



# AOP ACTIVITIES AT THE OECD

Workshop AOPs: From Research to Regulation  
3 - 5 September 2014

**Joop de Knecht**  
Principal Administrator  
OECD Test Guidelines Programme  
Environmental, Health and Safety Division



## Launch of the Programme at OECD

---

- The AOP Development Programme was launched at **OECD** in 2012, under the umbrella of the Advisory Group on Molecular Screening and Toxicogenomics (Programme on Chemical Safety).
- AOPs are a central concept in future work at OECD on predictive toxicology, improving uses and applications of mechanistic information for both future testing and assessment needs.
- Several OECD groups are involved, interdisciplinary nature of the work



# AOP Development Programme: an horizontal activity at OECD

---

The OECD programme on the development of AOPs addresses the needs of:

- the OECD [Test Guidelines Programme](#) for the identification of new *in vitro* test methods that are candidates to become OECD Test Guidelines;
- The OECD [QSAR Project](#) for the identification of new methods/profilers for grouping chemicals;
- the OECD [Hazard Assessment activities](#) for the development of IATAs for defined hazard endpoints.



## ***Framework for the development and use of IATAs***

---

- Approaches to decide on the adverse effect of a chemical by using existing information, alternative methods and tailored testing strategies.
- Starts with the formulation of plausible and testable hypotheses about the toxicological potential of a chemical based on existing information and/or information derived from lower tier testing.
- The information would then be used to evaluate data gaps and what testing approaches if any would be most appropriate to undertake in order to elucidate the toxicological profile of that substance



## ***Integrated Approaches to Testing and Assessment (IATA)***

---

- The vision is that the results from appropriate combinations of selected *in silico*, *in chemico*, and *in vitro* tests that target key events along well defined AOPs could provide sufficient information for hazard and risk assessments with minimal, but well-tailored need for further testing.
- The knowledge of an adverse outcome pathway or mode of action can provide the scientific framework for developing and using IATAs.



## *Development of an IATA based on the AOP / MoA concept*

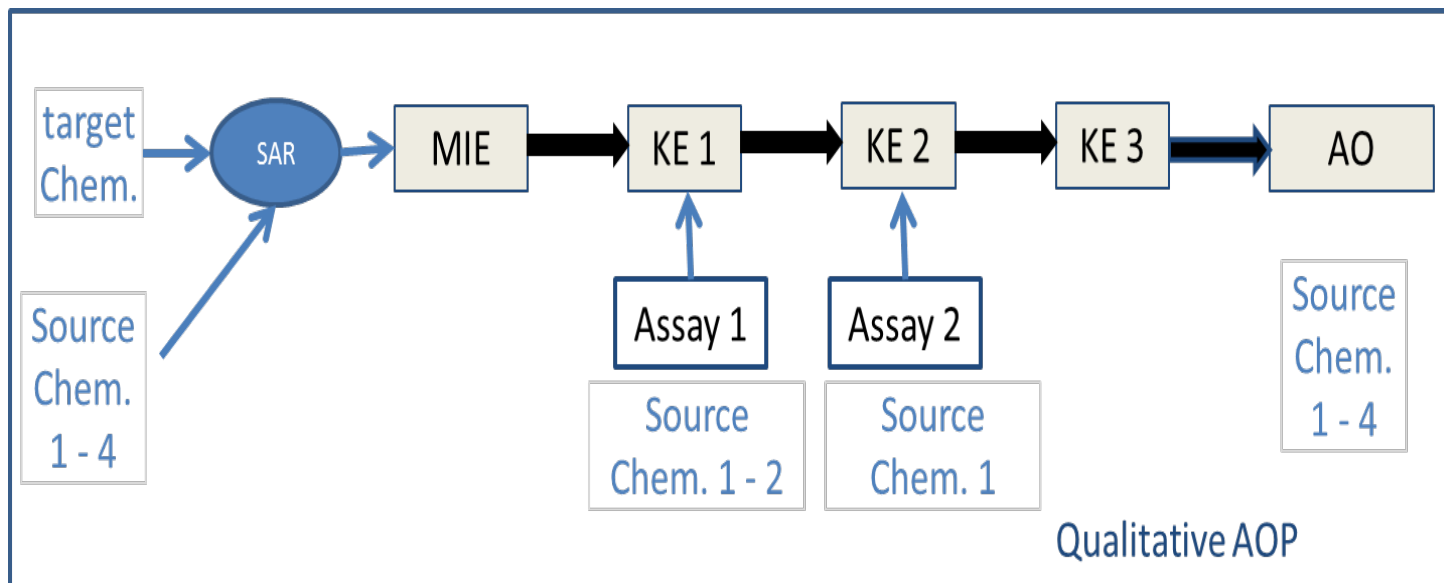
---

AOPs/MoAs could be used to:

- develop (Q)SARs
- support grouping of chemicals into chemical categories for subsequent data gap filling for a specific endpoint using read-across or trend analysis
- develop testing strategies
- select methods for TG development
- interpret results from non-standard test methods

