An introduction to Navigating the AOP-Wiki

NAMs Training Workshop

RTP, NC

April 25, 2024

Dan Villeneuve, US EPA, Great Lakes Toxicology and Ecology Division

2004

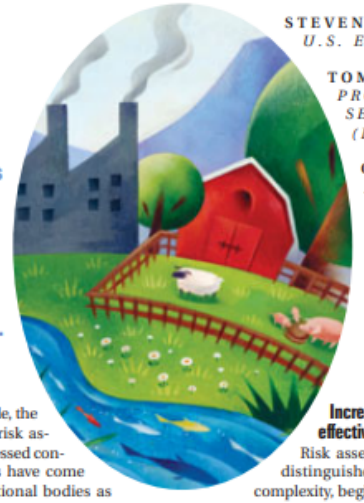
Meeting *the* Scientific Needs *of* Ecological RISK Assessment *in* a Regulatory Context

STEVEN P. BRADBURY
U.S. EPA

TOM C. J. FEIJTEL
PROCTER & GAMBLE SERVICES COMPANY NV/SA (BELGIUM)

CORNELIS J. VAN LEEUWEN
EUROPEAN COMMISSION

Three strategies could move both science and regulation forward.



During the past decade, the field of ecological risk assessment has progressed considerably. Advances have come from such international bodies as the Organisation for Economic Co-operation and Development (OECD), the World Health Organisation (WHO), the European and Mediterranean Plant Protection Organisation (EPPO), and the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) (*1–8*). Risk assessments have played a critical role in the development of various regulations within the European Commission (EC) as well as in other parts of the world, including the United States, Canada, and Japan (*9–17*). But scientists and regulators are faced with three significant challenges: streamlining the risk-assessment process, quantifying risks in a spatially explicit manner, and acquiring the correct kind of environmental data to enable regulatory programs to effectively focus on future environmental protection activities.

Increasing efficiency, cost-effectiveness, and focus

Risk assessment is a tiered process distinguished by levels of increasing complexity, beginning with the preliminary categorization step, followed by a refined or screening assessment, and progressing to the full, comprehensive risk assessment (*4, 18, 19*). For each tier, a minimum level of information is required. For example, OECD has established an international program—called the Screening Information Data Sets (SIDS)—for surveying high-production-volume chemicals (HPV) for potential effects. SIDS include the basic information needed to perform a preliminary assessment of a chemical's potential risk (*20*).

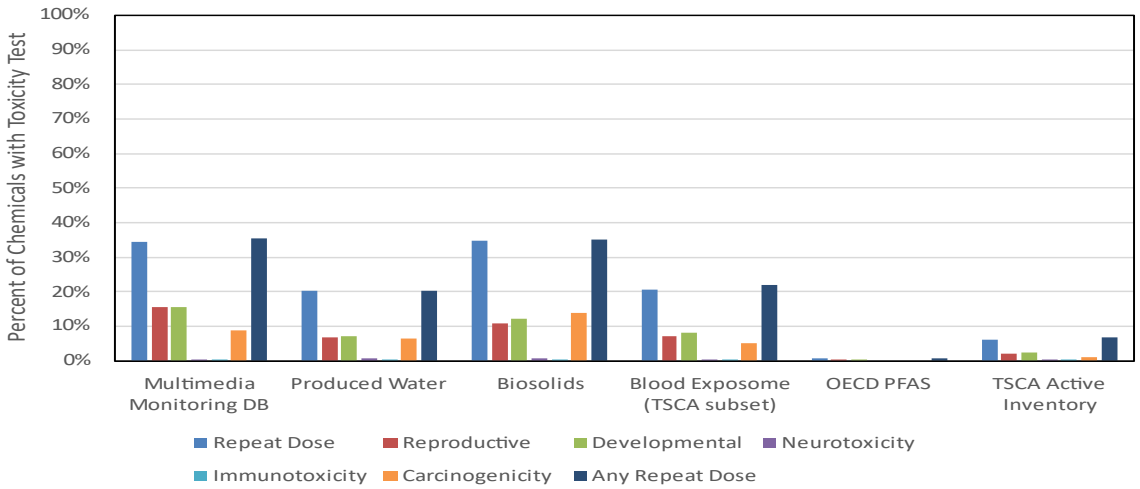
Applying the current risk-assessment paradigm and meeting the associated data-generation requirements, combined with the increased need to evaluate the potential effects posed by thousands of industrial chemicals, are big challenges for the chemical industry, national and international regulatory

