

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

**I04G: Mean Body Weight Gain**  
**Test Compound:** 4-Methylimidazole  
**CAS Number:** 822-36-6

**Date Report Requested:** 07/25/2018  
**Time Report Requested:** 10:46:43  
**Lab:** RTI

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

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F0 Females

Treatment Groups (ppm)

Phase	Litter ID	Days	0		750		2500		5000	
			Wt Gain (g)	N	Wt Gain (g)	N	Wt Gain (g)	N	Wt Gain (g)	N
Gestation	A	0 - 3	14.6 ± 0.9 **	21	15.6 ± 0.6	21	11.1 ± 0.7 *	16	3.4 ± 5.3 **	6
		3 - 6	11.1 ± 0.7 **	21	9.4 ± 0.4	21	8.5 ± 0.7	16	12.0 ± 4.8	6
		6 - 9	10.8 ± 0.7 **	21	10.0 ± 0.8	21	4.2 ± 1.8 **	16	8.7 ± 2.3 *	6
		9 - 12	13.0 ± 0.5	21	13.5 ± 0.6	21	14.1 ± 1.7	16	9.1 ± 0.9	6
		12 - 15	19.4 ± 0.7 **	21	15.6 ± 0.9 **	21	14.4 ± 0.8 **	16	18.2 ± 2.9 *	6
		15 - 18	41.7 ± 1.5 **	21	37.0 ± 1.6 *	21	28.8 ± 1.2 **	16	29.4 ± 2.8 **	6
		18 - 21	48.1 ± 1.2 **	21	45.1 ± 2.0	21	34.9 ± 1.6 **	16	21.2 ± 5.4 **	6
		0 - 21	158.8 ± 2.7 **	21	146.2 ± 4.7 *	21	116.1 ± 3.0 **	16	101.9 ± 7.1 **	6
Lactation	A	1 - 4	11.1 ± 1.3 *	22	10.1 ± 1.0	22	6.8 ± 1.1 *	15	-15.8	1
Gestation	B	0 - 3	11.8 ± 1.2 *	18	11.9 ± 0.8	20	9.0 ± 0.9	16	9.8 ± 1.6	6
		3 - 6	7.8 ± 0.7 **	18	5.9 ± 0.7	20	4.8 ± 0.7 **	16	5.1 ± 1.2 *	6
		6 - 9	7.9 ± 0.8	18	6.4 ± 0.6	20	6.3 ± 0.6	16	7.0 ± 1.6	6
		9 - 12	10.1 ± 0.7	18	12.1 ± 0.4	20	10.4 ± 0.6	16	8.0 ± 1.6	6
		12 - 15	17.2 ± 1.0 **	18	15.5 ± 0.7	20	12.3 ± 0.7 **	16	9.5 ± 1.9 **	6
		15 - 18	39.0 ± 1.5 **	18	37.9 ± 1.4	20	26.3 ± 1.8 **	16	23.4 ± 4.5 **	6
		18 - 21	48.8 ± 2.0 **	18	46.8 ± 1.8	20	35.4 ± 2.1 **	16	16.7 ± 3.5 **	6
		0 - 21	142.6 ± 3.7 **	18	136.6 ± 3.5	20	104.4 ± 4.5 **	16	79.5 ± 7.8 **	6
Lactation	B	1 - 4	13.2 ± 2.0 *	19	8.6 ± 1.2	23	7.0 ± 1.5 *	17	4.4	1
Gestation	C	0 - 3	9.8 ± 0.7	17	10.7 ± 1.1	20	7.4 ± 0.9	15	NR	
		3 - 6	4.6 ± 0.7 *	17	3.9 ± 0.8	20	2.9 ± 0.5	15	NR	
		6 - 9	8.2 ± 0.8 *	17	7.4 ± 0.7	20	5.8 ± 0.5 *	15	NR	
		9 - 12	10.8 ± 0.9	17	5.4 ± 5.7	20	10.2 ± 0.6	15	NR	
		12 - 15	17.2 ± 0.9 **	17	21.5 ± 6.0	20	11.7 ± 1.2	15	NR	
		15 - 18	39.7 ± 1.8 **	17	34.7 ± 1.3	20	30.0 ± 3.0 **	15	NR	
		18 - 21	45.5 ± 2.0 **	17	43.1 ± 1.7	20	31.9 ± 2.7 **	15	NR	
		0 - 21	135.7 ± 4.9 **	17	126.7 ± 3.1	20	99.9 ± 5.4 **	15	NR	

