HIGH THROUGHPUT ASSESSMENTS OF CONVENTIONAL AND ALTERNATIVE COMPOUNDS

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High throughput approaches for quantifying chemical hazard, exposure, and sustainability have the potential to dramatically impact the pace and nature of risk assessments. Integrated evaluation strategies developed at the US EPA incorporate inherency, bioactivity, bioavailability, metabolism and other properties critical to predicting and modeling toxicodynamics and toxicokinetics. Combined hazard and exposure predictions make it possible to derive relative estimates of risk for chemicals and proposed "green" alternatives. The U.S. EPA's ToxCast research project uses high throughput screening (HTS) and a pathway-based approach to predict chemical hazard. Phase I and II of ToxCast tested 1060 unique compounds, including 135 failed pharmaceuticals donated by industry partners, reference compounds known to be endocrine disruptors, carcinogens or reproductive/developmental toxicants, high-production volume chemicals, food additives, cosmetic ingredients, and proposed alternatives to commonly used plasticizers and surfactants. HTS results are presented from this large-scale high throughput screen using cutting edge research on bioactivity, dosimetry and exposure, with a specific focus on practical incorporation of sustainability metrics. Initial analysis of 51 chemicals in Phase I and II of ToxCast included BPA and TGSA; the surfactants PFOA, PFOS and 4 alternatives; 18 phthalate plasticizers and 25 alternatives. Predictive models for reproductive and developmental toxicity, based on ToxCast data, were used to generate Toxicological Prioritization Index (ToxPi) rankings of chemicals. In general alternatives had lower predicted reproductive or developmental toxicity than conventional plasticizers or surfactants. An in silico vasculogenesis model was also used to compare chemicals potential to disrupt this important cellular process in tissue development. This work demonstrates the ability for rapid *assessment of* "green" alternatives supporting timely, transparent and sustainable decisions.