

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

R19G: Pup Mean Body Weight Gain
Test Compound: 4-Methylimidazole
CAS Number: 822-36-6

Date Report Requested: 07/26/2018
Time Report Requested: 10:43:10
Lab: RTI

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

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F1 Pups

Phase	Litter ID	Days	Treatment Groups (ppm)							
			0		750		2500		5000	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	3.45 ± 0.11 **	22 (296)	2.90 ± 0.15 **	22 (275)	2.05 ± 0.19 **	15 (119)	1.58	1 (2)
PND	B	1 - 4	3.47 ± 0.12 **	19 (253)	3.13 ± 0.11	23 (288)	2.37 ± 0.16 **	17 (133)	1.52	1 (2)
PND	C	1 - 4 ^a	2.94 ± 0.19 *	19 (224)	2.50 ± 0.18	22 (270)	2.26 ± 0.24 *	15 (141)	NR	
		4 - 7	4.48 ± 0.21 **	19 (200)	4.07 ± 0.16	22 (235)	3.32 ± 0.24 **	15 (132)	NR	
		7 - 10	5.86 ± 0.28 **	19 (200)	5.58 ± 0.17	22 (234)	4.67 ± 0.23 **	15 (131)	NR	
		10 - 13	6.41 ± 0.38 **	19 (199)	6.30 ± 0.16	22 (232)	5.66 ± 0.20 **	15 (128)	NR	
		13 - 16	6.32 ± 0.30	19 (198)	6.48 ± 0.20	22 (232)	6.24 ± 0.18	15 (127)	NR	
		16 - 19	7.68 ± 0.35 **	19 (198)	6.90 ± 0.27	22 (232)	6.09 ± 0.32 **	15 (127)	NR	
		19 - 21	7.15 ± 0.25 **	19 (198)	6.49 ± 0.32	22 (232)	5.27 ± 0.21 **	15 (127)	NR	
		21 - 25	17.93 ± 0.59 **	19 (198)	17.09 ± 0.23	22 (232)	13.08 ± 0.35 **	15 (127)	NR	
		25 - 28	15.52 ± 0.44 **	19 (198)	14.45 ± 0.21 *	22 (232)	11.99 ± 0.34 **	15 (127)	NR	
		4 - 28	71.42 ± 2.09 **	19 (198)	67.47 ± 1.06 **	22 (232)	56.63 ± 1.35 **	15 (127)	NR	
PND	D	1 - 4	2.61 ± 0.29	12 (126)	NR		2.21 ± 0.26	9 (97)	NR	
PND	E	1 - 4	NR		NR		NR		NR	

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F1 Pups

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0 NF		2500 NF		5000 NF	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	NR		NR		NR	
PND	B	1 - 4	NR		NR		NR	
PND	C	1 - 4 ^a	NR		NR		NR	
		4 - 7	NR		NR		NR	
		7 - 10	NR		NR		NR	
		10 - 13	NR		NR		NR	
		13 - 16	NR		NR		NR	
		16 - 19	NR		NR		NR	
		19 - 21	NR		NR		NR	
		21 - 25	NR		NR		NR	
		25 - 28	NR		NR		NR	
		4 - 28	NR		NR		NR	
PND	D	1 - 4	NR		NR		NR	
PND	E	1 - 4	3.07 ± 0.13	16 (209)	2.72 ± 0.30	15 (152)	3.04 ± 0.16	6 (68)

