

**Title:** A Quantitative Source-to-Outcome Case Study To Demonstrate the Integration of Human Health and Ecological End Points Using the Aggregate Exposure Pathway and Adverse Outcome Pathway Frameworks

**Abstract:**

Exposure to environmental contaminants can lead to adverse outcomes in both human and nonhuman receptors. The Aggregate Exposure Pathway (AEP) and Adverse Outcome Pathway (AOP) frameworks can mechanistically inform cumulative risk assessment for human health and ecological end points by linking together environmental transport and transformation, external exposure, toxicokinetics, and toxicodynamics. This work presents a case study of a hypothetical contaminated site to demonstrate a quantitative approach for implementing the AEP framework and linking this framework to AOPs. We construct an AEP transport and transformation model and then quantify external exposure pathways for humans, fishes, and small herbivorous mammals at the hypothetical site. A Monte Carlo approach was used to address parameter variability. Source apportionment was quantified for each species, and published pharmacokinetic models were used to estimate internal target site exposure from external exposures. Published dose-response data for a multispecies AOP network were used to interpret AEP results in the context of species-specific effects. This work demonstrates (1) the construction, analysis, and application of a quantitative AEP model, (2) the utility of AEPs for organizing mechanistic exposure data and highlighting data gaps, and (3) the advantages provided by a source-to-outcome construct for leveraging exposure data and to aid transparency regarding assumptions.

**Bio:**

Dr. Hines is a senior computational toxicologist at Integrated Laboratory Systems Inc. in Research Triangle Park, North Carolina. He specializes in network flow modeling, environmental transport and transformation modeling, Physiologically Based Pharmacokinetic (PBPK) modeling, Bayesian approaches, and statistical analyses. His research focuses on the integration and evaluation of complex data sets to inform risk assessment and decision making, and in recent work he has developed applications of mechanistic frameworks such as Aggregate Exposure Pathways and Adverse Outcome Pathways to integrate data and inform both environmental and human health risk assessments. The work being presented by Dr Hines today on the integration of human health and ecological endpoints uses these frameworks in a source-to-outcome approach, and was conducted while he was in a previous position at the US Environmental Protection Agency.