JUN ISHIDA

Traditional testing with defined batteries of in vivo tests

- Too many chemicals
- Too costly
- Too much time to generate and interpret
- Too many animals
- Inefficient
  - Typically only a subset of the data are used for the assessments

Bradbury SP, Feijtel TC, Van Leeuwen CJ. Meeting the scientific needs of ecological risk assessment in a regulatory context. Environ Sci Technol. 2004 Dec 1;38(23):463A-470A. doi: 10.1021/es040675s.



Meeting *the* Scientific Needs *of* Ecological RISK Assessment *in* a Regulatory Context

STEVEN P. BRADBURY
U.S. EPA

TOM C. J. FEIJTEL
PROCTER & GAMBLE SERVICES COMPANY NV/SA (BELGIUM)

CORNELIS J. VAN LEEUWEN
EUROPEAN COMMISSION

Three strategies could move both science and regulation forward.

During the past decade, the field of ecological risk assessment has progressed considerably. Advances have come from such international bodies as the Organisation for Economic Co-operation and Development (OECD), the World Health Organisation (WHO), the European and Mediterranean Plant Protection Organisation (EPPO), and the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) (*1–8*). Risk assessments have played a critical role in the development of various regulations within the European Commission (EC) as well as in other parts of the world, including the United States, Canada, and Japan (*9–17*). But scientists and regulators are faced with three significant challenges: streamlining the risk-assessment process, quantifying risks in a spatially explicit manner, and acquiring the correct kind of environmental data to enable regulatory programs to effectively focus on future environmental protection activities.

Increasing efficiency, cost-effectiveness, and focus

Risk assessment is a tiered process distinguished by levels of increasing complexity, beginning with the preliminary categorization step, followed by a refined or screening assessment, and progressing to the full, comprehensive risk assessment (*4, 18, 19*). For each tier, a minimum level of information is required. For example, OECD has established an international program—called the Screening Information Data Sets (SIDS)—for surveying high-production-volume chemicals (HPV) for potential effects. SIDS include the basic information needed to perform a preliminary assessment of a chemical's potential risk (*20*).

Applying the current risk-assessment paradigm and meeting the associated data-generation requirements, combined with the increased need to evaluate the potential effects posed by thousands of industrial chemicals, are big challenges for the chemical industry, national and international regulatory

- If one assumes all chemicals on “a list” do not need to be tested, and for those that do, not all can be tested for all possible endpoints at once, then the following questions must be addressed:
  - Which chemicals should be tested *[in vivo]*?
  - And of these, which should be tested first?
  - For what endpoints [*in vivo*]?
  - On the basis of what rationale?

