ASCCT-ESTIV Webinar

30 September 2022

EFSA's roadmap on NAMs and related case studies

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Trusted science for safe food

European Food Safety Authority

Disclaimer: The views, thoughts and opinions presented are not necessarily those of EFSA

Regulated products

Contaminants

Applicants

No commercial producer

New chemicals or already on market

II

(Non-legislative acts)

REGULATIONS

COMMISSION REGULATION (EU) No 283/2013

of 1 March 2013

setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

(Text with EEA relevance)

EFSA Journal 2012;10(7):2760

SCIENTIFIC OPINION

Guidance for submission for food additive evaluations[1]

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

Main sources and types of data received by EFSA

EFSA's use of alternative approaches in chemical risk assessment: the past two decades

In vitro approaches for genotoxicity testing

- Established battery of in vitro tests
- When clear absence of genotoxicity there is no need for in vivo tests

TTC approach in chemical risk assessment

- Used by EFSA since 2004 for flavourings (EFSA Guidance from 2010 under review)
- For some impurities, metabolites and degradation products
- Pharmacologically active substances present in food of animal origin
- Combined exposure to multiple chemicals
- 2019 Guidance

Read-across in chemical risk assessment

- Flavourings
  - ✓ 1996-2006: Grouping of ~2650 existing flavourings into 34 groups of substances of structurally related compounds expected to show similar metabolic and biological behaviour
  - ✓ Flavouring Group Evaluations (FGEs)
  - ✓ Procedure for evaluation of new flavourings
- Combined exposure to multiple chemicals
  - ✓ Read-across from similar mixtures (sometimes referred to as sufficiently similar mixtures)
  - ✓ Grouping chemicals into assessment groups
- Food contact materials (ad-hoc)

Example: Pesticide metabolites

GUIDANCE

EFSA Journal

ADOPTED: 22 July 2016

doi: 10.2903/j.efsa.2016.4549

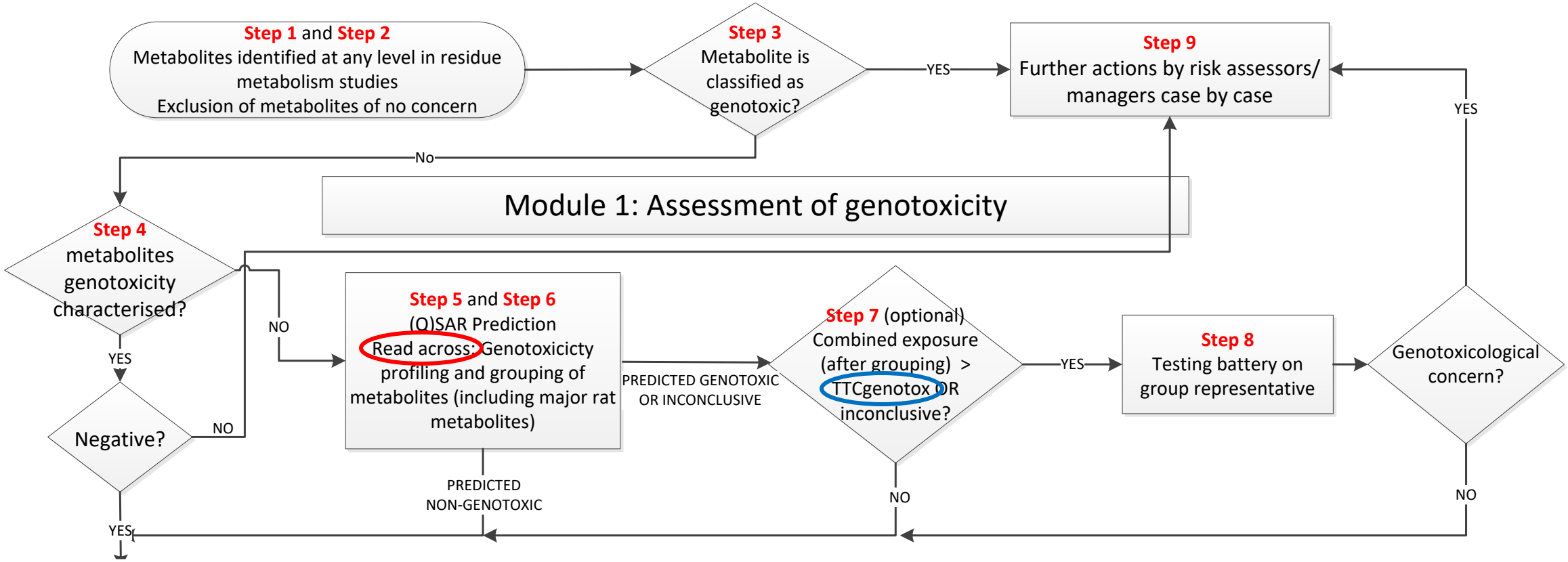
Guidance on the establishment of the residue definition for dietary risk assessment

