The OECD Framework for AOP Development and Application

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The Danish 3R-symposium: 3R-successes
13th and 14th September 2016,

OECD
BETTER POLICIES FOR BETTER LIVES

Presentation Outline

- OECD AOP Development Programme
  - Background
  - OECD work on predictive toxicology
  - Main milestones
  - IT tools

Background

Use of animals for human and ecological risk assessments

Skin sensitization

Dermal toxicity

Acute toxicity

Chronic toxicity

Genotoxicity

Carcinogenicity

Reproduction toxicity

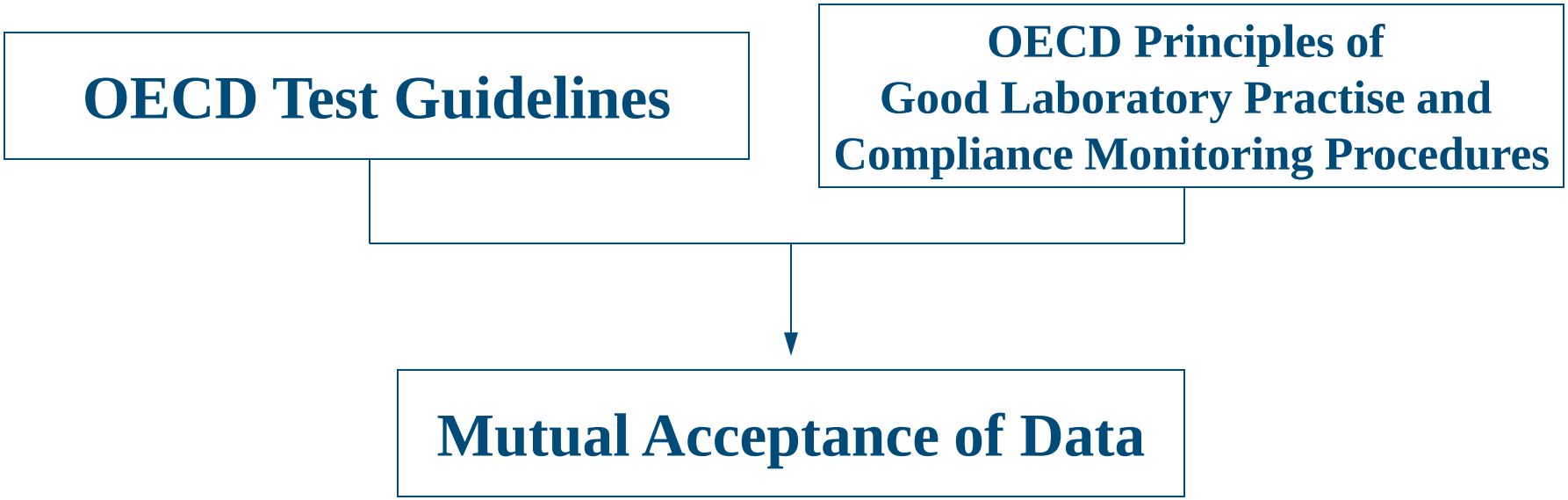
Eye irritation / corrosion

Skin irritation / corrosion

Neurotoxicity

Development toxicity

Data quality ensured by



Growing concern over lack of toxicological data

Chemicals

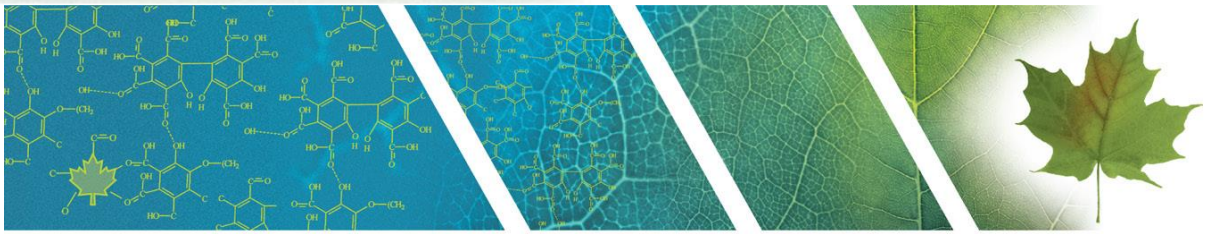
Chemicals on the market

Only 10 -20% has been fully assessed

1900

2000

Countries are improving their legislation to assess more chemicals in a shorter time frame



CHEMICALS
MANAGEMENT
PLAN

PLAN DE
GESTION DES
PRODUITS CHIMIQUES

Standard toxicity testing is costly, time consuming and requires many animals

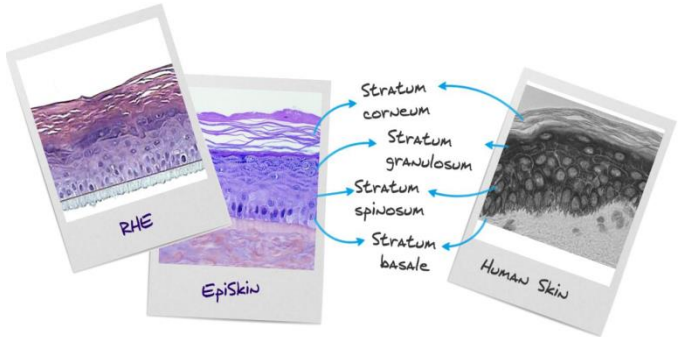
5000 animals / chemical

Test duration
30 – 720 days

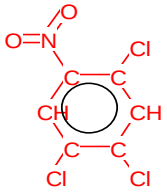
Costs
€2,000 - €2,000,000

Promoting the use of non-animal methods

- OECD Test Guidelines based on non-animal methods (skin and eye corrosion/irritation, phototoxicity, skin absorption and sensitisation, genotoxicity)
- Development of models to predict the toxicity of chemicals (grouping of chemicals and read across)
- Computational methods



