

“Scientific and Regulatory Advances in Safety Evaluation of Heavy Metals in Food” for the 2016 Society of Toxicology Meeting to be held in March 13–17 next year (2016) in New Orleans, Louisiana.

“Heavy Metals in ToxCast: Relevance to Food Safety”

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Human exposure to heavy metals occurs through food contamination due to industrial processes, vehicle emissions and farming methods. Specific toxicity endpoints have been associated with metal exposures, e.g. lead and neurotoxicity; however, numerous varieties of heavy metals have not been systematically examined for potential toxicities. We describe results from testing a large set of heavy metal-containing compounds in extensive suites of in vitro assays to suggest possible molecular initiating events in toxicity pathways. A broad definition of heavy metals that includes As, Se and organometallics or inorganic salts containing metals in Group III or higher (MW > 40) was used to identify 75 different compounds tested in the EPA’s ToxCast assays encompassing biochemical, cellular and model organism assays. These 75, plus an additional 100 metal-containing compounds, were tested in Tox21 quantitative high-throughput screening (qHTS) assays covering nuclear receptor and stress pathways. Known activities were confirmed such as activation of stress pathways and nuclear receptors (RXR, PPAR γ) as well as overt cytotoxicity. Specifically, organotin and organomercury were among the most potent of over 8K chemicals tested. The HTS results support known toxicities, including promiscuous GPCR activity for mercury compounds consistent with the neuropsychiatric effects seen in mercury poisoning (Mad Hatter’s Syndrome). As such, HTS approaches provide an efficient method for surveying potential toxicities of heavy metals and suggest areas of focus to more thoroughly examine toxicity links and define safe exposure limits. These data may be of use to government and industry safety assessors as well as academics and others focused on mechanism of action. [This abstract does not necessarily reflect US EPA policy]