Short term fathead minnow reproduction assay generates response profiles broadly consistent with mechanism(s) of action.

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Small fish tests have been a recommended component of regulatory programs proposed for endocrine disrupting chemicals (EDCs). An ideal EDC test would not only identify chemicals with potential to disrupt normal endocrine function, but would also provide diagnostic information regarding likely mechanism(s) of action (MOA) and an assessment of wholeorganism responses relevant for risk assessment (e.g. reproduction). To address these needs, a short term reproduction assay utilizing reproductively-mature fathead minnows (Pimephales promelas) was developed. Endpoints evaluated include biochemical measures (e.g. plasma vitellogenin and steroid concentrations), histological evaluation of gonads and other sexually dimorphic tissues, morphological evaluation of secondary sex characteristics, and measures of general reproductive fitness (e.g. fecundity, fertility, F1 viability). The test has been evaluated using EDCs with known or suspected MOA including strong and weak estrogen receptor agonists (estradiol, methoxychlor), androgen receptor agonists (methyltestosterone, trenbolone), androgen receptor antagonists (vinclozolin, flutamide), and strong and weak inhibitors of steroid metabolism (fadrozole, prochloraz, fenarimol), some of which were expected to have mixed MOA. The test consistently detected the reproductive toxicity of the chemicals, indicating that it broadly meets the goal of providing data for higher-tier risk assessments. Furthermore, the profiles of biochemical, histological, and/or morphological responses observed were generally consistent with the presumed MOA. Correspondingly, chemicals known to have a mixed MOA gave mixed response profiles. Thus the test appears to have some diagnostic utility that may be enhanced through the inclusion of supplemental endpoints. The U.S. Environmental Protection Agency plans to use this assay to help fulfill screening and testing requirements associated with the current EDC regulatory program. The contents of this abstract do not necessarily reflect U.S. EPA policy.