**STATISTICAL ANALYSIS**

**PND1 Litter Data, Dam and Pup Weights**

**Toxico Genomic Study**

**of**

**DE-71 in Wistar Han Rats**

**(C20287B)**

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| **Table 1: DE71 Pregnancy Status in Female Wistar Han Rats** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **Pregnancy Statusb,c** |  |  |  |  |  |
| **Number Pregnant (%)** | 15 (79%) | 14 (70%) | 18 (90%) | 17 (89%) | 0.183+ |
| **Number Not Pregnant (%)** | 4 (21%) | 6 (30%) | 2 (10%) | 2 (11%) | 0.183- |
| **Resorptions** | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | . |
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| **Table 2: DE71 Pregnancy Status in Core Female Wistar Han Rats** | | | | | |
| **Parameter** | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **Pregnancy Statusb,c** |  |  |  |  |  |
| **Number Pregnant (%)** | 9 (100%) | 9 (100%) | 9 (100%) | 10 (100%) | . |
| **Number Not Pregnant (%)** | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | . |
| **Resorptions** | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | . |
| a: P-value and direction of Cochran-Amitage Trend Test | | | | | |
| b: Each dose is compared to the control with Fishers Exact test[\* = P<0.05, \*\* = P<0.01] | | | | | |
| c: Number observed (percent of total number of dams) | | | | | |
|  | | | | | |

| **Table 3: DE71 PND1 Litter Data in Female Wistar Han Rats** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **Litter Datab,c** |  |  |  |  |  |
| **Total Litter Size** | 6.12 ± 0.89 [17] | 6.83 ± 1.02 [18] | 9.28 ± 0.43 [18]\* | 8.94 ± 0.85 [18]\* | 0.004+ |
| **Male Litter Size** | 3.64 ± 0.43 [14] | 4.93 ± 0.50 [14] | 4.89 ± 0.46 [18] | 4.82 ± 0.50 [17] | 0.157+ |
| **Female Litter Size** | 3.64 ± 0.63 [14] | 3.86 ± 0.57 [14] | 4.39 ± 0.37 [18] | 4.65 ± 0.52 [17] | 0.116+ |
| **Percent Males (%)** | 53.53 ± 5.79 [14] | 58.51 ± 5.28 [14] | 48.05 ± 4.62 [18] | 51.72 ± 3.59 [17] | 0.514- |
| **Total Pup Body Weight (g)** | 49.79 ± 4.30 [14] | 63.95 ± 4.73 [14]\* | 65.31 ± 2.98 [18]\* | 66.12 ± 5.08 [17]\* | 0.007+ |
| **Total Male Pup Body Weight (g)** | 26.54 ± 2.96 [14] | 36.55 ± 3.77 [14] | 34.81 ± 2.99 [18] | 34.74 ± 3.77 [17] | 0.293+ |
| **Total Female Pup Body Weight (g)** | 23.24 ± 3.76 [14] | 29.51 ± 3.60 [13] | 30.51 ± 2.28 [18] | 31.38 ± 3.27 [17] | 0.082+ |
| **Pup Body Weight per Litter (g)** | 7.08 ± 0.24 [14] | 7.33 ± 0.18 [14] | 7.06 ± 0.12 [18] | 7.04 ± 0.17 [17] | 0.839- |
| **Male Pup BW per Litter (g)** | 7.34 ± 0.15 [14] | 7.44 ± 0.19 [14] | 7.38 ± 0.28 [18] | 7.25 ± 0.17 [17] | 0.468- |
| **Female Pup BW per Litter (g)** | 6.37 ± 0.69 [14] | 7.17 ± 0.22 [13] | 7.15 ± 0.33 [18] | 6.95 ± 0.22 [17] | 0.450+ |
| **Gestational Length (Day)** | 21.60 ± 0.16 [15] | 21.50 ± 0.14 [14] | 21.56 ± 0.12 [18] | 21.41 ± 0.12 [17] | 0.461- |
| a: P-value and direction of trend | | | | | |
| b: For body weight endpoints each dose was compared to the control with Williams test when a trend was present | | | | | |
| [P<.01 from Jonckheere’s trend test] or with Dunnetts test when no trend was present | | | | | |
| For other endpoints each dose was compared to the control with Shirleys test when a trend was present | | | | | |
| or with Dunns test when no trend was present [\* = P<0.05, \*\* = P<0.01] | | | | | |
| c: Mean ± standard error [number of dams] | | | | | |
|  | | | | | |