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**F0 Females**

**Treatment Groups (ppm)**

Phase	Litter ID	Days	0		750		2500		5000	
			Wt Gain (g)	N	Wt Gain (g)	N	Wt Gain (g)	N	Wt Gain (g)	N
Lactation	C	1 - 4	8.4 ± 1.3	19	8.7 ± 1.2	22	4.8 ± 1.3	15	NR	
		4 - 7	8.9 ± 1.2	19	5.1 ± 1.4	22	5.2 ± 2.8	15	NR	
		7 - 10	4.8 ± 1.7	19	4.2 ± 1.6	22	8.9 ± 3.6	15	NR	
		10 - 13	-2.6 ± 1.6	19	-0.5 ± 1.7	22	2.2 ± 2.3	15	NR	
		13 - 16	-1.3 ± 1.8	19	-6.4 ± 1.7 *	22	-4.3 ± 0.9	15	NR	
		16 - 19	-7.7 ± 1.6	19	-4.4 ± 2.0	22	-3.0 ± 1.8	15	NR	
		19 - 21	-7.8 ± 1.9	19	-6.6 ± 1.7	22	-3.4 ± 2.5	15	NR	
		21 - 25	-20.2 ± 2.4 **	19	-14.7 ± 1.8	22	-5.8 ± 1.6 **	15	NR	
		25 - 28	0.2 ± 2.7	19	-1.5 ± 1.8	22	-4.1 ± 1.5	15	NR	
	1 - 28	-17.3 ± 3.5 **	19	-16.0 ± 3.5	22	0.6 ± 2.7 **	15	NR		
Gestation	D	0 - 3	13.9 ± 1.7 **	11	NR		3.7 ± 1.4 **	9	NR	
		3 - 6	7.3 ± 1.3	11	NR		3.6 ± 1.1 *	9	NR	
		6 - 9	10.6 ± 0.6	11	NR		8.0 ± 1.2	9	NR	
		9 - 12	11.6 ± 0.6	11	NR		11.8 ± 2.0	9	NR	
		12 - 15	16.3 ± 1.8	11	NR		13.9 ± 1.8	9	NR	
		15 - 18	37.3 ± 3.9	11	NR		33.4 ± 4.2	9	NR	
		18 - 21	38.2 ± 4.8	11	NR		39.3 ± 4.7	9	NR	
			0 - 21	135.2 ± 11.8	11	NR		113.7 ± 10.6	9	NR
Lactation	D	1 - 4	10.1 ± 1.9 *	12	NR		3.1 ± 2.4 *	9	NR	

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**F0 Females: F0 Naive Females**

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0 NF		2500 NF		5000 NF	
			Wt Gain (g)	N	Wt Gain (g)	N	Wt Gain (g)	N
Gestation	E	0 - 3	14.2 ± 0.5	16	14.3 ± 0.7	15	13.5 ± 1.1	6
		3 - 6	11.9 ± 1.0	16	12.9 ± 0.7	15	9.7 ± 0.7	6
		6 - 9	12.6 ± 0.8	16	11.6 ± 0.6	15	11.7 ± 1.3	6
		9 - 12	13.7 ± 0.9	16	13.1 ± 1.0	15	12.9 ± 1.0	6
		12 - 15	19.4 ± 0.8 *	16	16.3 ± 1.2	15	15.6 ± 1.9	6
		15 - 18	38.3 ± 1.6	16	33.9 ± 2.5	15	34.0 ± 3.8	6
		18 - 21	48.8 ± 1.6	16	44.4 ± 3.3	15	41.0 ± 5.1	6
		0 - 21	158.9 ± 3.9	16	146.4 ± 7.7	15	138.4 ± 12.1	6
Lactation	E	1 - 4	10.3 ± 2.0	16	13.4 ± 1.8	15	12.6 ± 1.3	6

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F1 Females: F1 Parental Females

