) **	9.0 ± 0.7 (34)	5.9 ± 0.9 (31) **
	Total Dead ^a			
	PND 0	2.11 ± 0.41 (33)	1.70 ± 0.29 (34)	1.68 ± 0.30 (31)
	PND 1 - 4	0.84 ± 0.48 (33) **	0.48 ± 0.20 (32)	1.56 ± 0.34 (29) *
	Survival Ratio ^a			
	PND 0	0.83 ± 0.04 (33)	0.83 ± 0.03 (34)	0.74 ± 0.07 (31)
	PND 1 - 4	0.92 ± 0.05 (33) **	0.93 ± 0.04 (32)	0.72 ± 0.08 (29) **

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F2 Pups: F1 Parental Females

Litter ID		Treatment Groups (ppm)		
		0	750	2500
B	Total Litter Size ^a			
	PND 0	15.3 ± 0.5 (34) **	12.3 ± 0.5 (37) **	10.6 ± 0.9 (29) **
	Live Litter Size ^a			
	PND 0	13.6 ± 0.6 (34) **	11.9 ± 0.6 (37)	9.8 ± 0.8 (29) **
	PND 1	13.3 ± 0.6 (34) **	11.6 ± 0.6 (37)	9.0 ± 0.7 (29) **
	PND 4	13.2 ± 0.6 (34) **	11.4 ± 0.6 (37) *	8.8 ± 0.7 (29) **
	Total Dead ^a			
	PND 0	1.67 ± 0.32 (34)	0.45 ± 0.12 (37) **	0.89 ± 0.20 (29)
	PND 1 - 4	0.41 ± 0.13 (34)	0.45 ± 0.12 (36)	0.94 ± 0.34 (29)
	Survival Ratio ^a			
	PND 0	0.89 ± 0.02 (34)	0.94 ± 0.02 (37) *	0.92 ± 0.02 (29)
	PND 1 - 4	0.97 ± 0.01 (34) *	0.97 ± 0.01 (36)	0.91 ± 0.03 (29) *

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F2 Pups: F1 Parental Females

Litter ID		Treatment Groups (ppm)		
		0	750	2500
C	Total Litter Size ^a			
	PND 0	10.7 ± 0.8 (28)	9.8 ± 0.7 (35)	9.4 ± 0.9 (23)
	Live Litter Size ^a			
	PND 0	9.2 ± 0.7 (28)	8.8 ± 0.6 (35)	8.5 ± 0.9 (23)
	PND 1	8.7 ± 0.8 (28)	8.6 ± 0.7 (35)	7.9 ± 0.9 (23)
	PND 4 pre-cull	8.4 ± 0.9 (28)	8.5 ± 0.7 (35)	7.7 ± 0.9 (23)
	PND 4 post-cull	8.0 ± 0.8 (28)	8.2 ± 0.6 (35)	7.6 ± 0.8 (23)
	PND 7	7.2 ± 0.7 (28)	8.1 ± 0.6 (35)	7.1 ± 0.8 (23)
	PND 10	6.8 ± 0.8 (28)	7.8 ± 0.6 (35)	7.0 ± 0.8 (23)
	PND 13	6.7 ± 0.7 (28)	7.5 ± 0.6 (35)	6.8 ± 0.8 (23)
	PND 16	6.6 ± 0.7 (28)	7.5 ± 0.6 (35)	6.8 ± 0.8 (23)
	PND 19	6.6 ± 0.7 (28)	7.5 ± 0.6 (35)	6.8 ± 0.8 (23)
	PND 21	6.6 ± 0.7 (28)	7.5 ± 0.6 (35)	6.8 ± 0.8 (23)
	PND 25	6.6 ± 0.7 (28)	7.5 ± 0.6 (35)	6.8 ± 0.8 (23)
	PND 28	6.6 ± 0.7 (28)	7.5 ± 0.6 (35)	6.8 ± 0.8 (23)
	Total Dead ^a			
	PND 0	1.45 ± 0.38 (28)	1.00 ± 0.26 (35)	0.90 ± 0.35 (23)
	PND 1 - 4	0.82 ± 0.31 (28)	0.36 ± 0.11 (34)	0.85 ± 0.22 (23)
	PND 5 - 28	1.34 ± 0.58 (28)	0.76 ± 0.26 (33)	0.85 ± 0.26 (22)
	Survival Ratio ^a			
PND 0	0.87 ± 0.04 (28)	0.89 ± 0.03 (35)	0.90 ± 0.03 (23)	
PND 1 - 4	0.89 ± 0.05 (28)	0.92 ± 0.05 (34)	0.88 ± 0.04 (23)	
PND 5 - 28	0.83 ± 0.07 (28)	0.93 ± 0.02 (33)	0.89 ± 0.03 (22)	

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LEGEND

Data are displayed as the means and standard errors of the litter means, N is number of litters

All calculations are based on the last litter observation of the day

^aF1 litter size and survival endpoints were analyzed using Jonckheere's test for trend and Shirley's or Dunn's methods for pairwise comparison of controls to dose groups. F2 litters from the F1 Fertility females were analyzed using the bootstrapped Jonckheere for trend; pairwise comparisons were done using the Datta-Satten modified Wilcoxon test with the Hommel adjustment for multiple comparisons.

Data with sample sizes of 1 or 2 were excluded from the trend and multiple comparisons tests.

* Statistically significant at $P \leq 0.05$

** Statistically significant at $P \leq 0.01$

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

D Litter is crossover mating of dosed F0 Females with naive F0 Males

E Litter is crossover mating of F0 naive Females with dosed F0 Males (doses listed are for the doses of the F0 Males)

NF = Naive Females

**** END OF REPORT ****