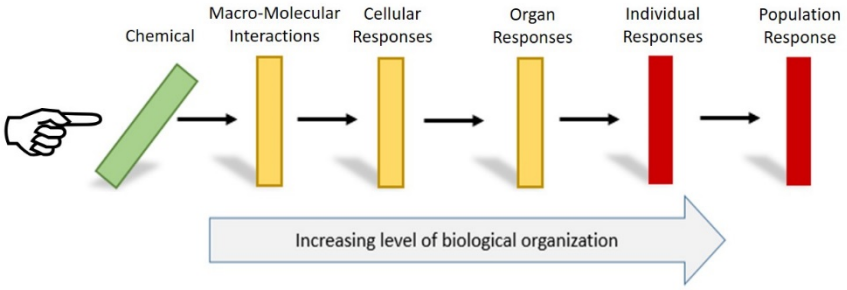
ADVERSE OUTCOME PATHWAY

Background

The same way you might piece together a jigsaw puzzle, scientists at the EPA are working hard to piece together information about the potential biological effects caused by chemicals in the environment. Their aim is to collect and connect biological information to create a fuller picture of how toxicity may be expressed in the body. The approach is helping to develop a consistent way for scientists worldwide to organize biological information-- a priority for the EPA. The science behind this approach is called Adverse Outcome Pathways, or "AOPs." An AOP is a framework for organizing these data, thereby creating context to help better understand the bigger picture.

Currently, only a relatively small percentage of chemicals we are exposed to everyday have been evaluated in traditional toxicity tests. The good news is that we have massive amounts of information from various sources that can help us understand potential effects of the remaining chemicals in the market. And, we have the additional benefit of newer high-throughput screening methodologies which can be used to inform the potential effects of chemical exposure. But until AOPs, there was no consistent way to pull all this data together to understand it in context.



AOPs enable us to better use all existing information to evaluate "data poor" chemicals, even though they have not gone through the time intensive and expensive traditional toxicity tests. They allow scientists and decision-makers to access the latest scientific information to efficiently and effectively evaluate the safety of chemicals.

Here's how it works

An AOP maps out how a stressor (e.g. chemical) interacts within an organism to cause adverse effects. If the amount of the chemical is sufficient, then cells can be affected, which can then affect tissues (which are collections of cells), organs (which are collections of tissues), and, ultimately, the health of the organism or even the population as a whole. By understanding the individual key events, one can better understand what the health outcome will be. Information used to develop AOPs can come from *in vitro* assays, animal studies and computational models. AOPs allow scientists to connect the *in vitro* results generated from rapid screening protocols to actual adverse outcomes.

Standardizing the Adverse Outcome Pathway Approach

The AOP approach requires coordination and consistency among scientists worldwide to ensure their ability to inform chemical risk assessments and regulatory decisions. The EPA, in collaboration with the international scientific community, the European Joint Research Center, the US Army Corp of Engineers, the Organization of Economic Cooperation and Development (OECD), and others are developing standardized approaches and tools to facilitate consistent development of AOPs. These collaborations enable global "crowd sourcing" of information and establish common standards for mutual acceptance of data across borders.

Adverse Outcome Pathway Databases and Tools

The AOP Knowledge Base is an internationally accessible and searchable web-based resource for AOP information. The AOP Knowledge Base was designed to bring together comprehensive knowledge on how chemicals can result in adverse outcomes. This platform serves as a portal to share AOP tools and resources as they become publicly available.

The AOP Wiki is an interactive and virtual encyclopedia for AOP development intended to help the international scientific community recognize and agree on AOPs. The AOP Wiki is maintained as part of the AOP Knowledge Base.

- 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 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.

- A controlled vocabulary promotes consistent terminology, avoiding unnecessary duplication of information in the Wiki.

- 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.

More information

- **EPA's AOP Research Brief:** https://www.epa.gov/chemical-research/adverse-outcome-pathway-aop-research-brief

- **AOP Knowledge Base:** http://aopkb.org/background.html

- **AOP Wiki:** http://aopwiki.org/

- **EPA's chemical safety research:** https://www.epa.gov/chemical-research

- **Organization of Economic Cooperation and Development:** http://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-_and-toxicogenomics.htm

- **For technical assistance/access:** aopwiki@googlegroups.com