EU-ToxRisk Final Symposium

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The Square, Brussels, Belgium

EU-ToxRisk and EFSA

A common journey towards NGRA

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Trusted science for safe food

efsa

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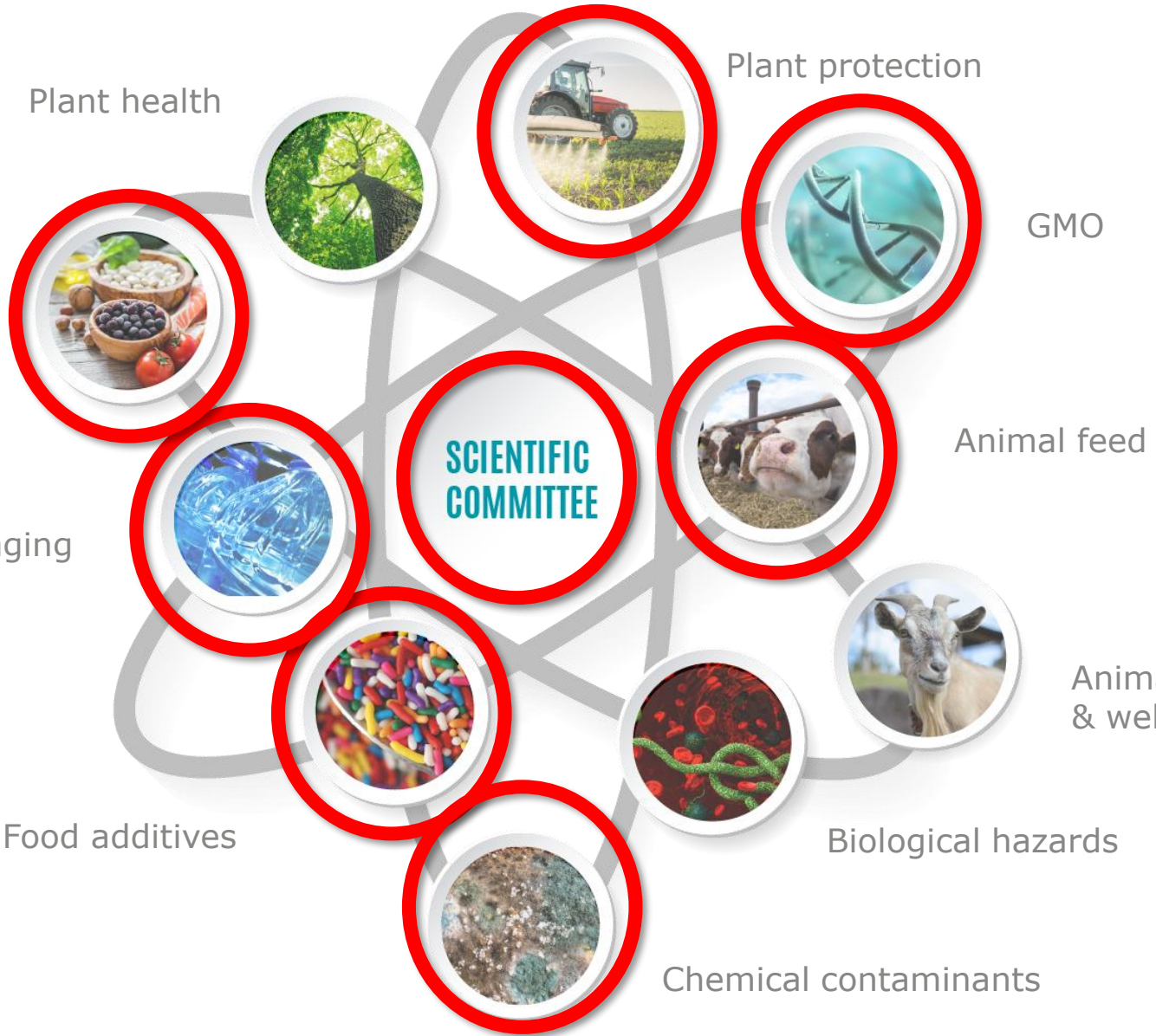
Disclaimer: The views, thoughts and opinions presented are not necessarily those of EFSA