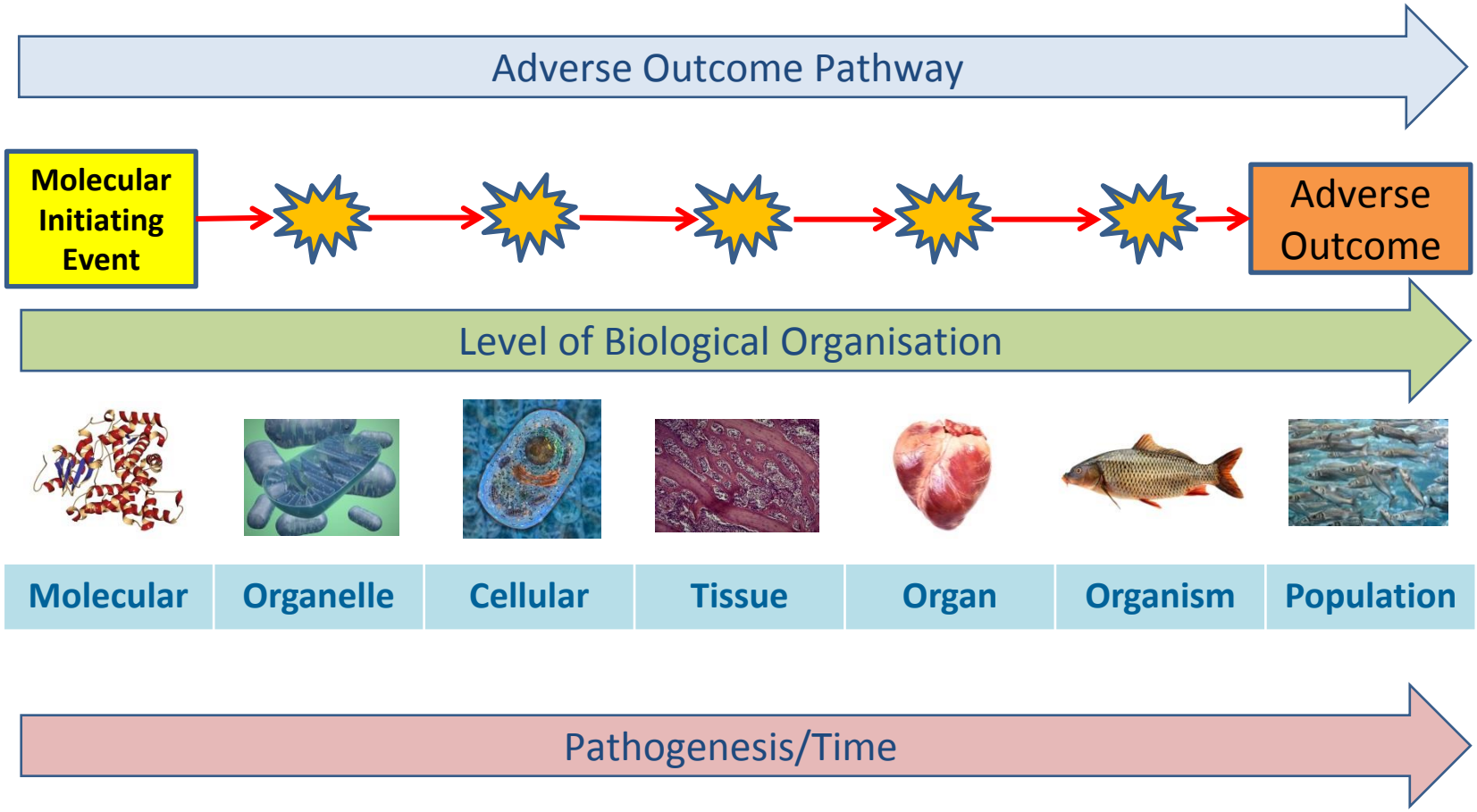
Need for mechanistic understanding



Test Chemical

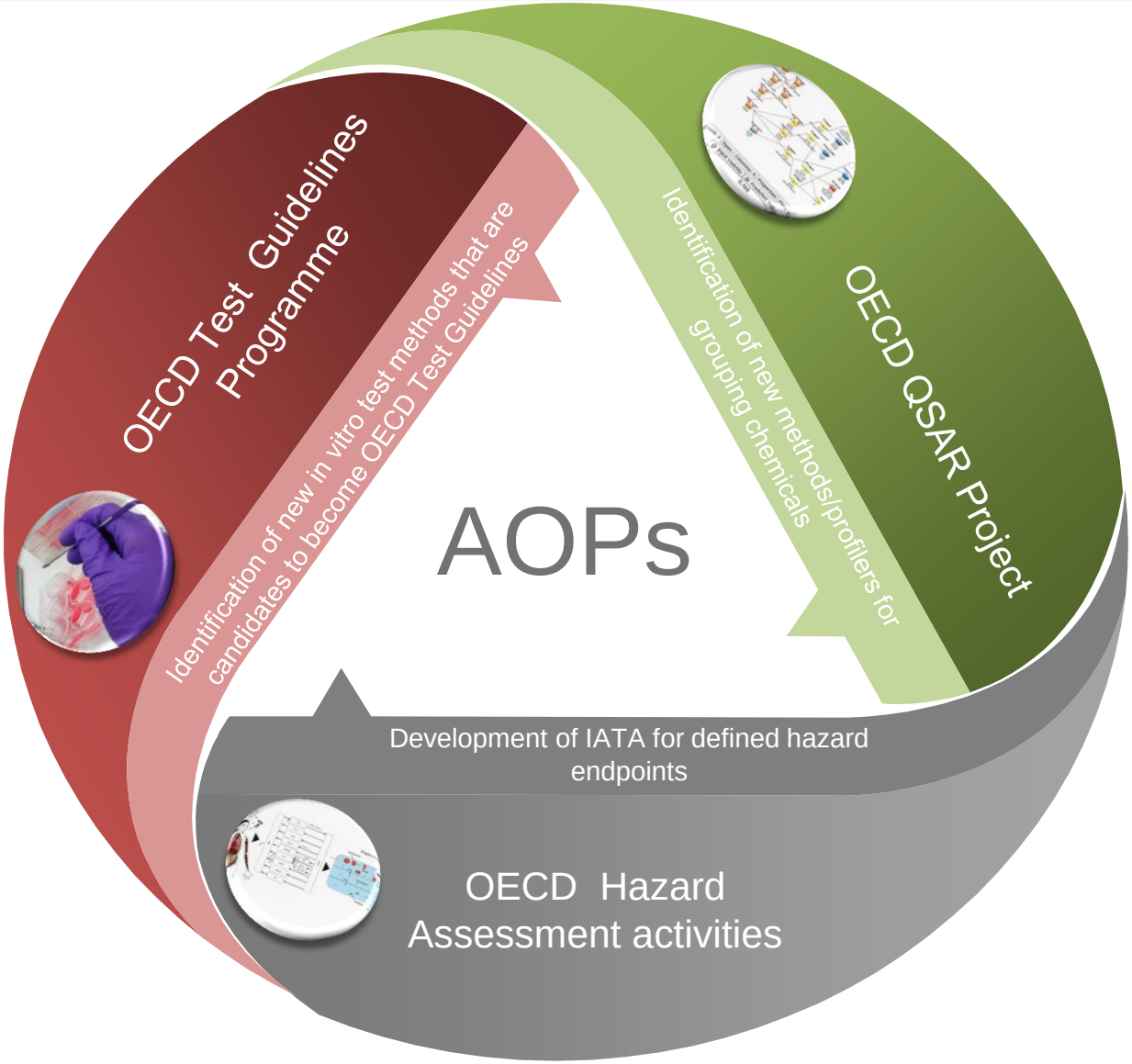
Developmental & Reproductive toxicity

Identifying the mechanism(s)

