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

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

R02: Reproductive Performance Summary
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 07/25/2018
Time Report Requested: 14:20:20
Lab: RTI

F0 Female

		Treatment Groups (ppm)			
Litter ID		**0**	**750**	**2500**	**5000**
A	No. Females Paired	23	23	22	23
	No. Females Mated	23	22	21	9
	No. Females Littering	22	22	17	6
	Percent of Mated Females/Paired[a]	100.0 **	95.7	95.5	39.1 **
	Percent of Littered Females/Paired[a]	95.7 **	95.7	81.0	27.3 **
	Percent of Littered Females/Mated[a]	95.7 *	100.0	85.0	75.0
	Pre-coital Interval[b]	5.9 ± 0.9 (22)	5.1 ± 0.8 (21)	4.9 ± 0.5 (20)	4.7 ± 1.2 (9)
	Gestational Length[b]	22.4 ± 0.1 (21)	22.1 ± 0.1 (21)	22.3 ± 0.1 (16)	23.0 ± 0.4 (6)

Experiment Number: R92025B
Test Type: RACB
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Date Report Requested: 07/25/2018
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F0 Female

		Treatment Groups (ppm)			
Litter ID		**0**	**750**	**2500**	**5000**
B	No. Females Paired	23	23	20	21
	No. Females Mated	22	23	19	12
	No. Females Littering	19	23	17	6
	Percent of Mated Females/Paired[a]	95.7 **	100.0	95.0	57.1 **
	Percent of Littered Females/Paired[a]	82.6 **	100.0	85.0	37.5 **
	Percent of Littered Females/Mated[a]	86.4	100.0	89.5	75.0
	Pre-coital Interval[b]	3.7 ± 0.8 (21)	4.0 ± 0.5 (20)	3.9 ± 0.3 (18)	2.6 ± 0.4 (12)
	Gestational Length[b]	22.3 ± 0.1 (18) **	22.2 ± 0.1 (20)	22.6 ± 0.1 (16)	23.5 ± 0.2 (6) **

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

R02: Reproductive Performance Summary
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Date Report Requested: 07/25/2018
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F0 Female

		Treatment Groups (ppm)		
Litter ID		**0**	**750**	**2500**
C	No. Females Paired	22	23	20
	No. Females Mated	21	23	20
	No. Females Littering	19	22	16
	Percent of Mated Females/Paired[a]	95.5	100.0	100.0
	Percent of Littered Females/Paired[a]	86.4	95.7	84.2
	Percent of Littered Females/Mated[a]	90.5	95.7	84.2
	Pre-coital Interval[b]	3.9 ± 0.9 (19)	2.8 ± 0.3 (21)	3.2 ± 0.6 (19)
	Gestational Length[b]	22.5 ± 0.2 (17)	22.1 ± 0.1 (20)	22.6 ± 0.1 (15)

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

R02: Reproductive Performance Summary
Test Compound: 4-Methylimidazole
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Date Report Requested: 07/25/2018
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F0 Female

		Treatment Groups (ppm)	
Litter ID		**0**	**2500**
D	No. Females Paired	22	19
	No. Females Mated	15	14
	No. Females Littering	12	10
	Percent of Mated Females/Paired[a]	68.2	73.7
	Percent of Littered Females/Paired[a]	54.5	52.6
	Percent of Littered Females/Mated[a]	80.0	71.4
	Pre-coital Interval[b]	2.3 ± 0.5 (14)	2.6 ± 0.4 (13)
	Gestational Length[b]	22.4 ± 0.2 (11)	22.4 ± 0.2 (9)

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

R02: Reproductive Performance Summary
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 07/25/2018
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Lab: RTI

F0 Female

		Treatment Groups (ppm)		
Litter ID		**0 NF**	**2500 NF**	**5000 NF**
E	No. Females Paired	23	20	21
	No. Females Mated	20	16	7
	No. Females Littering	16	15	6
	Percent of Mated Females/Paired[a]	87.0 **	80.0	33.3 **
	Percent of Littered Females/Paired[a]	69.6 **	75.0	28.6 *
	Percent of Littered Females/Mated[a]	80.0	93.8	85.7
	Pre-coital Interval[b]	3.6 ± 0.5 (20)	3.5 ± 0.5 (16)	5.4 ± 0.6 (7)
	Gestational Length[b]	21.9 ± 0.1 (16)	22.1 ± 0.1 (15)	22.0 ± 0.0 (6)