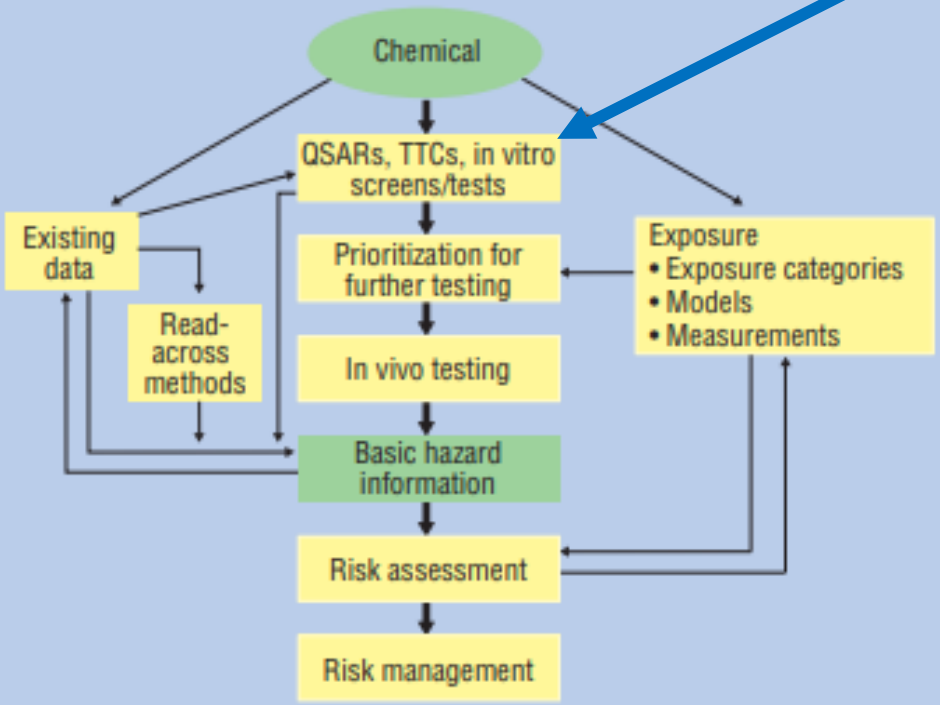
Bradbury SP, Feijtel TC, Van Leeuwen CJ. Meeting the scientific needs of ecological risk assessment in a regulatory context. Environ Sci Technol. 2004 Dec 1;38(23):463A-470A. doi: 10.1021/es040675s.

2004

FIGURE 1

Efficient risk assessment

Combining use and exposure information and effects information obtained from quantitative structure–activity relationships (QSARs), read-across methods, thresholds of toxicological concern (TTCs), and in vitro tests prior to in vivo testing is a more rapid, efficient, and cost-effective way to perform risk assessment of chemicals.