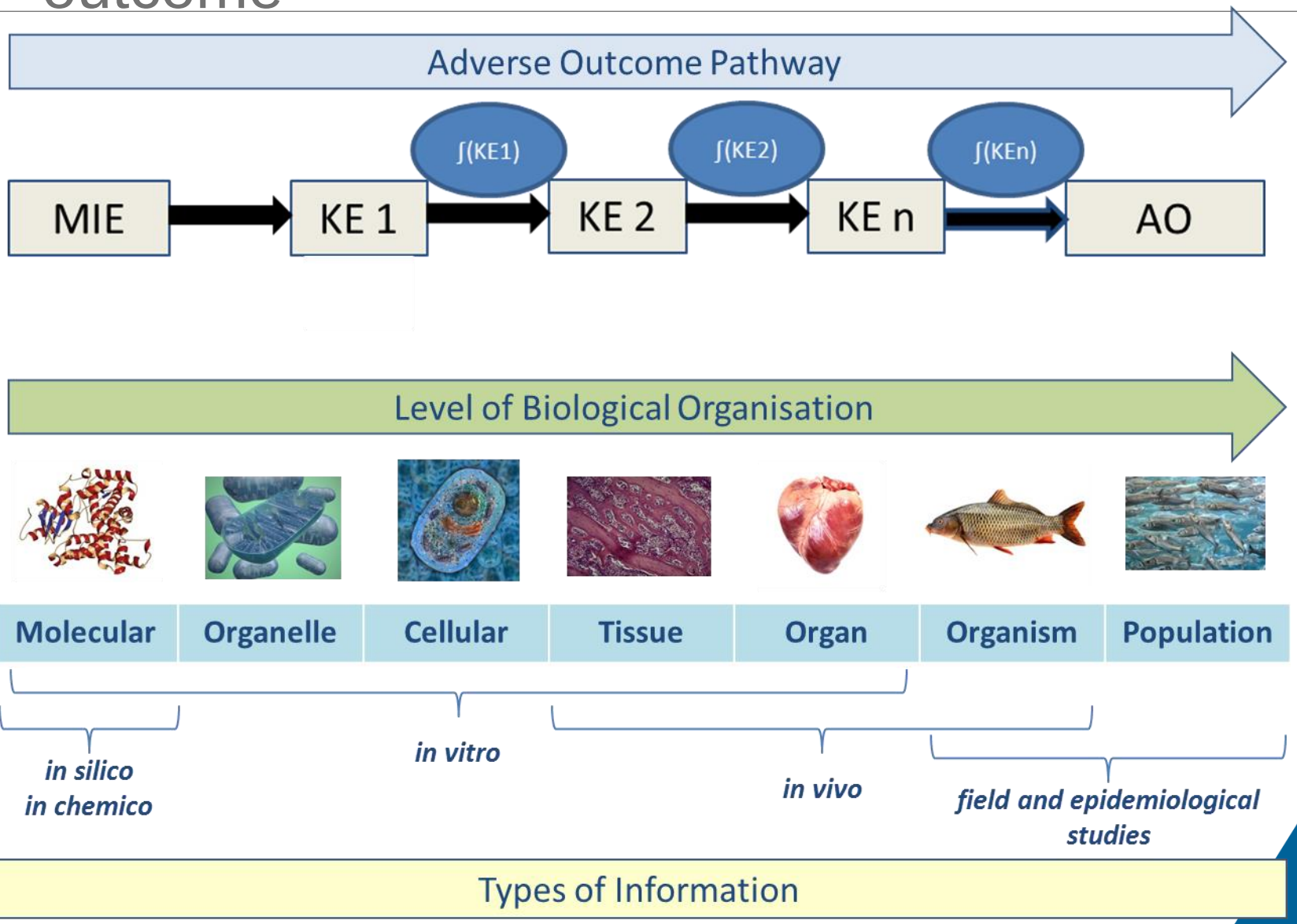


OECD work on Predictive Toxicology

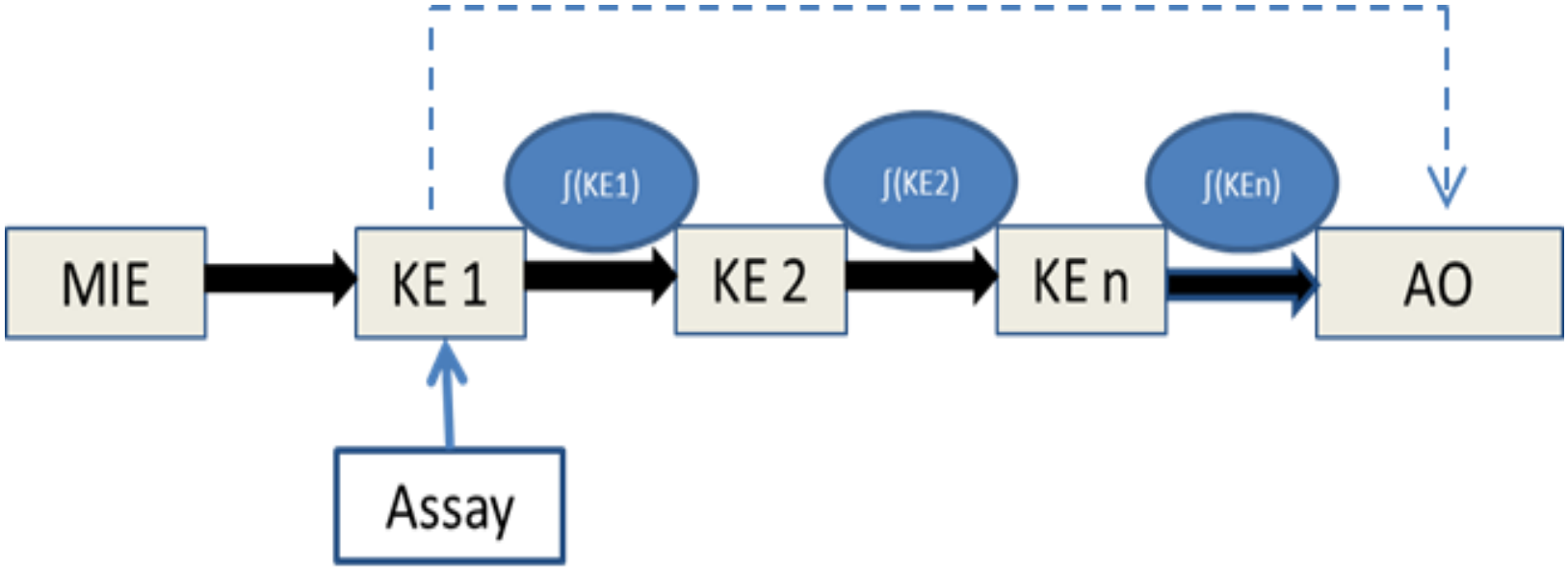
AOP's central role in OECD work on predictive toxicology



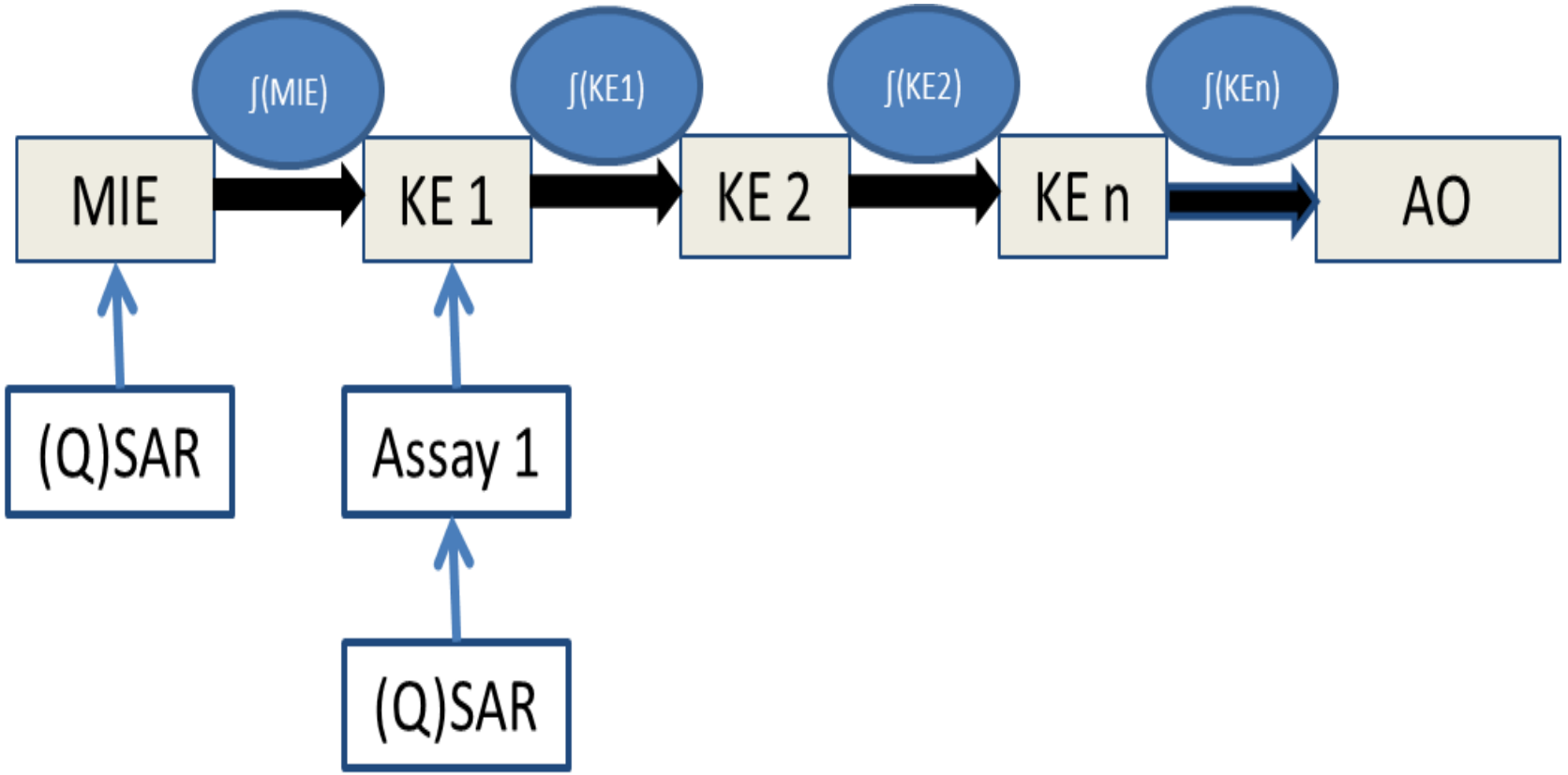
Key events can be measured with non-animal tests, which can be used to predict the adverse outcome



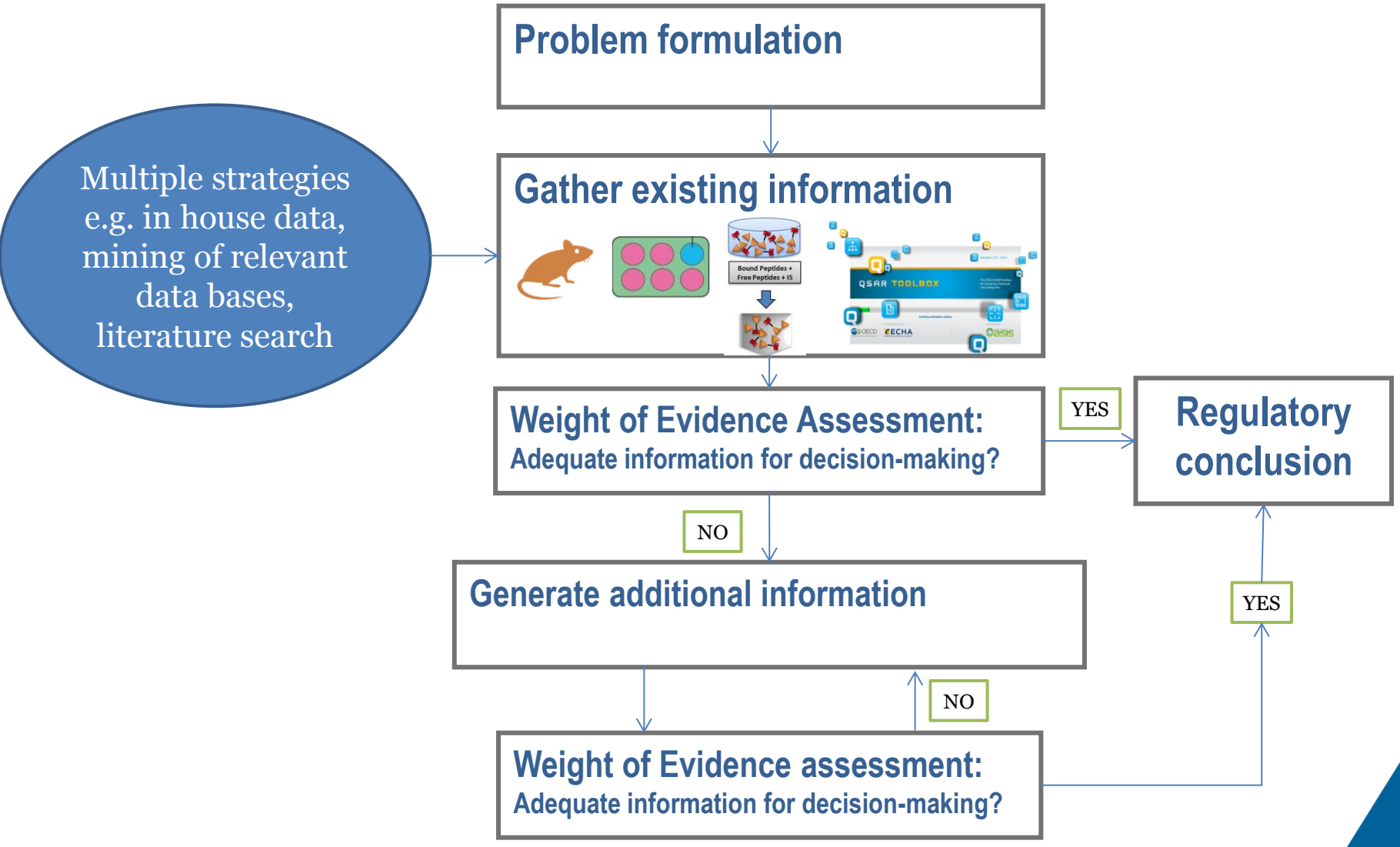
Selection of methods for Test Guideline development/refinement