| **Table 4: DE71 PND1 Litter Data in Core Female Wistar Han Rats** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **Litter Weightsb,c** |  |  |  |  |  |
| **Total Litter Size** | 8.22 ± 0.85 [9] | 9.33 ± 0.53 [9] | 9.44 ± 0.56 [9] | 10.90 ± 0.57 [10]\* | 0.011+ |
| **Male Litter Size** | 4.44 ± 0.38 [9] | 5.00 ± 0.65 [9] | 4.56 ± 0.47 [9] | 5.70 ± 0.52 [10] | 0.121+ |
| **Female Litter Size** | 3.78 ± 0.66 [9] | 4.33 ± 0.53 [9] | 4.89 ± 0.51 [9] | 5.20 ± 0.59 [10] | 0.108+ |
| **Percent Males (%)** | 57.90 ± 6.26 [9] | 53.09 ± 4.99 [9] | 48.32 ± 4.36 [9] | 52.65 ± 4.02 [10] | 0.633- |
| **Total Pup Body Weight (g)** | 55.11 ± 5.05 [9] | 68.86 ± 4.48 [9] | 65.27 ± 4.00 [9] | 74.03 ± 5.22 [10]\* | 0.022+ |
| **Total Male Pup Body Weight (g)** | 32.11 ± 2.35 [9] | 37.62 ± 5.26 [9] | 32.01 ± 3.18 [9] | 39.88 ± 4.51 [10] | 0.303+ |
| **Total Female Pup Body Weight (g)** | 23.00 ± 4.13 [9] | 31.23 ± 3.57 [9] | 33.26 ± 3.26 [9] | 34.15 ± 3.58 [10] | 0.041+ |
| **Pup Body Weight per Litter (g)** | 6.83 ± 0.23 [9] | 7.39 ± 0.26 [9] | 6.91 ± 0.16 [9] | 6.77 ± 0.25 [10] | 0.569- |
| **Male Pup BW per Litter (g)** | 7.31 ± 0.20 [9] | 7.51 ± 0.26 [9] | 7.06 ± 0.13 [9] | 6.92 ± 0.21 [10] | 0.090- |
| **Female Pup BW per Litter (g)** | 5.44 ± 0.74 [9] | 7.30 ± 0.30 [9]\* | 6.89 ± 0.33 [9] | 6.67 ± 0.32 [10] | 0.560+ |
| **Gestational Length (Day)** | 21.56 ± 0.18 [9] | 21.44 ± 0.18 [9] | 21.67 ± 0.17 [9] | 21.40 ± 0.16 [10] | 0.707- |
| a: P-value and direction of trend | | | | | |
| b: For body weight endpoints each dose was compared to the control with Williams test when a trend was present | | | | | |
| [P<.01 from Jonckheere’s trend test] or with Dunnetts test when no trend was present | | | | | |
| For other endpoints each dose was compared to the control with Shirleys test when a trend was present | | | | | |
| or with Dunns test when no trend was present [\* = P<0.05, \*\* = P<0.01] | | | | | |
| c: Mean ± standard error [number of dams] | | | | | |
|  | | | | | |