EFSA Panel on Plant Protection Products and their Residues (PPR)

Abstract

EFSA has asked the Panel on Plant Protection Products and their Residues to prepare guidance on the establishment of the residue definition for dietary risk assessment. The residue definition for risk assessment is used by risk assessors to evaluate the potential risk of dietary intake of residues resulting from the application of a pesticide. This document guides the complex process of identifying

Module 1: Genotoxicity assessment



The future of chemical risk assessment in EFSA: New projects, new challenges and new ambitions

Changing the way to do Risk Assessment: EC Policies

EUROPEAN COMMISSION

Brussels, 14.10.2020
COM(2020) 667 final

Safety testing and chemical risk assessment need to innovate in order to reduce dependency on animal testing but also to improve the quality, efficiency and speed of chemical hazard and risk assessments.

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS

Chemicals Strategy for Sustainability
Towards a Toxic-Free Environment

SCIENCE-POLICY INTERFACE

The Commission will:

- foster multidisciplinary research and digital innovations for **advanced tools, methods and models, and data analysis capacities**[102] to also move away from animal testing;

mb210624-a2

EFSA Strategy 2027

Science

Safe food

Sustainability

Adopted at the Management Board meeting
held in virtual modality on 24 June 2021
For EFSA's Management Board
[SIGNED]
Raymond O'Rourke
Chair of the Management Board

efsa
European Food Safety Authority

STRATEGIC OBJECTIVE 2

Ensure preparedness for future risk analysis needs

2.1.3 The quality of scientific guidance and methodologies, with the necessary risk assessment capabilities is improved to address future challenges. Within its risk assessment approaches, EFSA will develop and integrate new scientific developments focusing on NAM-based methods and the minimisation of animal testing, innovations in food systems, data, and technology, and strive to meet One health policy needs.

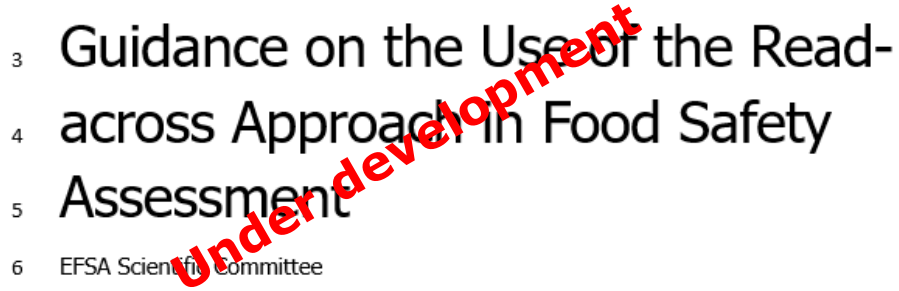
Expected Operational Result 2.1.3

The quality of scientific guidance and methodologies, with the necessary risk assessment capabilities, is improved to address future challenges

