



THE OECD PROGRAM ON ADVERSE OUTCOME PATHWAYS (AOP)

WC-9 Satellite meeting
AOP 101
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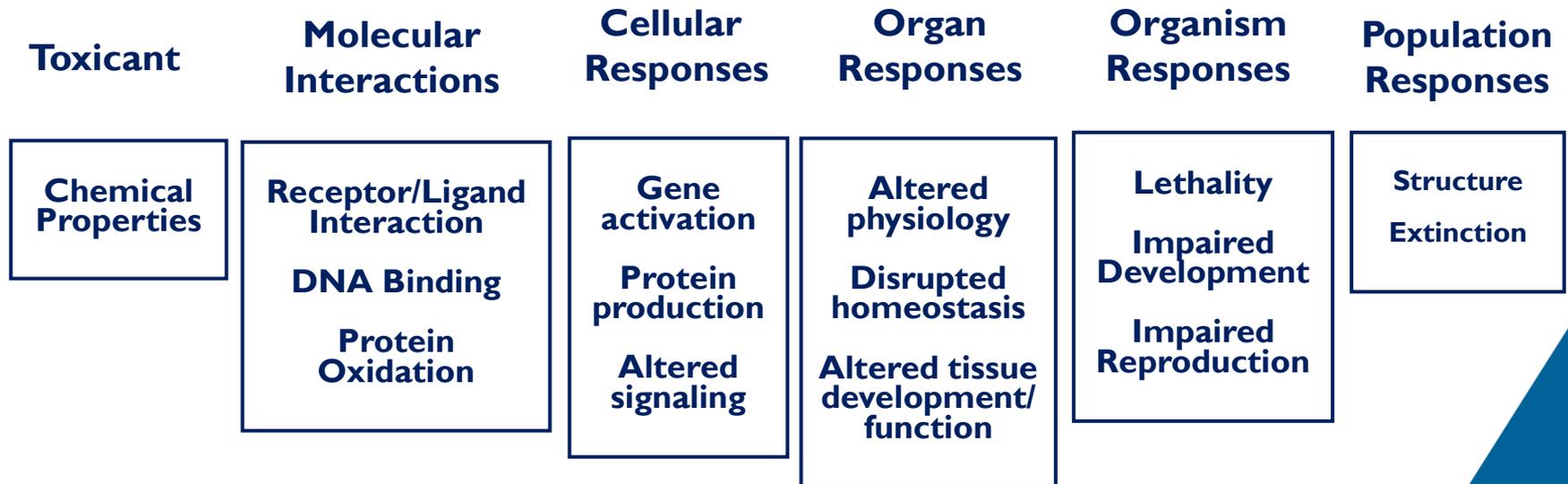
Launch of the Programme at OECD