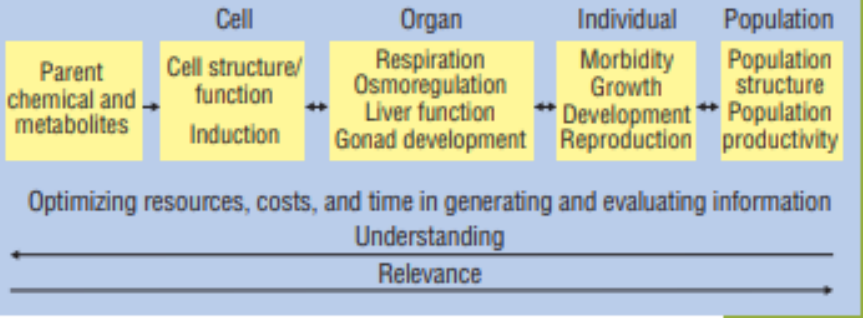
NAMs

FIGURE 2

Toxicity pathways

AOPs

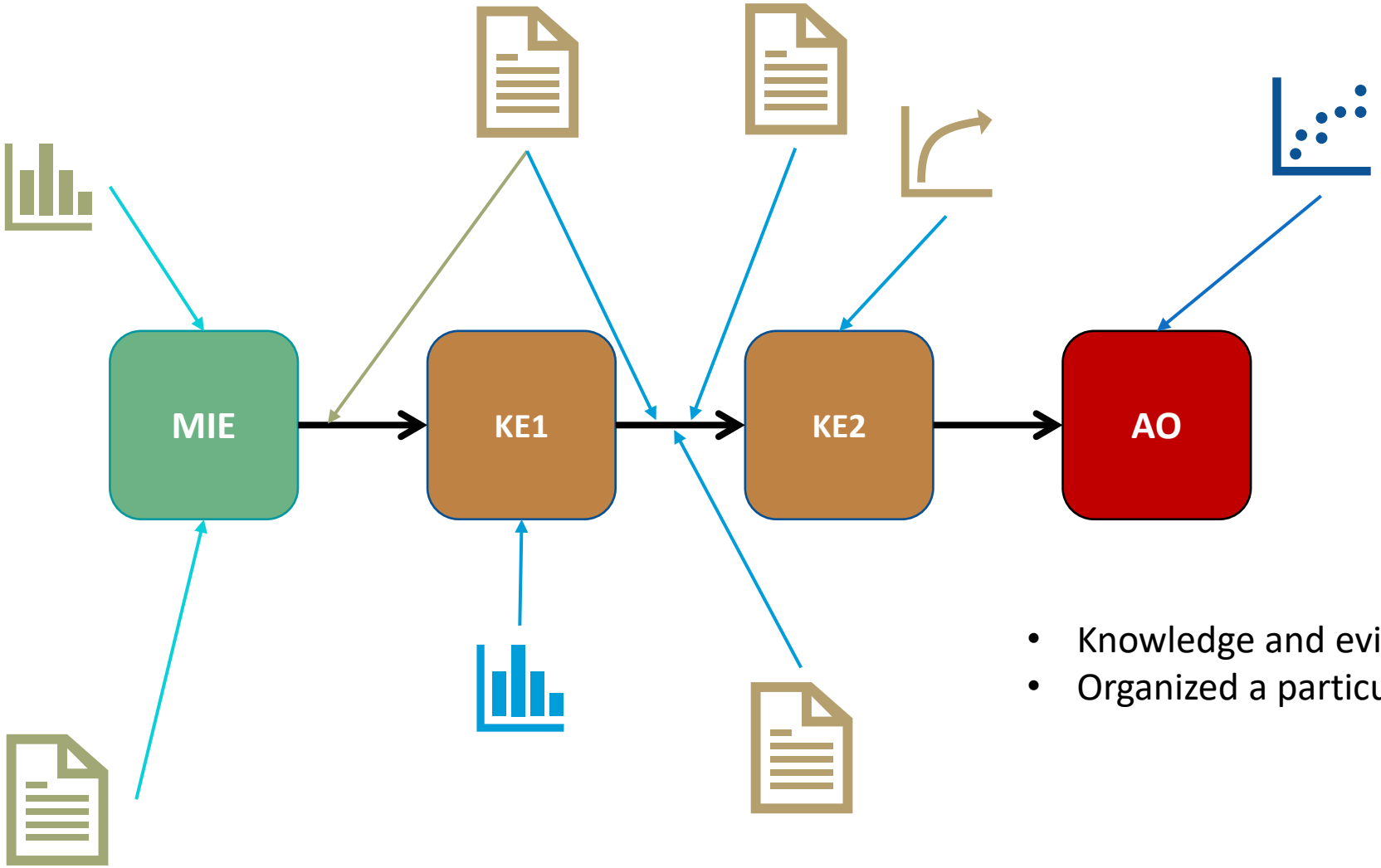
Linking toxicological responses across levels of biological organization would help prioritize risk-based assessment questions and associated data and information needs.



Bradbury SP, Feijtel TC, Van Leeuwen CJ. Meeting the scientific needs of ecological risk assessment in a regulatory context. Environ Sci Technol. 2004 Dec 1;38(23):463A-470A. doi: 10.1021/es040675s.

Adverse Outcome Pathways (AOPs)

Support inference from the properties we can measure (or model) rapidly, cost-effectively, efficiently (i.e., NAMs), to the effects that matter to decision-making/ policy-setting/ management.