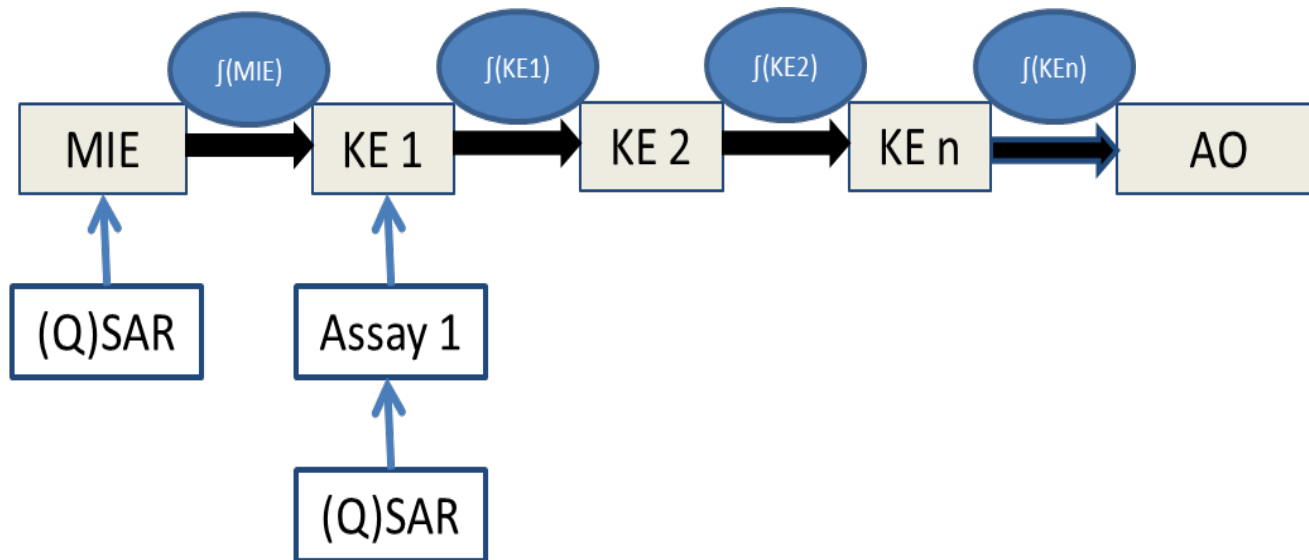


# Use of the AOP concept to categorise chemicals for a specific endpoint





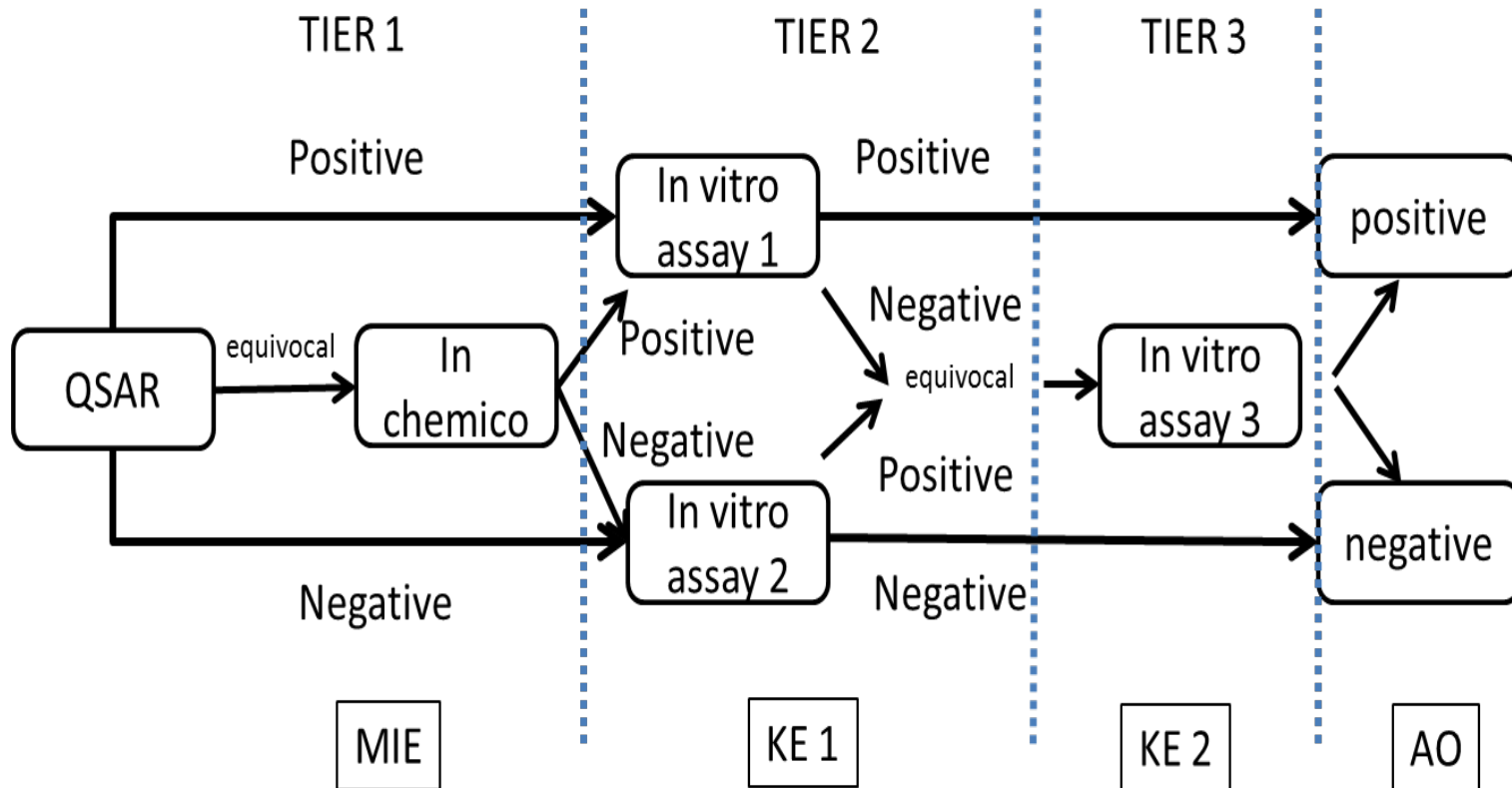
# Use of an AOP to develop QSARs







# Use of an AOP/MoA in a testing strategy





# OECD Workshop on a framework for the development and use of IATA

---

## Aim

- To test the applicability of the AOP/MoA concept as a framework for developing and using IATAs and to refine the framework as far as possible.
- Build consensus that the AOP/MoA concept is a good basis for developing and using IATAs,
- Determine for which type of IATA, the AOP/MoA concept can be used,
- Discuss and refine different stages of development of an AOP
- Decide which of the different stages is most suitable for each type of IATA and their associated purpose.



# Relevant documentation published at OECD

---

- [Template format](#) for project proposals
- [Guidance document on developing and assessing AOP](#) (2013), No. 184 Series Testing and Assessment
- [User handbook](#) (more practical and wiki-oriented than the guidance, *under preparation*)



# Functioning of the AOP Development Programme at OECD

---

- The OECD Advisory Group on Molecular Screening and Toxicogenomics (EAGMST) is a large group of experts from various areas of toxicology.
- Experts are designated by governmental or non-governmental affiliations (academia, agencies, industry, animal welfare groups, scientific societies, etc.)
- The EAGMST meets once a year before summer and holds a teleconference, usually in December to keep pace with new developments.



# Functioning of the AOP Development Programme at OECD

---

- Project proposals to develop new AOPs can be made by members of EAGMST or the public (academia, scientific societies, industry groups, etc.)
- Project proposals can be submitted any time of the year to the Secretariat who makes them available to the EAGMST for their review.
- The AOP Development Programme maintains a rolling work plan, updated twice a year with new project proposals and new information on existing projects.
  - Twice a year, project proposals are reviewed and included in the work plan if justified and in line with the objectives of the Programme.



# Where can I find relevant information?

---

- A public web-page provides summary information to the public on the AOP development programme, including **titles of AOP** on the workplan and **lead** organisations/countries, relevant **templates** for making proposals, **guidance** on how to develop AOPs, etc.

