**Table 3:   Adjusted Pup Body Weights (g)**

| Parameter | Control | 75 mg/kg | 250 mg/kg | 750 mg/kg | Trend[a] |
|---|---|---|---|---|---|
| **Male[b,c,i]** | | | | | |
| **PND 4[d,f]** | 10.24 ± 0.17 [197/30] | 9.88 ± 0.18 [206/30] | 9.96 ± 0.17 [210/32] | 9.17 ± 0.17 [208/34]** | <0.001- |
| **PND 4[e,g]** | 10.19 ± 0.19 [122/30] | 9.95 ± 0.21 [123/30] | 9.94 ± 0.22 [121/30] | 9.43 ± 0.20 [125/30]* | 0.008- |
| **PND 7[g]** | 15.36 ± 0.35 [122/30] | 14.90 ± 0.38 [123/30] | 14.84 ± 0.44 [121/30] | 14.03 ± 0.34 [124/30]* | 0.014- |
| **PND 12[g]** | 26.80 ± 0.45 [121/30] | 26.14 ± 0.50 [123/30] | 25.63 ± 0.58 [117/29] | 24.14 ± 0.54 [122/30]** | <0.001- |
| **PND 15[g]** | 34.20 ± 0.50 [121/30] | 33.47 ± 0.58 [122/30] | 32.64 ± 0.60 [117/29] | 31.44 ± 0.65 [122/30]** | 0.001- |
| **PND 18[g]** | 41.51 ± 0.70 [121/30] | 40.71 ± 0.69 [122/30] | 40.01 ± 0.74 [117/29] | 38.00 ± 0.78 [122/30]** | <0.001- |
| **PND 21[g]** | 53.66 ± 0.81 [121/30] | 52.41 ± 0.89 [122/30] | 50.67 ± 1.06 [117/29] | 47.96 ± 1.00 [122/30]** | <0.001- |
| **PND 24[g]** | 67.94 ± 1.09 [121/30] | 66.24 ± 1.10 [122/30] | 63.88 ± 1.31 [117/29]* | 60.30 ± 1.24 [122/30]** | <0.001- |
| **PND 28[g]** | 88.35 ± 1.31 [121/30] | 86.75 ± 1.24 [122/30] | 83.85 ± 1.60 [117/29] | 79.26 ± 1.56 [122/30]** | <0.001- |
| **Female[b,c,h,i]** | | | | | |
| **PND 4[d,f]** | 9.75 ± 0.18 [200/30] | 9.28 ± 0.18 [177/31] | 9.29 ± 0.16 [201/32] | 8.70 ± 0.17 [189/34]** | <0.001- |
| **PND 4[e,g]** | 9.76 ± 0.22 [118/30] | 9.28 ± 0.19 [116/30] | 9.19 ± 0.19 [119/30] | 8.86 ± 0.18 [115/30]** | 0.005- |
| **PND 7[g]** | 14.75 ± 0.38 [118/30] | 13.91 ± 0.35 [117/30] | 13.73 ± 0.41 [119/30] | 13.18 ± 0.34 [115/30]** | 0.009- |
| **PND 12[g]** | 26.00 ± 0.53 [117/30] | 24.52 ± 0.52 [117/30] | 24.14 ± 0.55 [115/29]* | 22.89 ± 0.53 [112/30]** | <0.001- |
| **PND 15[g]** | 33.24 ± 0.57 [117/30] | 31.31 ± 0.57 [117/30] | 30.91 ± 0.58 [115/29]* | 29.96 ± 0.65 [112/30]** | 0.001- |
| **PND 18[g]** | 40.39 ± 0.76 [117/30] | 38.11 ± 0.68 [117/30] | 37.83 ± 0.73 [115/29]* | 36.45 ± 0.76 [112/30]** | 0.001- |
| **PND 21[g]** | 51.29 ± 0.85 [117/30] | 48.43 ± 0.85 [117/30] | 47.29 ± 0.92 [115/29]** | 45.40 ± 0.99 [112/30]** | <0.001- |
| **PND 24[g]** | 63.70 ± 1.13 [117/30] | 60.34 ± 1.01 [117/30] | 59.03 ± 1.14 [115/29]* | 56.64 ± 1.18 [112/30]** | <0.001- |
| **PND 28[g]** | 80.26 ± 1.17 [116/30] | 77.06 ± 1.09 [117/30] | 75.21 ± 1.34 [115/29]* | 72.22 ± 1.39 [112/30]** | <0.001- |
| **Combined[b,c,h,i]** | | | | | |
| **PND 4[d,f]** | 10.00 ± 0.17 [397/30] | 9.57 ± 0.18 [383/31] | 9.64 ± 0.16 [411/32] | 8.94 ± 0.16 [397/34]** | <0.001- |
| **PND 4[e,g]** | 9.98 ± 0.20 [240/30] | 9.63 ± 0.20 [239/30] | 9.57 ± 0.20 [240/30] | 9.16 ± 0.18 [240/30]** | 0.005- |
| **PND 7[g]** | 15.05 ± 0.35 [240/30] | 14.42 ± 0.36 [240/30] | 14.29 ± 0.41 [240/30] | 13.64 ± 0.31 [239/30]* | 0.010- |
| **PND 12[g]** | 26.41 ± 0.47 [238/30] | 25.37 ± 0.50 [240/30] | 24.90 ± 0.55 [232/29] | 23.57 ± 0.50 [234/30]** | <0.001- |
| **PND 15[g]** | 33.73 ± 0.50 [238/30] | 32.42 ± 0.56 [239/30] | 31.79 ± 0.57 [232/29]* | 30.76 ± 0.61 [234/30]** | 0.001- |
| **PND 18[g]** | 40.96 ± 0.70 [238/30] | 39.45 ± 0.67 [239/30] | 38.93 ± 0.71 [232/29] | 37.25 ± 0.74 [234/30]** | <0.001- |
| **PND 21[g]** | 52.49 ± 0.79 [238/30] | 50.46 ± 0.86 [239/30] | 49.01 ± 0.97 [232/29]* | 46.79 ± 0.94 [234/30]** | <0.001- |
| **PND 24[g]** | 65.86 ± 1.07 [238/30] | 63.34 ± 1.03 [239/30] | 61.49 ± 1.19 [232/29]* | 58.58 ± 1.14 [234/30]** | <0.001- |
| **PND 28[g]** | 84.41 ± 1.19 [237/30] | 82.00 ± 1.13 [239/30] | 79.58 ± 1.43 [232/29]* | 75.94 ± 1.38 [234/30]** | <0.001- |

# Black Cohosh Chronic Perinatal Study-Rats (C00058-03)

a: Statistical analysis was performed using linear mixed models with litter as random effect and with Dunnett-Hsu adjustment for multiple comparisons [* = P<0.05, ** = P<0.01]

b: Mean of litter means ± standard error [Number of pups/Number of litters]

c: PND=Postnatal Day

d: Body weights at pre-cull, all pups

e: Body weights at pre-cull, but only animals that were not culled are included.

f: Individual pup weights first adjusted for live litter size on PND 1. Litters with differing pup counts between PND 1 and PND 4 excluded.

g: Individual pup weights first adjusted for live litter size on PND 4 postcull

h: PND 4 weight for female animal 204-6 in the 75 mg/kg dose was removed as outlier

i: Statistical significance for a dosed group indicates a significant pairwise test compared to the vehicle control group.