KEY ACTIONS

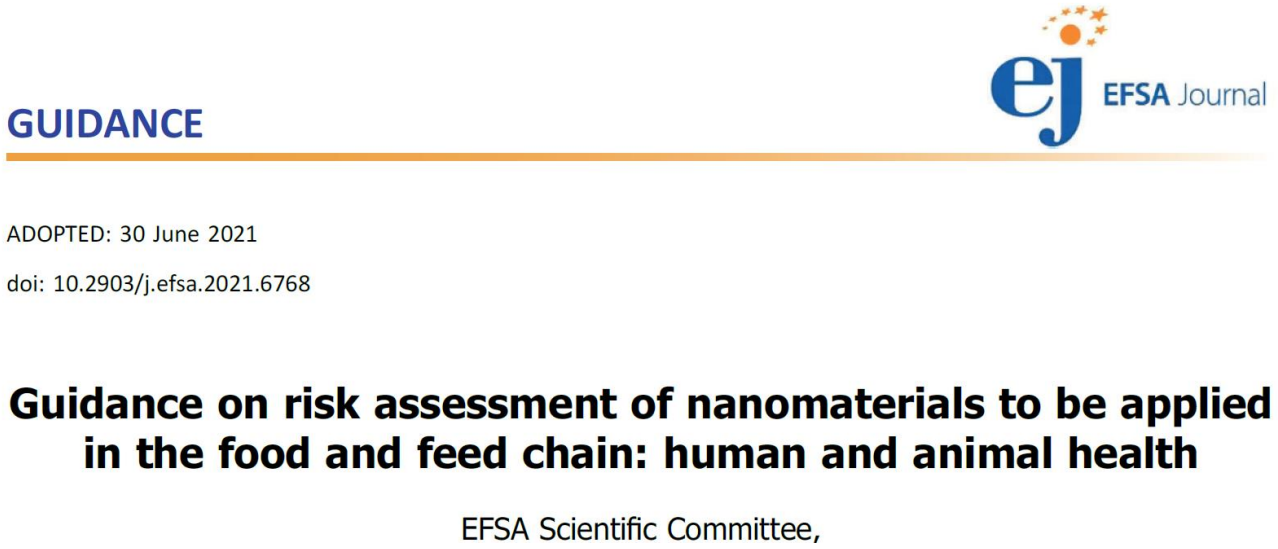
- Develop and integrate new approach methodologies (NAMs) and omics for regulatory risk assessment

Read-Across Approaches for Food Safety



- Development for a **horizontal Guidance** on the use of RAx in EFSA and by its Scientific Panels
  - Testing the **regulatory applicability** of RAx to chemicals in remit of food safety
  - Testing opportunities for biological RAx
  - Testing opportunities to underpin RAx with NAM
- Procurement to test RAx using EFSA's database on plant protection products

Risk Assessment of Nanomaterials



GUIDANCE

EFSA Journal

ADOPTED: 30 June 2021

doi: 10.2903/j.efsa.2021.6768

Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health

EFSA Scientific Committee,

- In vitro tests may provide insights into a **nanomaterial's hazard and its mode of action** upon e.g. **internal exposure**.
- In vitro toxicity tests have an advantage, because, when properly designed, it is usually possible to **monitor directly the cellular internalisation and subsequent fate of the nanoparticles**.
- In vitro studies may provide mechanistic information on the **toxicokinetics and toxicodynamics** of the nanomaterials.
- Informing the weight of evidence approach.