| **Table 5: DE71 Male Wistar Han Rats:  PND Body Weights** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **PND22 Core Pup Body Wts(g)b,d** |  |  |  |  |  |
| **PND4** | 10.58 ± 0.60 [9] | 10.50 ± 0.36 [9] | 10.78 ± 0.32 [9] | 9.63 ± 0.48 [10] | 0.260- |
| **PND7** | 17.84 ± 0.79 [8] | 17.35 ± 0.43 [8] | 17.62 ± 0.50 [8] | 15.75 ± 0.72 [10] | 0.049- |
| **PND10** | 25.49 ± 0.95 [9] | 26.00 ± 0.86 [9] | 24.98 ± 0.74 [9] | 22.63 ± 0.69 [10]\* | 0.012- |
| **PND12** | 32.06 ± 1.45 [9] | 31.80 ± 0.98 [9] | 31.61 ± 0.58 [9] | 28.95 ± 0.93 [10] | 0.051- |
| **PND14** | 37.91 ± 1.75 [9] | 37.45 ± 1.12 [9] | 37.11 ± 0.67 [9] | 33.91 ± 1.28 [10] | 0.056- |
| **PND18** | 47.25 ± 2.12 [9] | 47.87 ± 1.27 [9] | 48.20 ± 0.94 [9] | 44.71 ± 1.57 [10] | 0.524- |
| **PND21** | 58.57 ± 2.67 [9] | 59.63 ± 1.64 [9] | 59.66 ± 1.47 [9] | 54.93 ± 2.26 [10] | 0.393- |
| **PND22** | 63.06 ± 2.68 [9] | 63.54 ± 1.75 [9] | 64.53 ± 1.78 [9] | 59.12 ± 2.33 [10] | 0.524- |
| **PND22 Core + NonCore Pup Body Wts(g)c,e** |  |  |  |  |  |
| **PND4** | 10.65 ± 0.57 [26/9] | 10.52 ± 0.35 [27/9] | 10.64 ± 0.27 [27/9] | 9.87 ± 0.37 [30/10] | 0.131- |
| **PND7** | 17.56 ± 0.72 [23/8] | 17.94 ± 0.51 [24/9] | 17.49 ± 0.37 [24/8] | 16.03 ± 0.57 [30/10] | 0.009- |
| **PND10** | 25.16 ± 0.84 [26/9] | 26.03 ± 0.82 [26/9] | 24.96 ± 0.73 [27/9] | 22.92 ± 0.52 [30/10] | 0.003- |
| **PND12** | 31.84 ± 1.33 [26/9] | 31.84 ± 0.99 [26/9] | 31.50 ± 0.62 [27/9] | 29.13 ± 0.82 [30/10] | 0.018- |
| **PND14** | 37.60 ± 1.58 [26/9] | 37.53 ± 1.11 [26/9] | 36.99 ± 0.69 [27/9] | 34.36 ± 1.10 [30/10] | 0.020- |
| **PND18** | 47.31 ± 1.99 [26/9] | 47.97 ± 1.29 [26/9] | 47.63 ± 0.99 [27/9] | 45.00 ± 1.31 [30/10] | 0.113- |
| **PND21** | 58.52 ± 2.47 [26/9] | 59.70 ± 1.63 [26/9] | 58.85 ± 1.36 [27/9] | 55.23 ± 1.79 [30/10] | 0.074- |
| **PND22** | 63.18 ± 2.57 [26/9] | 63.79 ± 1.74 [26/9] | 63.56 ± 1.64 [27/9] | 59.62 ± 1.88 [30/10] | 0.094- |
| a: P-value and direction of Trend Test | | | | | |
| b: Each dose was compared to the control with Williams test when a trend was present [P<.01 from Jonckheere’s trend test] | | | | | |
| or with Dunnetts test when no trend was present [\* = P<0.05, \*\* = P<0.01] | | | | | |
| c: Random litter effects model used for trend and pairwise [\* = P<0.05, \*\* = P<0.01] | | | | | |
| d: Mean ± standard error [number of pups] (for core animals only 1 pup per sex per litter was used) | | | | | |
| e: Mean ± standard error [number of pups/number of dams] | | | | | |