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

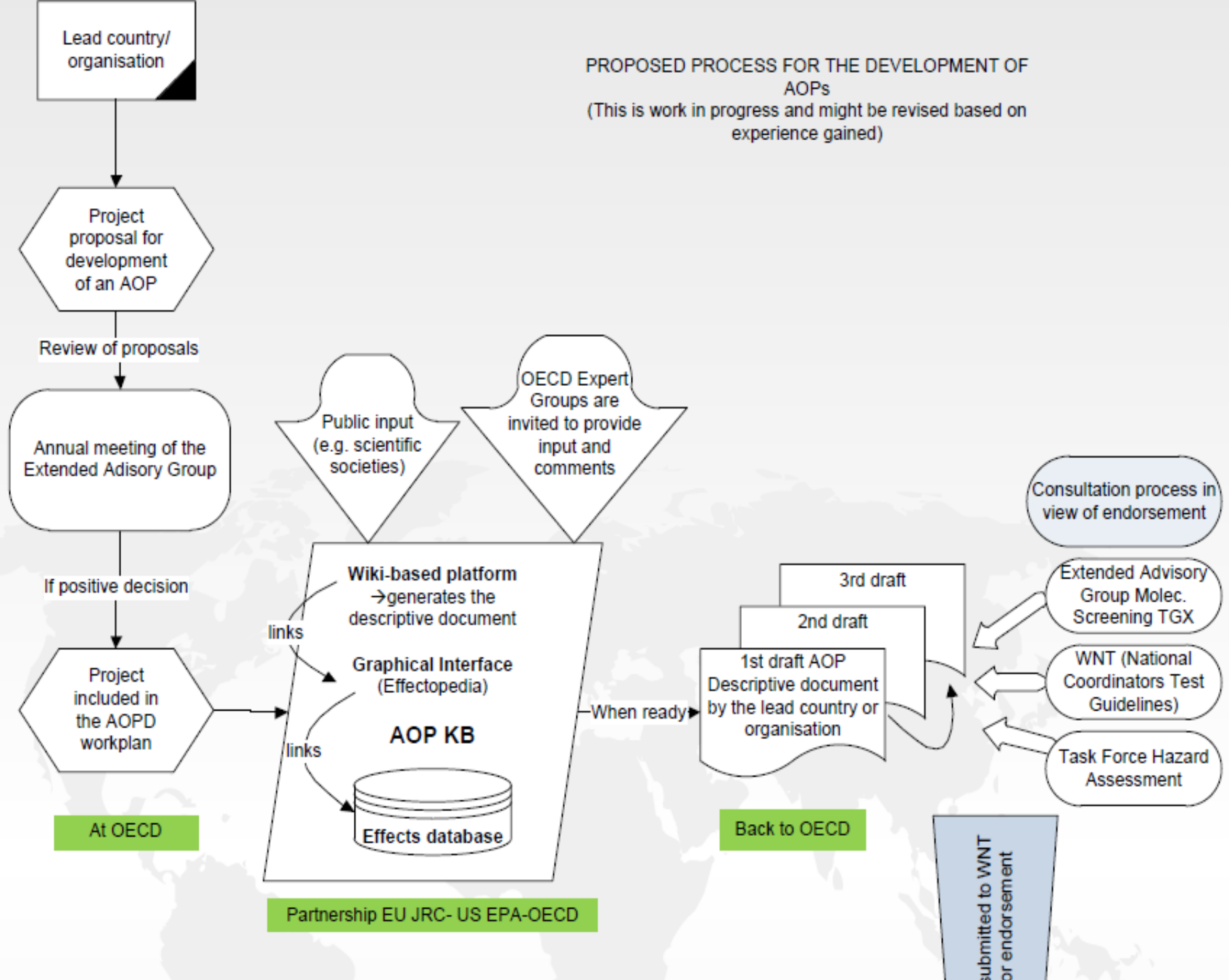


# Where can AOPs under development be found?

---

- A **wiki-based** interface has been developed to enable AOP description (MIE, KE, KER, AO)
  - <http://aopwiki.org>  
→ *see Stephen Edwards presentation*
- The AOP wiki will be **publicly launched** by end of September 2014
- All AOPs should be considered at this stage as drafts under development

PROPOSED PROCESS FOR THE DEVELOPMENT OF AOPs  
(This is work in progress and might be revised based on experience gained)





At OECD

Effects database

Back to OECD

Partnership EU JRC- US EPA-OECD

Document is submitted to WNT and TFHA for endorsement

Lead country or organisation:  
Identification of possible Test  
Guidelines to be developed under the  
WNT

Lead country or organisation:  
Proposal for Integrated Testing  
Strategy under the TFHA

