EFSA'S PERSPECTIVE ON EVOLUTION OF SAFETY ASSESSMENT

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EFSA STRATEGY 2027

Goals:

- Improve the **quality** of scientific guidance and methodologies
- Develop and integrate **New Assessment methods (NAM)-based approaches** for regulatory risk assessment
- Minimisation of **animal testing**
- Ensure more **informative** risk assessments
- Make use of wider, improved and new **data streams**

Actions:

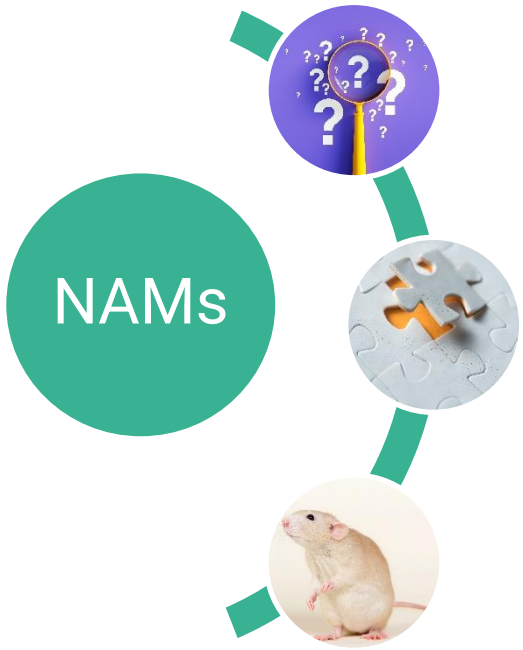
- Launch **experimental case studies** for filling data gaps identified in EFSA risk assessments using NAMs
- Explore the use of **Artificial Intelligence for integrating NAMs data** in risk assessments
- Define in parallel the **mid-term strategy** (i.e. development of a Roadmap for action)
- **Increase international cooperation** (i.e. via NanoNetwork, APCRA, and ILMERAC Working Group on NAMs, PARC, ECVAM)

EFSA ONGOING PROJECTS ON NAMS METHODOLOGIES

NAMS4NANO: EFSA NAMs roadmap data integration nanomaterials (case studies and guidance)	Practical implementation NAMs - RA of pesticide metabolites	Environmental neurotoxicants (testing for DNT and NT)	AOP for ED
New approach methodologies for RA of chemicals in food (ADME4NGRA)	Inter-human variability in toxicodynamic	Integrating new approaches in chemical risk assessment (case studies)	Protein Safety
	TGX-MAP (translational quantitative TG mechanism based AOP mapping for human NAM based RA)	Brain Health (NAMs to study developmental glial cell toxicity)	Waiving of the Dog for agrochemical RA

Projects highlighted in green are of direct interest for the pesticide RA process

NAMs - INTENDED USES IN SAFETY AND RISK ASSESSMENT



Filling a data gap, in case of no existing data, no existing toxicity testing method, and/or only a default approach available that does not rely on data (e.g. Tebufenpyrad case study).

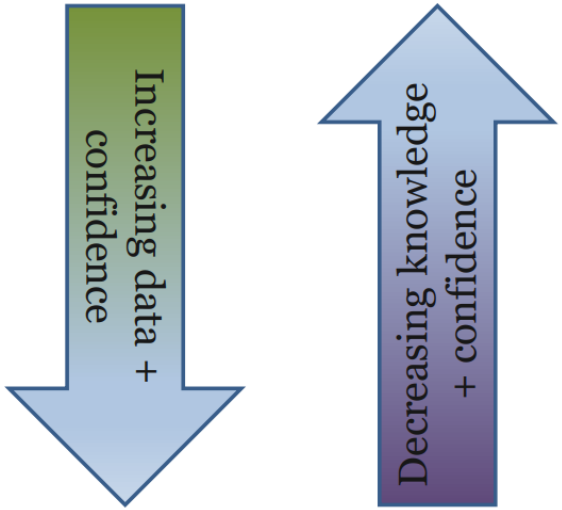
Complementing existing data to corroborate evidence and decrease uncertainty in the evaluation of an outcome; offering an alternative to another test method, such as a mammalian toxicity test method (e.g. DNT IATA for Deltamethrin).

Offering alternatives to mammalian toxicology test methods with the same or a similar target human population/exposure, including but not limited to the one-to-one replacement situation (Commission road map for phasing out animal studies).

