



# An introduction to Navigating the AOP-Wiki

NAMs Training Workshop

RTP, NC

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

# 2004

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

Three strategies could move both science and regulation forward.

**D**uring 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.



STEVEN P. BRADBURY  
U.S. EPA

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

CORNELIS J. VAN LEEUWEN  
EUROPEAN COMMISSION

### Increasing efficiency, cost-effectiveness, and focus

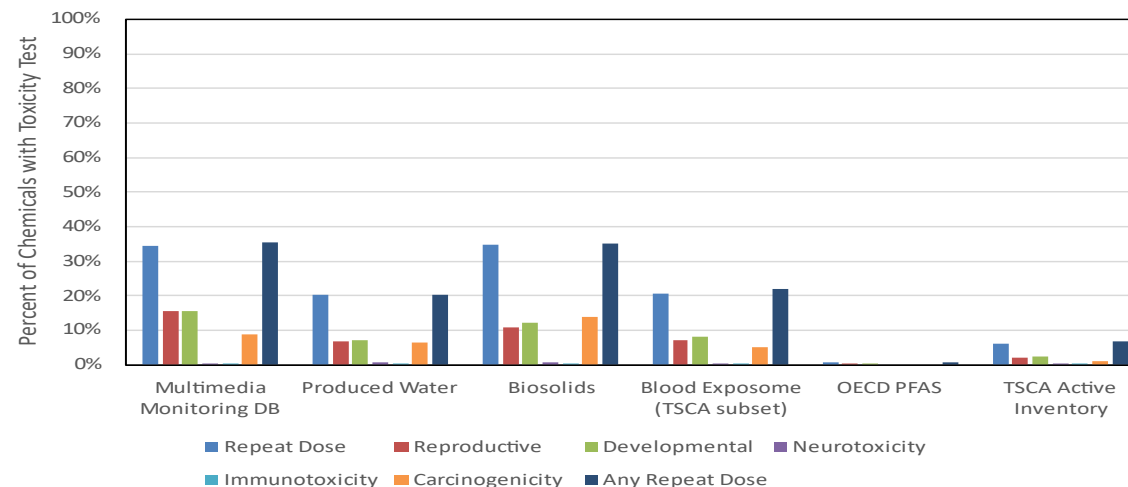
Risk assessment is a tiered process distinguished by levels of increasing complexity, beginning with the preliminary categorization step, followed by a refined or screening assessment, and progressing to the full, comprehensive risk assessment (4, 18, 19). For each tier, a minimum level of information 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

### 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

Three strategies could move both science and regulation forward.



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### Increasing efficiency, cost-effectiveness, and focus

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- 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:

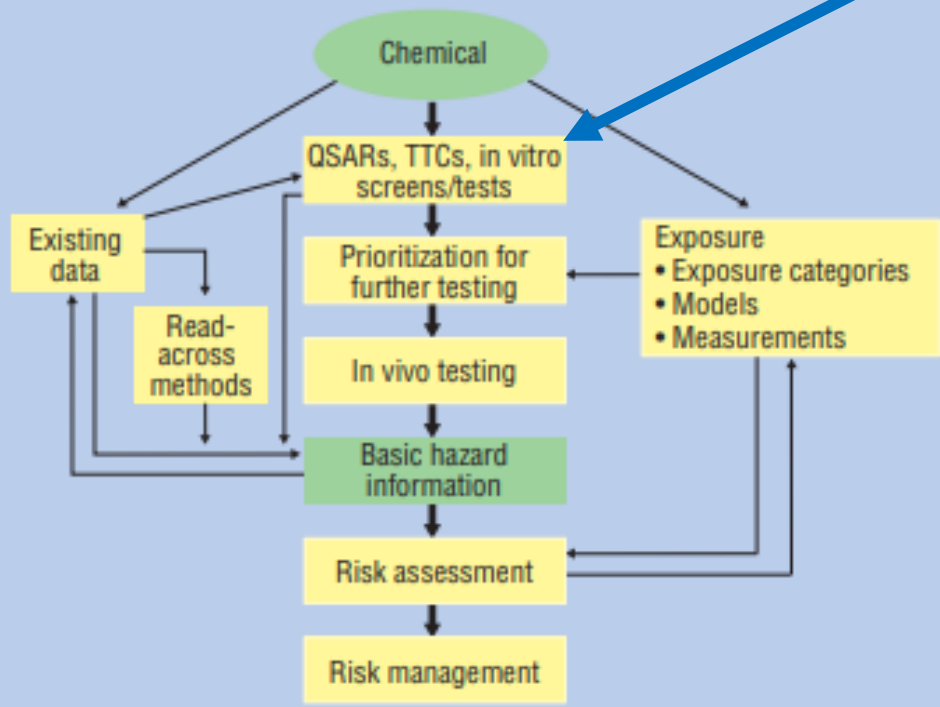
- Which chemicals should be tested [*in vivo*]?
- And of these, which should be tested first?
- For what endpoints [*in vivo*]?
- On the basis of what rationale?

