

## **Fish early life stage: developing AOPs to support targeted reduction and replacement**

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There is an interest in developing alternatives to the fish early-life stage (FELS) test (OECD test guideline 210), for predicting adverse chronic toxicity outcomes (e.g., impacts on growth and survival). Development and characterization of adverse outcome pathways (AOPs) related to FELS toxicity can provide a foundation for the design and acceptance of less resource-intensive methods alternative test methods. In May 2012, a HESI-sponsored expert workshop yielded a proposed research strategy for systematically discovering, characterizing, and annotating fish early life-stage (FELS) adverse outcome pathways (AOPs). This presentation illustrates aspects of that strategy using specific examples. Key anatomical and physiological events occurring during the developmental period covered by the FELS test were identified. Review of the extant peer-reviewed literature identified existing knowledge concerning the normal regulation of those developmental events and associated physiological functions. Using the key event of swim bladder development and inflation as an example, we illustrate how basic biological knowledge was mined to develop a series of putative AOPs applicable to FELS development, including one linking thyroid peroxidase inhibition to reduced young of year survival. Empirical testing of this putative AOP led to refined understanding of the life-stage specificity of the AOP and identification of other molecular initiating events and key events that are linked within a broader adverse outcome pathway network. Results illustrate the utility of the AOP framework for aiding the development and evaluation of alternative methods for potential use in regulatory toxicology. *The contents of this abstract neither constitute, nor necessarily reflect, US EPA views or policies.*