National Academies on Sciences, Engineering and Medicine, 2023

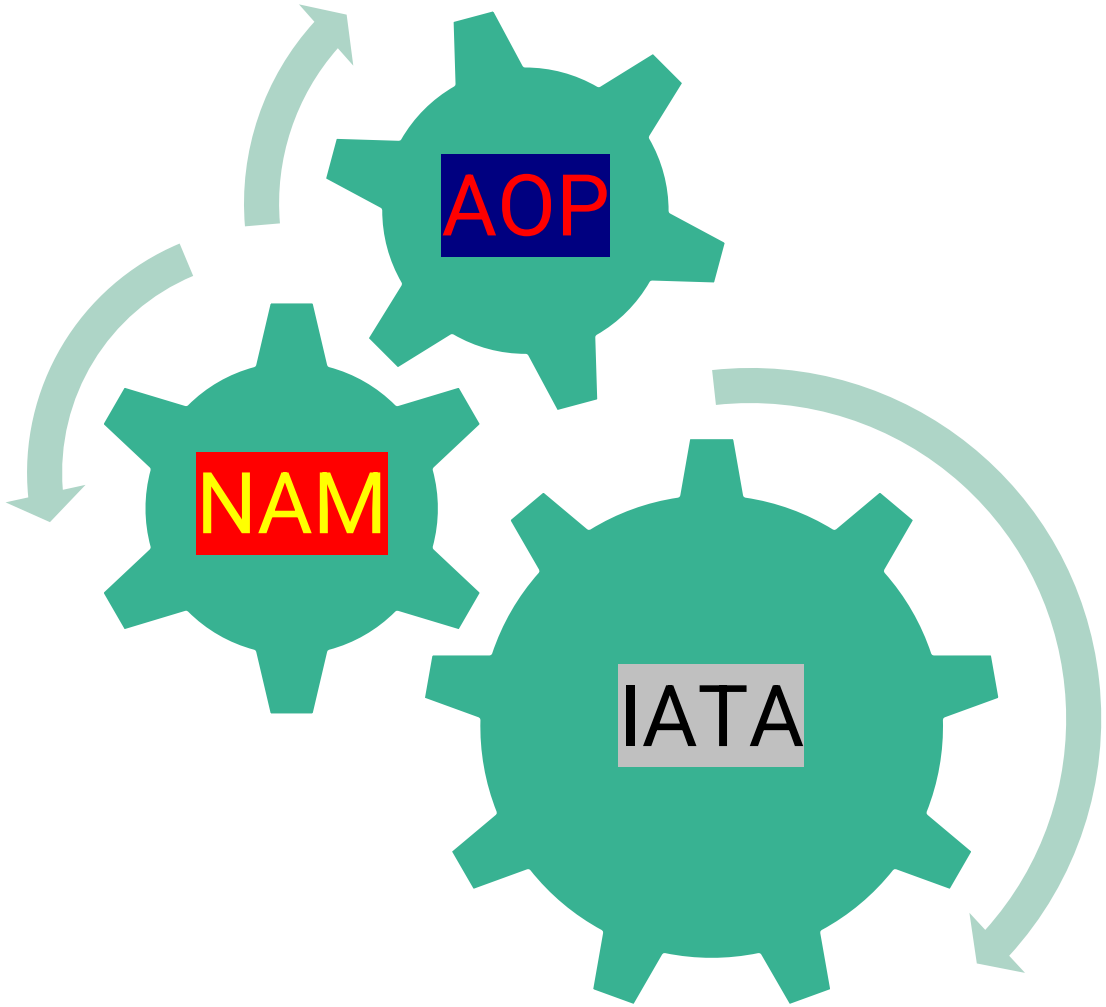
REGULATORY CONTEXT OF USE

- Need examples of NAM solutions for a variety of regulatory contexts
  - data rich/data poor chemicals
  - across chemical sectors/regulations
  - various regulatory problem formulations
    - Prioritisation
    - Hazard identification
    - Hazard characterisation
    - POD
    - Risk assessment



- Likely to be a continuum
  - more data/less uncertainty as more experience/knowledge is acquired

STANDARD APPROACH FOR NAM IMPLEMENTATION IN RA



- NAMs are intended to measure Key Events in the Adverse Outcome Pathway (AOP) conceptual framework.
- The AOP informs an Integrated Approach to Testing and Assessment (IATA)
- To conclude on the hazard characterization and setting of points of departure, well-established IATAs including data on toxicolkinetics is needed.

NAM REGULATORY IMPLEMENTATION

- **Intended purpose and context of use** relates to the regulatory problem formulation
- **Internal validity (reliability)** relates to the extent to which systematic error (bias) can influence the extent to which a study answers it research question correctly
- **External validity (relevance)** refers to whether the study is addressing the relevant research question
- **Biological and experimental variability (standardization)**
  - **Biological variability**: true biological differences due to heterogenicity or diversity (not possible to eliminate but possible to characterize)
  - **Experimental variability**: encompasses inter- and intra-laboratory variability, repeatability, and all aspects of reproducibility
- **Transparency**

REGULATORY IMPLEMENTATION

- **Assay qualification**: refers to assays intended to resolve a concern for which data requirement and validated assays are not existing and the context of use for the assays is appropriate
  - Qualification requires that the NAM have a well-defined context of use. One of the purposes of qualification is to enable industry and other stakeholders to **use the NAM for its qualified purpose during product development**, enabling regulators to apply the results generated using the NAM without needing to re-review the underlying supporting data
- For data that are included in the regulatory data requirement, a **validation process** is necessary and should include method standardization, transferability and reproducibility of the data and accessibility to the performing laboratories. Testing Guidance and interpretative Guidance (OECD) represents the best option for the mutual acceptance of data.

OVERALL CONSIDERATIONS

- Paradigm shifting in safety and risk assessment is possible but requires efforts from all sides (risk assessors, regulators, industry and society at large).
- Safety assessment is shifting from rigid data requirement schemes to evidence-based approaches (e.g. ED assessment, tiered approach for assessing pathogenicity of biopesticides).
- A full and wider acceptability of NAMs at regulatory levels requires development of robust NAM-AOP-IATA frameworks, method validation and experimental application in real study cases.
- Data sharing is essential to progress in certain areas (e.g. impact of new application techniques on non-dietary exposure assessment).

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