Functional Assays and Alternative Species: Using Larval Zebrafish in Developmental Neurotoxicity Screening Stephanie Padilla[1], Megan Culbreth[1,2], Robert C. MacPhail[3,4], Deborah L. Hunter[1], Kimberly Jarema[3], Karl Jensen[3], Jeanene Olin[1], and AlanTennant[1]. [1]ISTD, NHEERL, ORD, US EPA, RTP, NC; [2]Albert Einstein College of Medicine, Bronx, NY; [3]TAD, NHEERL, ORD, U.S. EPA, RTP, NC; [4] VA Tech, Blacksburg, VA; USA

The U.S. Environmental Protection Agency is evaluating methods to screen and prioritize large numbers of chemicals for developmental toxicity. As such, we are exploring a behavioral testing paradigm, which can assess the effects of sublethal and subteratogenic concentrations of developmental neurotoxicants on 6 day larval zebrafish (*Danio rerio*). This assay simultaneously tests individual zebrafish under both light and dark conditions in a 96-well plate using a video tracking system. By controlling the duration and intensity of light, we are able to detect changes in locomotion during light-dark transitions, and adaptation to both light and dark during the approximate 1.5 hour testing period. Multiple chemicals at several concentrations (≤ 120 µM nominal concentration) can be tested in large numbers of larvae using this method. We have evaluated a training set of chemicals (n=22) that are generally considered positive (n=16) or negative (n=6) controls for developmental neurotoxicity in mammals. Many of the developmentally neurotoxic compounds perturbed behavior at subteratogenic doses (*e.g,* lead, heptachlor, chlorpyrifos, chlorpyrifos oxon), while many non-neurotoxic compounds did not (*e.g.*, acetaminophen, saccharin, glyphosate). Exposure to developmental neurotoxicants altered the overall activity level in light and dark conditions, and/or the activity pattern. The zebrafish neurodevelopmental assay using this training set of chemicals had a sensitivity of 0.875 and a specificity of 0.833. The training set results, therefore, indicate that careful evaluation of zebrafish larvae behavior is capable of identifying mammalian developmental neurotoxicants. *This abstract may not necessarily reflect official Agency policy.*