

## Evaluating High Throughput Toxicokinetics and Toxicodynamics for IVIVE

Authors: John Wambaugh, Robert Pearce, Greg Honda, Mike Hughes, Caroline Ring, Ly Pham, Barbara Wetmore, R. Woodrow Setzer

High-throughput screening (HTS) generates *in vitro* data for characterizing potential chemical hazard. TK models are needed to allow *in vitro* to *in vivo* extrapolation (IVIVE) to real world situations. The U.S. EPA has created a public tool (R package “httk” for high throughput toxicokinetics) for TK and physiologically-based TK (PBTk). We are now able to rapidly parameterize generic PBPK models using *in vitro* data to allow IVIVE for 543 chemicals. We evaluate using four R’s: We have (1) Reused existing TK data by compiling a library of TK time course data in, this data has (2) Refined the design of *in vivo* TK studies, allowing us to perform new, informative experiments for high value chemicals using a (3) Reduced (n=6) study design. Careful evaluation of the existing and new data allows comparison of the results of *in vitro* HTS bioactivity assays with previously collected *in vivo* toxicity studies. In some cases, we may be able to (4) Replace *in vivo* animal studies with HTS and HTTK. *This abstract does not necessarily reflect U.S. EPA policy.*