

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

**R22: Cross Generational Summary of Litters**

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

**Date Report Requested:** 10/02/2018  
**Time Report Requested:** 09:38:39  
**Lab:** RTI

**C Number:**

R92025B

**Study Gender:**

Both

**PWG Approval Date**

See web page for date of PWG Approval

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	Litter ID	F0				F1		
		Treatment Groups (ppm)				Treatment Groups (ppm)		
		0	750	2500	5000	0	750	2500
Mating Pairs <sup>a</sup>		22	23	20	21	39	41	35
Number of Litters/Pair <sup>b,c</sup>		2.6 ± 0.2	2.9 ± 0.1	2.4 ± 0.2	0.1 ± 0.1	2.5 ± 0.1	2.5 ± 0.1	2.3 ± 0.1
Number of Pairs without a Litter <sup>d</sup>		1	0	2	18	1	2	1
Live Pups/Pair <sup>e,f</sup>		36.7 ± 1.8	36.8 ± 1.1	24.4 ± 1.8	0.7 ± 0.5	29.7 ± 1.9 *	27.0 ± 1.8 **	20.3 ± 2.2
Average Live Litter Size/Pair <sup>f,g</sup>	A	14.0 ± 0.5	12.7 ± 0.6	8.3 ± 1.0	2.2 ± 2.0	10.8 ± 0.8 **	9.7 ± 0.6 **	7.9 ± 0.7
Average Live Litter Size/Pair <sup>f,g</sup>	B	13.6 ± 0.5	12.7 ± 0.5	8.5 ± 0.6	0.5 ± 0.5	13.6 ± 0.6	11.9 ± 0.6	9.8 ± 0.8
Average Live Litter Size/Pair <sup>f,g</sup>	C	12.2 ± 0.8	12.4 ± 0.5	9.8 ± 1.2		9.2 ± 0.7 **	8.8 ± 0.6 **	8.5 ± 0.9
Average Live Litter Size/Pair - All Litters <sup>f,g,h</sup>		13.2 ± 0.4	12.6 ± 0.3	9.0 ± 0.7	0.6 ± 0.5	11.4 ± 0.4 **	10.0 ± 0.5 **	8.2 ± 0.7
Average Live Litter Size/Pair <sup>f,i</sup> (Excluding non-viable litters)	A	14.0 ± 0.5	12.7 ± 0.6	8.9 ± 0.9	5.5 ± 4.5	10.8 ± 0.8 **	9.7 ± 0.6 **	8.0 ± 0.7
Average Live Litter Size/Pair <sup>f,i</sup> (Excluding non-viable litters)	B	13.6 ± 0.5	12.7 ± 0.5	8.5 ± 0.6	3.0	13.6 ± 0.6	12.2 ± 0.6	9.8 ± 0.8
Average Live Litter Size/Pair <sup>f,i</sup> (Excluding non-viable litters)	C	12.2 ± 0.8	12.4 ± 0.5	10.4 ± 1.1		9.2 ± 0.7 **	8.9 ± 0.6 **	8.5 ± 0.9
Average Live Litter Size/Pair - All Litters <sup>f,h,i</sup> (Excluding non-viable litters)		13.2 ± 0.4	12.6 ± 0.3	9.2 ± 0.6	2.0 ± 1.0	11.4 ± 0.4 **	10.1 ± 0.5 **	8.3 ± 0.6

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## LEGEND

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Data are displayed as mean  $\pm$  SEM

Comparisons are between generations for each dose group. Only mated pairs included in the analysis.

Dams that died before littering were not removed from the "Average live litter size/pair" endpoints that were specific to litter A,B, or C. For example, if an animal died before littering on C the animal was still included for litters A and B.

<sup>a</sup>Pairs that were bred three times to produce Litters A, B, and C

<sup>b</sup>Pair may have 0,1,2 or 3 litters. Pairs not littering or that have no live pups are counted as having 0 litters. Animals that died prior to litter A,B or C not included.

<sup>c</sup>Generalized linear mixed model using multinomial distribution and maternal dam (F1 generation) as random effect and with Hommel p-value adjustment.

<sup>d</sup>Mating pairs that did not produce a single live litter over the course of three breedings

<sup>e</sup>Total number of live pups per pair over the three breedings. Animals that died prior to littering A, B or C not included.

<sup>f</sup>Non-trend multiple comparisons used Datta-Satten modified Wilcoxon test with a Hommel p-value adjustment.

<sup>g</sup>Pairs with live litter size of 0 included.

<sup>h</sup>Live litter size averaged over each mating pair used in the analysis. Animals that died prior to littering A, B or C not included.

<sup>i</sup>Pairs with live litter size of 0 excluded.

\* Statistically significant at  $P \leq 0.05$

\*\* Statistically significant at  $P \leq 0.01$

F0 5000 ppm dose group pairs were only bred two times to produce Litters A and B and this group was not included in the statistical tests.

**\*\* END OF REPORT \*\***