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

R02: Reproductive Performance Summary
Test Compound: 4-Methylimidazole
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Date Report Requested: 07/25/2018
Time Report Requested: 14:20:20
Lab: RTI

F1 Female: F1 Parental Females

		Treatment Groups (ppm)		
Litter ID		**0**	**750**	**2500**
A	No. Females Paired	40	44	40
	No. Females Mated	36	40	35
	No. Females Littering	33	34	31
	Percent of Mated Females/Paired[a]	90.0	90.9	87.5
	Percent of Littered Females/Paired[a]	82.5	77.3	81.6
	Percent of Littered Females/Mated[a]	91.7	85.0	93.9
	Pre-coital Interval[b]	4.5 ± 0.7 (19)	4.7 ± 0.7 (22)	3.4 ± 0.3 (14)
	Gestational Length[b]	22.7 ± 0.1 (19)	22.5 ± 0.1 (22)	22.6 ± 0.1 (14)

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

R02: Reproductive Performance Summary
Test Compound: 4-Methylimidazole
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Date Report Requested: 07/25/2018
Time Report Requested: 14:20:20
Lab: RTI

F1 Female: F1 Parental Females

		Treatment Groups (ppm)		
Litter ID		**0**	**750**	**2500**
B	No. Females Paired	39	41	36
	No. Females Mated	37	41	35
	No. Females Littering	34	37	29
	Percent of Mated Females/Paired[a]	94.9	100.0	97.2
	Percent of Littered Females/Paired[a]	87.2	90.2	82.9
	Percent of Littered Females/Mated[a]	91.9	90.2	85.3
	Pre-coital Interval[b]	3.5 ± 0.3 (18)	2.8 ± 0.3 (22)	3.1 ± 0.4 (14)
	Gestational Length[b]	22.5 ± 0.1 (18)	22.2 ± 0.1 (21) *	22.3 ± 0.1 (14)

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

R02: Reproductive Performance Summary
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Date Report Requested: 07/25/2018
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Lab: RTI

F1 Female: F1 Parental Females

		Treatment Groups (ppm)		
Litter ID		**0**	**750**	**2500**
C	No. Females Paired	39	41	35
	No. Females Mated	36	41	34
	No. Females Littering	28	35	23
	Percent of Mated Females/Paired[a]	92.3	100.0	97.1
	Percent of Littered Females/Paired[a]	75.7	85.4	71.9
	Percent of Littered Females/Mated[a]	80.0	85.4	71.9
	Pre-coital Interval[b]	3.8 ± 0.4 (19)	3.3 ± 0.5 (22)	3.2 ± 0.3 (14)
	Gestational Length[b]	22.4 ± 0.1 (19)	22.3 ± 0.1 (22)	22.3 ± 0.1 (14)

LEGEND

When reported, pre-coital interval in days is calculated for sperm positive females; results shown as mean ± SEM (N)

Gestation length in days calculated for sperm positive females that delivered a litter; results shown as mean ± SEM (N)

Animals removed from study between mating and littering excluded from calculations of percent littered females

[a]For binary endpoints for the F0 animals, statistical analysis was performed by Cochran-Armitage (trend) and Fisher Exact (pairwise) 2-sided test. For F1 animals, binary endpoints with litter-mates were analyzed using the Rao-Scott Cochran-Armitage test for both trend and pairwise tests.

[b]Statistical analysis for F0 animals performed by Jonckheere (trend) and Shirley or Dunn (pairwise) tests. For F1 animal non-normally distributed continuous endpoints with litter-mates, a bootstrapped Jonckheere trend test was used. Pairwise comparisons were done using the Datta-Satten modified Wilcoxon test with Hommel adjustment for multiple comparisons. To obtain the bootstrap distribution, the litters were permuted across the dose groups, and animals having the same maternal dam were sampled with replacement.

* Statistically significant at P <= 0.05

** Statistically significant at P <= 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

No p-values are reported unless there are at least two observations in one or more of the dose groups.

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 **