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F1 Males

Phase	Litter ID	Days	Treatment Groups (ppm)							
			0		750		2500		5000	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	3.41 ± 0.12 **	22 (158)	2.90 ± 0.14 **	22 (136)	2.14 ± 0.21 **	14 (46)	1.50	1 (2)
PND	B	1 - 4	3.59 ± 0.13 **	19 (120)	3.19 ± 0.12 *	23 (148)	2.37 ± 0.22 **	17 (53)	1.34	1 (1)
PND	C	1 - 4 ^a	3.21 ± 0.19 *	18 (110)	2.70 ± 0.20	22 (136)	2.50 ± 0.26 *	15 (66)	NR	
		4 - 7	4.69 ± 0.17 **	18 (100)	4.20 ± 0.15	22 (116)	3.30 ± 0.33 **	15 (63)	NR	
		7 - 10	6.24 ± 0.14 **	18 (100)	5.76 ± 0.18	22 (115)	4.79 ± 0.23 **	15 (62)	NR	
		10 - 13	6.77 ± 0.14 **	18 (99)	6.46 ± 0.17	22 (115)	5.54 ± 0.27 **	15 (61)	NR	
		13 - 16	6.79 ± 0.08 *	18 (99)	6.72 ± 0.20	22 (115)	6.26 ± 0.19	15 (60)	NR	
		16 - 19	7.99 ± 0.35 **	18 (99)	7.17 ± 0.29	22 (115)	6.25 ± 0.36 **	15 (60)	NR	
		19 - 21	7.95 ± 0.23 **	18 (99)	7.08 ± 0.35	22 (115)	5.58 ± 0.30 **	15 (60)	NR	
		21 - 25	19.32 ± 0.54 **	18 (99)	18.39 ± 0.29	22 (115)	14.18 ± 0.44 **	15 (60)	NR	
		25 - 28	17.33 ± 0.44 **	18 (99)	15.72 ± 0.27 **	22 (115)	13.17 ± 0.31 **	15 (60)	NR	
		4 - 28	77.14 ± 1.11 **	18 (99)	71.57 ± 1.16 **	22 (115)	59.42 ± 1.70 **	15 (60)	NR	
PND	D	1 - 4	2.61 ± 0.31	12 (58)	NR		2.25 ± 0.29	9 (46)	NR	
PND	E	1 - 4	NR		NR		NR		NR	

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F1 Males

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0 NF		2500 NF		5000 NF	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	NR		NR		NR	
PND	B	1 - 4	NR		NR		NR	
PND	C	1 - 4 ^a	NR		NR		NR	
		4 - 7	NR		NR		NR	
		7 - 10	NR		NR		NR	
		10 - 13	NR		NR		NR	
		13 - 16	NR		NR		NR	
		16 - 19	NR		NR		NR	
		19 - 21	NR		NR		NR	
		21 - 25	NR		NR		NR	
		25 - 28	NR		NR		NR	
		4 - 28	NR		NR		NR	
PND	D	1 - 4	NR		NR		NR	
PND	E	1 - 4	3.01 ± 0.14	16 (104)	2.60 ± 0.33	14 (72)	3.04 ± 0.21	6 (33)

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F1 Females

Phase	Litter ID	Days	Treatment Groups (ppm)							
			0		750		2500		5000	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	3.44 ± 0.11 **	22 (138)	2.87 ± 0.17 *	22 (139)	2.02 ± 0.19 **	15 (73)	NR	
PND	B	1 - 4	3.39 ± 0.13 **	19 (133)	3.05 ± 0.12	23 (140)	2.30 ± 0.16 **	17 (80)	1.67	1 (1)
PND	C	1 - 4 ^a	2.68 ± 0.20 *	19 (114)	2.29 ± 0.18	22 (134)	1.98 ± 0.25	15 (75)	NR	
		4 - 7	4.40 ± 0.20 **	19 (100)	3.91 ± 0.18 *	22 (119)	3.23 ± 0.23 **	15 (69)	NR	
		7 - 10	5.73 ± 0.29 **	19 (100)	5.35 ± 0.19	22 (119)	4.42 ± 0.32 **	15 (69)	NR	
		10 - 13	6.36 ± 0.37 *	19 (100)	6.10 ± 0.16	22 (117)	5.90 ± 0.16	15 (67)	NR	
		13 - 16	6.15 ± 0.26	19 (99)	6.20 ± 0.21	22 (117)	6.07 ± 0.25	15 (67)	NR	
		16 - 19	7.43 ± 0.35 **	19 (99)	6.58 ± 0.26	22 (117)	5.95 ± 0.36 **	15 (67)	NR	
		19 - 21	6.59 ± 0.28 **	19 (99)	5.90 ± 0.31	22 (117)	4.73 ± 0.25 **	15 (67)	NR	
		21 - 25	16.86 ± 0.55 **	19 (99)	15.85 ± 0.25	22 (117)	11.87 ± 0.43 **	15 (67)	NR	
		25 - 28	13.96 ± 0.41 **	19 (99)	13.25 ± 0.21	22 (117)	11.01 ± 0.38 **	15 (67)	NR	
		4 - 28	67.62 ± 1.81 **	19 (99)	63.27 ± 1.07 *	22 (117)	53.44 ± 1.45 **	15 (67)	NR	
PND	D	1 - 4	2.63 ± 0.28	12 (68)	NR		2.10 ± 0.22	9 (51)	NR	
PND	E	1 - 4	NR		NR		NR		NR	