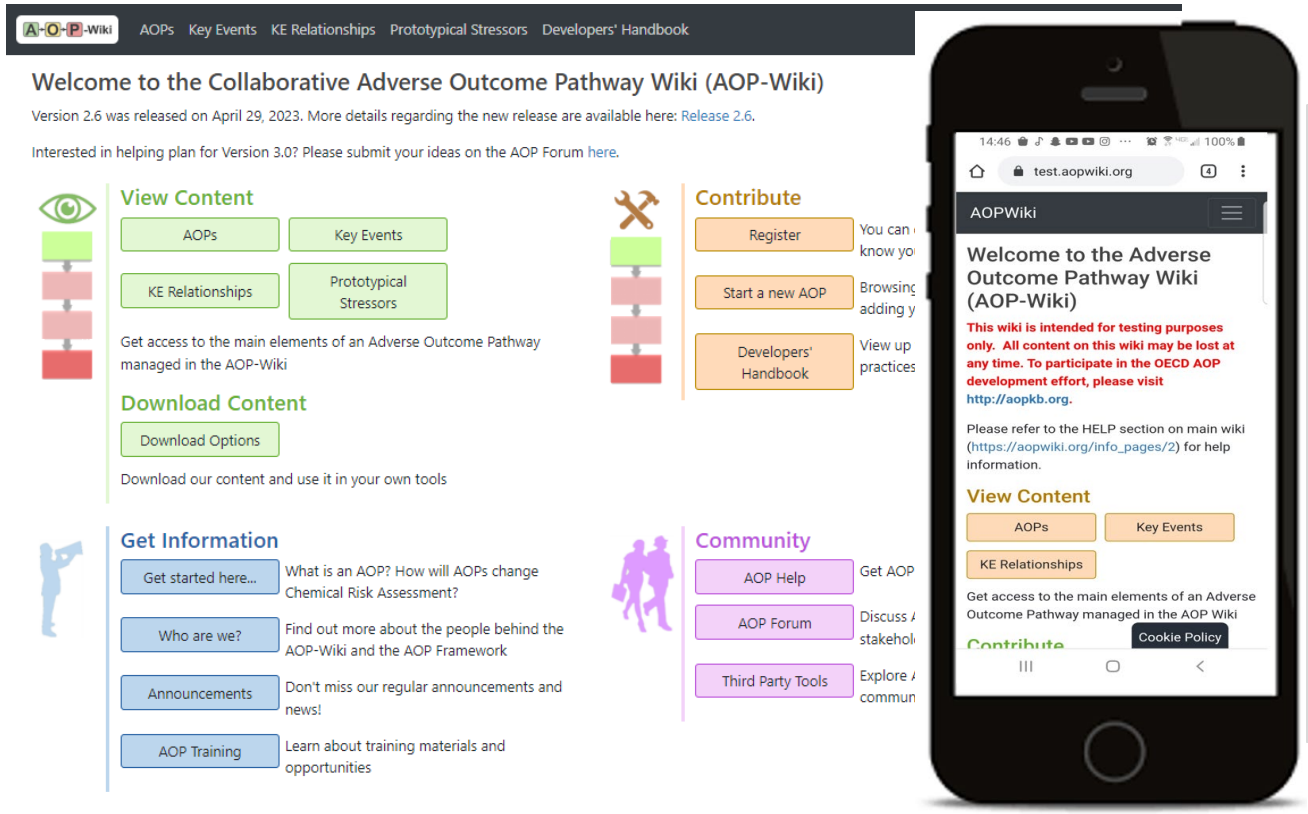


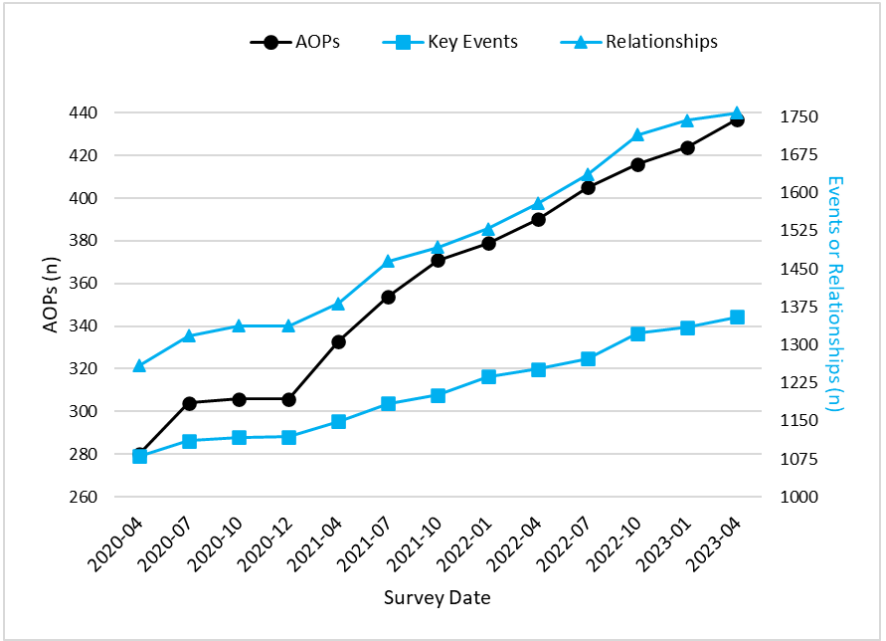
- Knowledge and evidence
- Organized a particular way

