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Human Exposure Estimates and Oral Equivalents of *In Vitro* Bioactivity for Prioritizing, Monitoring and Testing of Environmental Chemicals

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High-throughput, lower-cost, *in vitro* toxicity testing is currently being evaluated for use in prioritization and eventually for predicting *in vivo* toxicity. Interpreting *in vitro* data in the context of *in vivo* human relevance remains a formidable challenge. A key component in using *in vitro* data to predict *in vivo* toxicity is dosimetry sufficient to establish dose-response relationships. We modeled dosimetry using metabolic clearance rates from cryopreserved human hepatocytes, human plasma protein binding, and the population-based kinetic simulation software and database Simcyp© to calculate human oral equivalent doses of the *in vitro* AC50 (50% activity concentration) or LEC (lowest effective concentration) for 36 chemicals in 467 ToxCast Phase I assays. SimCyp results were compared to published PBPK models to assess model performance. Human oral equivalents of ToxCast *in vitro* results were compared to EPA chronic aggregate human oral exposure estimates, chronic population adjusted doses (cPAD) for humans, and no observed and lowest observed adverse effect levels (NOAEL and LOAEL) from animal toxicity studies. EPA estimates of human exposure and cPAD were available for 19 of the 36 chemicals. NOAEL and LOAEL were available for almost all 36 chemicals. These data were used to develop prioritization methods applicable to environmental chemicals and based on doses associated with *in vitro* bioactivity, estimates of human exposure, doses considered acceptable for human populations, and doses in animal studies that do and do not cause adverse effects. *In vivo* bioactivity based on predicted oral equivalents and estimated human exposures could be interpreted as a higher priority for further testing and monitoring. *Approved for publication but does not necessarily reflect Agency policy.*