

Experiment Number: C91069

Test Type: TOX

Route: Oral Gavage

Species/Strain: Rat/Harlan Sprague Dawley

C Number:

C91069

Cage Range:

All

Date Range:

All

Reasons For Removal:

All

Removal Date Range:

All

Treatment Groups:

All

Study Gender:

Both

PA41: Clinical Chemistry Summary

Test Compound: Wyeth 14,643 (WY)

CAS Number: 50892-23-4

Date Report Requested: 04/04/2018

Time Report Requested: 13:48:10

Lab: Battelle

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Male

| | Phase Day | Treatment Groups (mg/kg/day) | | | | | | | |
|----------------------------|-----------|------------------------------|---------------------|---------------------|----------------------|------|--|----|--|
| | | 0 | | 6.25 | | 12.5 | | 25 | |
| Urea Nitrogen (mg/dL) | SD 28 | 18.6 ± 0.7 (10) ** | 20.2 ± 0.5 (10) * | 21.3 ± 0.5 (10) ** | 23.1 ± 0.6 (10) ** | | | | |
| Percent of Control | | | 108.6 | 114.5 | 124.2 | | | | |
| Creatinine (mg/dL) | SD 28 | 0.76 ± 0.02 (10) | 0.75 ± 0.02 (10) | 0.72 ± 0.01 (10) | 0.74 ± 0.02 (10) | | | | |
| Percent of Control | | | 98.68 | 94.74 | 97.37 | | | | |
| Glucose (mg/dL) | SD 28 | 178.1 ± 6.4 (10) | 203.0 ± 17.1 (10) | 172.3 ± 6.7 (10) | 182.4 ± 9.4 (10) | | | | |
| Percent of Control | | | 114.0 | 96.7 | 102.4 | | | | |
| Total Protein (g/dL) | SD 28 | 6.59 ± 0.05 (10) ** | 6.24 ± 0.13 (10) * | 6.37 ± 0.05 (10) * | 6.25 ± 0.07 (10) ** | | | | |
| Percent of Control | | | 94.69 | 96.66 | 94.84 | | | | |
| Globulin (g/dL) | SD 28 | 2.29 ± 0.03 (10) ** | 1.50 ± 0.07 (10) ** | 1.59 ± 0.04 (10) ** | 1.39 ± 0.04 (10) ** | | | | |
| Percent of Control | | | 65.50 | 69.43 | 60.70 | | | | |
| A/G Ratio | SD 28 | 1.88 ± 0.02 (10) ** | 3.22 ± 0.13 (10) ** | 3.02 ± 0.08 (10) ** | 3.53 ± 0.14 (10) ** | | | | |
| Percent of Control | | | 171.21 | 160.94 | 187.80 | | | | |
| Albumin (g/dL) | SD 28 | 4.30 ± 0.03 (10) ** | 4.74 ± 0.06 (10) ** | 4.78 ± 0.04 (10) ** | 4.86 ± 0.09 (10) ** | | | | |
| Percent of Control | | | 110.23 | 111.16 | 113.02 | | | | |
| Total Bilirubin (mg/dL) | SD 28 | 0.201 ± 0.018 (10) | 0.195 ± 0.013 (10) | 0.163 ± 0.006 (10) | 0.177 ± 0.011 (10) | | | | |
| Percent of Control | | | 97.013 | 81.234 | 88.303 | | | | |
| Direct Bilirubin (mg/dL) | SD 28 | 0.024 ± 0.003 (10) ** | 0.021 ± 0.002 (10) | 0.025 ± 0.002 (10) | 0.030 ± 0.002 (10) * | | | | |
| Percent of Control | | | 85.417 | 102.917 | 126.667 | | | | |
| Indirect Bilirubin (mg/dL) | SD 28 | 0.177 ± 0.015 (10) * | 0.174 ± 0.014 (10) | 0.139 ± 0.006 (10) | 0.147 ± 0.011 (10) | | | | |
| Percent of Control | | | 98.587 | 78.293 | 83.098 | | | | |
| Cholesterol (mg/dL) | SD 28 | 125.0 ± 2.7 (10) ** | 106.6 ± 5.0 (10) ** | 116.2 ± 4.0 (10) * | 101.8 ± 3.5 (10) ** | | | | |
| Percent of Control | | | 85.3 | 93.0 | 81.4 | | | | |