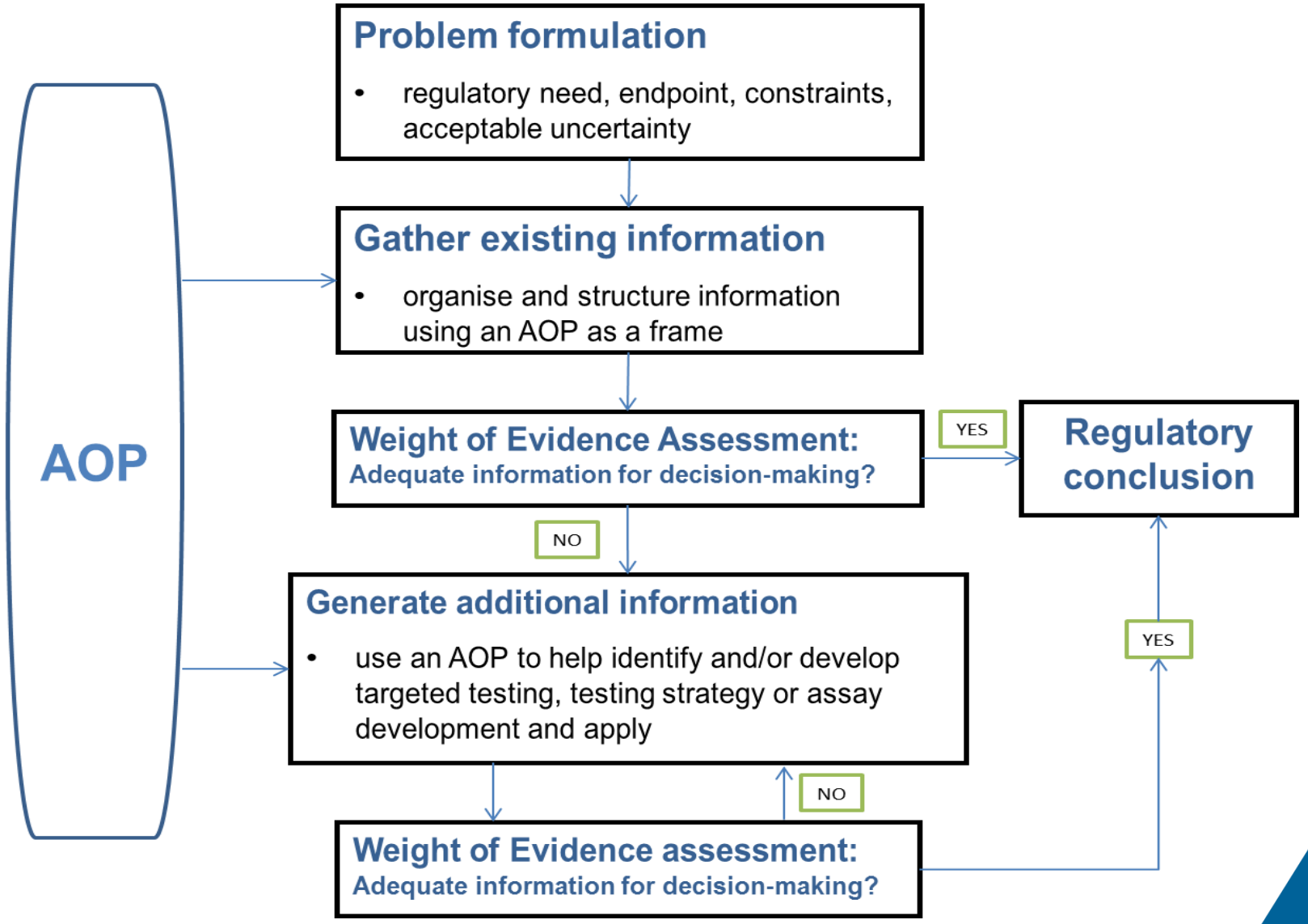
Development of (Q)SARs



General workflow in IATA

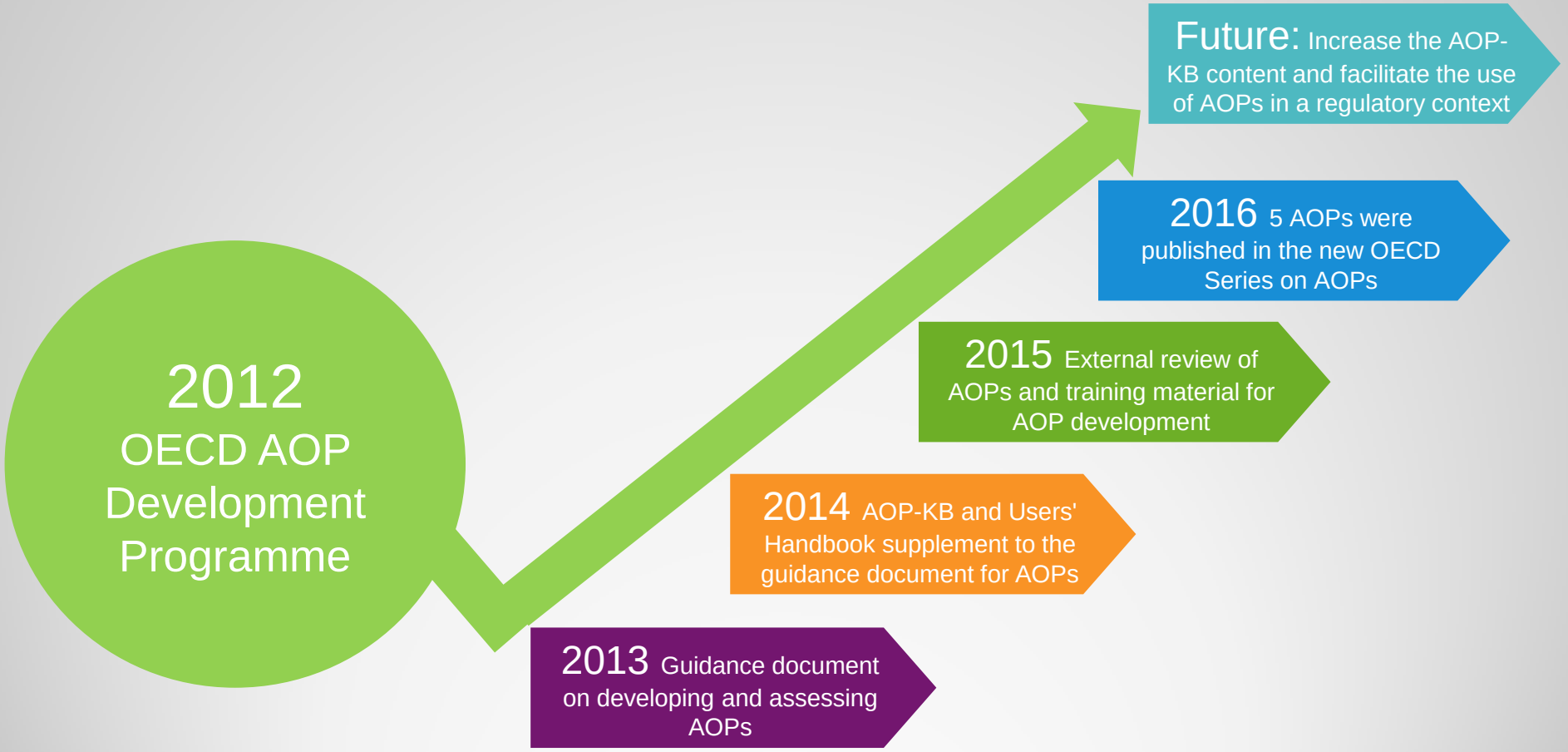


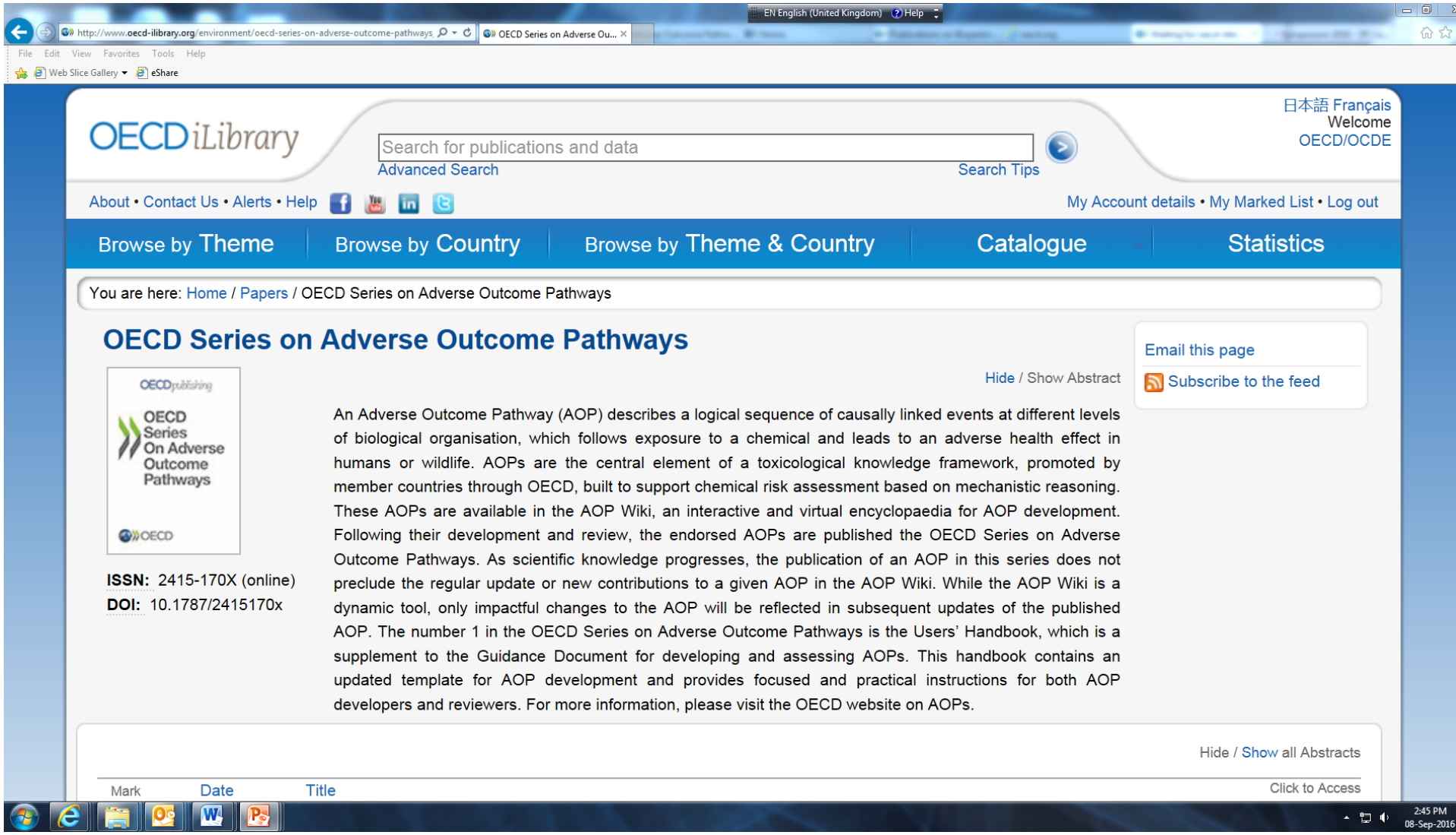