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0		750		2500	
			Wt Gain (g)	N	Wt Gain (g)	N	Wt Gain (g)	N
Gestation	A	0 - 3	15.8 ± 0.7 **	33	14.1 ± 0.7	33	12.2 ± 0.8 **	30
		3 - 6	9.8 ± 0.7 **	33	9.0 ± 0.5	33	7.8 ± 0.5 *	30
		6 - 9	10.3 ± 0.7 *	33	9.3 ± 0.5	33	8.3 ± 0.5 *	30
		9 - 12	12.5 ± 0.8 *	33	12.6 ± 0.8	33	10.3 ± 0.6	30
		12 - 15	15.7 ± 0.7	33	13.1 ± 0.9 *	33	14.0 ± 0.5	30
		15 - 18	41.9 ± 1.2 **	33	34.2 ± 1.3 **	33	30.3 ± 1.2 **	30
		18 - 21	46.1 ± 1.7 **	33	41.0 ± 1.9	33	35.5 ± 1.5 **	30
		0 - 21	152.0 ± 3.4 **	33	133.3 ± 4.0 **	33	118.4 ± 3.2 **	30
Lactation	A	1 - 4	11.1 ± 2.1 *	32	8.0 ± 0.9	32	5.8 ± 1.3 *	28
Gestation	B	0 - 3	12.0 ± 1.4	33	12.6 ± 0.7	36	8.9 ± 0.9	27
		3 - 6	7.3 ± 0.7 *	33	6.3 ± 0.5	36	5.0 ± 0.5 *	27
		6 - 9	9.7 ± 0.6	33	7.5 ± 0.7 *	36	7.8 ± 0.8	27
		9 - 12	13.4 ± 0.8	33	12.1 ± 0.6	36	11.4 ± 0.9	27
		12 - 15	16.8 ± 1.0 *	33	14.5 ± 0.7	36	13.5 ± 0.9 *	27
		15 - 18	45.3 ± 1.6 **	33	36.3 ± 1.6 **	36	33.8 ± 1.9 **	27
		18 - 21	49.2 ± 1.7 **	33	44.5 ± 1.9	36	35.7 ± 2.6 **	27
		0 - 21	153.6 ± 4.7 **	33	133.8 ± 3.9 **	36	116.0 ± 4.7 **	27
Lactation	B	1 - 4	6.5 ± 1.4	34	5.9 ± 1.4	36	4.0 ± 1.3	29
Gestation	C	0 - 3	11.7 ± 0.7 **	26	10.3 ± 0.8	35	8.1 ± 0.6 **	23
		3 - 6	7.7 ± 0.5 *	26	5.7 ± 0.7 *	35	5.3 ± 0.6 **	23
		6 - 9	8.6 ± 0.8	26	6.8 ± 0.6	35	7.9 ± 0.8	23
		9 - 12	11.6 ± 0.7 **	26	11.4 ± 0.7	35	9.4 ± 0.7 *	23
		12 - 15	15.2 ± 0.9 *	26	12.7 ± 1.1	35	12.3 ± 1.2	23
		15 - 18	36.1 ± 2.1 *	26	31.0 ± 1.6 *	35	30.5 ± 2.1 *	23
		18 - 21	41.2 ± 2.8	26	39.6 ± 2.7	35	35.3 ± 3.9	23
		0 - 21	132.1 ± 5.6 **	26	117.5 ± 5.0 *	35	108.8 ± 6.9 **	23

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**F1 Females: F1 Parental Females**

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0		750		2500	
			Wt Gain (g)	N	Wt Gain (g)	N	Wt Gain (g)	N
Lactation	C	1 - 4	6.0 ± 1.5	28	8.0 ± 1.1	33	6.8 ± 1.3	22
		4 - 7	5.6 ± 1.1	27	3.1 ± 1.4	33	5.5 ± 1.6	22
		7 - 10	1.9 ± 1.4	27	0.9 ± 1.6	33	5.1 ± 1.6	22
		10 - 13	0.6 ± 1.7	27	1.9 ± 1.2	33	2.9 ± 1.4	22
		13 - 16	2.2 ± 1.4	27	0.3 ± 1.3	33	3.1 ± 2.3	22
		16 - 19	-6.7 ± 1.6	27	-6.2 ± 1.3	33	-5.8 ± 2.1	22
		19 - 21	-3.3 ± 1.6	27	-3.7 ± 1.4	33	-1.9 ± 1.3	22
		21 - 25	-11.1 ± 1.6	27	-8.5 ± 1.9	33	-6.9 ± 1.4	22
		25 - 28	-7.1 ± 2.3	27	-4.6 ± 1.4	33	-2.3 ± 1.5	22
		1 - 28	-11.3 ± 4.4 **	27	-8.8 ± 1.9	33	6.5 ± 2.9 **	22

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#### LEGEND

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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 animals performed by Jonckheere (trend) and Williams or Dunnett (pairwise) tests.

Statistical analysis of normally distributed endpoints for F1 animals was performed using mixed models, with dam ID as a random effect for both trend and pairwise tests, with Dunnett-Hsu adjustment for multiple comparisons.

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

\* Statistically significant at  $P \leq 0.05$

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

GD - Gestation Day; LD - Lactation Day

Naive females that were not pregnant were excluded from the analysis of gestational and lactational body weight data.

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

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

NR not recorded

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