Slide adapted from – Elizabeth Huliganga

AOPwiki.org

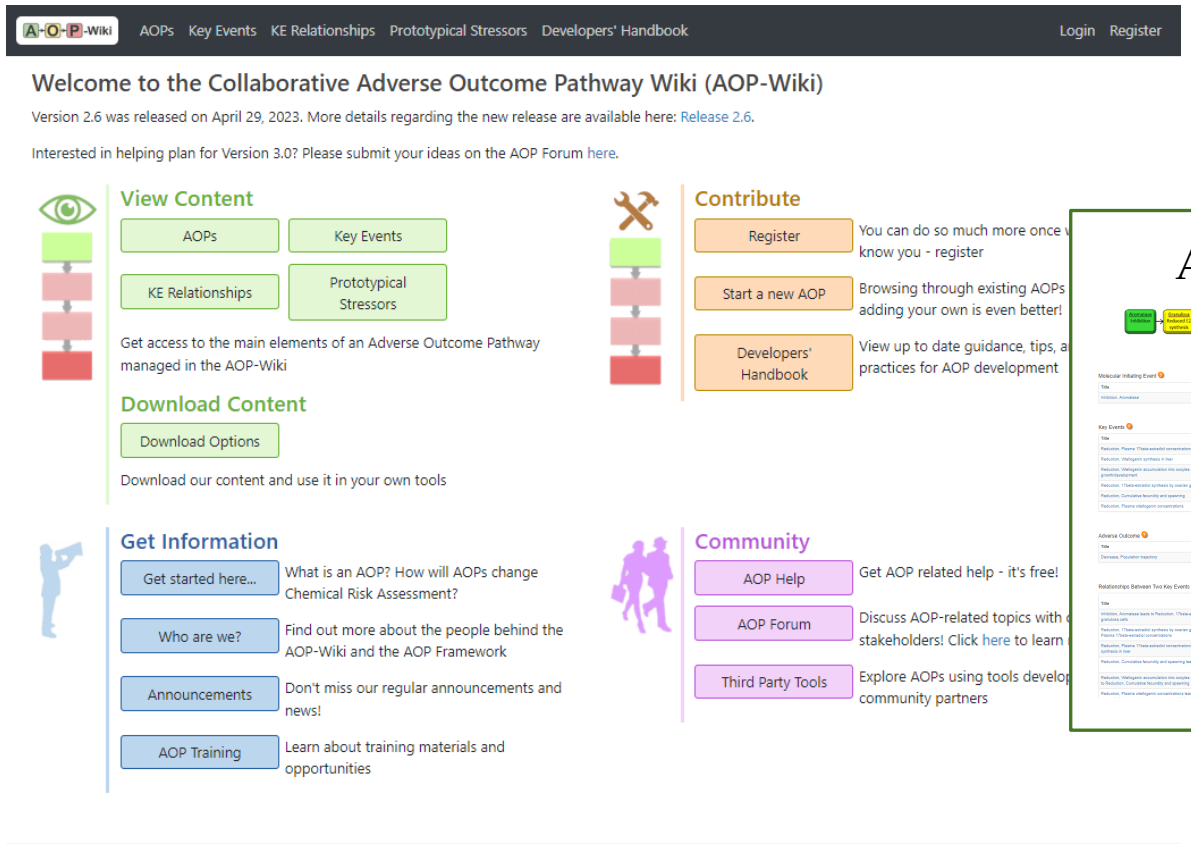
- Harmonized, globally accessible source of scientific information organized according to the AOP framework.
- Intended to support a wide range of NAMs-based decision-making