DNT

SCIENTIFIC OPINION

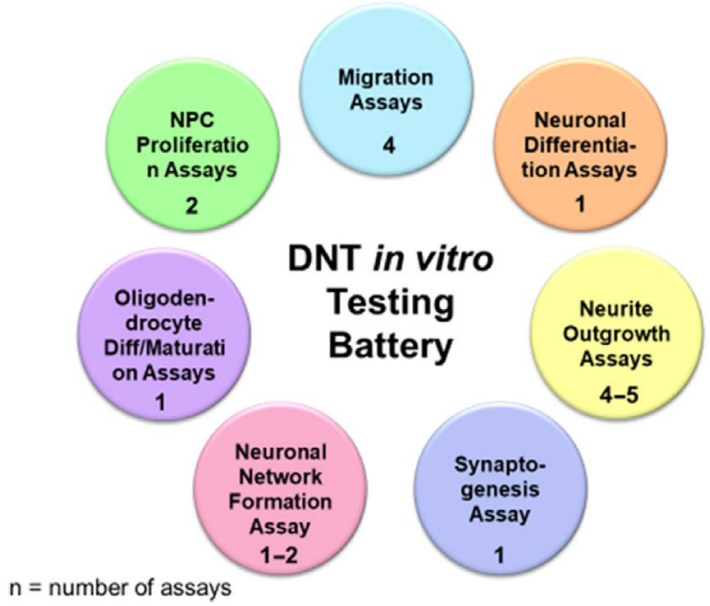
EFSA Journal

ADOPTED: 21 April 2021

doi: 10.2903/j.efsa.2021.6599

Development of Integrated Approaches to Testing and Assessment (IATA) case studies on developmental neurotoxicity (DNT) risk assessment

EFSA Panel on Plant Protection Products and their Residues (EFSA PPR Panel),



- **The IATA were developed to assess the applicability of the DNT in vitro testing battery (IVB), designed to explore fundamental neuro-developmental processes, in the regulatory risk assessment of pesticides**
- **Case studies** show the applicability of the DNT-IVB for hazard identification and characterisation and illustrate the usefulness of an AOP-informed IATA for regulatory decision making.

Non-Monotonic Dose-responses

- To facilitate the assessment, and also minimise the need for repeating animal studies, **NAM-based studies** should be considered.
- The integration of available animal and human studies with NAMs may provide the **mechanistic understanding** required for implementing the use of **AOP approaches**.

