**E11.5 LIVERS**

Yellow highlights indicate scanned images

**Summary of Results for E11.5 Livers**

*Vehicle control livers* were all within normal limits (WNL). There was no evidence of centrilobular hypertrophy. One liver (118-11) had a small focal area of confluent liver necrosis.

*2mg/kg/day of GenX livers* had minimal centrilobular hepatocellular hypertrophy with cytoplasmic alteration and decreased glycogen in periportal regions. There were also occasional mitotic figures and cell death within the centrilobular regions.

*10mg/kg/day GenX livers* had centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions, moderate cytoplasmic alteration and decreased glycogen in periportal regions. The frequency of cell death (apoptotic and necrotic) and mitoses were increased in centrilobular hepatocytes. One liver in this group (118-02) had a small focal area of liver necrosis with inflammation.

*1mg/kg/day PFOA livers* all had minimal centrilobular hepatocellular hypertrophy with cytoplasmic alteration.

*5mg/kg/day PFOA livers* all had centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions, marked cytoplasmic alteration and decreased glycogen in periportal regions. There was increased cell death and degeneration in centrilobular hepatocytes with accumulation of cytoplasmic small vacuoles with distinct borders. Two livers in this group had foci of confluent liver necrosis.

*Not pregnant livers:* Two were within normal limits, three had moderate cytoplasmic alteration with associated lesions and 2 had marked cytoplasmic alteration with associated lesions.

**Vehicle Control**

114-07, 116-07, 116-08, 117-06, 118-11: WNL

118-11: small ( ¼ 40x field) focal liver necrosis (gross lesion of 2x3 mm tan focal area on left lobe of liver)

**GenX 2mg/kg/day**

114-04, 115-03, 117-04, 116-03, 118-04: Minimal cytoplasmic alteration with centrilobular hepatocellular hypertrophy and decreased glycogen in periportal regions.

114-04 gross: excess abdominal fluid in dam

**GENX 10mg/kg/day**

114-02, 115-01, 117-01, 118-01, 118-02: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions, and decreased glycogen in periportal regions. Increased cell death in centrilobular hepatocytes.

118-02: Small focus (1/8 of 40x field) of hepatocellular necrosis with inflammation.

**PFOA 1mg/kg/day**

114-05, 115-05, 115-06, 116-06, 117-05: Minimal cytoplasmic alteration with centrilobular hepatocellular hypertrophy.

**PFOA 5mg/kg/day**

114-09, 115-09, 116-09, 117-08, 118-13: Marked cytoplasmic alteration with centrilobular hepatocellular hypertrophy with extension into the midzonal and periportal regions, and decreased glycogen in periportal regions. Increased cell death and degeneration in centrilobular hepatocytes with accumulation of cytoplasmic small vacuoles with distinct borders.

115-09: One small (1/3 of 40x field) focus of liver necrosis.

117-08: Multiple (4) foci of necrosis. (¼ 40x field; ¼ 40x field; ½ 40x field; 1/3 40x field)

**Not pregnant**

116-01: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy extending into the midzonal and periportal regions. Diffuse decreased glycogen. Occasional cell death.

Gross lesion of 2x2mm tan area on the left lobe with no histological correlate in section of tissue provided for evaluation.

114-08: WNL

115-02: Marked cytoplasmic alteration with centrilobular hepatocellular hypertrophy extending into the midzonal and periportal regions. Diffuse decreased glycogen. Increased cell death.

115-08: WNL

116-02: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy extending into the midzonal and periportal regions. Diffuse decreased glycogen. Occasional cell death.

116-04: Moderate cytoplasmic alteration with centrilobular hepatocellular hypertrophy extending into the midzonal and periportal regions. Diffuse decreased glycogen. Occasional cell death.

116-10: Marked cytoplasmic alteration with centrilobular hepatocellular hypertrophy extending into the midzonal and periportal regions. Diffuse decreased glycogen. Increased cell death.

**E11.5 KIDNEYS**

LS=longitudinal section; XS=cross section; WNL=within normal limits

**Vehicle Control**

114-07: WNL (one focus of mixed perivascular infiltrates adjacent to papilla LS)

116-07: WNL

116-08: WNL

117-06: WNL

118-11: WNL (2 foci of mineralization in papilla XS and 3 in LS)

**GenX 2mg/kg/day**

114-04: WNL (gross lesion of excess abdominal fluid in dam)

115-03: WNL (one focus of mineralization in papilla LS)

116-03: WNL (one focus of mineralization in papilla XS)

117-04: WNL (one focus of mixed perivascular infiltrates adjacent to papilla LS)

118-04: WNL (two dilated tubules)

**GENX 10mg/kg/day**

114-02: WNL (multifocal perivascular cellular infiltrates adjacent to papilla in renal pelvis and two minimal foci of urothelial hyperplasia LS)

115-01: WNL (focal dilated cortical tubule XS, small focus of hyperplasia of the surface epithelium of the renal papilla, one focus of tubule mineralization in renal papilla XS)