# 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.



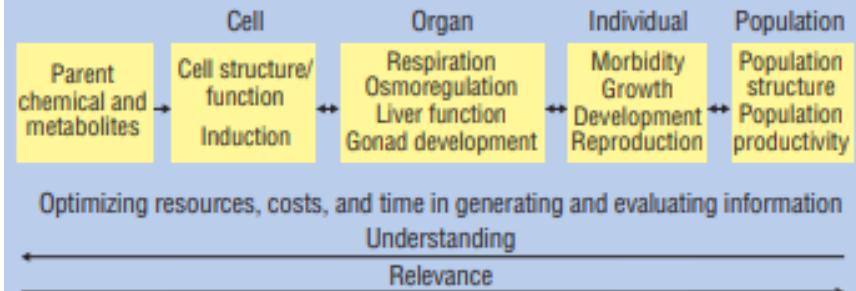
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**FIGURE 2**

## Toxicity pathways

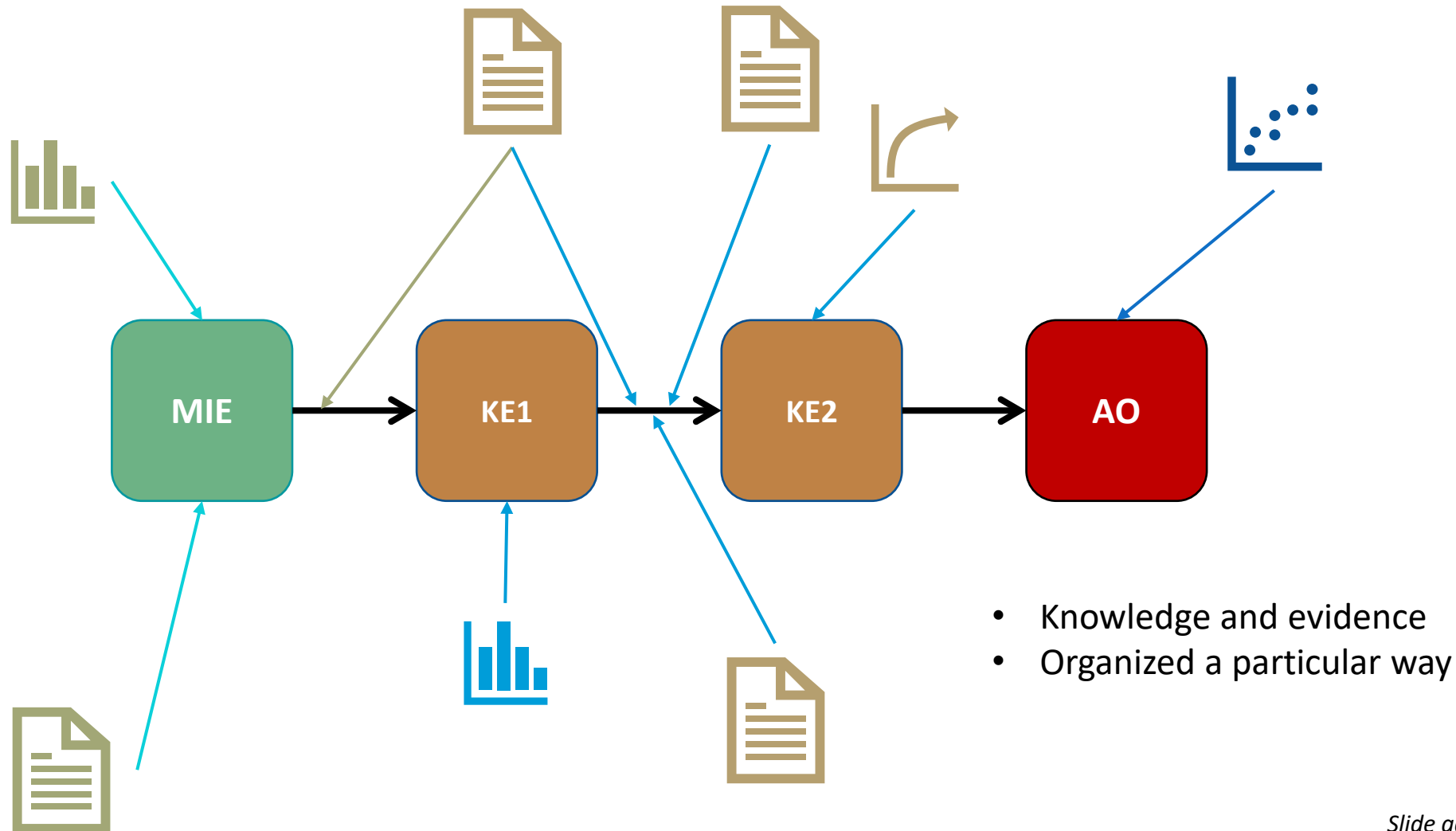
# AOPs

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



# 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.



# 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



**Welcome to the Collaborative Adverse Outcome Pathway Wiki (AOP-Wiki)**  
Version 2.6 was released on April 29, 2023. More details regarding the new release are available here: [Release 2.6](#).  
Interested in helping plan for Version 3.0? Please submit your ideas on the AOP Forum here.

**View Content**

- AOPs
- Key Events
- KE Relationships
- Prototypical Stressors

Get access to the main elements of an Adverse Outcome Pathway managed in the AOP-Wiki