SCIENTIFIC OPINION

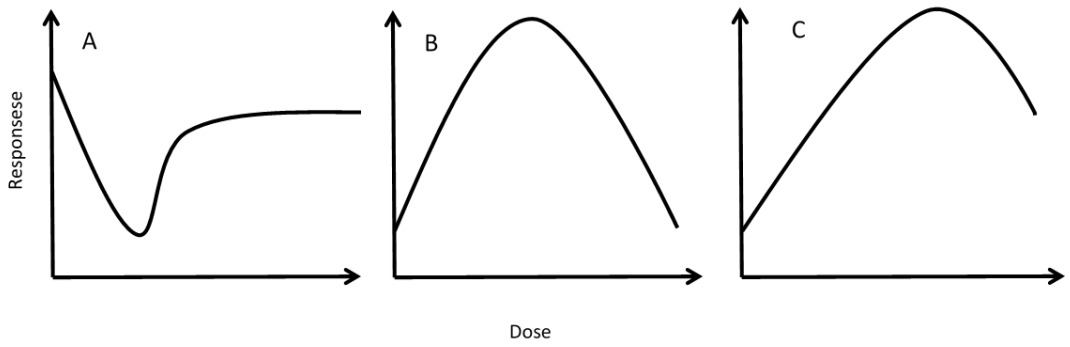
EFSA Journal

ADOPTED: 22 September 2021

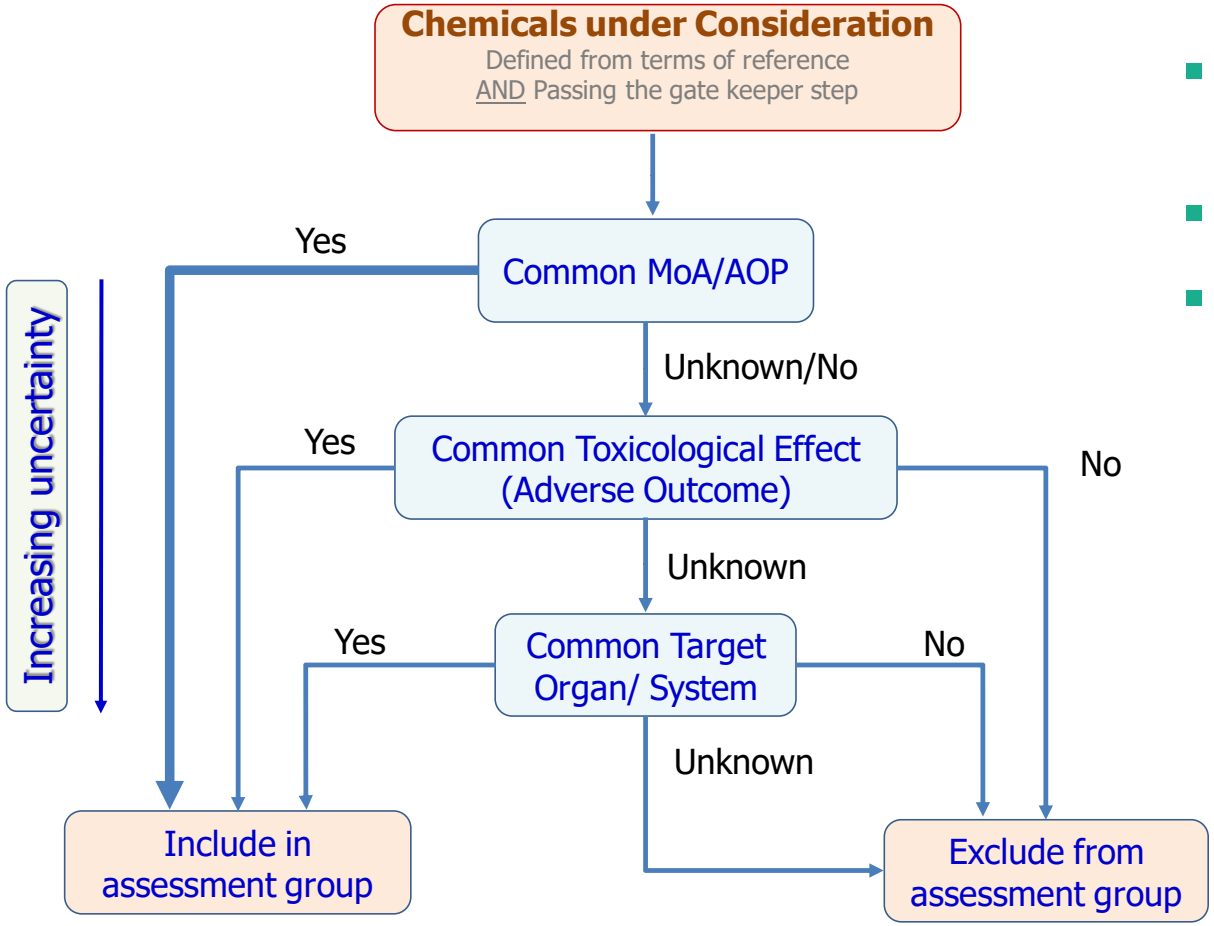
doi: 10.2903/j.efsa.2021.6877

Opinion on the impact of non-monotonic dose responses on EFSA's human health risk assessments

