Discovering and Annotating Fish Early Life-Stage (FELS) Adverse Outcome Pathways: Putting the Research Strategy into Practice

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ABSTRACT

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) as well as prioritizing AOP development in light of current restrictions and calls for reduction in the use of animals in testing, particularly in the European Union. This presentation illustrates that strategy using specific examples. The scope of AOP development was defined by the desire to develop alternatives to the OECD 210 FELS toxicity test which could increase efficiency and reduce cost. 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. One set of putative AOPs focused on disruptions to swim bladder development while another focused on disruptions to swim bladder function. These putative swim bladder-specific AOPs can be used to identify potential molecular screening assays that may be predictive of impaired swim bladder development or inflation or additional endpoints for inclusion in an extended fish embryo test, as well as to identify critical research gaps. Finally, we discuss the relative priority of conducting research to develop and fill gaps in swim bladder-related AOPs in the context of the overall strategy. *The contents of this abstract neither constitute nor reflect official US EPA policy.*