

Development of alternatives to chronic ecotoxicity tests: predicting early-life stage and endocrine-mediated toxicity in aquatic vertebrate species

SETAC meeting in Portland, OR, November, 2010-06-04

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In June 2010, the ILSI Health and Environmental Sciences Institute (HESI) with support from sanofi-aventis, NC3Rs, the Humane Society, L'Oreal, and ECVAM, held a workshop aimed at examining critical science needs related to the development of alternatives to chronic fish toxicity and endocrine disruption tests. It is estimated that demands for long-term (chronic) fish toxicity testing represents approximately 6% of the total animal testing needs for REACH. Though various strategies such as the use of fish cell lines, modelling, and integration of new technologies (such as 'omics') are promising strategies to improve testing strategies and should ultimately result in reducing animal use, their application to chronic toxicity hinges on an understanding of chemical modes of action. Endocrine disruption represents an ideal chronic ecotoxicity case-study, where numerous alternative strategies are already under development, due in large part to the detailed understanding of the specific modes of action. No single replacement, refinement or reduction approach will fit every testing scenario and the need to understand the chronic modes of action are critical for finding viable testing strategies for the variety of applications of ecotoxicological testing. The first half of the workshop focused on the state of data availability for a representative chronic test, the fish early life state test (FELS), addressing the realm of chemicals that have been tested, knowledge of modes of action / adverse outcome pathways for specific chemicals, and what additional supporting information may be available or useful for interpreting these studies. By identifying data quality and availability the workshop participants began the design of a long-term platform to address animal alternative testing strategies for chronic toxicity to fish. The second half of the workshop was dedicated to a detailed evaluation of the current state of the science for non in-vivo detection of endocrine disrupting chemicals in fish and amphibians, including a include a critical discussion of several promising methodologies and the identification of data gaps, research needs, and progression towards validation. Endocrine disruption is a prime example of well-known modes of action for which in vitro / in silico methodologies are already under development and provide promising non- in vivo approaches. Prior to the workshop, a literature search was prepared, with an initial analysis of the advantages and disadvantages of each assay in the context of potential use in an integrated testing strategy, which will be presented in a separate platform session. This poster will present a summary of the workshop outcomes, conclusions, and next steps.