Framework for how an AOP can be applied to inform and structure IATA



Milestones achieved

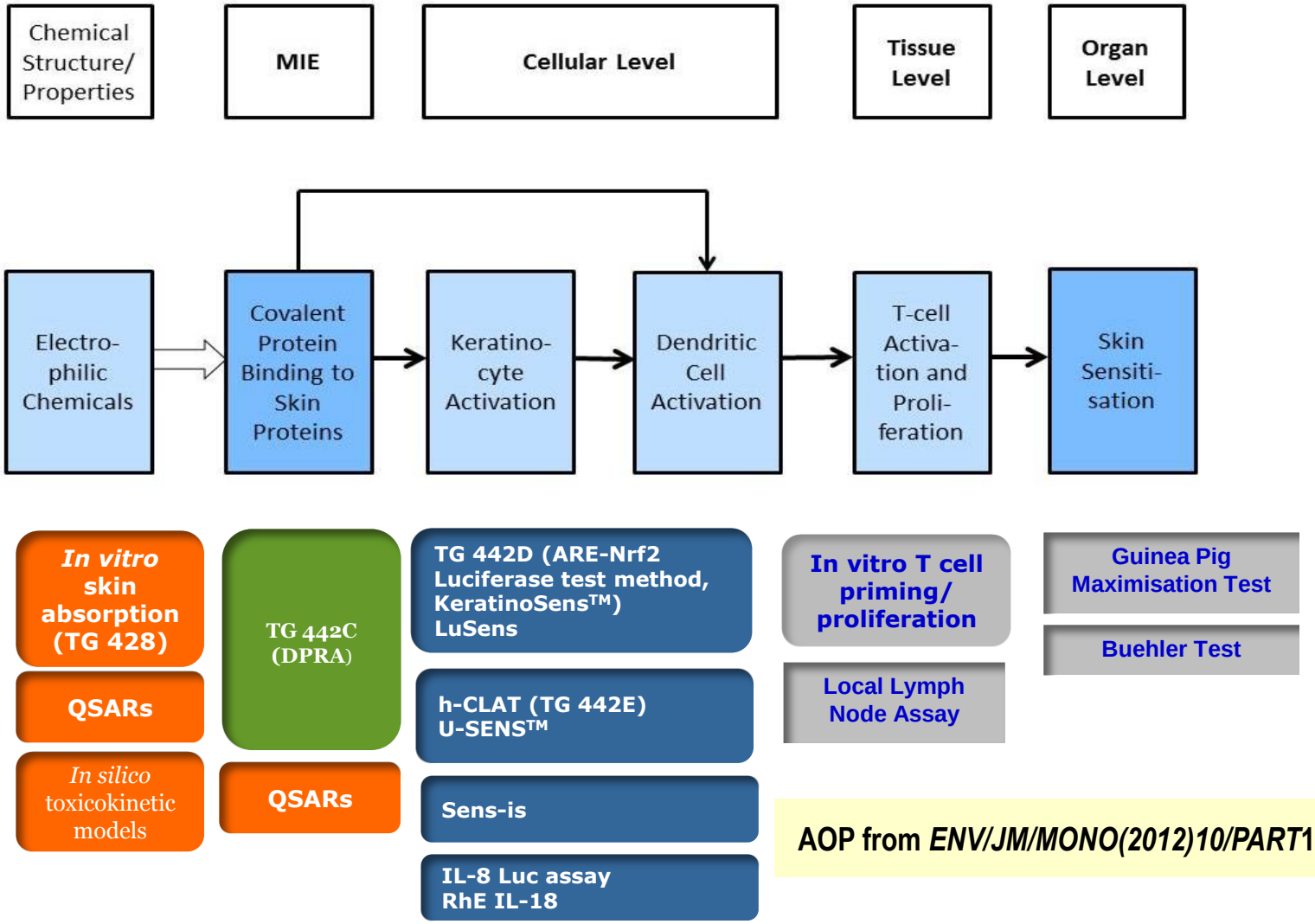
Main milestones achieved since the launch of the OECD AOP Development Programme