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Lab: Battelle

Male

| | Phase Day | Treatment Groups (mg/kg/day) | | | | | | | | | | | |
|----------------------------------|-----------|------------------------------|--------|---------|--------|--------|---------|--------|--------|---------|--------|--------|---------|
| | | 0 | | 6.25 | | 12.5 | | 25 | | | | | |
| Triglyceride (mg/dL) | SD 28 | 116.4 | ± 9.9 | (10) | 110.9 | ± 6.9 | (10) | 89.9 | ± 8.0 | (10) | 102.2 | ± 9.3 | (10) |
| Percent of Control | | | | | 95.3 | | | 77.2 | | | 87.8 | | |
| Alanine Aminotransferase (IU/L) | SD 28 | 52.20 | ± 1.32 | (10) ** | 62.80 | ± 4.29 | (10) * | 59.50 | ± 2.36 | (10) * | 62.70 | ± 2.10 | (10) ** |
| Percent of Control | | | | | 120.31 | | | 113.98 | | | 120.11 | | |
| Alkaline Phosphatase (IU/L) | SD 28 | 202.8 | ± 7.5 | (10) ** | 286.2 | ± 12.2 | (10) ** | 325.1 | ± 14.7 | (10) ** | 386.5 | ± 31.2 | (10) ** |
| Percent of Control | | | | | 141.1 | | | 160.3 | | | 190.6 | | |
| Aspartate Aminotransferase (U/L) | SD 28 | 60.00 | ± 1.26 | (10) * | 64.70 | ± 3.45 | (10) | 62.50 | ± 1.90 | (10) | 70.00 | ± 3.35 | (10) * |
| Percent of Control | | | | | 107.83 | | | 104.17 | | | 116.67 | | |
| Creatine Kinase (IU/L) | SD 28 | 98.1 | ± 3.8 | (10) | 88.4 | ± 6.1 | (10) | 84.2 | ± 3.1 | (10) | 87.6 | ± 4.2 | (10) |
| Percent of Control | | | | | 90.1 | | | 85.8 | | | 89.3 | | |
| Sorbitol Dehydrogenase (IU/L) | SD 28 | 5.7 | ± 0.4 | (10) ** | 9.9 | ± 1.4 | (10) ** | 7.9 | ± 0.5 | (10) ** | 8.4 | ± 0.4 | (10) ** |
| Percent of Control | | | | | 173.7 | | | 138.6 | | | 147.4 | | |
| Bile salt/acids (umol/L) | SD 28 | 11.8 | ± 1.6 | (10) ** | 40.9 | ± 6.5 | (10) ** | 73.1 | ± 11.2 | (10) ** | 83.2 | ± 9.5 | (10) ** |
| Percent of Control | | | | | 346.6 | | | 619.5 | | | 705.1 | | |

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Lab: Battelle

Species/Strain: Rat/Harlan Sprague Dawley

Female

| | Phase Day | Treatment Groups (mg/kg/day) | | | | | | | |
|----------------------------|-----------|------------------------------|---------------------|---------------------|---------------------|------|--|----|--|
| | | 0 | | 6.25 | | 12.5 | | 25 | |
| Urea Nitrogen (mg/dL) | SD 28 | 17.5 ± 0.4 (10) | 17.7 ± 0.6 (10) | 18.7 ± 0.7 (10) | 17.6 ± 0.6 (10) | | | | |
| Percent of Control | | | 101.1 | 106.9 | 100.6 | | | | |
| Creatinine (mg/dL) | SD 28 | 0.79 ± 0.02 (10) | 0.84 ± 0.02 (10) | 0.85 ± 0.02 (10) | 0.83 ± 0.02 (10) | | | | |
| Percent of Control | | | 106.33 | 107.59 | 105.06 | | | | |
| Glucose (mg/dL) | SD 28 | 247.0 ± 6.7 (10) | 242.0 ± 9.6 (10) | 233.6 ± 8.1 (10) | 256.1 ± 8.6 (10) | | | | |
| Percent of Control | | | 98.0 | 94.6 | 103.7 | | | | |
| Total Protein (g/dL) | SD 28 | 6.37 ± 0.08 (10) ** | 6.54 ± 0.05 (10) | 6.85 ± 0.12 (10) ** | 6.85 ± 0.08 (10) ** | | | | |
| Percent of Control | | | 102.67 | 107.54 | 107.54 | | | | |
| Globulin (g/dL) | SD 28 | 1.91 ± 0.05 (10) | 1.51 ± 0.04 (10) ** | 1.65 ± 0.05 (10) * | 1.65 ± 0.05 (10) * | | | | |
| Percent of Control | | | 79.06 | 86.39 | 86.39 | | | | |
| A/G Ratio | SD 28 | 2.34 ± 0.05 (10) ** | 3.35 ± 0.10 (10) ** | 3.17 ± 0.08 (10) ** | 3.17 ± 0.09 (10) ** | | | | |
| Percent of Control | | | 142.95 | 135.28 | 135.37 | | | | |
| Albumin (g/dL) | SD 28 | 4.46 ± 0.05 (10) ** | 5.03 ± 0.05 (10) ** | 5.20 ± 0.08 (10) ** | 5.20 ± 0.05 (10) ** | | | | |
| Percent of Control | | | 112.78 | 116.59 | 116.59 | | | | |
| Total Bilirubin (mg/dL) | SD 28 | 0.148 ± 0.008 (10) | 0.126 ± 0.005 (10) | 0.137 ± 0.007 (10) | 0.135 ± 0.005 (10) | | | | |
| Percent of Control | | | 85.193 | 92.427 | 90.940 | | | | |
| Direct Bilirubin (mg/dL) | SD 28 | 0.023 ± 0.001 (10) | 0.021 ± 0.002 (10) | 0.020 ± 0.002 (10) | 0.020 ± 0.002 (10) | | | | |
| Percent of Control | | | 89.130 | 87.391 | 86.957 | | | | |
| Indirect Bilirubin (mg/dL) | SD 28 | 0.125 ± 0.008 (10) | 0.106 ± 0.006 (10) | 0.117 ± 0.007 (10) | 0.115 ± 0.004 (10) | | | | |
| Percent of Control | | | 84.468 | 93.355 | 91.673 | | | | |
| Cholesterol (mg/dL) | SD 28 | 107.5 ± 3.7 (10) | 92.6 ± 3.7 (10) * | 100.5 ± 3.3 (10) | 110.4 ± 4.3 (10) | | | | |
| Percent of Control | | | 86.1 | 93.5 | 102.7 | | | | |