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]

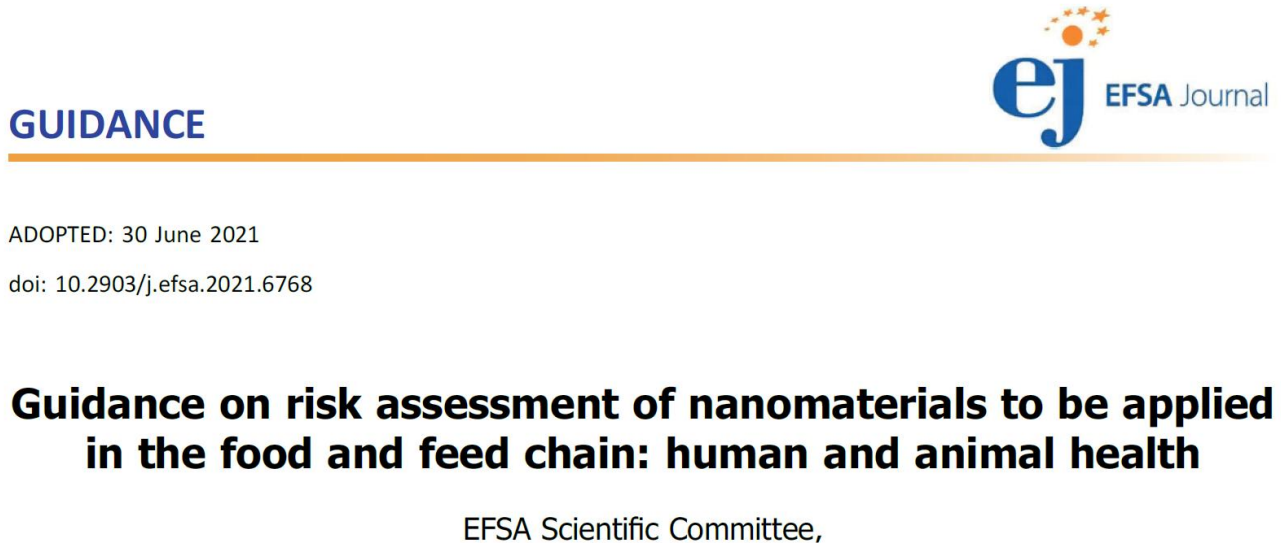
European Food Safety Authority (EFSA), Parma, Italy

EFSA's Journey towards NGRA

Read-Across Approaches for Food Safety

- Started in 2020
- 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
  - Opportunities for biological RAx
  - Underpinning of 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