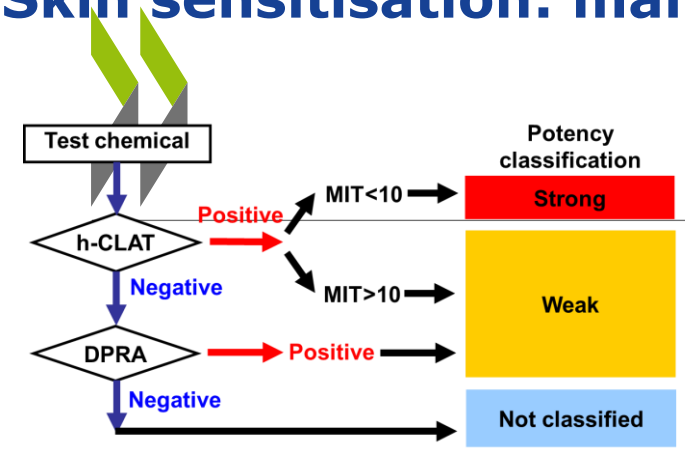
http://www.oecd-ilibrary.org/environment/oecd-series-on-adverse-outcome-pathways_2415170x;jsessionid=20oo8q54271qt.x-oecd-live-03

Skin sensitisation AOP and alternative method toolbox



https://aopwiki.org/wiki/index.php/Aop:40

Skin sensitisation: many possibilities of combining information

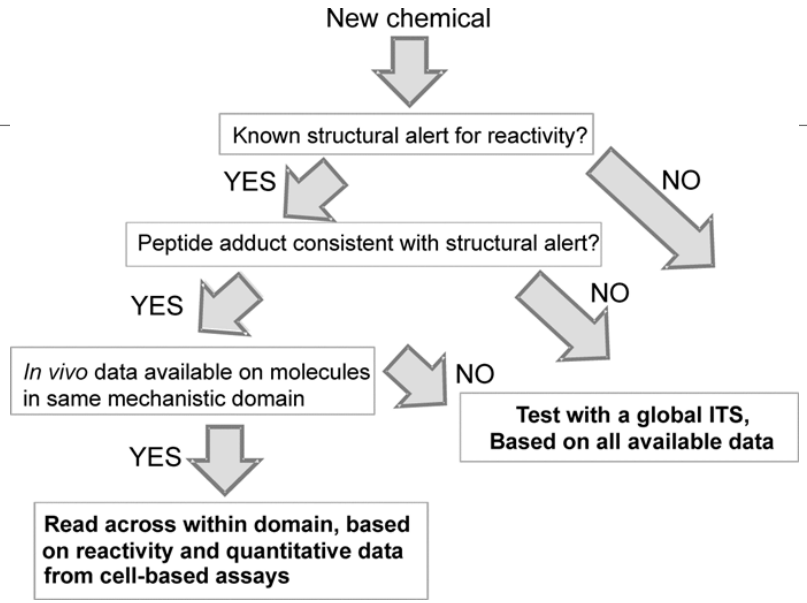


Takenouchi et al. (2015) J. Appl. Toxicol.: STS & ITS

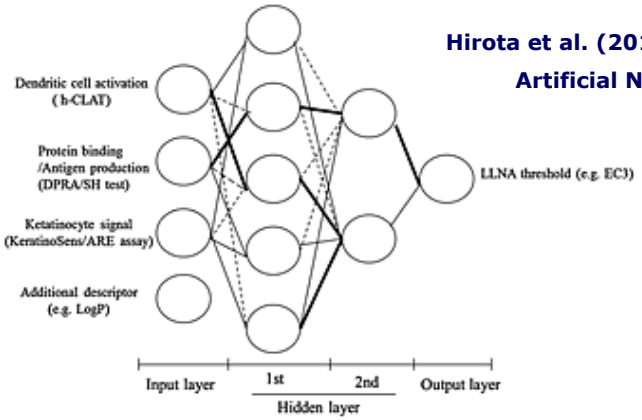
Score	h-CLAT MIT	DPRA depletion	DEREK
3	≤10 µg/mL	≥42.47%	-
2	>10, ≤150 µg/mL	≥22.62, <42.47%	-
1	>150, ≤5000 µg/mL	≥6.376, <22.62%	Alert
0	not calculated	<6.376%	No alert

Potency: Total battery score

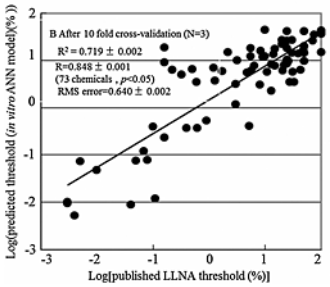
Strong :	7
Weak :	2-6
Not classified :	0-1

