Adverse Outcome Pathway (AOP) Development: Guiding Principles and Best Practices

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Adverse outcome pathways (AOPs) represent a conceptual framework that can support greater application of mechanistic data in regulatory decision-making. However, in order for the scientific community to collectively address the daunting challenge of describing relevant toxicological response motifs that cover the diversity of biological and exposure contexts of concern to human health and ecological risk assessment, it is critical that AOPs be developed in accordance with a set of core principles and best practices. For example, a set of fundamental principles that guide AOP development is that (1) AOPs are not chemical specific; (2) AOPs are modular and composed of reusable components – notably key events (KEs) and key event relationships (KERs); (3) individual AOPs are a pragmatic unit of development and evaluation; (4) AOP networks are expected to be the functional unit of prediction; and (5) AOPs are living documents. Key events are the functional unit of measurement/observation within an AOP. Best practices for KE description suggest that each KE should be defined with sufficient specificity to bound it within a particular level of biological organization, but only as specifically as needed to define function. Molecular initiating events and adverse outcomes are specialized cases of KEs that bound the upstream and downstream ends of an AOP, respectively. Key event relationships represent the functional unit of inference and extrapolation within the AOP, define directed relationships between KEs, and support the assembly of a weight of evidence. This presentation will introduce core principles and best practices underlying AOP development and the rationale behind them. *The contents of this abstract neither constitute nor necessarily represent official US EPA views and policies.*