An EU strategy on aggregate exposure: The ExpoAdvance Roadmap

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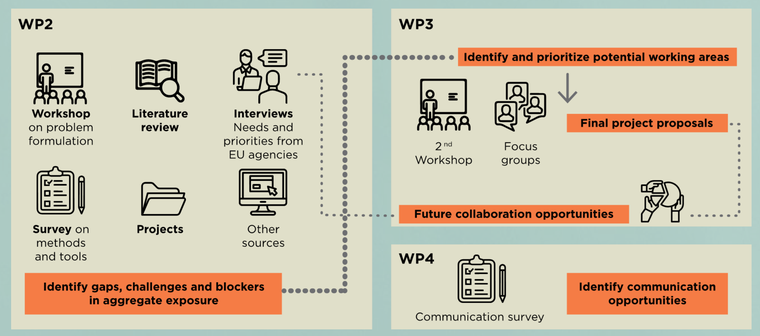
Introduction

Traditionally, chemical risk assessment has focused on evaluating risks associated with individual sources. However, individuals are exposed to the same chemical through multiple pathways. Aggregate exposure (AE) is the total exposure to a chemical — the combined dose received from all sources.

The ExpoAdvance roadmap presents the state-of-the-art on AE and identifies key projects by reviewing relevant scientific literature and projects and gathering insights and interests from key stakeholders. Eight key strategic projects are designed to support the actualization of the roadmap through 2030.

Methods

To identify relevant research gaps and challenges in AE, several engagement activities were organized with the involvement of relevant stakeholders (industry, regulators, public institutes, and Academia). A workshop was aimed at updating the original problem formulation. Interviews were organized with experts from EC agencies, DGs, and Committees. A survey was launched on methods and tools used in AE. In parallel, literature reviews were performed, and projects were screened to look for applications in the field of AE.



Information was collected and organized in working areas (WAs). A second expert workshop was held to refine WAs. A list of 24 project proposals were generated according to the WAs.

WA prioritization, and derived project proposals refinement and revision were obtained through focus groups.

In parallel, collaboration opportunities based on past and ongoing projects were identified. An online questionnaire was used to collect data on how to effectively communicate AE assessment to both stakeholders and the general public.

Results

Gaps and Challenges

A. Characterising source-specific exposures

- The **variability in the characteristics** of different exposures to chemicals will require a **wide range of source-specific models**.
- The **large number of chemicals** used in commerce require **significant resources to identify, collect, and curate data**. Additional research may be required to define the exposed populations.
- Such **data are complex** and include variability e.g. depending on the measurement methods. **Synthesis of multiple sources** of data may be required.
- For some sources, data may need to be created by **monitoring programs or surveys of human behaviors**.

B. Screening assessments of chemical's AE

- **Confidentiality** may affect data availability, e.g. on personal exposure.
- **Databases** would be large and include chemical-specific data for large numbers of chemicals and tables of default values for other model inputs.

C. Higher tier exposure models

- Developing **guidance** could be a complex process. Higher-tier exposure models will be source- and chemical-specific, regularly updated to reflect new data.
- **Surveys** could be designed to reflect AE, e.g. to flag concurrent use of consumer products and dietary exposure.
- New approaches are needed for **modeling** the potential for **co-exposures**.
- Measurements of exposure are limited to time scales of days and weeks.
- **Human biomonitoring** (HBM) provides an independent measure of AE.

D. PBK modelling

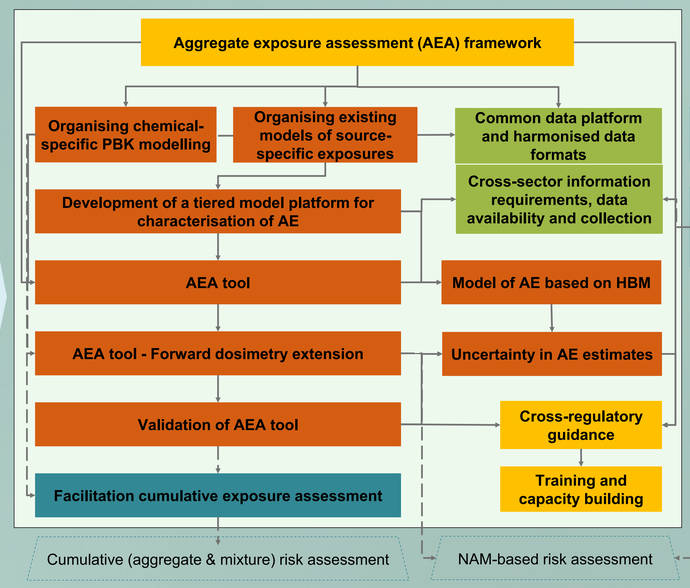
- Generating in-vitro and in-silico data to capture the biological mechanisms and organizing a centralized curated database with **ADME data**.
- Harmonize the reporting of models' **uncertainty and variability**.
- Data on **metabolites** are difficult to generate and predict.
- **Targeted methodologies** for generating ***in vitro*** and ***in silico*** data are needed to develop more detailed PBK model platforms.
- Develop default **low-tier kinetic conversion factors**.
- Promote **model interoperability** and **curated data platforms**.
- Consider variation of chemical kinetics across **age groups**.
- **Harmonization** and **guidance** relevant to the application of **reverse dosimetry** approaches.

E. Data management

- The large **number of chemicals**, the **type** of relevant **data** and **data streams** needed for AE assessment is large and fall under different (regulatory) domains.

F. Regulatory guidance for performing AEAS

- AE is dependent on **sources of exposure** that may be addressed by **different regulations**.
- Some data may be **confidential**. Complete data sharing may not be possible due to the confidential nature of some data. Shared data management systems would need to be developed.
- **Regulatory harmonization** may be required.



Gap area	Project	Working area category		
C, F	P1. AEA methodological framework	Framework and guidance		
A, B, C, F	P2. AEA open-source model system	Methodology		
A, C	P3. Higher-tier probabilistic AE model and inter-individual variability	Methodology		
C, D	P4. The use of HBM as a tool for supporting AE	Methodology	Data	
A, B, D, E	P5. Data platform	Data		
B, C, D, F	P6. AEA model system: forward and reverse dosimetry	Methodology		
A, B, E, F	P7. Exposure and risk repository	Data	Framework and guidance	
A, B, E	P8. AEA Prioritization	Methodology	Data	Innovation

Reference

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Disclaimer

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