| **Table 6: DE71 Male Wistar Han Rats:  Liver and Body Weights** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **PND4 Liver and Body Wt-Culled Pupsc,e** | |  |  |  |  |  |
| **Body weight(g)** | | 10.62 ± 0.37 [16/10] | 10.72 ± 0.52 [17/9] | 10.77 ± 0.25 [21/12] | 10.35 ± 0.36 [30/15] | 0.460- |
| **Liver Weight(g)** | | 0.40 ± 0.02 [16/10] | 0.38 ± 0.02 [17/9] | 0.45 ± 0.02 [21/12] | 0.50 ± 0.02 [30/15]\*\* | <0.001+ |
| **Liver/BW Ratio(%)** | | 3.73 ± 0.17 [16/10] | 3.55 ± 0.11 [17/9] | 4.18 ± 0.11 [21/12] | 4.87 ± 0.17 [30/15]\*\* | <0.001+ |
| **PND22 Liver and Body Wt-Core Pupsb,d** | |  |  |  |  |  |
| **Body Weight(g)** | | 63.06 ± 2.68 [9] | 63.54 ± 1.75 [9] | 64.53 ± 1.78 [9] | 59.12 ± 2.33 [10] | 0.524- |
| **Liver Weight(g)** | | 2.58 ± 0.16 [9] | 2.50 ± 0.09 [9] | 3.35 ± 0.13 [9]\*\* | 3.98 ± 0.19 [10]\*\* | <0.001+ |
| **Liver/BW Ratio(%)** | | 4.06 ± 0.09 [9] | 3.93 ± 0.06 [9] | 5.18 ± 0.14 [9]\*\* | 6.71 ± 0.09 [10]\*\* | <0.001+ |
| **PND22 Liver and Body Wt-Core+Non-Core Pupsc,e** | |  |  |  |  |  |
| **Body Weight(g)** | | 63.18 ± 2.57 [26/9] | 63.79 ± 1.74 [26/9] | 63.56 ± 1.64 [27/9] | 59.62 ± 1.88 [30/10] | 0.094- |
| **Liver Weight(g)** | | 2.49 ± 0.12 [26/9] | 2.51 ± 0.08 [26/9] | 3.30 ± 0.13 [27/9]\*\* | 4.04 ± 0.17 [30/10]\*\* | <0.001+ |
| **Liver/BW Ratio(%)** | | 3.94 ± 0.04 [26/9] | 3.93 ± 0.06 [26/9] | 5.18 ± 0.13 [27/9]\*\* | 6.76 ± 0.15 [30/10]\*\* | <0.001+ |
| a: P-value and direction of Trend Test | | | | | | |
| b: Each dose was compared to the control with Williams test when a trend was present [P<.01 from Jonckheere’s trend test] | | | | | | |
| or with Dunnetts test when no trend was present [\* = P<0.05, \*\* = P<0.01] | | | | | | |
| c: Random litter effects model used for trend and pairwise [\* = P<0.05, \*\* = P<0.01] | | | | | | |
| d: Mean ± standard error [number of pups] (for core animals only 1 pup per sex per litter was used) | | | | | | |
| e: Mean ± standard error [number of pups/number of dams] | | | | | | |
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| **Table 7: DE71 Female Wistar Han Rats:  PND Body Weights** | | | | | |
| **Parameter** | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **PND22 Core Pup Body Wts(g)b,d** |  |  |  |  |  |
| **PND4** | 9.23 ± 0.60 [8] | 10.35 ± 0.39 [9] | 9.74 ± 0.47 [9] | 9.71 ± 0.49 [10] | 0.977- |
| **PND7** | 15.46 ± 0.65 [7] | 17.07 ± 0.47 [8] | 16.07 ± 0.79 [8] | 15.52 ± 0.72 [10] | 0.736- |
| **PND10** | 23.08 ± 0.85 [8] | 25.44 ± 0.79 [9] | 22.88 ± 1.06 [9] | 22.03 ± 0.68 [10] | 0.194- |
| **PND12** | 29.18 ± 1.25 [8] | 31.26 ± 0.96 [9] | 29.09 ± 1.12 [9] | 28.35 ± 1.08 [10] | 0.330- |
| **PND14** | 34.58 ± 1.41 [8] | 36.63 ± 0.90 [9] | 34.36 ± 1.24 [9] | 34.00 ± 1.29 [10] | 0.309- |
| **PND18** | 43.43 ± 2.03 [8] | 46.31 ± 1.27 [9] | 44.61 ± 1.55 [9] | 43.92 ± 1.59 [10] | 0.788- |
| **PND21** | 53.51 ± 2.35 [8] | 56.99 ± 1.46 [9] | 54.77 ± 1.40 [9] | 53.48 ± 1.71 [10] | 0.601- |
| **PND22** | 57.38 ± 2.46 [8] | 61.15 ± 1.37 [9] | 59.01 ± 1.53 [9] | 58.08 ± 1.89 [10] | 0.563- |
| **PND22 Core + NonCore Pup Body Wts(g)c,e** |  |  |  |  |  |
| **PND4** | 9.54 ± 0.50 [22/8] | 10.27 ± 0.35 [26/9] | 9.96 ± 0.27 [25/9] | 9.67 ± 0.40 [28/10] | 0.533- |
| **PND7** | 15.81 ± 0.48 [19/7] | 17.03 ± 0.38 [23/8] | 16.48 ± 0.45 [22/8] | 15.63 ± 0.59 [27/10] | 0.118- |
| **PND10** | 23.37 ± 0.78 [22/8] | 25.49 ± 0.70 [26/9] | 23.51 ± 0.81 [25/9] | 22.29 ± 0.60 [28/10] | 0.014- |
| **PND12** | 29.45 ± 1.08 [22/8] | 31.26 ± 0.87 [26/9] | 29.92 ± 0.70 [25/9] | 28.44 ± 0.96 [28/10] | 0.068- |
| **PND14** | 34.79 ± 1.20 [22/8] | 36.86 ± 0.93 [26/9] | 35.18 ± 0.78 [25/9] | 33.88 ± 1.19 [28/10] | 0.104- |
| **PND18** | 43.94 ± 1.78 [22/8] | 46.67 ± 1.15 [26/9] | 45.27 ± 1.01 [25/9] | 44.13 ± 1.41 [28/10] | 0.418- |
| **PND21** | 53.95 ± 2.16 [22/8] | 57.54 ± 1.28 [26/9] | 56.09 ± 1.16 [25/9] | 54.16 ± 1.65 [28/10] | 0.351- |
| **PND22** | 57.94 ± 2.25 [22/8] | 61.81 ± 1.28 [26/9] | 60.61 ± 1.32 [25/9] | 58.63 ± 1.78 [28/10] | 0.465- |
| a: P-value and direction of Trend Test | | | | | |
| b: Each dose was compared to the control with Williams test when a trend was present [P<.01 from Jonckheere’s trend test] | | | | | |
| or with Dunnetts test when no trend was present [\* = P<0.05, \*\* = P<0.01] | | | | | |
| c: Random litter effects model used for trend and pairwise [\* = P<0.05, \*\* = P<0.01] | | | | | |
| d: Mean ± standard error [number of pups] (for core animals only 1 pup per sex per litter was used) | | | | | |
| e: Mean ± standard error [number of pups/number of dams] | | | | | |
|  | | | | | |