EFSA Scientific Committee,



Criteria for grouping for RA

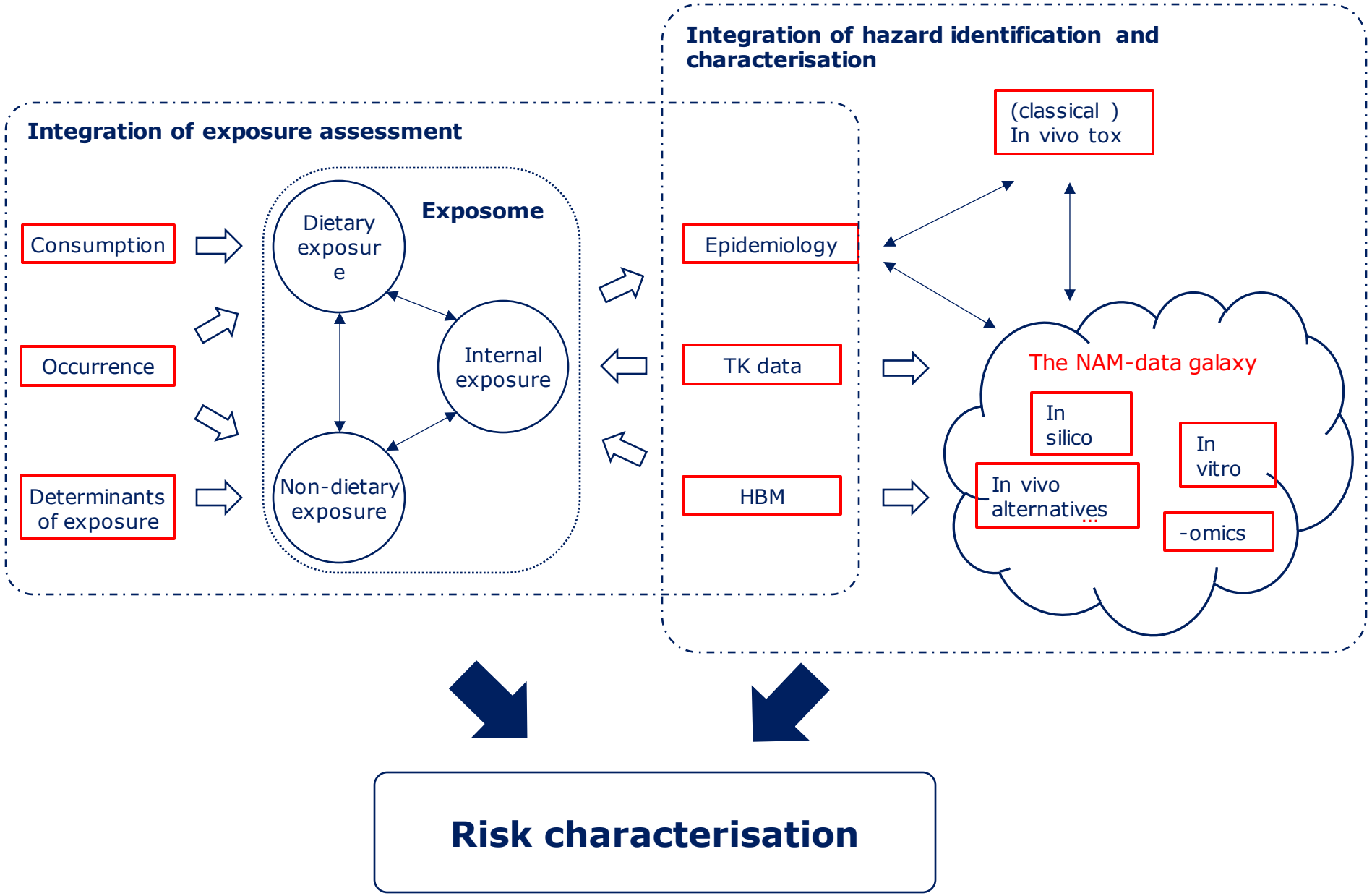


- Human risk assessment of combined exposure to multiple chemicals
- Incorporation of MoA/AOP
- Recommendations
  - Support **integration of data** generated from NAMs as currently investigated world-wide (OECD, US EPA, EFSA) and Horizon 2020 and Horizon Europe programmes (EuroMix, EUTOXRISK, HBM4EU, PARC etc.).
  - Further develop and implement in silico approaches that could support grouping of chemicals. This will support the **development of NAMs for grouping multiple chemicals** based on a) predictions of the interaction between chemicals and their molecular targets, b) predictions of toxicological endpoints.