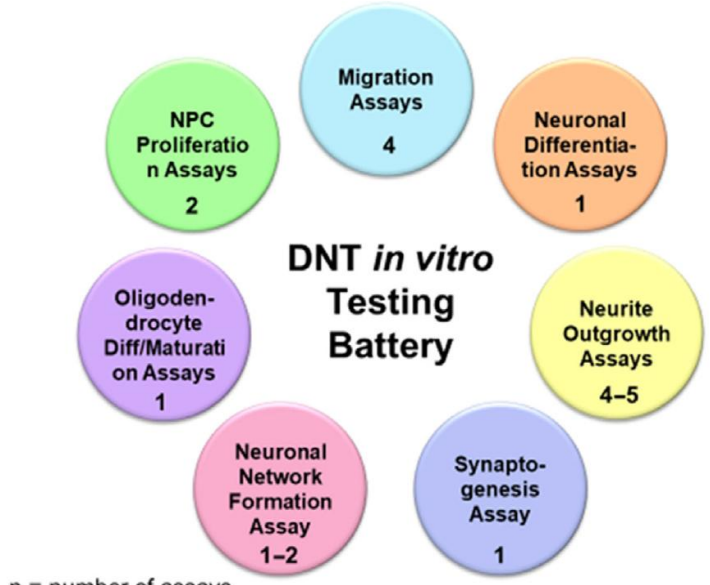
EFSA Journal

ADOPTED: 21 April 2021

doi: 10.2903/j.efsa.2021.6599

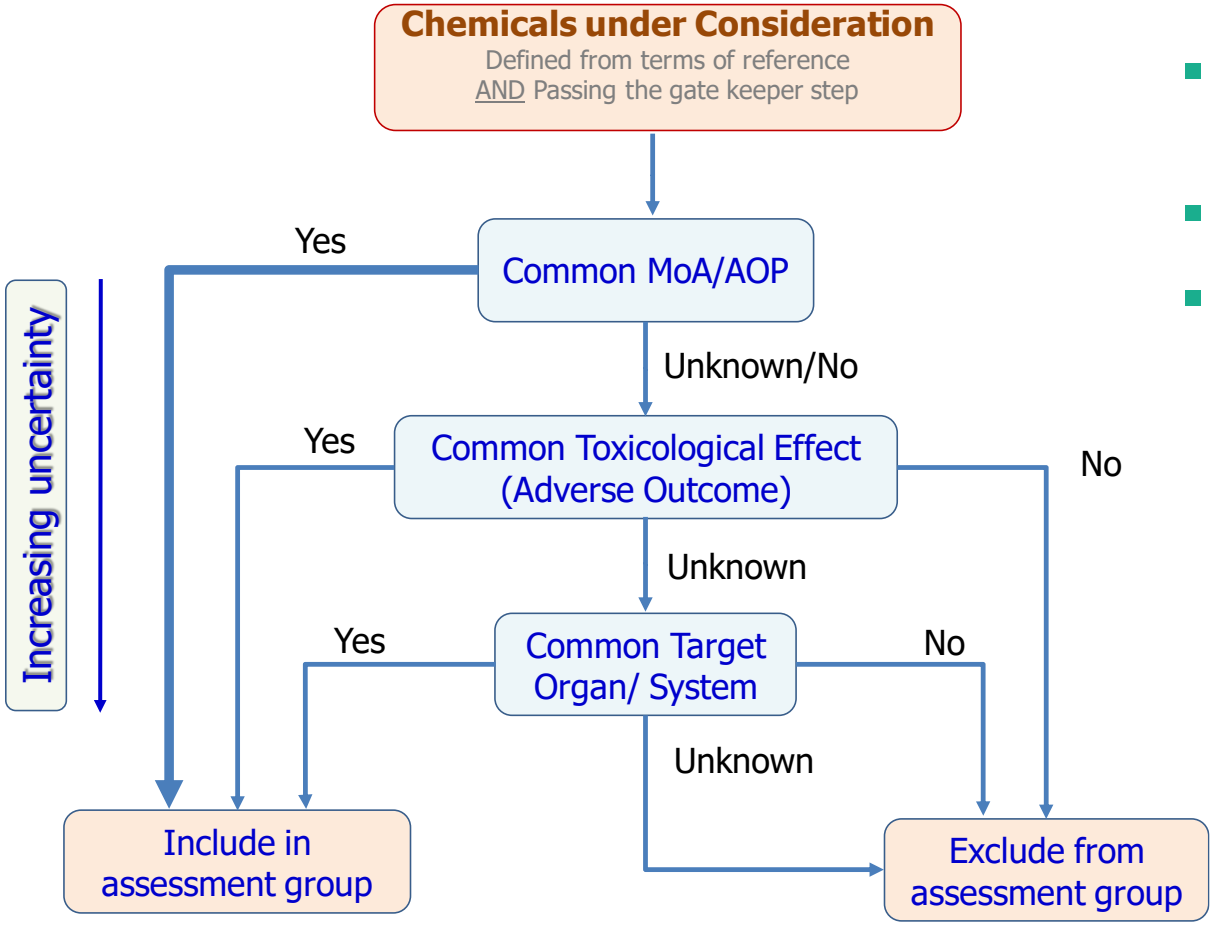
Development of Integrated Approaches to Testing and Assessment (IATA) case studies on developmental neurotoxicity (DNT) risk assessment

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.