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F1 Females

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0 NF		2500 NF		5000 NF	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	NR		NR		NR	
PND	B	1 - 4	NR		NR		NR	
PND	C	1 - 4 ^a	NR		NR		NR	
		4 - 7	NR		NR		NR	
		7 - 10	NR		NR		NR	
		10 - 13	NR		NR		NR	
		13 - 16	NR		NR		NR	
		16 - 19	NR		NR		NR	
		19 - 21	NR		NR		NR	
		21 - 25	NR		NR		NR	
		25 - 28	NR		NR		NR	
		4 - 28	NR		NR		NR	
PND	D	1 - 4	NR		NR		NR	
PND	E	1 - 4	3.03 ± 0.13	16 (105)	2.61 ± 0.32	15 (80)	3.06 ± 0.17	6 (35)

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F2 Pups

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0		750		2500	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	3.20 ± 0.21 **	32 (344)	3.09 ± 0.24	32 (301)	2.49 ± 0.19 *	26 (181)
PND	B	1 - 4	2.63 ± 0.17 *	34 (443)	2.88 ± 0.13	36 (420)	2.25 ± 0.11	29 (255)
PND	C	1 - 4 ^a	2.65 ± 0.26 **	28 (253)	2.89 ± 0.18	33 (297)	1.80 ± 0.22 *	22 (165)
		4 - 7	3.78 ± 0.25	27 (222)	3.97 ± 0.20	33 (284)	3.21 ± 0.20	22 (153)
		7 - 10	5.23 ± 0.26 **	27 (212)	4.98 ± 0.22	33 (276)	3.92 ± 0.24 **	22 (150)
		10 - 13	6.16 ± 0.25 *	27 (207)	6.04 ± 0.25	33 (266)	5.41 ± 0.24 *	22 (145)
		13 - 16	6.76 ± 0.22 **	27 (206)	6.74 ± 0.25	33 (265)	5.94 ± 0.18 **	22 (145)
		16 - 19	6.46 ± 0.26 *	27 (205)	6.20 ± 0.31	33 (265)	5.54 ± 0.26 *	22 (145)
		19 - 21	7.51 ± 0.36 **	27 (205)	7.37 ± 0.39	33 (264)	4.95 ± 0.28 **	22 (145)
		21 - 25	16.49 ± 0.56 **	27 (205)	16.18 ± 0.43	33 (264)	11.97 ± 0.50 **	22 (145)
		25 - 28	15.12 ± 0.39 **	27 (205)	15.00 ± 0.32	33 (264)	12.14 ± 0.41 **	22 (145)
		4 - 28	67.70 ± 1.96 **	27 (205)	66.75 ± 2.06	33 (264)	53.35 ± 1.65 **	22 (145)