Organization of the AOP-Wiki

- Three main page-types



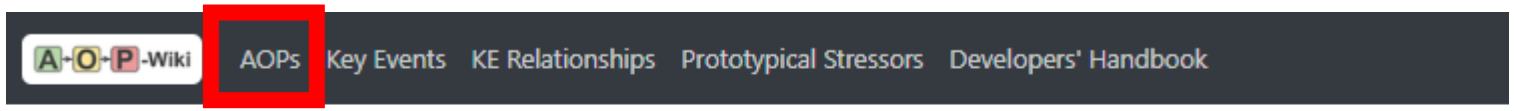
KE Pages

- Description
- Measurement/ detection
- Domain of applicability

KER Pages

- Title
- Description
- Biological plausibility
- Empirical support
- Inconsistencies and uncertainties
- Quantitative understanding

Navigating the AOP-Wiki



Welcome to the Collaborative Adverse Outcome Pathway Wiki (AOP-Wiki)

Version 2.7 was released on March 30, 2024. More details regarding the new release are available here: Release 2.7.

Search AOPs... Search | Find by ID Find by ID | OECD View | API

AOPs

Filtered AOP Count: 469

ID	Title	Point of Contact	License	MIE	AO	OECD Status	OECD Project
			Clear			Clear	
443	DNA damage and mutations leading to Metastatic Breast Cancer	Usha Adiga	BY-SA	• Increased, DNA damage and mutation	• metastatic breast cancer	Under Development	1.103
450	Inhibition of AChE and activation of CYP2E1 leading to sensory axonal peripheral neuropathy and mortality	SAROJ AMAR	BY-SA	• Acetylcholinesterase (AchE) Inhibition	• Sensory axonal peripheral neuropathy • Increased Mortality		
202	Inhibitor binding to topoisomerase II leading to infant leukaemia	Andrea Terron	BY-SA	• Binding to (interferes with) topoisomerase II enzyme	• Infant leukaemia	WPHA/WNT Endorsed	1.53
389	Oxygen-evolving complex damage leading to population decline via inhibition of photosynthesis	Knut Erik Tollefsen	BY-SA	• Increase, Oxygen-evolving complex damage	• Decrease, Reproduction • Decrease, Population growth rate		
423	Toxicological mechanisms of hepatocyte apoptosis through the PARP1 dependent cell death pathway	Fei Li	BY-SA	• Activation, PARP1 • ROS formation	• Apoptotic cell death		
98	5-hydroxytryptamine transporter (5-HTT; SERT) inhibition leading to	Ksenia Groh	BY-SA	• Inhibition, 5-hydroxytryptamine transporter (5-	• Increased, predation		1.29

List pages

Search AOPs... Search

- In title
- Anywhere on page

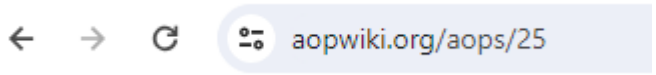
Find by ID Find by ID

- Must click “find by ID”
- Enter will not work

Similar search and filter options are available on the Key Events and Key Event Relationships list pages as well

Navigating the AOP-Wiki

Content pages



URL will always tell you what page type you're on
Unique identifier for each page (citable)

