PRELIMINARY ASSESSMENTS OF *IN VITRO* PHARMACOKINETIC DATA AND EXPOSURE INFORMATION FOR THE TOXCAST PHASE II CHEMICALS

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Momentum has been growing in Toxicology to assess the utility of high-throughput screening (HTS) assays in the determination of chemical testing priorities. However, *in vitro* potencies determined in these assays do not consider *in vivo* bioavailability, clearance or exposure estimates, limiting their value as indicators of potential human health risk. We previously used ToxCast Phase I chemicals to assess the integration of *in vitro* pharmacokinetic (PK) and HTS data to extrapolate the daily dose required to obtain blood concentrations equivalent to those eliciting bioactivity in *in vitro* assays. This daily dose was then compared to human exposure estimates to aid in prioritization. Unlike the Phase I set, comprised primarily of food-use, data-rich pesticides, the ~700 chemicals in Phase II are much more diverse structurally and in their usage and exposures. *In vitro* hepatic clearance and plasma protein binding assay data generated for Phase II chemicals indicate similar distributions to those observed with the Phase I set. The majority of chemicals are highly bound to plasma proteins, with median and upper quartile values at ~3 and ~20% unbound, respectively, for both sets. *In vitro* hepatic metabolic clearance values are also similar, with median and upper quartile values at ~8 and ~18 µL/min/106 cells, respectively, for both. In contrast to the Phase I chemicals, review of USEPA and CDC documents revealed that human exposure estimates are available for <10% of the Phase II chemicals. Our data indicate that the PK behavior of Phase II chemicals is similar to that of the Phase I set. Strategies to provide human exposure estimations, in part through EPA's ExpoCast project, are being explored to compensate for the limited information available for these chemicals.
This abstract does not necessarily reflect EPA policy.