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Female

| | Phase Day | Treatment Groups (mg/kg/day) | | | | | | | | | | | |
|----------------------------------|-----------|------------------------------|--------|---------|--------|--------|---------|--------|--------|---------|--------|--------|---------|
| | | 0 | | 6.25 | | 12.5 | | 25 | | | | | |
| Triglyceride (mg/dL) | SD 28 | 72.5 | ± 5.5 | (10) * | 87.9 | ± 7.8 | (10) | 105.9 | ± 10.7 | (10) | 97.2 | ± 10.1 | (10) |
| Percent of Control | | | | | 121.2 | | | 146.1 | | | 134.1 | | |
| Alanine Aminotransferase (IU/L) | SD 28 | 41.80 | ± 1.24 | (10) ** | 49.50 | ± 3.85 | (10) | 46.80 | ± 1.85 | (10) | 54.80 | ± 2.58 | (10) ** |
| Percent of Control | | | | | 118.42 | | | 111.96 | | | 131.10 | | |
| Alkaline Phosphatase (IU/L) | SD 28 | 142.6 | ± 6.9 | (10) ** | 181.7 | ± 10.2 | (10) ** | 179.2 | ± 5.4 | (10) ** | 217.3 | ± 11.4 | (10) ** |
| Percent of Control | | | | | 127.4 | | | 125.7 | | | 152.4 | | |
| Aspartate Aminotransferase (U/L) | SD 28 | 55.30 | ± 1.08 | (10) * | 64.70 | ± 8.15 | (10) | 56.50 | ± 1.70 | (10) | 61.90 | ± 1.55 | (10) * |
| Percent of Control | | | | | 117.00 | | | 102.17 | | | 111.93 | | |
| Creatine Kinase (IU/L) | SD 28 | 87.0 | ± 4.9 | (10) | 96.9 | ± 5.6 | (10) | 87.5 | ± 3.1 | (10) | 84.9 | ± 5.0 | (10) |
| Percent of Control | | | | | 111.4 | | | 100.6 | | | 97.6 | | |
| Sorbitol Dehydrogenase (IU/L) | SD 28 | 4.2 | ± 0.5 | (10) ** | 9.9 | ± 2.4 | (10) ** | 7.7 | ± 0.7 | (10) ** | 8.3 | ± 0.6 | (10) ** |
| Percent of Control | | | | | 235.7 | | | 183.3 | | | 197.6 | | |
| Bile salt/acids (umol/L) | SD 28 | 17.4 | ± 1.7 | (10) | 20.0 | ± 4.5 | (10) | 20.3 | ± 4.4 | (10) | 21.2 | ± 4.7 | (10) |
| Percent of Control | | | | | 114.9 | | | 116.7 | | | 121.8 | | |

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LEGEND

Values given as mean \pm SEM (N) with Percent of Control calculated by (dosed group mean / control group mean) x 100

SD – Study Day; GD – Gestation Day; LD – Lactation Day; PND – Postnatal Day, adults post-weaning

Clinical Chemistry for gestation phase includes pregnant females only

Statistical analysis performed by Jonckheere (trend) and Shirley or Dunn (pairwise) tests (unless otherwise noted).

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 $P \leq 0.01$

Indirect Bilirubin calculated as Total Bilirubin - Direct Bilirubin.

**** END OF REPORT ****