Nanomaterial Toxicity Screening in Developing Zebrafish Embryos

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To assess nanomaterial vertebrate toxicity, a high-content screening assay was created using developing zebrafish, *Danio rerio.* This included a diverse group of nanomaterials (n=42 total) ranging from metallic (Ag, Au) and metal oxide (CeO_2, CuO, TiO_2, ZnO) nanoparticles, to non-metallic nanomaterials (SiO_2 nanoparticles and carbon nanotubes), as well as micro and ion counterparts. Overt toxicity (lethality, dysmorphology, and hatching) was assessed via visual inspection and/or high-content imaging analysis. At 5-7 hours post fertilization, individual embryos were treated in a 96-well plate with the testing material (8 doses, semi-log spacing, n≥3 at each dose). Solutions were renewed daily until 5 days post fertilization (dpf) when the larvae were placed into embryo rearing solution only. At 6 dpf, dysmorphology was assessed via visual inspection. Following visual inspection, fish were euthanized and positioned, and images were recorded and analyzed on the ArrayScan IV automated microscopy system using the Zebratox V3 bioapplication. Results showed little to no overt toxicity, with a few exceptions: some of the nano-Ag and nano-CuO compounds produced dose-related overt toxicity. This result was also seen in the Ag and Cu ions; however, in general, metal salts were more toxic than their corresponding nanoparticles at the same metal mass concentration. Also, nano-ZnO and $ZnCl_2$ did not typically cause lethality or dysmorphology, but did delay hatching. By employing few larvae per dose, we were able to assess toxicity for a relatively large number of different materials, demonstrating the utility of high-content screening of whole organisms as a valuable platform for nanomaterial or other chemical toxicity screening. These results in zebrafish will be combined with data from other ToxCast screening assays for nanomaterials to more fully characterize bioactivity.

This abstract does not necessarily reflect U.S. EPA policy.