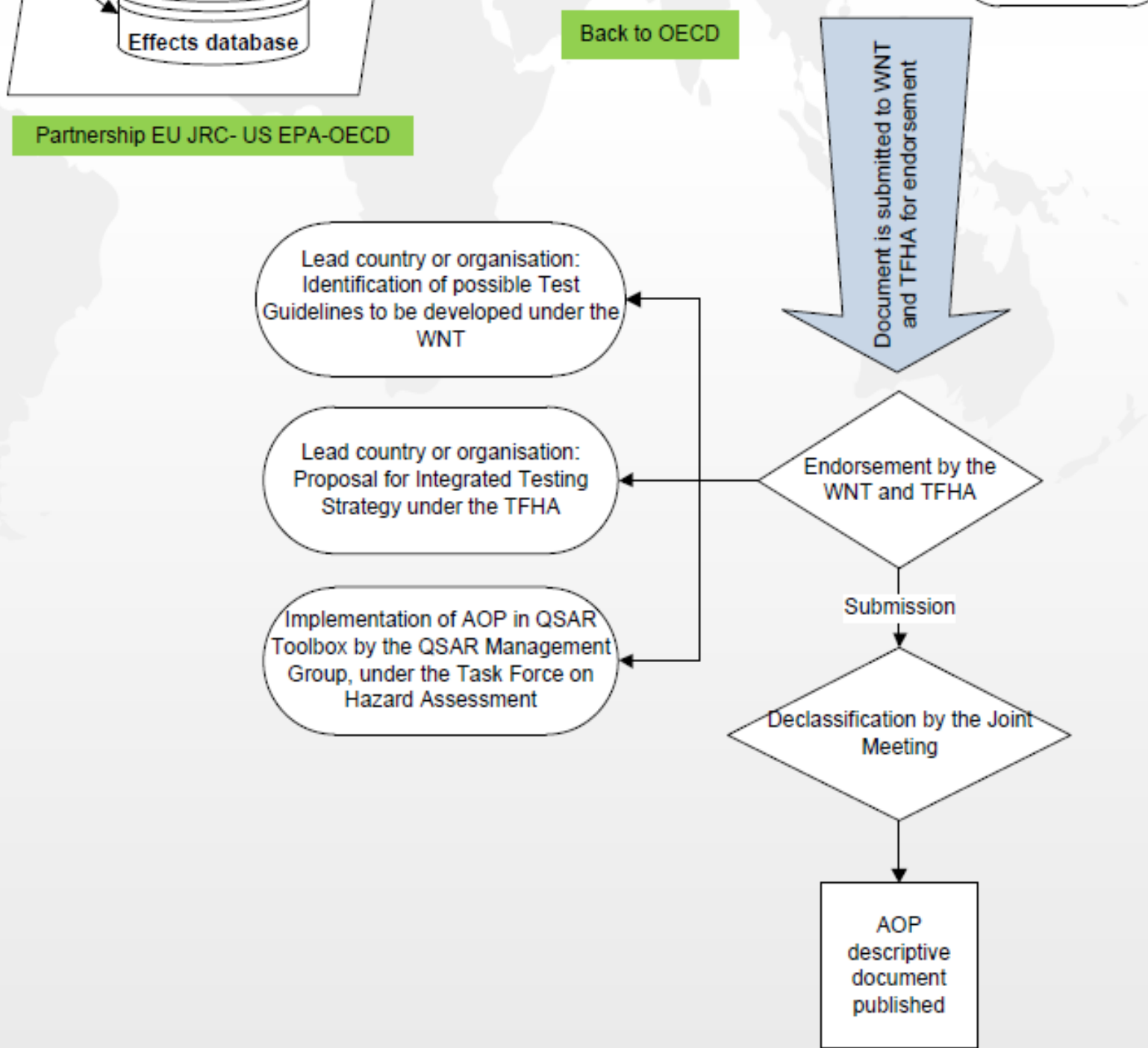
Implementation of AOP in QSAR  
Toolbox by the QSAR Management  
Group, under the Task Force on  
Hazard Assessment

Endorsement by the  
WNT and TFHA

Submission

Declassification by the Joint  
Meeting

AOP  
descriptive  
document  
published





## Status of AOPs developed at OECD

---

- AOPs are **scientific descriptive documents** depicting interactions, events, outcome, etc.: as such, they have **no regulatory implication**
- AOP can be developed in parallel of scientific publications (OECD work **does not preclude scientists to publish** in the literature)
- AOPs can be seen as continuously developing, and **OECD-agreed versions of AOPs can evolve** as science progresses



