

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

R06: Andrology Summary
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 09:35:29
Lab: RTI

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

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

R06: Andrology Summary
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 09:35:29
Lab: RTI

Male

Generation	Litter ID	Terminal Sac	Cohort	Treatment Groups (ppm)				
				0	750	2500	5000	
F0	SD 177 - 178			No. Examined	23	23	20	21
				Testis Weight (g)	2.075 ± 0.026	2.074 ± 0.026	2.096 ± 0.026	2.062 ± 0.029
				Spermatid Head Count (millions)	210.2 ± 9.7	207.1 ± 8.5	219.4 ± 7.8	216.0 ± 7.6
				Spermatid Head Concentration (millions/gram tissue)	101.4 ± 4.6	100.3 ± 4.2	104.6 ± 3.4	105.2 ± 4.0
				Percent Motile Sperm	83.3 ± 2.1 **	80.1 ± 1.6	76.2 ± 1.8 **	71.9 ± 2.5 **
				Percent Progressively Motile Sperm	70.0 ± 1.9 *	68.9 ± 1.3	67.2 ± 1.6	65.3 ± 2.5
				Epididymis Weight (g)	0.704 ± 0.009 **	0.718 ± 0.013	0.657 ± 0.011 **	0.635 ± 0.010 **
				Cauda Epididymis Weight (g)	0.266 ± 0.005 **	0.274 ± 0.006	0.243 ± 0.007 *	0.229 ± 0.005 **
				Cauda Epididymis Sperm Count (millions)	180.6 ± 8.2 **	206.6 ± 7.9	167.0 ± 11.3	135.1 ± 7.3 **
				Cauda Epididymis Sperm Concentration (millions/gram tissue)	682.4 ± 29.7 *	752.7 ± 21.2	676.5 ± 38.3	589.5 ± 28.5

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

R06: Andrology Summary
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 09:35:29
Lab: RTI

Male							
Generation	Litter ID	Terminal Sac	Cohort	Treatment Groups (ppm)			
				0	750	2500	
F1	C	PND 91 - 93	F1 NonParental Male	No. Examined (Litters)	49 (18)	56 (22)	20 (8)
				Testis Weight (g)	1.931 ± 0.029	1.911 ± 0.023	1.884 ± 0.038
				Spermatid Head Count (millions)	247.0 ± 4.7	249.8 ± 2.9	225.5 ± 11.9
				Spermatid Head Concentration (millions/gram tissue)	128.2 ± 2.2	131.1 ± 1.9	120.2 ± 6.9
				Percent Motile Sperm	68.9 ± 1.8	68.7 ± 2.0	61.9 ± 1.2 **
				Percent Progressively Motile Sperm	57.6 ± 1.6	57.4 ± 1.7	51.4 ± 1.4 *
				Epididymis Weight (g)	0.579 ± 0.010 **	0.561 ± 0.007	0.521 ± 0.012 **
				Cauda Epididymis Weight (g)	0.218 ± 0.005	0.216 ± 0.004	0.201 ± 0.007
				Cauda Epididymis Sperm Count (millions)	187.8 ± 8.9	168.8 ± 6.5	153.8 ± 11.4
				Cauda Epididymis Sperm Concentration (millions/gram tissue)	856.4 ± 26.1	780.1 ± 25.8 *	754.4 ± 40.8 *

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

R06: Andrology Summary
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 09:35:29
Lab: RTI

Male

Generation	Litter ID	Terminal Sac	Cohort	Treatment Groups (ppm)			
				0	750	2500	
F1	C	PND 218 - 224	F1 Parental Males	No. Examined (Litters)	40 (18)	44 (22)	39 (15)
				Testis Weight (g)	2.101 ± 0.038	2.106 ± 0.029	2.153 ± 0.048
				Spermatid Head Count (millions)	270.2 ± 7.3	268.3 ± 6.0	277.9 ± 6.9
				Spermatid Head Concentration (millions/gram tissue)	128.7 ± 3.1	127.9 ± 2.7	129.5 ± 3.1
				Percent Motile Sperm	80.1 ± 1.5 **	77.4 ± 1.2	71.7 ± 2.9
				Percent Progressively Motile Sperm	66.9 ± 1.3	66.5 ± 1.2	64.4 ± 2.9
				Epididymis Weight (g)	0.697 ± 0.013 **	0.698 ± 0.010	0.649 ± 0.012 *
				Cauda Epididymis Weight (g)	0.257 ± 0.004 *	0.263 ± 0.005	0.243 ± 0.006
				Cauda Epididymis Sperm Count (millions)	196.7 ± 9.0	190.2 ± 7.1	176.0 ± 10.6
				Cauda Epididymis Sperm Concentration (millions/gram tissue)	759.6 ± 27.3	723.0 ± 26.2	721.2 ± 35.0

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

R06: Andrology Summary
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 10/16/2018
Time Report Requested: 09:35:29
Lab: RTI

LEGEND

Data are displayed as mean \pm SEM for the F0 animals. Data are displayed as the mean of the litter mean \pm SEM for the F1 and/or F2 animals.

Statistical analysis for F0 data performed by Jonckheere (trend) and then a pairwise test. Williams/Dunnett pairwise tests are used for organ weights, Shirley/Dunn pairwise tests are used for all other endpoints.

Statistical analysis of F1 and/or F2 organ weight endpoints performed using linear mixed models with the dam ID as the random effect for both trend and pairwise test, and using the Dunnett-Hsu adjustment for multiple comparisons. For non-normally distributed continuous endpoints with litter-mates, for F1 and/or F2 endpoints, a bootstrapped Jonckheere trend test was used, and pairwise comparisons were done using the Datta-Satten modified Wilcoxon test with Hommel adjustment for multiple comparisons.

* 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

**** END OF REPORT ****