Adverse Outcome Pathways: From Research to Regulation
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Exposure and Dosimetry Considerations for AOPs

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Risk is a function of both of hazard and exposure. Toxicokinetic (TK) models can determine whether chemical exposures produce potentially hazardous tissue concentrations. Whether or not the initial molecular event (MIE) in an Adverse Outcome Pathway (AOP) occurs depends on both exposure and TK. As high throughput screening (HTS) identifies putative MIEs and key events, chemical-specific TK and exposure data will be needed to make prioritizations based on risk. For thousands of chemical currently undergoing HTS for bioactivity (*e.g.*, Tox21), information on TK and exposure are lacking. Successful methods have been developed for pharmaceutical compounds to determine TK from limited *in vitro* measurements and chemical structure-derived property predictions. These high throughput TK (HTTK) methods provide a more rapid and less resource–intensive alternative to traditional TK model development. Complementary exposure science is also needed to assess risk; and the U.S. Environmental Protection Agency (EPA)'s ExpoCast initiative has been developing mechanistic and heuristic models for high-throughput exposure (HTE). Jointly, HTS, HTTK, and HTE can move risk-based evaluation earlier in chemical management decisions. *This abstract does not necessarily reflect Agency policy.*