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Use of the Zebrafish Developmental Screen and Estimation of Internal Concentration to Assess Toxicity

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Abstract

Environmental chemicals from the ToxCastTM Phase I chemical library were screened to assess developmental toxicity endpoints. Zebrafish embryos were immersed in media containing one of 309 chemicals tested, at concentrations ranging from 0.001 to 80 μ M. The half-maximal activity concentration (AC₅₀) for toxicity (lethality, non-hatching, or dysmorphology) was determined. The relationship between lipophilicity (LogP) and bioconcentration was used to estimate a body burden associated with developmental toxicity (EC₅₀). Toxicity potency rankings derived from AC₅₀ and EC₅₀ calculations were compared. Some chemicals were highly toxic regardless of how toxicity was expressed while use of EC₅₀ values substantially affected the toxicity ranking of others. The pyrethroids (n=12) were among the most toxic chemicals with a mean AC₅₀ of 4.01 μ M. However, due to their high lipophilicity, the mean EC₅₀ for the class was estimated at 843.25 μ M. The ability of the zebrafish developmental screen to predict mammalian toxicity was assessed by examining the correlation between chemical potencies based on EC₅₀, chemical class, and known *in vivo* effects. *This abstract does not necessarily reflect EPA policy.* This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract Nos. N01-ES-35504 and HHSN27320140003C.