| **Table 8: DE71 Female Wistar Han Rats:  Liver and Body Weights** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | | **Control** | **.1 mg/kg** | **15 mg/kg** | **50 mg/kg** | **Trenda** |
| **PND4 Liver and Body Wt-Culled Pupsc,e** | |  |  |  |  |  |
| **Body weight(g)** | | 9.79 ± 0.64 [14/9] | 10.35 ± 0.17 [12/9] | 10.40 ± 0.37 [23/12] | 10.06 ± 0.41 [23/14] | 0.909- |
| **Liver Weight(g)** | | 0.37 ± 0.03 [14/9] | 0.38 ± 0.01 [12/9] | 0.43 ± 0.02 [23/12] | 0.49 ± 0.03 [23/14]\*\* | 0.001+ |
| **Liver/BW Ratio(%)** | | 3.74 ± 0.11 [14/9] | 3.62 ± 0.11 [12/9] | 4.13 ± 0.09 [23/12] | 4.86 ± 0.22 [23/14]\*\* | <0.001+ |
| **PND22 Liver and Body Wt-Core Pupsb,d** | |  |  |  |  |  |
| **Body Weight(g)** | | 57.38 ± 2.46 [8] | 61.15 ± 1.37 [9] | 59.01 ± 1.53 [9] | 58.08 ± 1.89 [10] | 0.563- |
| **Liver Weight(g)** | | 2.20 ± 0.11 [8] | 2.33 ± 0.08 [9] | 3.05 ± 0.11 [9]\*\* | 3.80 ± 0.19 [10]\*\* | <0.001+ |
| **Liver/BW Ratio(%)** | | 3.84 ± 0.06 [8] | 3.80 ± 0.05 [9] | 5.18 ± 0.20 [9]\*\* | 6.52 ± 0.17 [10]\*\* | <0.001+ |
| **PND22 Liver and Body Wt-Core+Non-Core Pupsc,e** | |  |  |  |  |  |
| **Body Weight(g)** | | 57.94 ± 2.25 [22/8] | 61.81 ± 1.28 [26/9] | 60.61 ± 1.32 [25/9] | 58.63 ± 1.78 [28/10] | 0.465- |
| **Liver Weight(g)** | | 2.18 ± 0.10 [22/8] | 2.41 ± 0.07 [26/9] | 3.15 ± 0.10 [25/9]\*\* | 3.90 ± 0.17 [28/10]\*\* | <0.001+ |
| **Liver/BW Ratio(%)** | | 3.75 ± 0.06 [22/8] | 3.89 ± 0.05 [26/9] | 5.20 ± 0.10 [25/9]\*\* | 6.63 ± 0.15 [28/10]\*\* | <0.001+ |
| a: P-value and direction of Trend Test | | | | | | |
| b: Each dose was compared to the control with Williams test when a trend was present [P<.01 from Jonckheere’s trend test] | | | | | | |
| or with Dunnetts test when no trend was present [\* = P<0.05, \*\* = P<0.01] | | | | | | |
| c: Random litter effects model used for trend and pairwise [\* = P<0.05, \*\* = P<0.01] | | | | | | |
| d: Mean ± standard error [number of pups] (for core animals only 1 pup per sex per litter was used) | | | | | | |
| e: Mean ± standard error [number of pups/number of dams] | | | | | | |