117-01: WNL (mild, multiple perivascular mononuclear cell infiltrates surrounding main renal vein LS, presumed lymphoid; one dilated cortical tubule with hypertrophied epithelium XS)

118-01: WNL

118-02: WNL

**PFOA 1mg/kg/day**

114-05: WNL

115-05: WNL (focus of urothelial hyperplasia XS)

115-06: WNL

116-06: WNL (one small focus of minimal cortical nephropathy LS- hyperplastic tubule, perviscular infiltrate; one small focus of interstitial and periglomerular (2) infiltrates with fibrosis of Bowman’s capsule XS, one single glomerulus with periglomerular fibrosis, two small foci of papillary tubule mineralization XS)

117-05: WNL (4 dilated hyperplastic tubules and focus of urothelial hyperplasia LS, 2 small foci of papillary tubular mineralization LS)

**PFOA 5mg/kg/day**

114-09: WNL (small focus of perivascular infiltrates XS and LS, papillary tubular lesion LS?)

115-09: WNL (small focus of perivascular infiltrates LS)

116-09: WNL (two small foci of papillary tubular mineralization LS, one focus XS

117-08: WNL

118-13: WNL

**Not Pregnant**

116-01: WNL

**E11.5 PLACENTAS**

**Vehicle Control** (2 out of 33 abnormal)

114-07: P1-P5 WNL

114-07 P2, P4, P5 (range of normal)

116-07: P1-P4 and P6-P10 WNL

P5 gross: Embryo was very pale but could still see heartbeat. No histo correlate.

116-08: P1-P8 WNL

P4 gross: vasculature in embryo was very prominent-no histo correlate-possibly tangential sectioning

117-06: P1-P4 and P6, P8 WNL

P5 gross: embryo was underdeveloped. histo correlate decreased area of labyrinth

P7 gross: no embryo was with the placenta-histo correlate increased thickness of trilaminar trophoblast layers

117-06 P7 (increased thickness of trilaminar trophoblast layers)

118-11: P1-P7 WNL

R6A and R6B embryos had a shared placenta-histo correlate P6 had a slightly malformed placenta consistent with twins

118-11 P6 (shared placenta)

**GenX 2mg/kg/day** (3 out of 43 abnormal)

114-04: P1-P9 WNL

Gross: Excess abdominal fluid in dam

115-03: P1-P11 WNL

L11 gross: A placenta was found with no embryo but the yolk sac was intact. The placenta was collected for histology. Histo correlate-labyrinth hypoplasia/atrophy

115-03 P6 (metrial gland)

116-03: P1-P10 WNL

117-04: P1-P4 WNL

P5-decidua and transitional zone only, labyrinth necrosis consistent with resporption

118-04: P1-P6, P8 WNL

P7 gross: entire embryonic sac was bloody/hemorrhagic but the embryo was still viable -histo correlate large focal labyrinth hemorrhage and thrombus.

118-04 LP1 – placenta on left that had area of hemorrhage-histo correlate labyrinth atrophy/hypoplasia

**GENX 10mg/kg/day** (5 out of 34 abnormal)

114-02: P1-P3 WNL

115-01: P1, P2, P4, P5, P6, P7 WNL

P3 gross: 2 embryos sharing same placenta. Histology consistent with fused placenta (twins)

P8-P10 gross: placentas collected from resorption embryos

P8 labyrinth necrosis and junctional zone hyperplasia with abundant giant cells

P9, P10 labyrinth necrosis

115-01 P3 (shared placenta), P7 (metrial gland)

117-01: P1-P4 WNL

118-01: P1-P11 WNL

118-02: P1-P6 WNL

**PFOA 1mg/kg/day** (4 out of 36 abnormal)

114-05: P1-P4 and P6-P10 WNL

P5-no labyrinth so check to see if a resorption

115-05: P1-P5 WNL

115-06: P1-P7 WNL

116-06: P1- P7 WNL

117-05: P1-P4-WNL

P5, P6, P7-necrotic labyrinth consistent with resorptions

P6 and P7 were resorptions identified grossly-check on P5

117-05 LP3 (shared placenta)

L3A and L3B – fused placentas. Images taken, placentas collected for histology and embryos submitted for genotyping-histo correlate malformed placenta consistent with a shared placenta (twins) check for gross notes or images

**PFOA 5mg/kg/day** (6 out of 39 abnormal)

114-09: P2, P4-P9 WNL

P1-embryo resorption grossly and marked necrosis histologically

P3: Two embryos sharing the same placenta grossly and malformed placenta histologically consistent with this finding

P10: mild labyrinth atrophy

P11: mild labyrinth atrophy

114-09 P3 (shared placenta), P10 (labryrinth atrophy)

115-09: P2-P6: WNL

Gross finding: areas of hemorrhage in the uterus, embryos appeared to be E10.5-E11.5

P1: multifocal moderate labyrinth necrosis

P7: mild labyrinth, decidua and transitional zone atrophy

115-09 P1 (labryrinth necrosis), P7 (labyrinth atrophy)

116-09: P1-P6: WNL

P7: resorption identified grossly and necrotic placenta histology

117-08: P1-P9 WNL

118-13: P1-P5 WNL