**E17.5 LIVERS**

Yellow highlights indicate scanned images

**Summary of Results for E17.5 Livers**

*Vehicle control livers* had centrilobular hepatocellular hypertrophy with karyomegaly, increased mitotic figures and decreased glycogen. There was increased basophilic granular cytoplasm in all hepatocytes.

*2mg/kg/day of GenX livers* showed the same changes as the vehicle control livers but with these additional lesions: extension of the centrilobular hepatocellular hypertrophy into the midzonal and periportal regions; minimal to mostly moderate (one minimal, one mild, three moderate) cytoplasmic alteration and decreased glycogen in periportal regions. One liver in this group had a small focal lesion of confluent liver necrosis.

*10mg/kg/day GenX livers* had centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions, marked cytoplasmic alteration and decreased glycogen in periportal regions. Occasional cell death in was present in the centrilobular hepatocytes. One liver in this group had a large focal lesion of confluent liver necrosis. Another liver had a hepatodiaphragmatic nodule (incidental finding).

*1mg/kg/day PFOA livers* showed centrilobular hepatocellular hypertrophy with moderate cytoplasmic alteration and occasional cell death.

*5mg/kg/day PFOA livers* had centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions, marked cytoplasmic alteration and decreased glycogen in periportal regions. There was also frequent cell death and degeneration in centrilobular hepatocytes with accumulation of cytoplasmic small vacuoles with distinct borders.

**Vehicle Control**

184-05, 184-06, 186-02, 187-07, 188-07: Centrilobular hepatocellular hypertrophy

**GenX 2mg/kg/day**

184-02: Minimal cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions, and decreased glycogen in periportal regions.

185-02: Mild cytoplasmic alteration with centrilobular hepatocellular hypertrophy.

187-03: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy and decreased glycogen in periportal regions.

188-03: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy.

One lobe had a smallfocal area (20X field) of liver necrosis Grossly, there was a tan lesion on the dam’s liver approximately 0.5mm(w) x 4mm(l).

188-04: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy.

**GENX 10mg/kg/day**

184-01, 185-01, 187-01, 187-02, 188-02: Marked cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions and decreased glycogen in periportal regions. Occasional cell death in centrilobular hepatocytes.

185-01: One lobe had a large focal area (two 10X fields) of confluent liver necrosis--- Grossly, there was a 4-5mm lesion on the median lobe of the liver. The other lobe had a medium focal area (1/2 20X field) of confluent liver necrosis.

187-01: One lobe had a hepatodiaphragmatic nodule. Grossly there was a ~1mm white area on right caudate lobe of liver.

**PFOA 1mg/kg/day**

187-04, 187-05, 187-06, 188-05, 188-06: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy and occasional cell death.

**PFOA 5mg/kg/day**

184-07, 185-05, 186-03, 187-08, 188-09, 188-10: Marked cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions and decreased glycogen in periportal regions. Frequent cell death and degeneration in centrilobular hepatocytes with accumulation of cytoplasmic small vacuoles with distinct borders.

**Female mice that were not pregnant**

184-03: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions.

184-04: WNL

185-04: WNL

186-01: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions.

188-01: Marked cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions and decreased glycogen in periportal regions. Frequent cell death and degeneration in centrilobular hepatocytes with accumulation of cytoplasmic small vacuoles with distinct borders.

188-08: Mild cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions.

**E17.5 KIDNEYS**

**Vehicle Control**

184-05: WNL (few minimal perivascular mononuclear cell infiltrates-mostly lymphocytes and fewer plasma cells)

184-06: WNL

186-02: WNL

187-07: WNL

188-07: WNL

**GenX 2mg/kg/day**

184-02: WNL

185-02: WNL

187-03: WNL

188-03: WNL

188-04: WNL (one minimal necrotic tubule with adjacent hyperplastic tubules)

**GENX 10mg/kg/day**

184-01: WNL

185-01: WNL

187-01: WNL (minimal perivascular mononuclear cell infiltrates, minimal focal mineralization in papilla XS and LS)

187-02: WNL (minimal focal mineralization in papilla LS)

188-02: WNL (one necrotic tubule with adjacent hyperplastic tubules LS)

**PFOA 1mg/kg/day**

187-04: WNL [minimal focal mineralization in papilla (XS and LS) and minimal perivascular mononuclear cell infiltrates (LS)]

187-05: WNL

187-06: WNL

188-05: WNL (no XS)

188-06: WNL

**PFOA 5mg/kg/day**

184-07: WNL [minimal focal mineralization in papilla (XS and LS)]

185-05: WNL

186-03: WNL

187-08: WNL [minimal focal tubular necrosis/hyperplasia (XS) and minimal focal mineralization in papilla (LS)]

188-09: WNL

188-10: WNL

**Female mice that were not pregnant**

184-03: WNL [minimal focal mineralization in papilla (XS and LS)]

184-04: WNL [minimal focal mineralization in papilla (XS and LS)]

185-04: WNL [minimal focal mineralization in papilla (XS)]