Collaborative (outsourced) NAM case studies

- Pesticides: neurodegenerative diseases
- Nanomaterials: GI uptake and genotoxicity
- Artificial intelligence for NAMs
- PFAS immunotoxicity
- Essential oils as feed additives and interspecies metabolic differences
- TKplate 2.0 (Open-Source Platform integrating PBTK Models and Machine Learning Models)
- Human variability in toxicodynamics (qAOPs)

Chemical Risk Assessment - a vision for the coming years



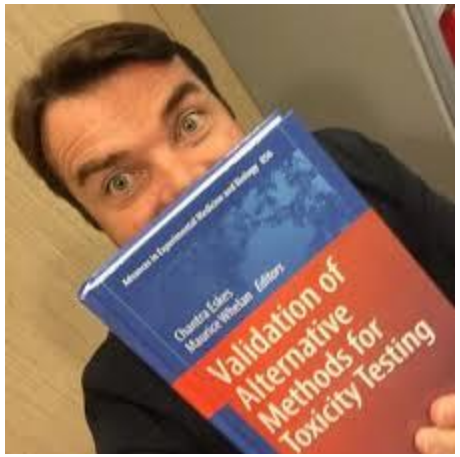
EFSA's Engagement: EU Landscape

Draft proposal for a European Partnership under Horizon Europe

Partnership for the Assessment of Risk from Chemicals (PARC)

Version 03/06/2020

EURL ECVAM
European Union Reference Laboratory for Alternatives to Animal Testing



ASPIS Consortium (RISK-HUNT3R, ONTOX and PrecisionTOX)

efsa
European Food Safety Authority

epaa
The European Partnership for Alternative Approaches to Animal Testing

EUTOXRISK

EFSA's Engagement: International Landscape

OECD

efsa
European Food Safety Authority

World Health Organization

Food safety agencies

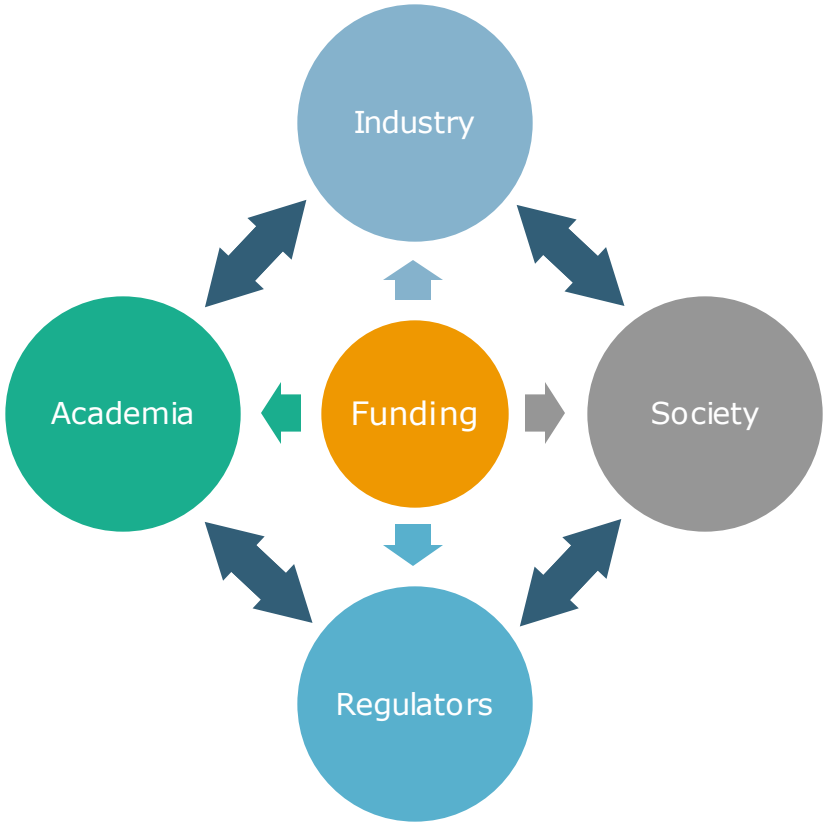
ILMERAC

Global Coalition for Regulatory Science Research

Some final thoughts – how to move to NGRA?

Vision, expectations and opportunities

Collaboration, acceptability and sustainability






Thank you!