Criteria for grouping for RA (Public Consultation)



- 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.

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

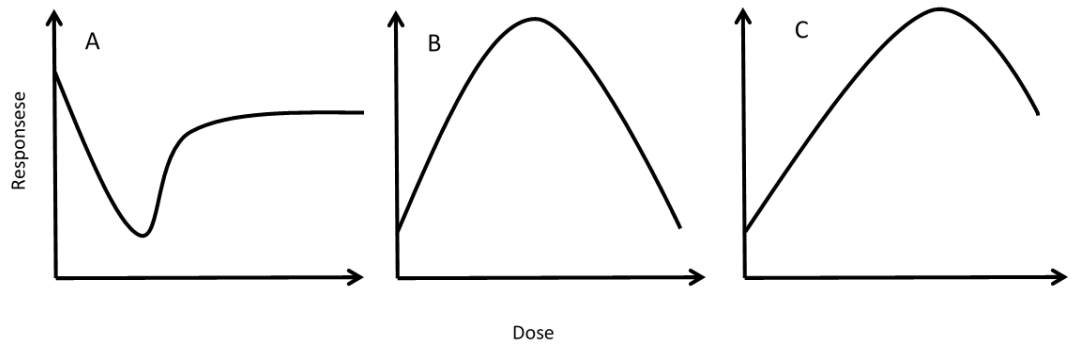
EFSA Journal

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,



Collaborative case studies

- Pesticides neurotoxicity: AOP on Parkinsonian motor deficiencies
  - *In vitro* neurotox Reference Point + PBPK model for QIVIVE
  - Ongoing, ANSES & Uni Konstanz
- Nanomaterials/GIT nanofibres uptake and genotoxicity
  - "Classical" *in vitro* models and exploring Gut-on-a-Chip models
  - Focus: Cellulose nanofibres
  - Ongoing, EU consortia lead by ISS & Italian CNR