| **TABLE 9: DE-71 Dam Body Weights (Core Study) in Female WH Rats** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Parametera** | **Vehicle Control** | **0.1 mg/kg** | **Pct Ctrl** | **15 mg/kg** | **Pct Ctrl** | **50 mg/kg** | **Pct Ctrl** | **Trendb** |
| **GD5** | 220.0 ± 5.190 [9] | 215.0 ± 5.100 [9] | 97.73 | 208.4 ± 3.956 [9] | 94.55 | 219.2 ± 4.800 [10] | 99.55 | 0.786 |
| **GD6** | 224.1 ± 5.854 [9] | 219.6 ± 5.562 [9] | 97.77 | 214.9 ± 4.303 [9] | 95.54 | 224.7 ± 5.511 [10] | 100.00 | 0.578 |
| **GD7** | 225.2 ± 6.453 [9] | 219.4 ± 5.600 [9] | 97.33 | 214.6 ± 4.251 [9] | 95.11 | 225.1 ± 5.555 [10] | 100.00 | 0.560 |
| **GD8** | 228.4 ± 7.211 [9] | 223.9 ± 6.173 [9] | 97.81 | 218.7 ± 4.512 [9] | 95.61 | 227.2 ± 5.648 [10] | 99.56 | 0.989 |
| **GD9** | 230.7 ± 6.860 [9] | 224.3 ± 5.266 [9] | 97.39 | 219.0 ± 3.819 [9] | 95.22 | 228.0 ± 5.141 [10] | 99.13 | 0.839 |
| **GD10** | 235.7 ± 6.919 [9] | 231.6 ± 5.806 [9] | 98.30 | 224.0 ± 3.902 [9] | 95.32 | 234.2 ± 5.754 [10] | 99.57 | 0.871 |
| **GD11** | 241.0 ± 7.312 [9] | 234.5 ± 5.528 [9] | 97.10 | 227.3 ± 4.374 [9] | 94.19 | 239.7 ± 5.761 [10] | 99.17 | 0.924 |
| **GD12** | 246.9 ± 7.407 [9] | 240.2 ± 5.302 [9] | 97.56 | 233.2 ± 4.184 [9] | 94.72 | 244.3 ± 5.844 [10] | 99.19 | 0.968 |
| **GD13** | 251.2 ± 7.266 [9] | 245.9 ± 5.823 [9] | 97.61 | 237.9 ± 3.776 [9] | 94.42 | 250.3 ± 6.228 [10] | 99.60 | 0.818 |
| **GD14** | 254.8 ± 7.323 [9] | 249.4 ± 5.372 [9] | 98.03 | 242.2 ± 4.444 [9] | 95.28 | 254.5 ± 5.976 [10] | 100.00 | 0.694 |
| **GD15** | 257.1 ± 6.930 [9] | 252.5 ± 5.644 [9] | 98.05 | 244.8 ± 3.696 [9] | 94.94 | 259.4 ± 5.995 [10] | 100.78 | 0.578 |
| **GD16** | 262.1 ± 7.685 [9] | 258.2 ± 5.711 [9] | 98.47 | 252.6 ± 4.622 [9] | 96.18 | 267.2 ± 6.379 [10] | 101.91 | 0.284 |
| **GD17** | 268.8 ± 7.863 [9] | 267.4 ± 5.780 [9] | 99.63 | 259.3 ± 4.794 [9] | 96.64 | 275.6 ± 6.534 [10] | 102.61 | 0.309 |
| **GD18** | 279.2 ± 8.540 [9] | 277.8 ± 6.293 [9] | 99.28 | 268.6 ± 4.953 [9] | 96.06 | 287.2 ± 6.952 [10] | 102.87 | 0.272 |
| **GD19** | 288.4 ± 8.662 [9] | 285.7 ± 6.434 [9] | 98.96 | 277.2 ± 5.906 [9] | 96.18 | 297.4 ± 7.046 [10] | 103.13 | 0.408 |
| **GD20** | 293.6 ± 8.913 [9] | 294.8 ± 6.997 [9] | 100.34 | 284.2 ± 6.103 [9] | 96.93 | 306.2 ± 7.950 [10] | 104.44 | 0.272 |
| **GD21** | 305.3 ± 9.211 [9] | 307.6 ± 7.878 [9] | 100.66 | 296.6 ± 5.811 [9] | 97.05 | 321.1 ± 8.376 [10] | 105.25 | 0.198 |
| **GD22** | 327.2 ± 15.13 [5] | 326.7 ± 3.847 [4] | 99.69 | 310.4 ± 9.486 [6] | 94.80 | 346.7 ± 5.539 [4] | 105.81 | 0.382 |
| **PND0** | 314.1 ± 9.705 [9] | 294.8 ± 12.80 [9] | 93.63 | 284.1 ± 8.470 [9] | 90.45 | 313.8 ± 14.33 [9] | 99.68 | 0.843 |
| **PND1** | 256.2 ± 9.084 [9] | 251.6 ± 5.780 [9] | 98.05 | 238.1 ± 5.939 [9] | 92.97 | 253.9 ± 5.991 [10] | 98.83 | 0.946 |
| **PND2** | 256.3 ± 8.164 [9] | 253.5 ± 5.695 [9] | 98.83 | 243.2 ± 5.479 [9] | 94.92 | 259.7 ± 6.023 [10] | 101.17 | 0.881 |
| **PND3** | 259.1 ± 8.388 [9] | 257.1 ± 6.304 [9] | 99.23 | 245.2 ± 4.836 [9] | 94.59 | 263.9 ± 5.978 [10] | 101.54 | 0.714 |
| **PND4** | 258.7 ± 7.971 [9] | 257.4 ± 4.950 [9] | 99.61 | 248.7 ± 5.510 [9] | 96.12 | 263.2 ± 5.897 [10] | 101.94 | 0.714 |
| **PND5** | 260.5 ± 7.862 [9] | 258.5 ± 4.752 [9] | 99.23 | 249.9 ± 5.204 [9] | 95.77 | 266.6 ± 6.334 [10] | 102.31 | 0.489 |
| Table Page 1 of 2 | | | | | | | | |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **TABLE 9 (cont): DE-71 Dam Body Weights (Core Study) in Female WH Rats** | | | | | | | | | |
