

*Xenopus laevis* Müllerian ducts are sensitive indicators of estrogenic or androgenic chemical exposure *in vivo*

J.T. Haselman<sup>1</sup>, P.A. Kosian<sup>1</sup>, J.J. Korte<sup>1</sup>, A.W. Olmstead<sup>2</sup>, R.D. Johnson<sup>1</sup>, S.J. Degitz<sup>1</sup>. <sup>1</sup>NHEERL/ORD, US EPA, Duluth, MN; <sup>2</sup>Bayer CropScience LP, Research Triangle Park, NC

The Larval Amphibian Growth and Development Assay (LAGDA) is one of a series of Tier 2 test guidelines being developed by the US EPA under the Endocrine Disruptor Screening Program. The LAGDA was designed to evaluate effects of lower-dose, longer-term chemical exposure on (a) amphibian metamorphosis mediated by the hypothalamic-pituitary-thyroid (HPT) axis, and (b) reproductive development mediated by the hypothalamic-pituitary-gonadal (HPG) axis. In the development phase of the assay, chemicals with known modes of action were chosen for testing to evaluate the assay's performance. Two of the chemicals were chosen to target the HPG axis; a weak estrogen receptor agonist, 4-*tert*-octylphenol, and an androgen receptor agonist, 17 $\beta$ -Trenbolone. *Xenopus laevis* embryos were constantly exposed (flow-through conditions) to various doses of either 4-*tert*-octylphenol (6.25, 12.5, 25, 50  $\mu$ g/L) or 17 $\beta$ -Trenbolone (12.5, 25, 50, 100 ng/L) and clean water controls until 8 weeks post-metamorphosis, at which time growth measurements were taken and histopathology assessments were made on gonads, reproductive ducts, liver and kidneys. There were no effects on growth in both studies and only minimal pathologies found in the liver, kidneys and gonads of frogs in the high treatments. However, Müllerian duct development was significantly affected following exposure to both chemicals, as maturation (oviduct formation) and Müllerian duct regression are estrogen and androgen-dependent processes respectively. 4-*tert*-octylphenol exposure caused dose-dependent formation and maturation of oviducts in both male and female frogs, whereas 17 $\beta$ -Trenbolone exposure caused accelerated regression in males and complete regression in >50% of the females in the 100ng/L treatment making them ostensibly unable to reproduce. Based on these results, it appears that the Müllerian ducts are more sensitive to estrogenic and androgenic influence than are the gonads or other reproductive tissues within the *Xenopus* HPG axis.