

Initial investigation of a hypothesized link between thyroid peroxidase inhibition and 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. The present study was designed to begin testing a hypothesized AOP linking inhibition of thyroid peroxidase (TPO) activity to FELS toxicity. Fathead minnow embryos were exposed to 1mg/L of the TPO inhibitor 2-mercaptobenzothiazole (MBT) from 2 hours post fertilization to 8 or 16 days post fertilization. Over the initial 8d of exposure survival of the MBT-exposed organisms was 95%. In contrast, mortality was observed in all fish treated with 4 mg 3,4-dichloroaniline/L, a positive control routinely used in zebrafish embryo toxicity assays. Hatching occurred for all MBT-exposed organisms between 96 and 144 hours post fertilization, similar to the control population. Growth, based on length measurements, was significantly different ( $p < 0.05$ ) between the control and MBT-exposed fish with average lengths of  $5.29 \pm 0.14$  mm ( $n=18$ ) and  $5.13 \pm 0.16$  mm ( $n=18$ ), respectively. Hypothesized impacts on jaw development and swim bladder inflation were also examined. This preliminary study will inform the design of additional experiments that will test the hypothesized AOP and identify key events which may serve as useful endpoints/assays to incorporate into an alternative testing strategy.

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

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