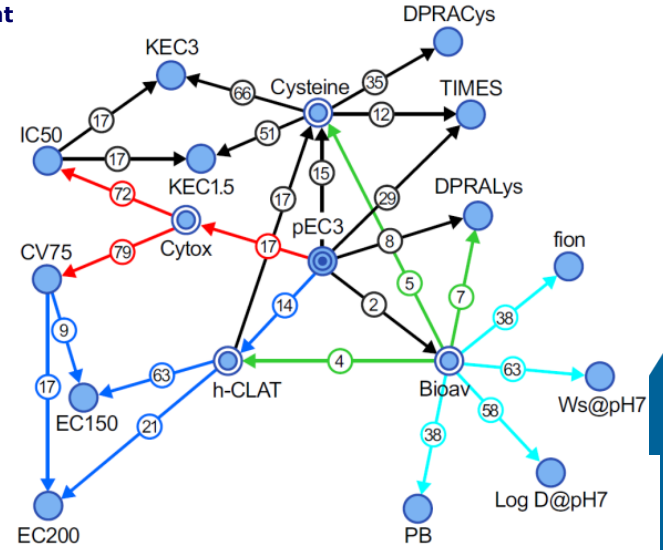


Natsch et al. (2015) Toxicological Science
Global/domain-based asssessment

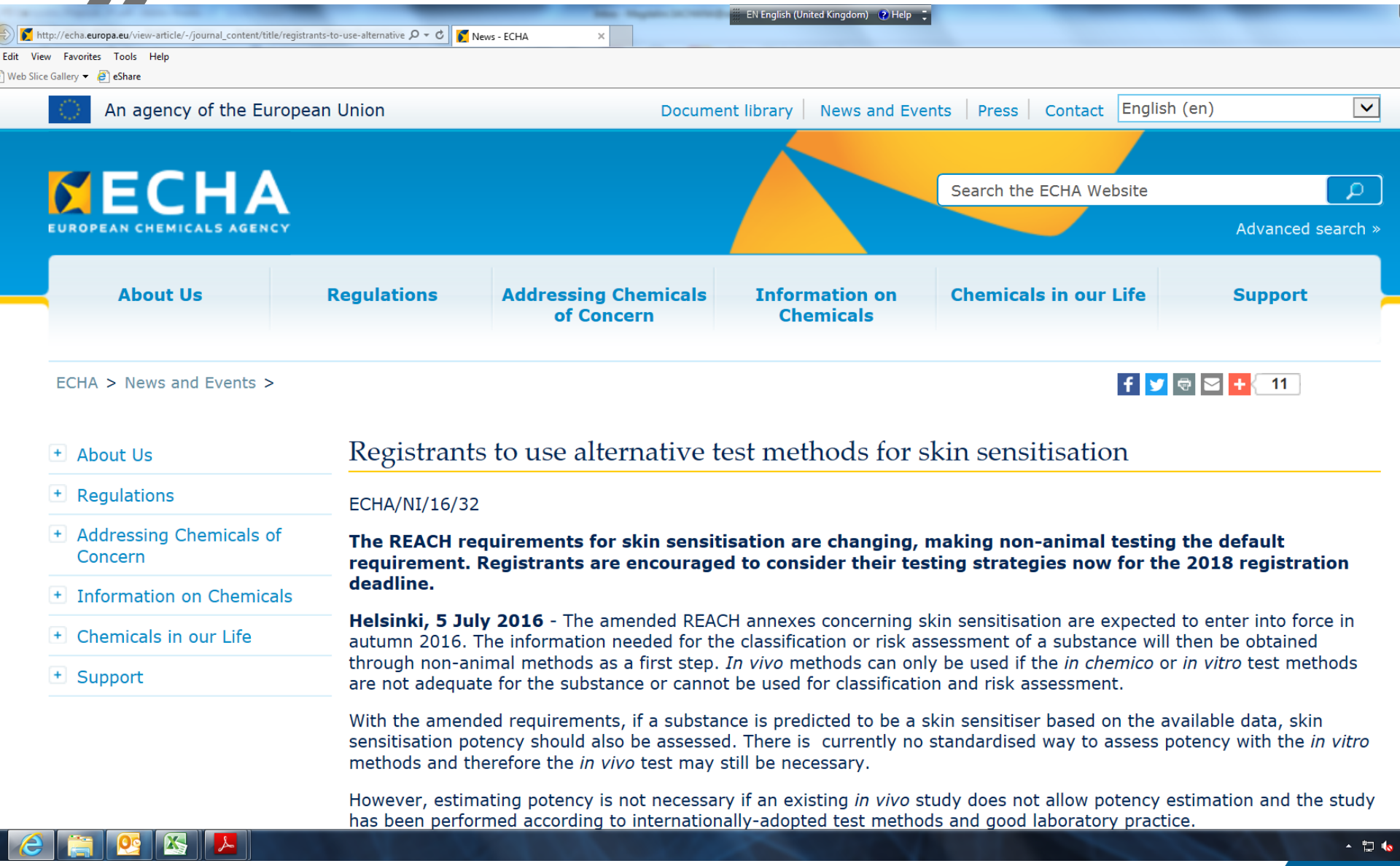


Hirota et al. (2015) J. Appl. Toxicol.:
Artificial Neural Network





Jaworska et al. (2015) Arch. Toxicol.:
Bayesian Network


http://echa.europa.eu/view-article/-/journal_content/title/registrants-to-use-alternative
News - ECHA
EN English (United Kingdom) Help
Edit View Favorites Tools Help
Web Slice Gallery eShare
An agency of the European Union
Document library News and Events Press Contact English (en)
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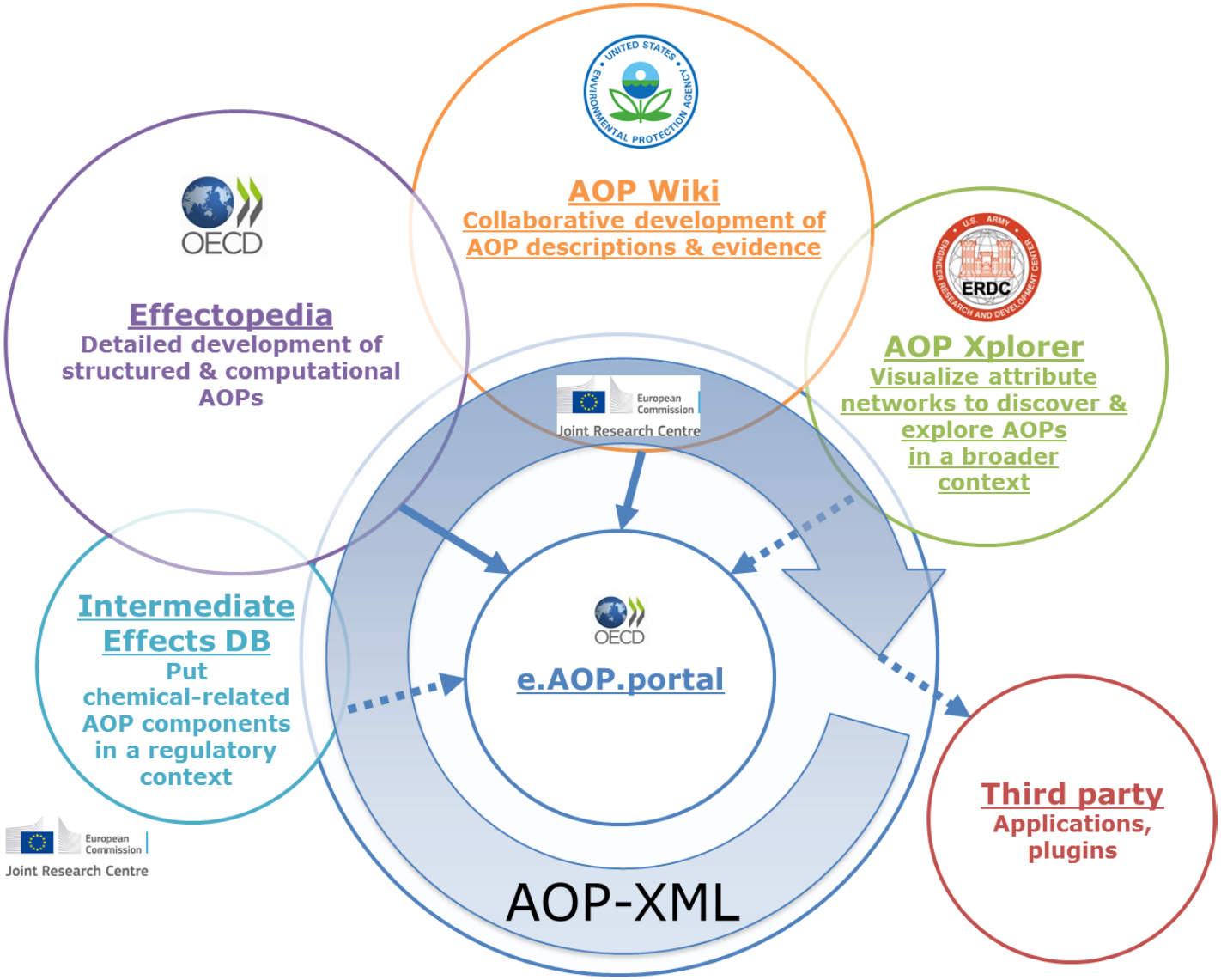
ECHA > News and Events >
11
About Us
Regulations
Addressing Chemicals of Concern
Information on Chemicals
Chemicals in our Life
Support
Registrants to use alternative test methods for skin sensitisation
ECHA/NI/16/32
The REACH requirements for skin sensitisation are changing, making non-animal testing the default requirement. Registrants are encouraged to consider their testing strategies now for the 2018 registration deadline.
Helsinki, 5 July 2016 - The amended REACH annexes concerning skin sensitisation are expected to enter into force in autumn 2016. The information needed for the classification or risk assessment of a substance will then be obtained through non-animal methods as a first step. In vivo methods can only be used if the in chemico or in vitro test methods are not adequate for the substance or cannot be used for classification and risk assessment.
With the amended requirements, if a substance is predicted to be a skin sensitiser based on the available data, skin sensitisation potency should also be assessed. There is currently no standardised way to assess potency with the in vitro methods and therefore the in vivo test may still be necessary.
However, estimating potency is not necessary if an existing in vivo study does not allow potency estimation and the study has been performed according to internationally-adopted test methods and good laboratory practice.

AOP-KB

AOP-KB modules



Main Page

Main Page

Navigation
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AOP List
AOP Table
EAGMST Approved AOPs
Help
FAQ
Recent changes
Release notes
Actions
Create new AOP
Feedback
Tools
What links here
Related changes
Special pages
Printable version
Permanent link
Page information

Announcements

There was a minor software upgrade for the AOP-Wiki on 2/13/2016. A list of the bug fixes and new features is available here: Release_Notes#Release_1.5_.281.2F17.2F2016.29. If you notice any problems, please email aopwiki@googlegroups.com and/or report here: Bug Reports.

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

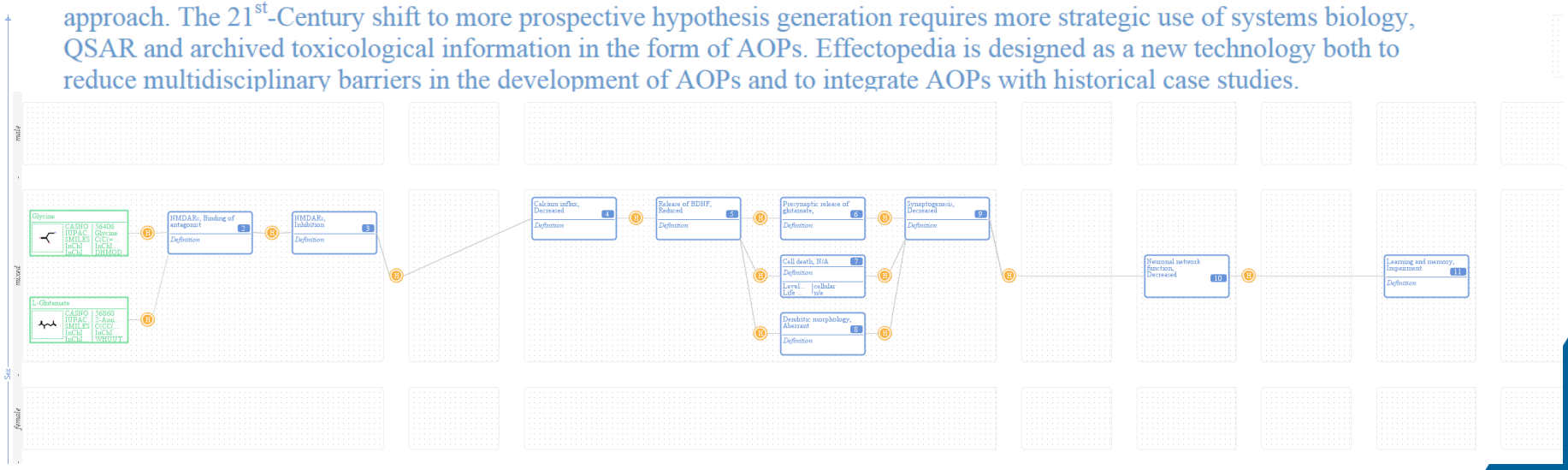
If you are interested in contributing AOP-related knowledge to the AOP-KB, please follow the instructions laid out at the OECD Adverse Outcome Pathways, Molecular Screening and Toxicogenomics page. The Guidance on Developing and Assessing AOPs document is the basis for all work related to contributing and sharing AOP-related knowledge. A Users' Handbook Supplement to this Guidance has been written to aid systematic development and transparent assessment of Adverse Outcome Pathways (AOPs). The handbook contains a template to guide AOP description and