- 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



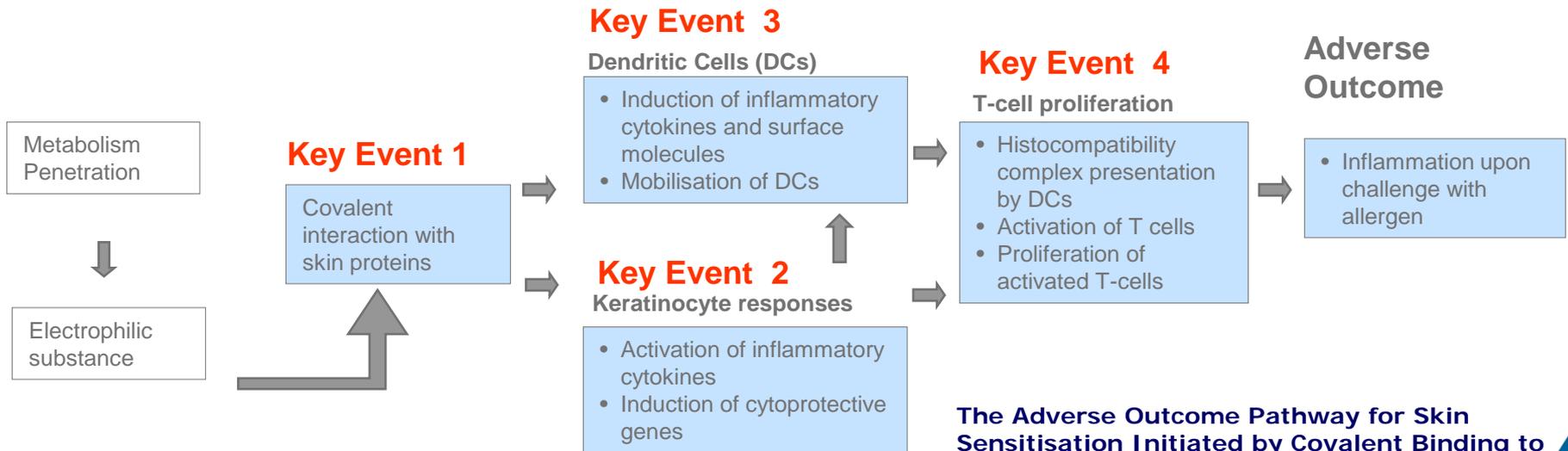
The Adverse Outcome Pathways concept

- AOPs delineate the documented, [plausible](#), and [testable](#) processes by which a chemical induces molecular perturbations ([Molecular Initiating Events](#)) and the associated biological responses ([Key Events](#)) that describe how the molecular perturbations cause effects at the subcellular, cellular, tissue, organ, whole animal, and population levels of observation.



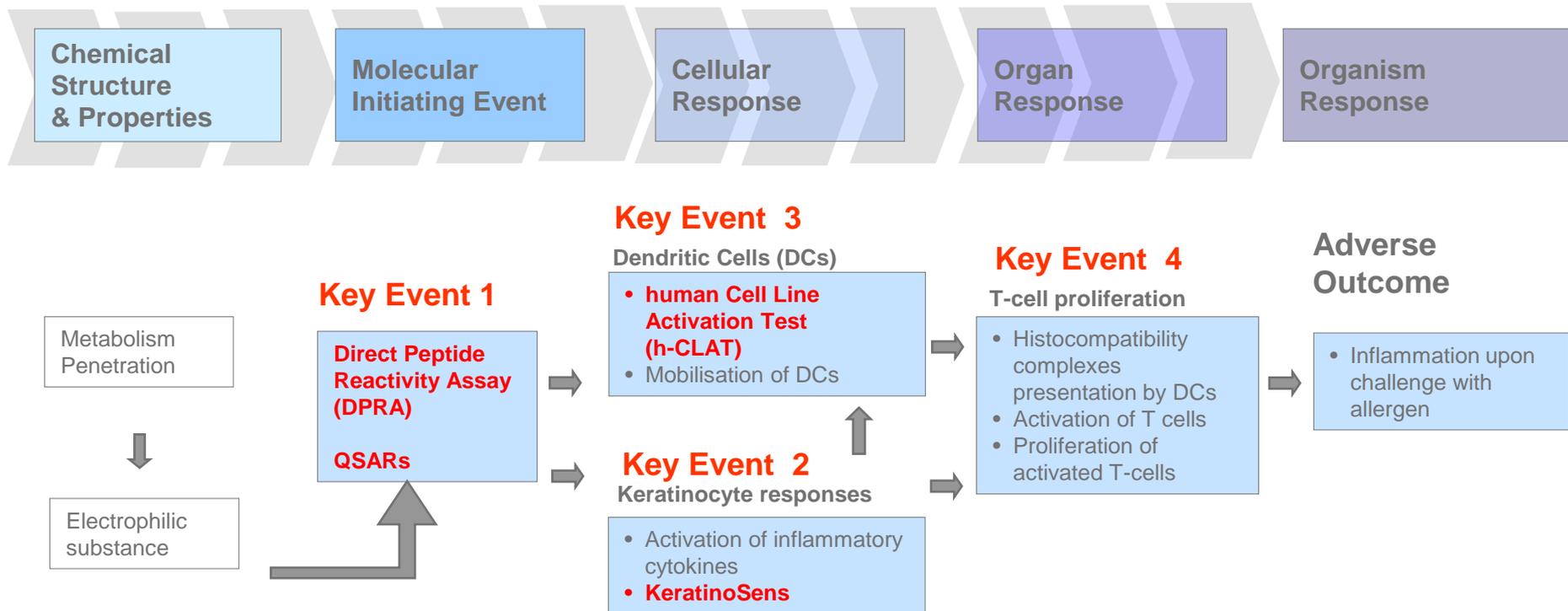


AOP for skin sensitisation



The Adverse Outcome Pathway for Skin Sensitisation Initiated by Covalent Binding to Proteins; Part 1: Scientific Evidence Series on Testing and Assessment No.168 ENV/JM/MONO(2012)10/PART1

Mapping alternative methods to key events





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.



