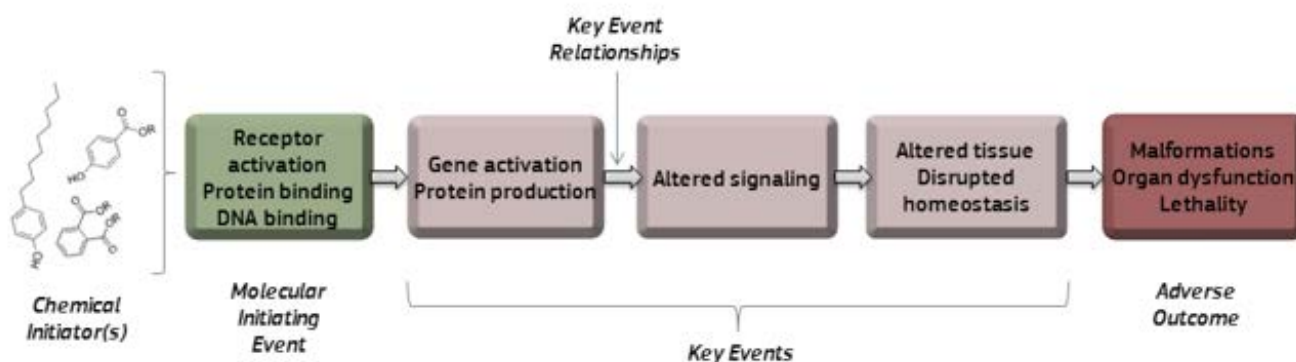


CHEMICAL SAFETY RESEARCH: ADVERSE OUTCOME PATHWAYS



Background

An adverse outcome pathway (AOP) is a conceptual framework that shows existing knowledge concerning the linkage between a chemical interacting with a biological process, a direct molecular initiating event and an adverse human or environmental health risk. The goal of an AOP is to provide the framework that connects the events of the chemical interaction that starts a molecular initiating event and leads to an adverse health outcome.

It is important to understand and map AOPs to be able to use high-throughput toxicological data, such as those available from the ToxCast program, for chemical risk assessments and regulatory decisions. Information used to help develop AOPs comes from *in*

vitro data, animal toxicity studies and computational systems. AOPs allow scientists to connect results from the *in-vitro* tools and rapid screening protocols to actual adverse outcomes.

The US Environmental Protection Agency, in collaboration with the international scientific community, the European Joint Research Center, the US Army Corp of Engineers and the Organization of Economic Cooperation and Development are developing AOP tools to facilitate using AOPs to help evaluate the safety of chemicals.

AOP Knowledge Base

The AOP Knowledge Base is the foundational web-based platform designed to bring together comprehensive

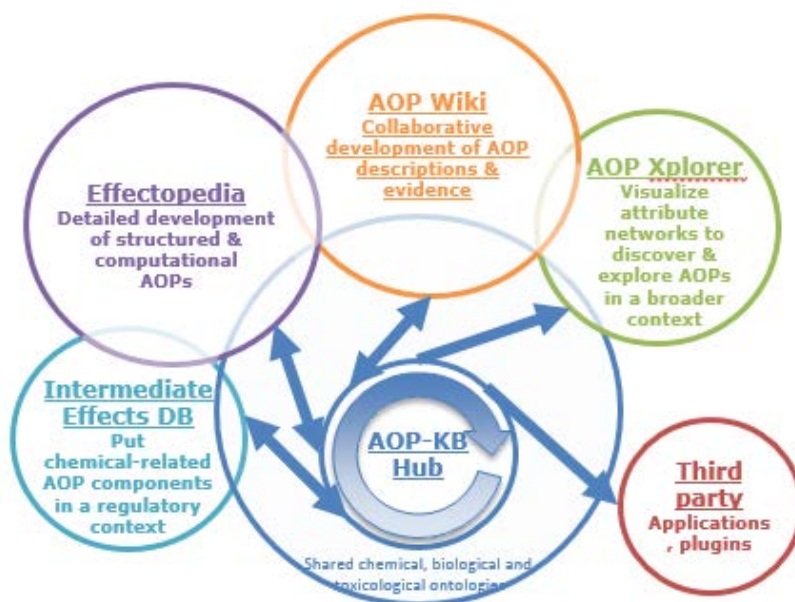
knowledge on how chemicals can prompt adverse outcomes. This platform develops and disseminates various AOP modules as they are publicly available.

AOP Wiki

The AOP Wiki is a module of the AOP Knowledge Base that is publicly available. It is an interactive and virtual encyclopedia for AOP development and is intended to help the international scientific community recognize and agree on AOPs.

The AOP Wiki allows users to develop new AOPs and take advantage of AOPs already developed. The easy-to-use tool stimulates open, crowd-sourced knowledge to capture and use AOPs. The Wiki uses templates to make it easy for users to include the information needed

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 for proper evaluation of an AOP. These templates are based on OECD guidance so that fully developed AOPs from the wiki can be used in a regulatory context. The idea is to develop AOPs using user-friendly widgets instead of requiring users to learn a wiki language. This simplifies the process for scientists and users who may not have extensive experience with editing wikis. In addition, a controlled vocabulary promotes consistent terminology, avoiding unnecessary duplication of information in the wiki.



The AOP KB will also contain additional modules to capture textual knowledge from existing chemical evaluation studies. The *AOP Xplorer* module will support AOP development and highlight the interconnections among AOPs via network viewing tools.

An *Intermediate Effects Database* module will provide AOP information in a format acceptable for regulatory purposes.

The *Effectopedia* module will facilitate the collaborative development and utilization of AOPs through a visually expressed modular structure.

Together, these modules will be able to share, exchange, and

synchronize information to form a comprehensive collection of AOP knowledge based on internationally accepted standards.

The AOP Wiki is publicly available for anyone to view. To be granted Wiki editing rights, interested users should request access and provide a summary of how they can contribute expertise to the development and evaluation of AOPs.

Timeline: 2014 and beyond

The AOP Wiki will be integrated with other components of the AOP KB as they become publicly available. The focus is on formalizing AOP information to facilitate computational modeling.

More information

AOP Wiki: <http://aopwiki.org/>

EPA's chemical safety research: <http://epa.gov/research/chemicalscience/>

OECD: <http://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm>

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