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F2 Males

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0		750		2500	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	3.18 ± 0.23 *	32 (151)	3.29 ± 0.15	31 (148)	2.53 ± 0.20	25 (82)
PND	B	1 - 4	2.70 ± 0.16 *	34 (209)	2.88 ± 0.14	35 (223)	2.31 ± 0.13	29 (131)
PND	C	1 - 4 ^a	2.74 ± 0.27 *	28 (124)	3.05 ± 0.19	32 (152)	2.09 ± 0.23	20 (77)
		4 - 7	4.01 ± 0.24 *	26 (114)	4.13 ± 0.23	32 (143)	3.20 ± 0.21 *	20 (72)
		7 - 10	5.77 ± 0.19 **	25 (109)	5.17 ± 0.25	32 (139)	4.00 ± 0.24 **	20 (71)
		10 - 13	6.43 ± 0.22 *	25 (108)	6.01 ± 0.27	32 (133)	5.67 ± 0.21 *	20 (69)
		13 - 16	7.14 ± 0.22 **	25 (107)	6.89 ± 0.27	32 (132)	5.93 ± 0.23 **	20 (69)
		16 - 19	6.69 ± 0.31 *	25 (107)	6.68 ± 0.36	32 (132)	5.68 ± 0.23	20 (69)
		19 - 21	8.09 ± 0.37 **	25 (107)	7.79 ± 0.43	32 (132)	5.45 ± 0.29 **	20 (69)
		21 - 25	18.24 ± 0.52 **	25 (107)	17.71 ± 0.54	32 (132)	13.35 ± 0.41 **	20 (69)
		25 - 28	16.93 ± 0.41 **	25 (107)	16.45 ± 0.41	32 (132)	13.45 ± 0.55 **	20 (69)
		4 - 28	73.54 ± 1.54 **	25 (107)	71.21 ± 2.42	32 (132)	56.97 ± 1.65 **	20 (69)

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F2 Females

Phase	Litter ID	Days	Treatment Groups (ppm)					
			0		750		2500	
			WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)	WT Gain (g)	N (# of pups)
PND	A	1 - 4	3.20 ± 0.20 **	30 (193)	3.03 ± 0.24	32 (153)	2.53 ± 0.15 *	24 (99)
PND	B	1 - 4	2.58 ± 0.18 *	34 (234)	2.85 ± 0.12	36 (197)	2.23 ± 0.13	29 (124)
PND	C	1 - 4 ^a	2.67 ± 0.18 **	27 (129)	2.67 ± 0.20	32 (145)	1.63 ± 0.21 **	22 (88)
		4 - 7	3.53 ± 0.26	27 (108)	3.75 ± 0.19	32 (141)	3.16 ± 0.21	22 (81)
		7 - 10	4.91 ± 0.29 **	27 (103)	4.83 ± 0.20	32 (137)	3.87 ± 0.26 *	22 (79)
		10 - 13	6.07 ± 0.26 **	27 (99)	6.24 ± 0.16	32 (133)	5.26 ± 0.26 *	22 (76)
		13 - 16	6.51 ± 0.23 **	27 (99)	6.82 ± 0.22	32 (133)	5.97 ± 0.16 *	22 (76)
		16 - 19	6.25 ± 0.26 *	27 (98)	6.09 ± 0.22	32 (133)	5.51 ± 0.26	22 (76)
		19 - 21	7.06 ± 0.32 **	27 (98)	7.07 ± 0.26	32 (132)	4.63 ± 0.29 **	22 (76)
		21 - 25	15.07 ± 0.49 **	27 (98)	14.88 ± 0.32	32 (132)	10.92 ± 0.48 **	22 (76)
		25 - 28	13.65 ± 0.34 **	27 (98)	13.78 ± 0.25	32 (132)	11.18 ± 0.28 **	22 (76)
		4 - 28	63.30 ± 1.83 **	27 (98)	63.70 ± 1.04	32 (132)	50.81 ± 1.44 **	22 (76)

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LEGEND

N(# of pups) = the number of litters examined (number of pups)

PND4 weights are precull if litters are culled on postnatal day 4.

Data are displayed as the means and standard errors of the litter means.

PND - Postnatal Day, pups pre-weaning

Pup weights are adjusted for covariate litter size. Total live on PND 1 for day 1 to cull day, and number of live pups after culling for later weight days if litters culled. If litters were not culled, the total live on PND 1 was used for the entire postnatal period.

Statistical analysis was performed using mixed models with dam ID as a random effect for both trend and pairwise tests, using Dunnett-Hsu 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

NF = Naive Females

NR not recorded

**** END OF REPORT ****