**Download Content**

Download Options

Download our content and use it in your own tools

**Get Information**

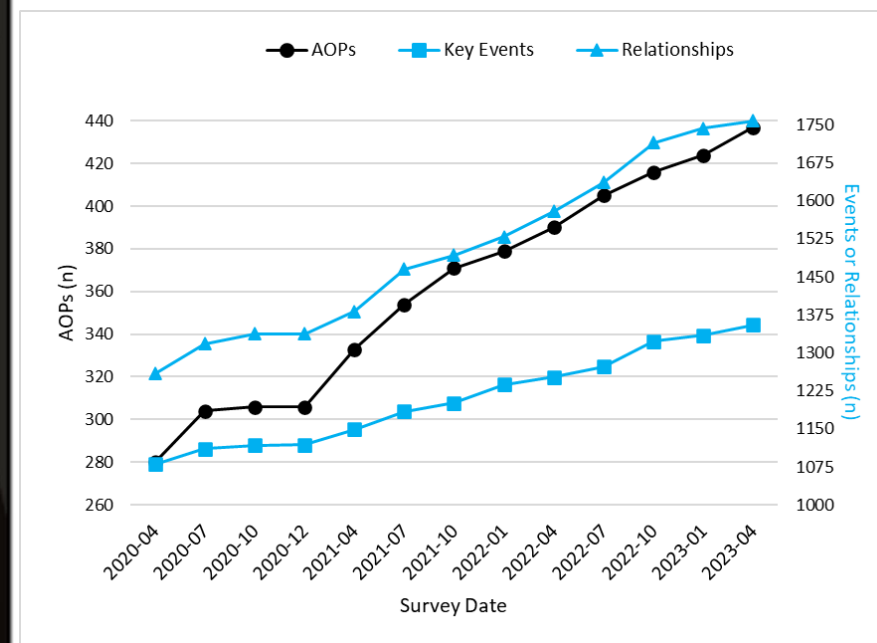
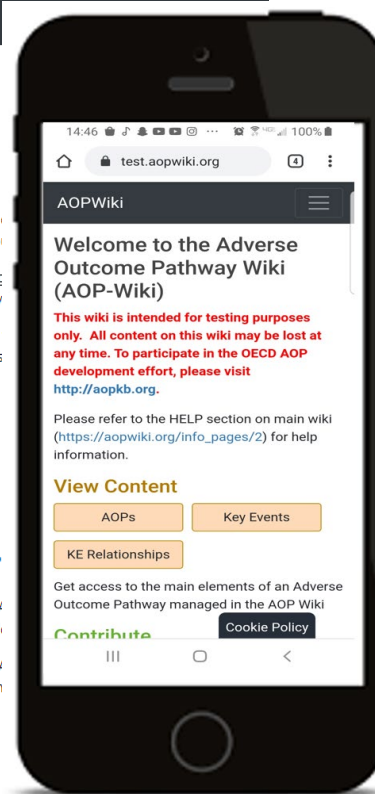
- Get started here... What is an AOP? How will AOPs change Chemical Risk Assessment?
- Who are we? Find out more about the people behind the AOP-Wiki and the AOP Framework
- Announcements Don't miss our regular announcements and news!
- AOP Training Learn about training materials and opportunities

**Contribute**

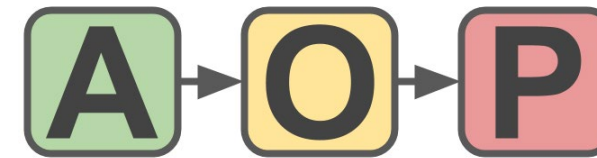
- Register You can know yo
- Start a new AOP Browsing adding y
- Developers' Handbook View up practices

**Community**

- AOP Help Get AOP
- AOP Forum Discuss / stakehol
- Third Party Tools Explore / commun



# Organization of the AOP-Wiki



- Three main page-types

**View Content**

- AOPs
- Key Events
- KE Relationships
- Prototypical Stressors

Get access to the main elements of an Adverse Outcome Pathway managed in the AOP-Wiki

**Download Content**

Download Options

Download our content and use it in your own tools

**Contribute**

- Register: You can do so much more once you know you - register
- Start a new AOP: Browsing through existing AOPs adding your own is even better!
- Developers' Handbook: View up to date guidance, tips, and practices for AOP development

**Community**

- AOP Help: Get AOP related help - it's free!
- AOP Forum: Discuss AOP-related topics with stakeholders! Click [here](#) to learn more!
- Third Party Tools: Explore AOPs using tools developed by community partners

**Get Information**

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### AOP Page

Flow diagram: Molecular Initiating Event → Key Event 1 → Key Event 2 → Key Event 3 → Adverse Outcome

**Key Events**

Title	Short name	Relationship
Key Event 1	KE1	Key Event 1
Key Event 2	KE2	Key Event 2
Key Event 3	KE3	Key Event 3

**Adverse Outcomes**

Title	Short name	Relationship
Adverse Outcome 1	AO1	Adverse Outcome 1
Adverse Outcome 2	AO2	Adverse Outcome 2

