Cross-Species Extrapolation of Chemical Effects: Challenges and New Insights. Gerald Ankley, USEPA, ORD, Duluth, MN, USA.

One of the greatest uncertainties in chemical risk assessment is extrapolation of effects from tested to untested species. While this undoubtedly is a challenge in the human health arena, species extrapolation is a particularly daunting task in ecological assessments, where it is not uncommon for toxicity data from a few (perhaps one) species to be extrapolated to thousands. Past approaches to dealing with this have relied on the application of uncertainty factors which, only occasionally, can be based on empirical toxicity data. Pathway-based approaches offer an opportunity to conduct effective cross-species extrapolations in the absence of comparative whole-animal toxicity information. Specifically, through an understanding of taxonomic conservation of biological pathways whose perturbation results in unacceptable effects on survival, growth, and reproduction, predictions can be made as to the relative susceptibility of different taxa to chemicals that impact these pathways. Adverse outcome pathways (AOPs) offer a logical framework through which to understand and assess conservation of the molecular initiating events (MIEs), and subsequent key events through which chemicals affect biological processes. Emerging bioinformatic, genomic, and cellular tools offer substantial opportunities to evaluate and quantify evolutionary relationships of AOPs across species in the context MIEs/key events, thereby providing a technically-defensible foundation for cross-species extrapolation of chemical effects in the absence of extensive empirical data. This presentation will provide the background and conceptual basis for several subsequent talks focused on the use of new technologies for cross-species toxicological extrapolation. *The contents of this abstract do not reflect EPA policy.*