186-01: WNL [one dilated cortical tubule (XS) and minimal focal mineralization in papilla (LS) one minimal hyperplastic medullary tubule (LS)]

188-01: Multiple dilated tubules (9 profiles) in cortical region with hyperplastic epithelium and adjacent associated hyperplastic tubules, interstitial inflammatory cellular infiltrates, and occasional necrotic debris

188-08: WNL

**E17.5 Placentas**

**Vehicle Control**

184-05

P1-P8: WNL

P2 gross: head and neck appear thin and elongated. No placenta histology correlate

P8 gross: embryo is very small (0.65g) and the neck appears thin and elongated. No placenta histo correlate

184-05 P2 (metrial gland), P4 (nodule of transitional tissue)

184-06

P1-P8: WNL

184-06 P5 (normal labyrinth)

186-02

P1-P8: WNL

P5 gross: placenta torn. No histo correlate.

186-02 P1 (normal labyrinth)

187-07

P1-P7: WNL

187-07 P5 (normal labyrinth)

188-07

P1-P10: WNL

P8 head gross: there was a small, dark spot on the head of the embryo. Histology: Cortical necrosis with inflammatory cells (probably lymphocytes).

**GenX 2mg/kg/day**

184-02

P1-P7: moderate labyrinth atrophy and decreased giant cells in junctional zone

184-02 P2, P5, P7 (moderate labyrinth atrophy)

185-02

P1: minimal labyrinth atrophy

P2-P7: mild labyrinth atrophy

P1-P7: decreased giant cells in junctional zone

P4: nodule of transitional tissue on one end of placenta-focal developmental malformation

P4 gross: Nodule on the placenta from the right horn. Histology correlate: focal developmental malformation

185-02 P1 (minimal labyrinth atrophy)

185-02 P5, P6 (mild labyrinth atrophy)

185-02 P4 nodule

187-03

P1 and P3-P6: all WNL

P2: minimal labyrinth atrophy

188-03

P1-P2: WNL

P2 gross - embryo is small and its face/neck appear elongated (no placenta histology correlate)

188-04

P1-P6: WNL

P7-dilated and congested chorionic vessels and early clot formation (intravascular thrombosis) at interface of labyrinth and chorion

P7 gross: placenta rounded and slightly pale

**GENX 10mg/kg/day**

184-01

P1-P2: mild labyrinth atrophy with early formation of blood clots (intravascular thrombosis) at interface of labyrinth and chorion

Necropsy notes: two reabsorptions on the right uterine horn with no tissue for histology

185-01

P1, P2, P4, P5, P8, P10 - mild labyrinth atrophy

P3, P5, P7, P9 – minimal labyrinth atrophy

187-01

P1, P3-P7: WNL

P2: moderate labyrinth necrosis with degeneration and mineralization. Increased fibrin clots (intravascular thrombosis) in the chorion and dilation of maternal sinuses

P2 gross: the embryo was a resorption and was not collected. The placenta was pale and was collected

P8, P9: minimal labyrinth atrophy

187-02

P1: early clot formation (intravascular thrombosis) in decidua

P2, P3: minimal labyrinth atrophy

187-02 P1

188-02

P1-P8: diffuse mild labyrinth congestion

P2 gross: placenta increased in size. Embryo is pale

P7 gross: enlarged placenta

188-02 P5 & P8

**PFOA 1mg/kg/day**

187-04: P1-P5: WNL

187-05: P1-P8: WNL

187-06: P2-P6: WNL

188-06 P7 (junctional zone nodule)

P1 gross: Dark area of possible necrosis beside the placenta. Images were taken

P1 histo correlate-large area of decidua and labyrinth necrosis

188-05: P1-P7

P1-P5: WNL P1 and P2?

LP1: minimal atrophy

LP2: moderate atrophy, umbilical artery mild inflammation and minimal to marked necrosis

Left horn gross: There was one early-death embryo on the left horn. Images were taken of the embryo and placenta. The placenta was collected for histology and placed in a cassette labeled “188-05-L-P2.” There was a remarkable placenta on the left horn that was imaged and collected for histology. It was placed in a cassette labeled “188-05-L-P1.”

188-06: P1-P7

P1-P6: WNL

P7-nodule of tissue from junctional zone

P7 gross: There was a growth on the side of the placenta from P7 noted at necropsy. Images were taken

**PFOA 5mg/kg/day**

184-07: P1-P5: WNL

185-05: P1-P6: WNL

186-03: P1-P6

P1, P4, P5-mild labyrinth atrophy

P3: Intravascular thrombus in decidua and labyrinth congestion

P2, P6: WNL

187-08: P1-P8

P1-P8: moderate diffuse congestion,

P1-P8 gross: Edema seen in the mammary area / edema in abdominal cavity when opened

187-08 P1-P8

188-09: P1-P9

P1-P9: mild diffuse congestion

P1-P9 gross: There was excess fluid in the dam’s abdominal cavity; There was white foam coming out of the dam’s nose after sac; The placentas were rounded and slightly puffy

188-10: P1-P5

P1-P5: mild diffuse congestion

P1-P5 gross: There was excess fluid in the dam’s abdominal cavity