Effectopedia

The Online Encyclopedia of Adverse Outcome Pathways

Effectopedia

Effectopedia is an open-knowledge aggregation and collaboration tool designed to facilitate the interdisciplinary efforts for delineating adverse outcome pathways (AOPs) in an encyclopedic manner with greater predictive power. As a response to the growing awareness that a paradigm shift in chemical risk assessment is needed, Effectopedia provides a capability to move beyond the last half-century's phenomenological approach with animal testing to a more mechanistic and hypothesis-driven approach. The 21st-Century shift to more prospective hypothesis generation requires more strategic use of systems biology, QSAR and archived toxicological information in the form of AOPs. Effectopedia is designed as a new technology both to reduce multidisciplinary barriers in the development of AOPs and to integrate AOPs with historical case studies.



e.AOP.Portal

Retrieve all Adverse Outcome Pathways

Enter query to retrieve matching AOP titles, or leave blank to display all AOPs

Title containing...

Example: Androgen

START QUERY »

Results

8 page(s) | next page

AOP Title	View in native app	AOP Source
5-hydroxytryptamine transporter (5-HTT) inhibition leading to population increase	AOP195	https://aopwiki.org/
5-hydroxytryptamine transporter (5-HTT; SERT) inhibition leading to decreased shelter seeking and increased predation	AOP98	https://aopwiki.org/

OECD
BETTER POLICIES FOR BETTER LIVES

AOP-KB

- AOP
  - Background
  - OECD Guidance
  - OECD Handbook
- AOP-KB
  - AOP-Wiki
  - AOP-Xplorer
  - Effectopedia
  - IEDB
- AOP-Lists
- AOP-KB Search
- Contribute
- Resources
- Partners

• Enter your search phrase here

Available sorting options:
status, title , creation date, last modification date

Search

200 adverse outcome pathways found from 2

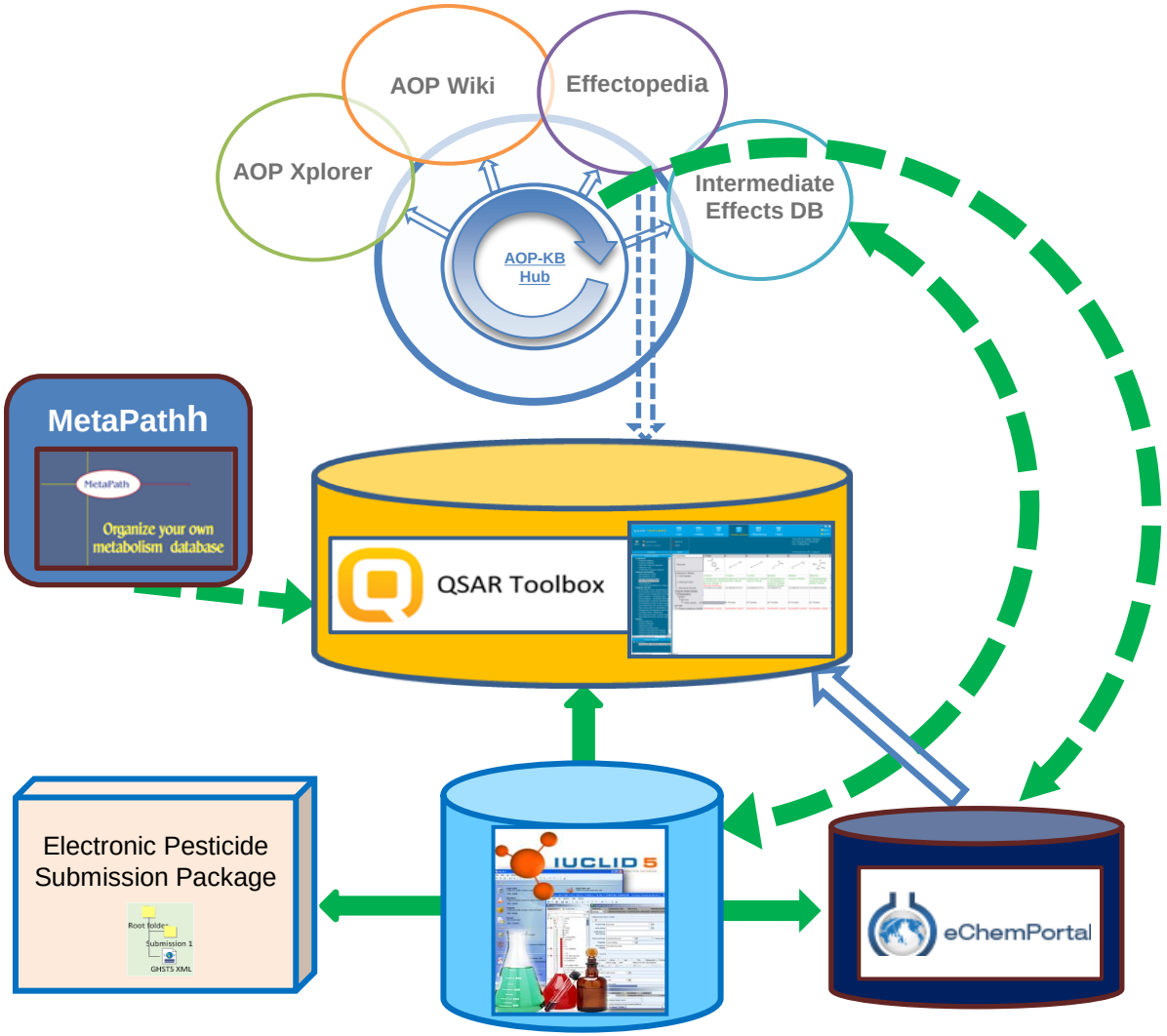
3000 key events found from 2 modules

Sort by title ▼

As in the current e.AOP.Portal show a paginated list of AOPs sorted in alphabetic order of the titles form all available data sources (AOP-Wiki and Effectopedia). Allow user to choose different sorting criteria arrange with combo box or list of options: (which can allow users to choose between ascending or descending order)
Sort by: status, **title**▼ , creation date, last modification date

Aromatase inhibition leading to reproductive dysfunction (in fish)
https://aopkb.org/aopwiki/index.php/Aop:25
Aromatase, Inhibition; 17beta-estradiol synthesis by ovarian granulosa cells, Reduction; Cumulative fecundity and spawning, Reduction; Plasma 17beta-estradiol concentrations, Reduction; Plasma vitellogenin concentrations, Reduction; Transcription and translation of vitellogenin in liver, Reduction; Vitellogenin uptake into oocytes and oocyte growth/development, Reduction; Population trajectory, Decrease …
Created on 01.01.2014, Last updated 14.01.2016, Status: EAGMST Approved , Project number, Review Report, i-Library
Source AOP-Wiki

Interlinkages between systems - data exchange



Websites for further information

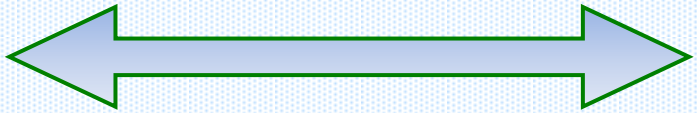
- OECD public website on Adverse Outcome Pathways:
  http://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm
- e.AOP.Portal:
  - Test platform http://aopkb-pp.oecd.org/
  - Production platform http://aopkb.oecd.org/ when the domain name will be transferred
- Wiki platform: https://aopkb.org/aopwiki
- Effectopedia: http://www.effectopedia.org/

THANK YOU

Types of IATA

Flexible

Judgement-based



Prescriptive

Rule-based

Non-formalised approaches

e.g. grouping and read-across

"Structured approaches"

e.g. Integrated Testing Strategy (ITS)

OECD IATA Case Studies Project

OECD Project on defined approaches

Defined approaches

- A defined approach to testing and assessment consists of a fixed data interpretation procedure (DIP) (e.g. sequential testing strategies, regression models, 2 out of 3 WoE, scoring systems, machine learning approaches, Bayesian networks, etc…) applied to data generated with a defined set of information sources (formalised decision-making approach)
- The result can either be used on its own, or together with other information sources within an IATA

OECD ENV/JM/HA(2016)10