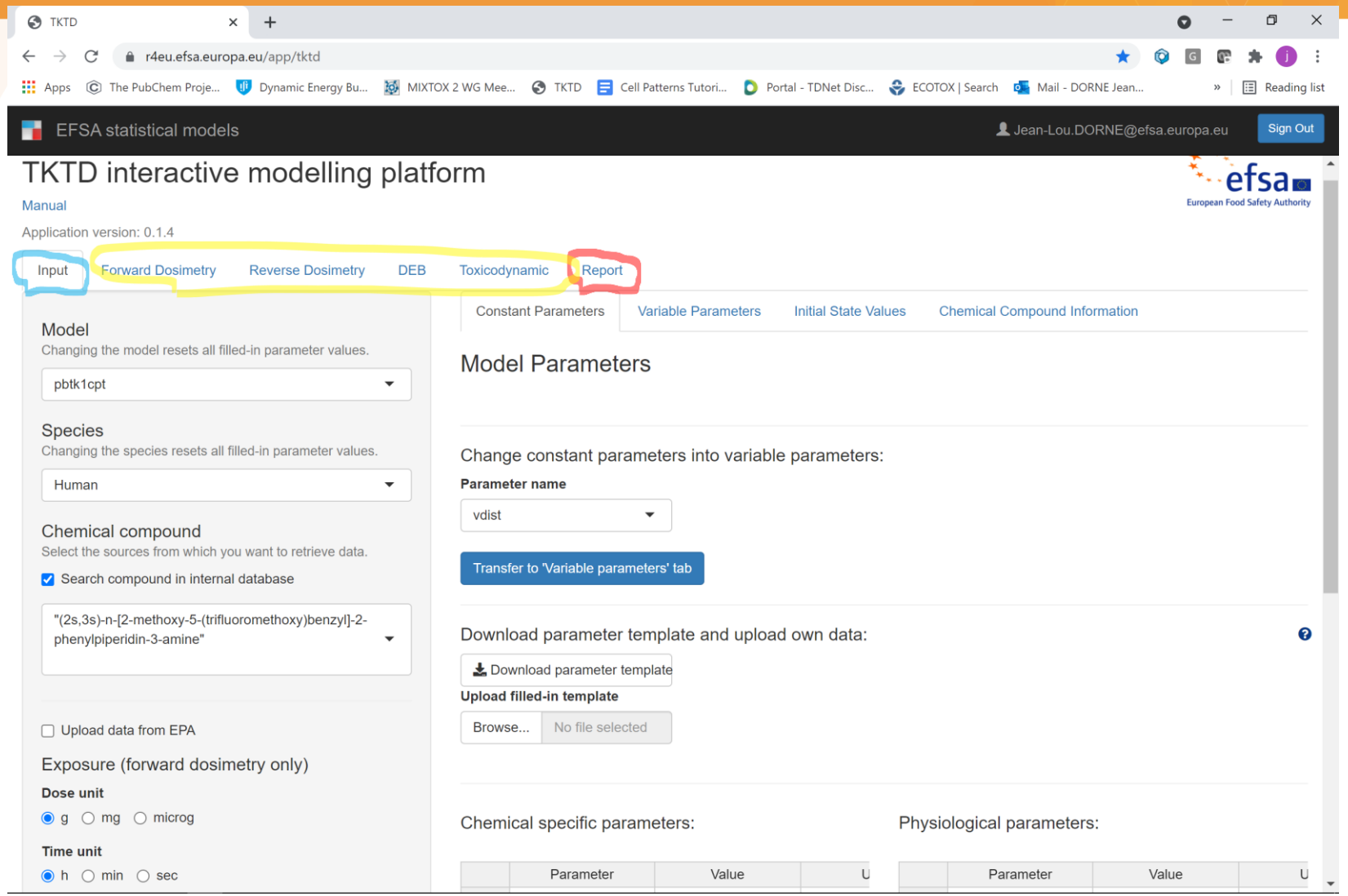
Collaborative case studies

- Artificial intelligence for NAMs
  - AI for NAMs data search, extraction, appraisal and integration in AOPs
  - Starting soon.
- PFAS immunotoxicity
  - The immune system is a prime target of PFASs, but:
  - A clear mode of action of immunotoxicity by PFOS and PFOA has not been established.
- Essential oils as feed additives and interspecies metabolic differences
  - To start soon

TKplate 2.0

- An **Open-Source Platform** integrating PBTK Models and Machine Learning Models for Risk Assessment of single and multiple chemicals and biological stressors in animal species.
  - Species of interest (human, farm animals, fish etc)
  - TK and TD data
  - PBK models for regulatory applications
  - Quantitative In vitro In Vivo extrapolation for Human RA
  - TK and TD human variability

