Track: Aquatic Toxicology and Ecology

Session Title: Alternative Methods for Evaluating Aquatic Toxicity: New Methods, Endpoints, and Testing Strategies

Abstract Title:
Evaluation of hypothesized adverse outcome pathway linking thyroid peroxidase inhibition to fish early life stage toxicity

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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 outcomes (e.g., impacts on growth and survival) using less resource-intensive methods. Development and characterization of adverse outcome pathways (AOPs) related to FELS toxicity can provide a foundation for the design and acceptance of alternative test methods. Two experiments were conducted to begin testing a proposed AOP linking disruption of the thyroid axis via inhibition of thyroid peroxidase to adverse outcomes in fish. Thyroid peroxidase (TPO) is an enzyme necessary for thyroid hormone production. Fathead minnow embryos were exposed to 1 or 5 mg/L of the TPO inhibitor 2-mercaptobenzothiazole (MBT) until 16 or 5 days post fertilization (dpf), respectively. Embryos exposed to 1 mg/L MBT did not show any obvious phenotypic changes as a result of the MBT exposure. However, in fish exposed to the 1 mg/L MBT for 16 dpf, the anterior swim bladder failed to inflate in 16 of 18, likely due to the inhibition of TPO and decreased thyroid hormone synthesis. Embryos exposed to 5 mg/L MBT showed a lack of pigmentation within two days of exposure which continued throughout embryonic development. This observation occurred prior to TPO function, suggesting MBT was impacting another target. Maternally-derived T4 in the yolk is known to be important for early thyroid-dependent development processes. We hypothesize that MBT is inhibiting deiodinase, the enzyme that converts T4 to its more active form T3, during early embryonic development. Our findings suggest that relevant molecular initiating events associated with thyroid axis disruption are life-stage dependent, with thyroid disruption via deiodinase being relevant at embryonic stages and thyroid peroxidase inhibition only becoming relevant when maternally-derived thyroid hormone is depleted. Further studies will be conducted to better link thyroid axis enzyme inhibition to the previously observed biological endpoints. *The contents of this abstract neither constitute, nor necessarily reflect, official US EPA policy.*

Key words: Adverse outcome pathway, thyroid disruption, embryo, fish early-life stage

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