## Conclusions and take home messages

---

- AOP Development Programme is evolving fast with **participation of multiple groups** of experts in various areas of toxicology
- The **public can make project proposals** to develop AOPs (published guidance for users)
- **AOPwiki soon publicly available** (end Sept. 2014) to enable crowd-sourcing



International QSAR Foundation

# Effectopedia

The Online Encyclopedia of Adverse Effect Pathways

Organizing the adverse outcome pathways knowledge – the Effectopedia way.

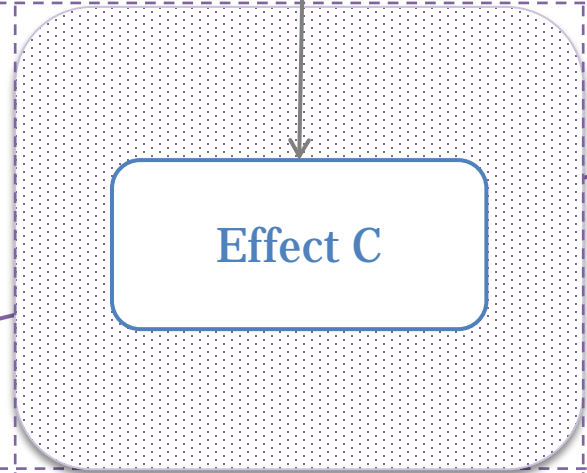
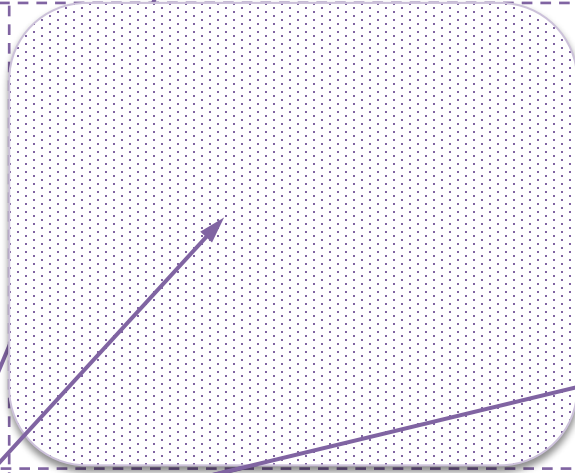
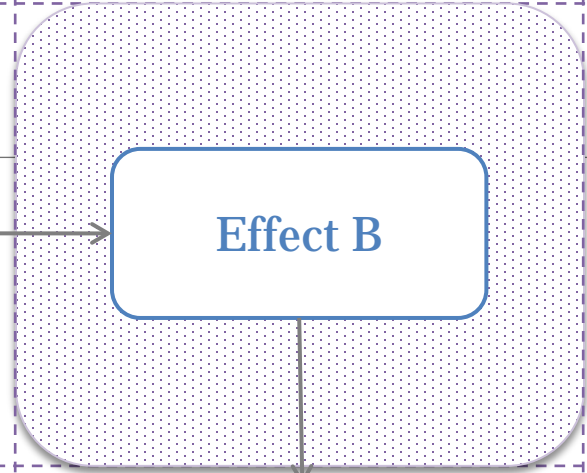
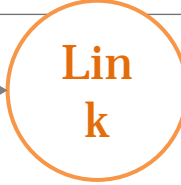
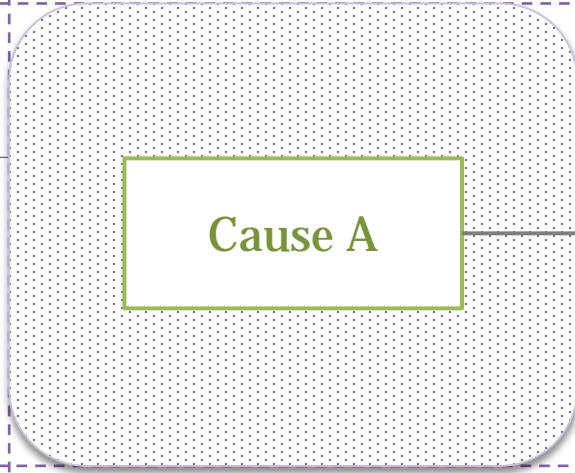
Hristo Aladjov, 27 August, Prague