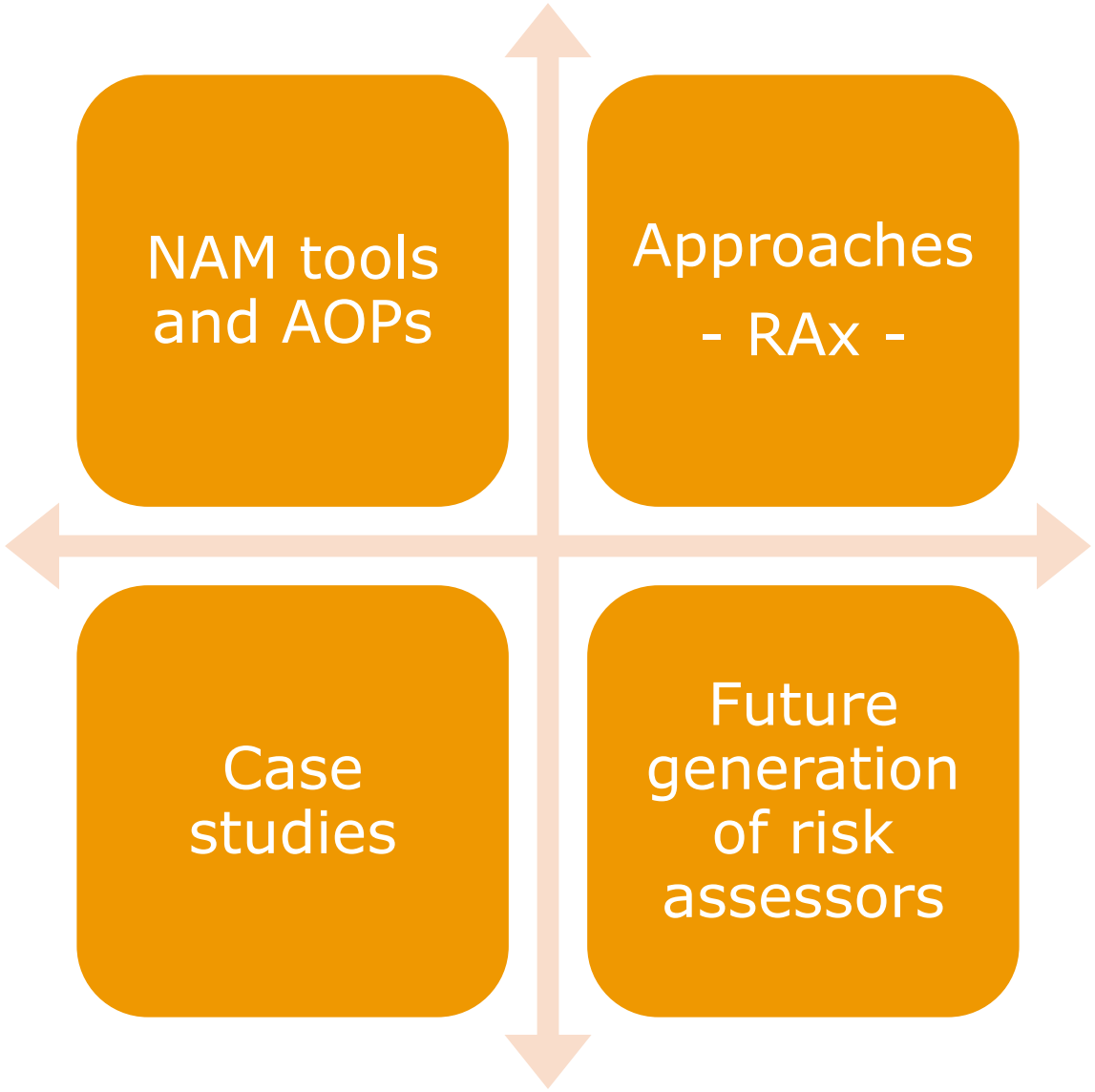
TKPlate Prototype



TK Plate contains different modules

- **Input**: Input data (model, expo, chemical specific, physiological data)
- **Outputs** :
  - ✓ **Forward dosimetry** : predict [c] in organs and kinetic parameters
  - ✓ **Reverse Dosimetry** : predict exposure from internal dose (e.g.biomomitoring)
  - ✓ **DEB and TD module** (DEB models individual and populations for ERA, and TD (BMD) modelling)
- **Automated Report**

EFSA's journey to NGRA: Impact of EU ToxRisk



Thank you!