C Number:	R88007B
Study Gender:	Both
PWG Approval Date	See web page for date of PWG Approval

Study Number: R88007B
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

R14: Developmental Markers Summary
Test Compound: Butyl Paraben
CAS Number: 94-26-8

Date Report Requested: 03/20/2019
Time Report Requested: 14:48:24
Lab: RTI

F1 Male

Generation	Litter	Cohort		Treatment Groups (ppm) 0	5000	15000	40000
F1	C		**PND 13**				
		All Males	No. Examined (litters)	98 (19)	76 (14)	102 (18)	72 (16)
			No. of areolae/nipples per litter[a]	0.09 ± 0.06	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
			No. pups with areolae/nipples (%)[b]	2 (2.04)	0 (0.00)	0 (0.00)	0 (0.00)
			No. litters with areolae/nipples (%)[b]	2 (10.53)	0 (0.00)	0 (0.00)	0 (0.00)
			Testicular Descent				
			No. Examined (litters)	98 (19)	75 (14)	102 (18)	72 (16)
			No. Removed (litters)[c]	0 (0)	1 (1)	0 (0)	0 (0)
			No. Not Attaining Testes Descent (litters)[d]	0 (0)	0 (0)	1 (1)	1 (1)
			Day of Testes Descent				
			Mean Analysis[e]				
			Litter Mean ± SE[f]	15.3 ± 0.2	15.9 ± 0.4	15.4 ± 0.3	15.6 ± 0.3
			Proportional Hazards Analysis[g]				
			Litter-based Model[h]	p=0.141	p=0.851	p=0.877	p=0.877

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F1 Male

Generation	Litter	Cohort		Treatment Groups (ppm) 0	5000	15000	40000
F1	C		**PND 13**				
		F1c NonParent Males	No. Examined (litters)	43 (16)	34 (12)	46 (18)	6 (5)
			No. of areolae/nipples per litter[a]	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
			No. pups with areolae/nipples (%)[b]	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
			No. litters with areolae/nipples (%)[b]	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
			Testicular Descent				
			No. Examined (litters)	45 (16)	34 (12)	46 (18)	45 (14)
			No. Removed (litters)[c]	0 (0)	0 (0)	0 (0)	0 (0)
			No. Not Attaining Testes Descent (litters)[d]	0 (0)	0 (0)	1 (1)	1 (1)
			Day of Testes Descent				
			Mean Analysis[e]				
			Litter Mean ± SE[f]	15.6 ± 0.3	15.5 ± 0.3	15.4 ± 0.2	16.0 ± 0.4
			Proportional Hazards Analysis[g]				
			Litter-based Model[h]	p=0.061	p=0.935	p=0.935	p=0.935

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F1 Male

Generation	Litter	Cohort		Treatment Groups (ppm) 0	5000	15000	40000
F1	C		**PND 13**				
		F1c Parental Males	No. Examined (litters)	39 (19)	37 (13)	39 (18)	26 (7)
			No. of areolae/nipples per litter[a]	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
			No. pups with areolae/nipples (%)[b]	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
			No. litters with areolae/nipples (%)[b]	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
			Testicular Descent				
			No. Examined (litters)	40 (19)	40 (14)	40 (18)	26 (7)
			No. Removed (litters)[c]	0 (0)	0 (0)	0 (0)	0 (0)
			No. Not Attaining Testes Descent (litters)[d]	0 (0)	0 (0)	0 (0)	0 (0)
			Day of Testes Descent				
			Mean Analysis[e]				
			Litter Mean ± SE[f]	15.2 ± 0.2	15.9 ± 0.4	15.4 ± 0.3	15.0 ± 0.2
			Proportional Hazards Analysis[g]				
			Litter-based Model[h]	p=0.110	p=0.630	p=0.630	p=0.630

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Species/Strain: Rat/Sprague-Dawley

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F2 Male

Generation	Litter	Cohort		Treatment Groups (ppm) 0	5000	15000	40000
F2	C		**PND 13**				
		All Males	No. Examined (litters)	121 (27)	133 (30)	130 (29)	98 (24)
			No. of areolae/nipples per litter[a]	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.04 ± 0.04
			No. pups with areolae/nipples (%)[b]	0 (0.00)	0 (0.00)	0 (0.00)	2 (2.04)
			No. litters with areolae/nipples (%)[b]	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.17)
			Testicular Descent				
			No. Examined (litters)	121 (27)	133 (30)	130 (29)	98 (24)
			No. Removed (litters)[c]	0 (0)	0 (0)	0 (0)	0 (0)
			No. Not Attaining Testes Descent (litters)[d]	4 (3)	0 (0)	1 (1)	3 (3)
			Day of Testes Descent				
			Mean Analysis[e]				
			Litter Mean ± SE[f]	15.5 ± 0.2 **	15.5 ± 0.2	14.8 ± 0.1 *	14.9 ± 0.2
			Proportional Hazards Analysis[g]				
			Litter-based Model[h]	p=0.005	p=0.674	p=0.015	p=0.067

LEGEND

In multiple breeding/littering studies Litter A is the default designation for the first litter; subsequent litters would be B, C etc.

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

The number of areolae/nipples per litter are shown as mean ± SEM

No. of pups with areolae/ nipples reported as number of affected pups (%)

No. of litters with areolae/ nipples reported as number of affected litters (%)

If measured, the No. of areolae/nipples at terminal sacrifice are shown as mean ± SEM

[a]Statistical analysis for the F1 generation performed by Jonckheere (trend) and Shirley or Dunn (pairwise) tests. Statistical analysis for the F2 generation performed using a bootstrapped Jonckheere trend test; pairwise comparisons were done using the Datta-Satten modified Wilcoxon tests with Hommel adjustment for multiple comparisons.

[b]Statistical analysis for the F1 generation was performed using Cochran-Armitage (trend) and Fisher Exact (pairwise) tests. Statistical analysis for the F2 generation was performed using a Rao-Scott Cochran-Armitage test for both trend and pairwise tests.

[c]Animals that died or were removed prior to the end of the observation period and did not attain. These animals were excluded from all analyses.

[d]Animals that survived to the end of the observation period without attaining.

[e]Summary statistics and mixed model results are presented for animals that attained during the observation period.

[f]Means of litter means presented. 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.

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

[h]P-values for trend and pairwise comparisons were calculated from a Cox proportional hazards model with random effect for litter and a Hommel 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 <= 0.05

** Statistically significant at P <= 0.01

** END OF REPORT **