# Visually Express Biological Context



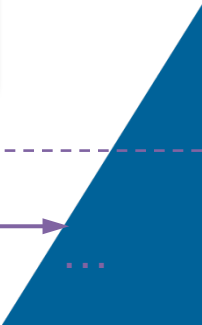
short term

mid term



cellular

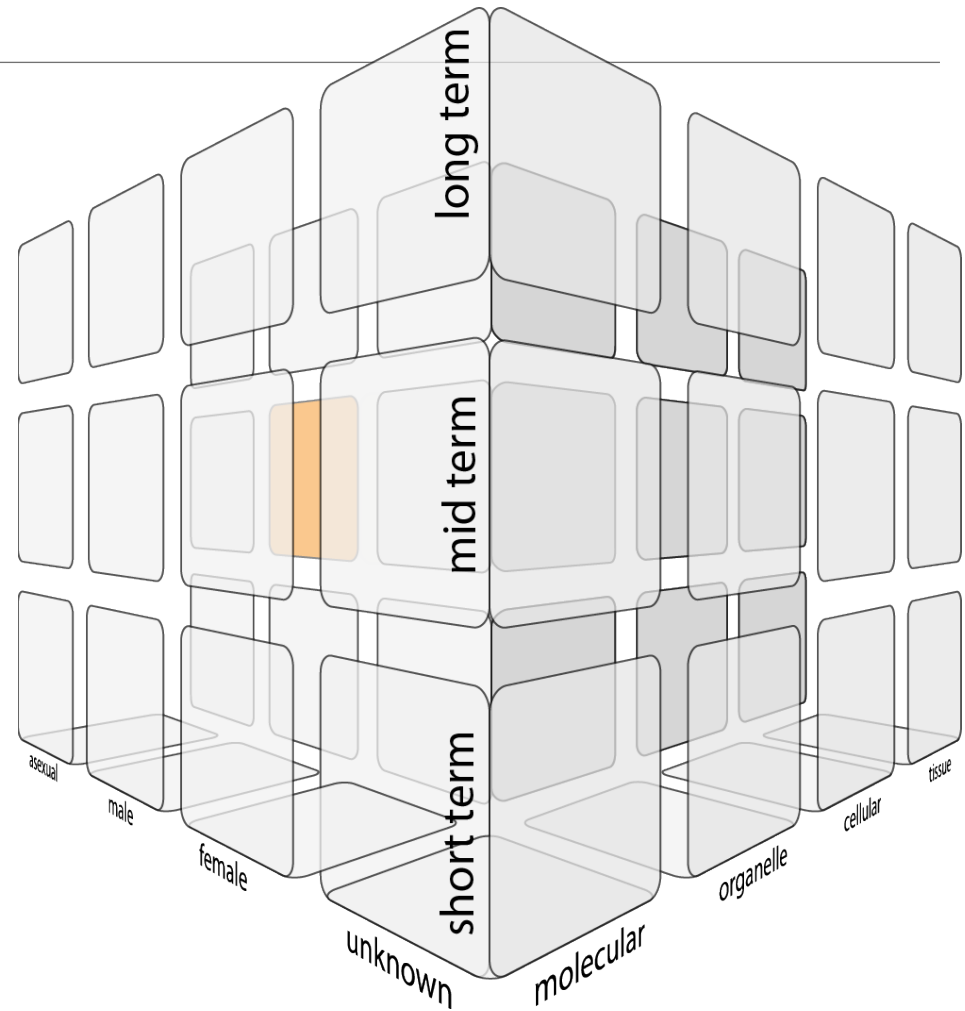
tissue





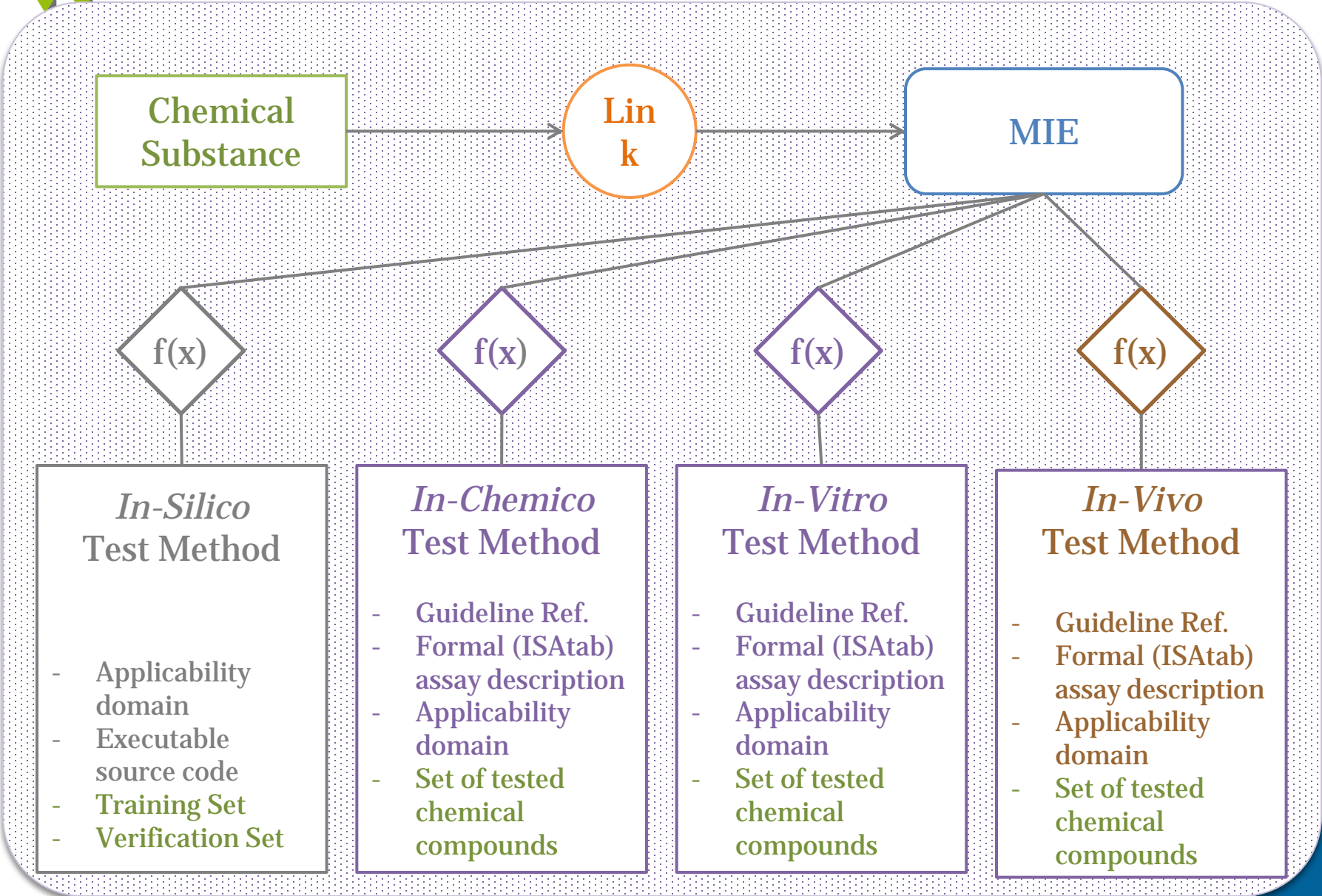
# Effectopedia's Pathway Space

- Life stage
- Taxonomy
- Gender
- Generation
- Time to effect
- Level of biological organization
- ...
- **User expandable set of biological context dimensions**
- **Interface allows easy switching between pathway space 2D projections**

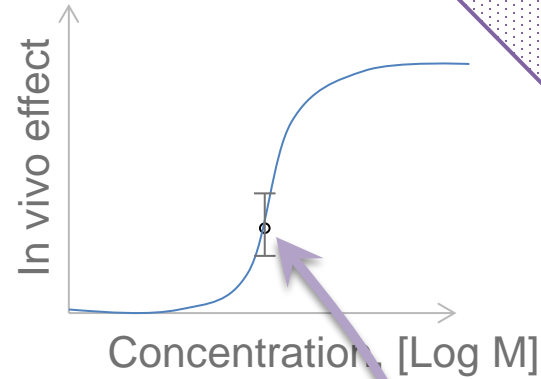
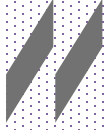