Application of the AOP concept to support grouping of chemicals

- As the MIE in each AOP involves a rather specific interaction of chemicals with biological systems, it can be used as the basis for generating structure–activity relationships, whether or not quantifiable.
- In turn, such information can be used for chemical grouping and read-across approaches, thus facilitating predictive and mechanism-based toxicology



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.

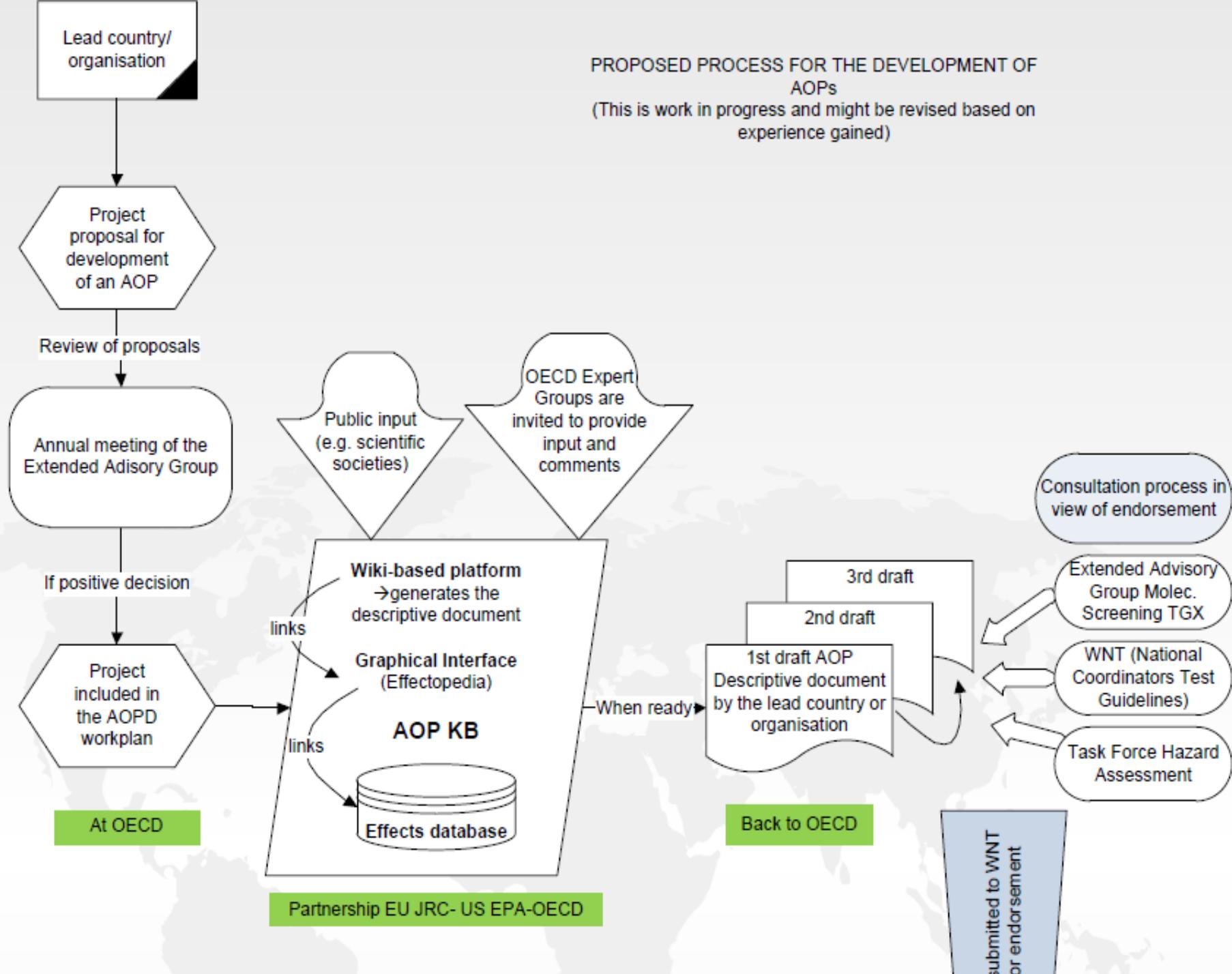
<http://www.oecd.org/env/ehs/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm>