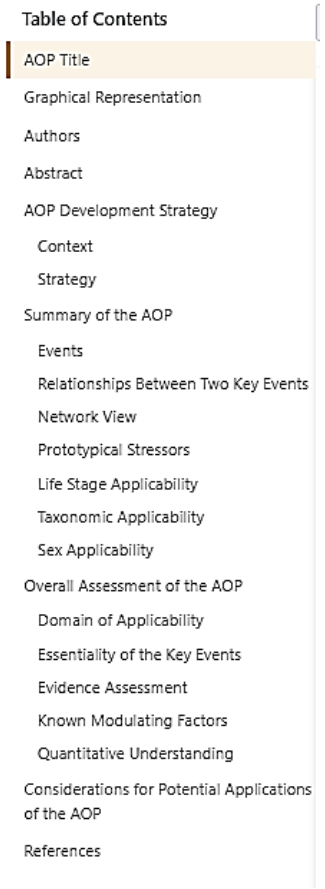
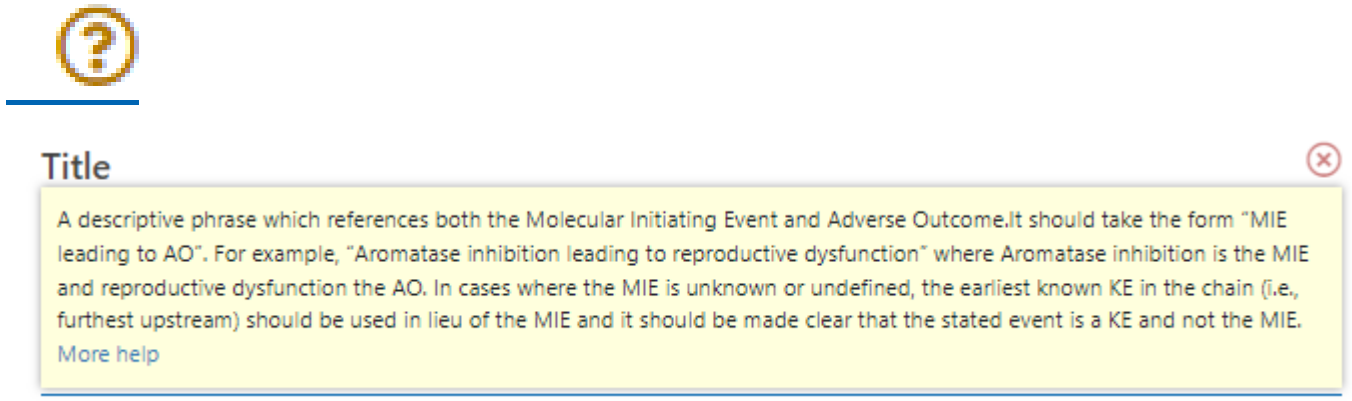


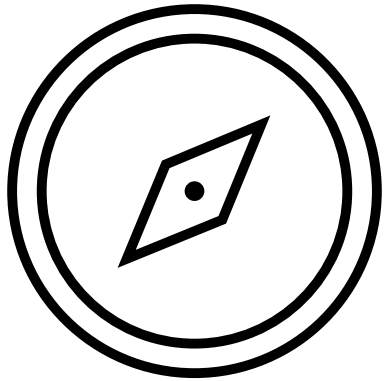
Table of contents

- Outlines the information fields on each page
- Can click any of the headings/sub-headings to navigate directly to that section of the page

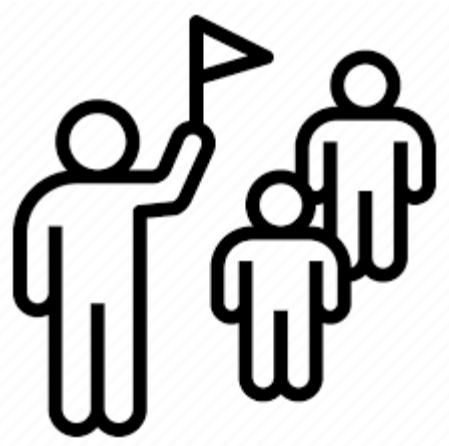


Quick tour of an AOP Page

Quick tour of an Event Page



Quick tour of a Relationship Page



Time to get hands on

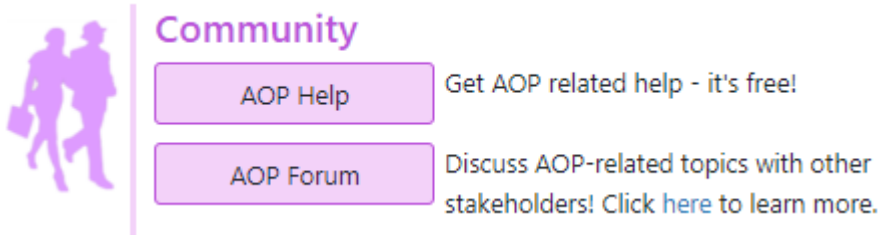
AOPwiki.org

Points of Contact

Dan Villeneuve
CCTE/GLTED
Villeneuve.dan@epa.gov

AOP Wiki

aopwiki@googlegroups.com.



https://forum.aopwiki.org/