The rapidly expanding field of nanotechnology is introducing a large number and diversity of engineered nanomaterials into research and commerce with concordant uncertainty regarding the potential adverse health and ecological effects. With costs and time of traditional animal toxicology being prohibitive for testing all of the many materials being produced, alternative methods using high-throughput screening (HTS) technologies have begun to be used. Here, we tested a broad array of engineered nanomaterials, including many reference materials being tested in other laboratories, across a variety of HTS screening platforms using standard cell lines, primary cells and zebrafish embryos. Standardized protocols were developed that permit parallel testing of many diverse materials in a variety of assays. Nanomaterial physicochemical properties were extensively characterized both as received from the manufacturer and during preparation and treatment of assays. Endpoints measured included cytotoxicity, transcription factor activation, cellular toxicity phenotypes, signaling pathway perturbations and signaling protein level changes in cells, as well as zebrafish embryotoxicity. A limited set of toxicity-associated endpoints were affected including indicators of oxidative stress, generalized cellular stress, cytokine induction and overt cytotoxicity. The results were generally consistent across diverse assay platforms both qualitatively and quantitatively. The HTS assays discriminated between different classes of nanomaterials (e.g. silver vs. zinc vs. carbon nanotubes); however, little qualitative difference was seen between nano- forms of specific materials compared with their atomic form. This suggests that a focus of understanding the toxicology of engineered nanomaterials should be the exposure, absorption, distribution and excretion of nanoparticles as delivery vehicles for their core component, as well as interactions with other chemicals. A caveat of this approach is the lack of HTS assays specific for inhalation toxicity, which is a likely route of exposure to most nanomaterials. These results support the value of using HTS approaches in profiling samples as unique as nanomaterials for understanding their potential for toxicity.

This work was reviewed by U.S. EPA and approved for publication but does not necessarily reflect official Agency policy.