

**Study Number:** MOG003B

**Test Type:** MOG

**Route:** Dosing in Feed

**Species/Strain:** Rat/Sprague-Dawley

**C Number:**

**Study Gender:**

**PWG Approval Date**

**R16: Pubertal Markers Summary**

**Test Compound:** 2-Ethylhexyl p-Methoxycinnamate

**CAS Number:** 5466-77-3

MOG003B

Both

See web page for date of PWG Approval

**Date Report Requested:** 01/14/2020

**Time Report Requested:** 12:38:05

**Lab:** RTI

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Generation	Cohort		Male			
			Treatment Groups (ppm)			
			0	1000	3000	6000
F1	All Males	No. Examined (litters)	72 (21)	84 (24)	69 (19)	74 (22)
		No. Removed (litters)	0 (0)	0 (0)	0 (0)	0 (0)
		No. Not Attaining BPS (litters)	0 (0)	0 (0)	0 (0)	0 (0)
		Day of BPS				
		Mean Analysis				
		Litter Mean ± SE	44.9 ± 0.3 **	45.4 ± 0.6	45.3 ± 0.4	48.4 ± 0.6 **
		Litter Mean of Adjusted ± SE	45.6 ± 0.3 **	45.6 ± 0.6	45.2 ± 0.3	47.8 ± 0.5 **
		Proportional Hazards Analysis				
		Litter-based Model	p<0.001	p=0.645	p=0.645	p=0.012
		BW at Attainment (g)	207.9 ± 3.5	203.5 ± 4.0	199.2 ± 1.9	214.1 ± 3.4
		BW at Weaning (g)	84.5 ± 1.6 **	80.9 ± 1.2	78.2 ± 0.9 **	73.6 ± 1.5 **

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Generation	Cohort	Female				
		Treatment Groups (ppm)				
		0	1000	3000	6000	
F1	All Females	No. Examined (litters)	80 (20)	94 (24)	79 (19)	84 (22)
		No. Removed (litters)	0 (0)	0 (0)	0 (0)	1 (1)
		No. Not Attaining VO (litters)	0 (0)	0 (0)	0 (0)	0 (0)
		Day of VO				
		Mean Analysis				
		Litter Mean ± SE	34.1 ± 0.3 **	35.0 ± 0.2	35.8 ± 0.4 **	36.8 ± 0.3 **
		Litter Mean of Adjusted ± SE	34.4 ± 0.3 **	35.1 ± 0.2	35.7 ± 0.3 *	36.5 ± 0.3 **
		Proportional Hazards Analysis				
		Litter-based Model	p<0.001	p=0.107	p=0.002	p<0.001
		BW at Attainment (g)	106.7 ± 2.0	107.3 ± 1.3	107.1 ± 1.4	107.7 ± 2.4
BW at Weaning (g)	77.5 ± 1.8 **	73.0 ± 1.1	69.4 ± 1.0 **	66.1 ± 1.6 **		

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## LEGEND

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BPS = Balanopreputial separation; BW = Body weight; VO = Vaginal opening

The All Males cohort includes all males that were weaned and present at the beginning of the observation period for BPS. The All Females cohorts includes all females that were weaned except the F1 Extra Females and the PND 28 Biosample Females.

No. Examined (litters) = the number of animals or pups examined (number of litters)

No. Removed (litters) is the number of animals (number of litters contributing) that died or were removed prior to the end of the observation period and did not attain. These animals were excluded from all analyses.

No. Not Attaining BPS (litters) and No. Not Attaining VO (litters) is the number of animals (number of litters contributing) that survived to the end of the observation period without attaining.

Summary statistics and mixed model results are presented for animals that attained during the observation period for Day of BPS and Day of VO Mean Analysis endpoint.

Means of litter means presented for Day of BPS and Day of VO Litter Mean  $\pm$  SE. Trend and pairwise tests were based on mixed models for day of attainment with dose as a covariate and a random effect for litter. The Dunnett-Hsu adjustment was used for multiple comparisons.

Mean adjusted day of attainment was calculated from the mean of the litter means of the weaning weight-adjusted attainment days for individual pups. Trend and pairwise tests were based on mixed models for day of attainment with dose and weaning weight as covariates and a random effect for litter. The Dunnett-Hsu adjustment was used for multiple comparisons.

Animals that did not attain by the end of the observation period were included in the proportional hazards analysis.

P-values for trend and pairwise comparisons for the Litter-based Model of the Proportional Hazards Analysis were calculated from a Cox proportional hazards model with dose and weaning weight as covariates and a random effect for litter, and a Hommel adjustment for multiple comparisons.

Analysis of body weight at attainment and body weight at weaning were performed using mixed effects models with dose as covariate and a random effect for litter. The Dunnett-Hsu adjustment was used for multiple comparisons. Animals that attained during the observation period were used for analysis.

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  $P \leq 0.01$

The body weight at acquisition for BPS for male 1503 (dam 102, pup 1) was excluded from analysis as an outlier.

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