| **Parametera** | | **Vehicle Control** | **0.1 mg/kg** | **Pct Ctrl** | **15 mg/kg** | **Pct Ctrl** | **50 mg/kg** | **Pct Ctrl** | **Trendb** |
| **PND6** | | 262.4 ± 8.875 [9] | 260.5 ± 4.755 [9] | 99.24 | 250.1 ± 4.910 [9] | 95.42 | 265.2 ± 6.081 [10] | 101.15 | 0.560 |
| **PND7** | | 266.1 ± 8.735 [9] | 262.0 ± 3.931 [9] | 98.50 | 252.2 ± 3.777 [9] | 94.74 | 267.8 ± 5.566 [10] | 100.38 | 0.560 |
| **PND8** | | 269.7 ± 8.899 [9] | 265.5 ± 4.759 [9] | 98.51 | 255.8 ± 4.076 [9] | 94.80 | 269.2 ± 5.282 [10] | 100.00 | 0.946 |
| **PND9** | | 273.8 ± 8.944 [9] | 272.3 ± 4.651 [9] | 99.63 | 262.4 ± 4.355 [9] | 95.97 | 275.2 ± 5.384 [10] | 100.73 | 0.797 |
| **PND10** | | 275.3 ± 9.215 [9] | 274.4 ± 4.213 [9] | 99.64 | 264.6 ± 4.228 [9] | 96.00 | 278.8 ± 5.192 [10] | 101.09 | 0.655 |
| **PND11** | | 277.5 ± 9.626 [9] | 271.4 ± 5.741 [9] | 97.83 | 266.3 ± 4.614 [9] | 96.03 | 279.8 ± 7.188 [10] | 100.72 | 0.694 |
| **PND12** | | 280.2 ± 8.634 [9] | 277.7 ± 3.548 [9] | 98.93 | 267.6 ± 4.358 [9] | 95.36 | 279.3 ± 5.914 [10] | 99.64 | 0.755 |
| **PND13** | | 283.1 ± 8.545 [9] | 281.0 ± 3.662 [9] | 99.29 | 270.3 ± 5.047 [9] | 95.41 | 283.4 ± 5.325 [10] | 100.00 | 0.714 |
| **PND14** | | 284.2 ± 8.698 [9] | 279.9 ± 2.614 [9] | 98.24 | 270.7 ± 4.212 [9] | 95.07 | 286.8 ± 5.483 [10] | 100.70 | 0.616 |
| **PND15** | | 283.4 ± 9.664 [9] | 281.7 ± 4.444 [9] | 99.29 | 273.8 ± 4.603 [9] | 96.47 | 285.9 ± 6.134 [10] | 100.71 | 0.714 |
| **PND16** | | 282.2 ± 8.308 [9] | 282.0 ± 3.737 [9] | 100.00 | 274.8 ± 4.463 [9] | 97.16 | 288.7 ± 6.058 [10] | 102.13 | 0.440 |
| **PND17** | | 281.5 ± 7.862 [9] | 277.3 ± 2.950 [9] | 98.58 | 269.8 ± 2.775 [9] | 95.73 | 286.5 ± 6.285 [10] | 101.78 | 0.489 |
| **PND18** | | 279.1 ± 7.505 [9] | 277.0 ± 3.328 [9] | 99.28 | 269.5 ± 4.603 [9] | 96.42 | 281.6 ± 5.825 [10] | 100.72 | 0.818 |
| **PND19** | | 278.6 ± 8.042 [9] | 273.7 ± 3.683 [9] | 98.20 | 265.1 ± 5.047 [9] | 95.32 | 278.8 ± 6.561 [10] | 100.00 | 0.968 |
| **PND20** | | 273.4 ± 6.904 [9] | 276.3 ± 3.936 [9] | 101.10 | 266.7 ± 4.832 [9] | 97.44 | 278.4 ± 7.445 [10] | 101.83 | 0.456 |
| **PND21** | | 279.2 ± 7.213 [9] | 277.6 ± 3.995 [9] | 99.28 | 267.6 ± 5.588 [9] | 95.70 | 279.9 ± 6.668 [10] | 100.00 | 0.850 |
| **PND22** | | 280.2 ± 7.500 [9] | 278.9 ± 4.345 [9] | 99.29 | 266.0 ± 5.389 [9] | 95.00 | 278.2 ± 6.468 [10] | 99.29 | 0.755 |
| **GD6\_21** | | 81.22 ± 4.978 [9] | 87.97 ± 5.107 [9] | 107.41 | 81.75 ± 4.526 [9] | 100.00 | 96.41 ± 3.459 [10] | 118.52 | 0.049 |
| **GD6\_9** | | 6.63 ± 1.721 [9] | 4.74 ± 1.117 [9] | 66.67 | 4.08 ± 1.896 [9] | 66.67 | 3.35 ± 0.941 [10] | 50.00 | 0.193 |
| **GD9\_12** | | 16.20 ± 1.194 [9] | 15.87 ± 1.347 [9] | 93.75 | 14.28 ± 1.345 [9] | 87.50 | 16.28 ± 1.332 [10] | 100.00 | 0.776 |
| **GD12\_15** | | 10.19 ± 0.660 [9] | 12.26 ± 1.477 [9] | 120.00 | 11.58 ± 0.830 [9] | 110.00 | 15.16 ± 0.931 [10]\*\* | 150.00 | 0.002 |
| **GD15\_18** | | 22.07 ± 2.291 [9] | 25.36 ± 1.899 [9] | 113.64 | 23.76 ± 2.130 [9] | 104.55 | 27.75 ± 1.573 [10] | 122.73 | 0.096 |
| **GD18\_21** | | 26.12 ± 1.975 [9] | 29.75 ± 2.419 [9] | 111.54 | 28.04 ± 1.366 [9] | 107.69 | 33.87 ± 1.670 [10]\* | 126.92 | 0.015 |
| Table Page 2 of 2 | | | | | | | | | |
| a: All values shown as mean ± standard error [number]  b: Each dose was compared to the control with Williams’ test when a trend was present (P <0.01 from Jonckheere’s trend test), otherwise Dunnett’s test was   applied. [\* = P<0.05, \*\* = P<0.01]  c: Due to small sample sizes, effect of experiment round was not considered in this analysis. | | | | | | | | | |