**Relationships Between Two Key Events (Including MEs and AOs)**

Title	Direction	Evidence	Quantitative Understanding
Relationship 1	One-way	Strong	High
Relationship 2	Two-way	Medium	Low
Relationship 3	One-way	Weak	None

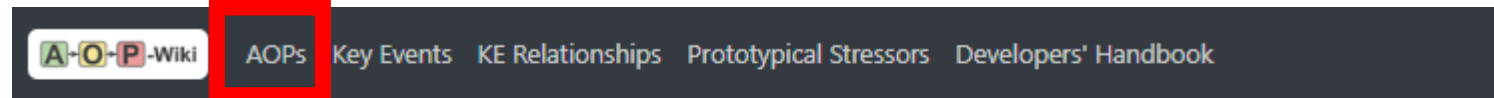
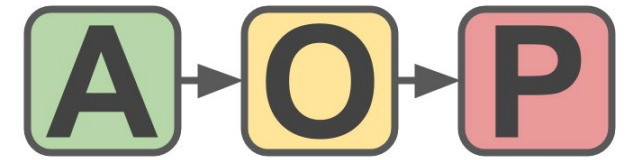
### KE Pages

- 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...  Find by ID

### AOPs

Filtered AOP Count: 469

ID	Title	Point of Contact	License	MIE	AO	OECD Status	OECD Project
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

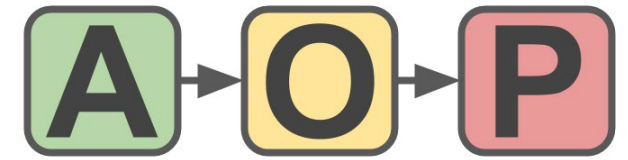
Search AOPs...  Find by ID

- In title
- Anywhere on page
- Must click “find by ID”
- Enter will not work

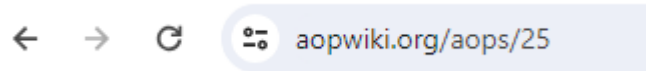
Similar search and filter options are available on the Key Events and Key Event Relationships list pages as well



# 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

- AOP Title
- Graphical Representation
- Authors
- Abstract
- AOP Development Strategy
  - Context
  - Strategy
- Summary of the AOP
  - Events
- Relationships Between Two Key Events
  - Network View
- Prototypical Stressors
- Life Stage Applicability
- Taxonomic Applicability
- Sex Applicability
- Overall Assessment of the AOP
  - Domain of Applicability
  - Essentiality of the Key Events
  - Evidence Assessment
  - Known Modulating Factors
  - Quantitative Understanding
- Considerations for Potential Applications of the AOP
- References

### 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



### Title

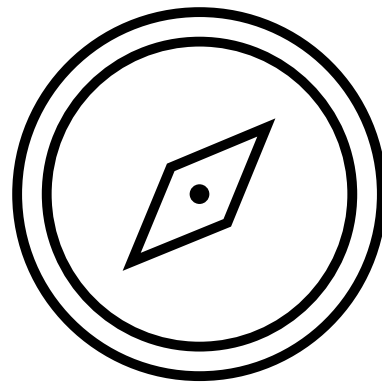
A descriptive phrase which references both the Molecular Initiating Event and Adverse Outcome. It should take the form "MIE leading to AO". For example, "Aromatase inhibition leading to reproductive dysfunction" where Aromatase inhibition is the MIE and reproductive dysfunction the AO. In cases where the MIE is unknown or undefined, the earliest known KE in the chain (i.e., furthest upstream) should be used in lieu of the MIE and it should be made clear that the stated event is a KE and not the MIE.

[More help](#)

# 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



[aopwiki@googlegroups.com](mailto:aopwiki@googlegroups.com)



## Community

AOP Help

Get AOP related help - it's free!

AOP Forum

Discuss AOP-related topics with other stakeholders! [Click here](#) to learn more.

<https://forum.aopwiki.org/>