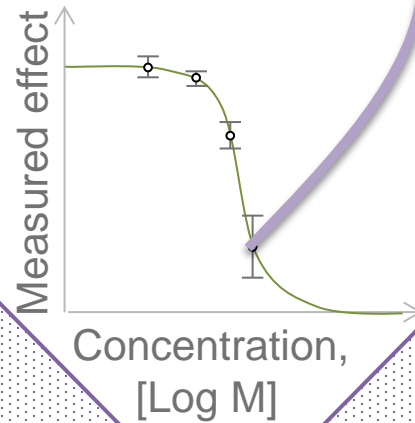
# Pathway elements



# Pathway elements – test response mapping

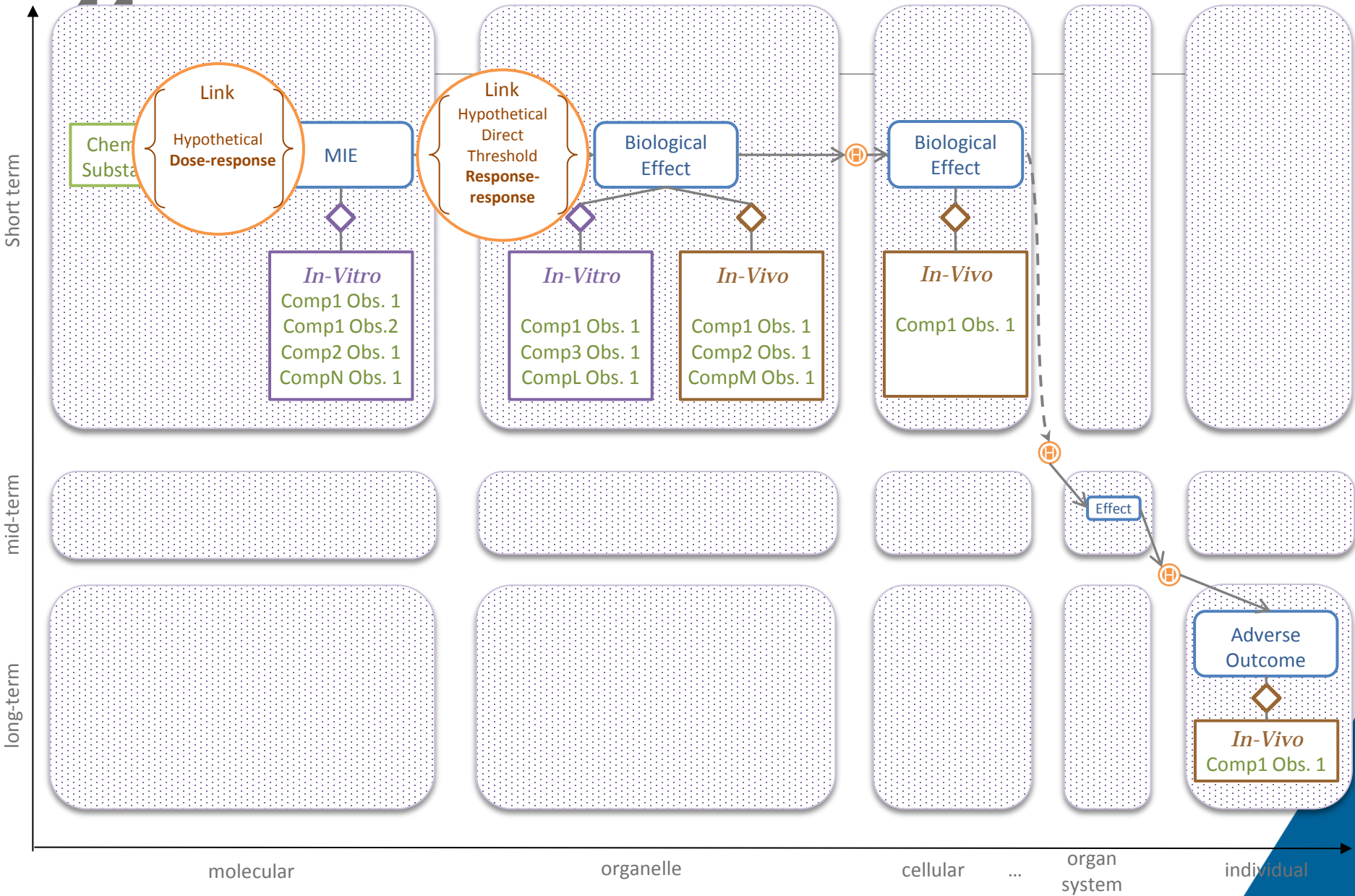


**Test response mapping (function)**





# Pathway elements



# FUTURE PENETRATION MODELS AND METABOLISM