**Appendix A: Extreme Values**

No observations were removed from the analysis as outliers.

**Appendix B: Statistical Methods**

Analysis of Continuous Variables

Two approaches were employed to assess the significance of pairwise comparisons between dosed and control groups in the analysis of continuous variables. Organ and body weight data, which have approximately normal distributions, were analyzed using the parametric multiple comparison procedures of Williams (1971, 1972) and Dunnett (1955). Hematology, clinical chemistry and thyroid hormone data , which typically have skewed distributions, were analyzed using the nonparametric multiple comparison methods of Shirley (1977) and Dunn (1964). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of dose-response trends and to determine whether a trend-sensitive test (Williams' or Shirley's test) was more appropriate for pairwise comparisons than a test that does not assume a monotonic dose-response (Dunnett's or Dunn's test). Trend-sensitive tests were used when Jonckheere's test was significant at p<0.01.

Core + Noncore pup PND body weights and liver weights were analyzed using a mixed model with dam as a random effect.

Prior to analysis, extreme values identified by the outlier test of Dixon and Massey (1951) were examined by NTP personnel. Implausible values, extreme values from animals that were suspected of being sick due to causes other than treatment, and values that the laboratory indicated as being inadequate due to measurement problems were eliminated from the analysis. A list of these values is provided in the Appendix.

**Appendix C: References**

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