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 Kristie Sullivan's 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

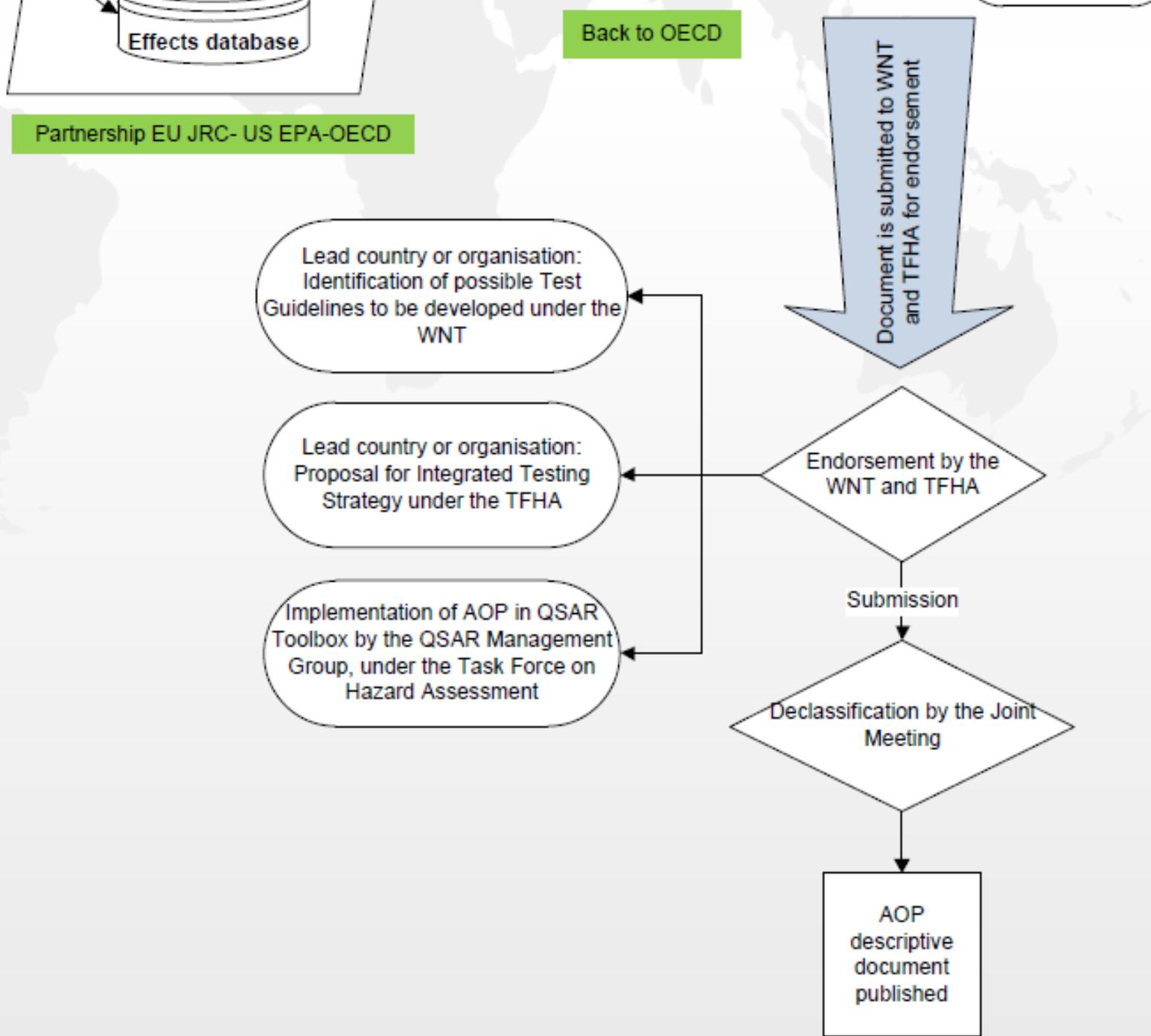
Implementation of AOP in QSAR
Toolbox by the QSAR Management
Group, under the Task Force on
Hazard Assessment

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



**Thank you for listening
on a Sunday morning!**

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