FURTHER DEVELOPING METHODOLOGIES: IMPLEMENTATION OF NAMS INTO RISK ASSESSMENT

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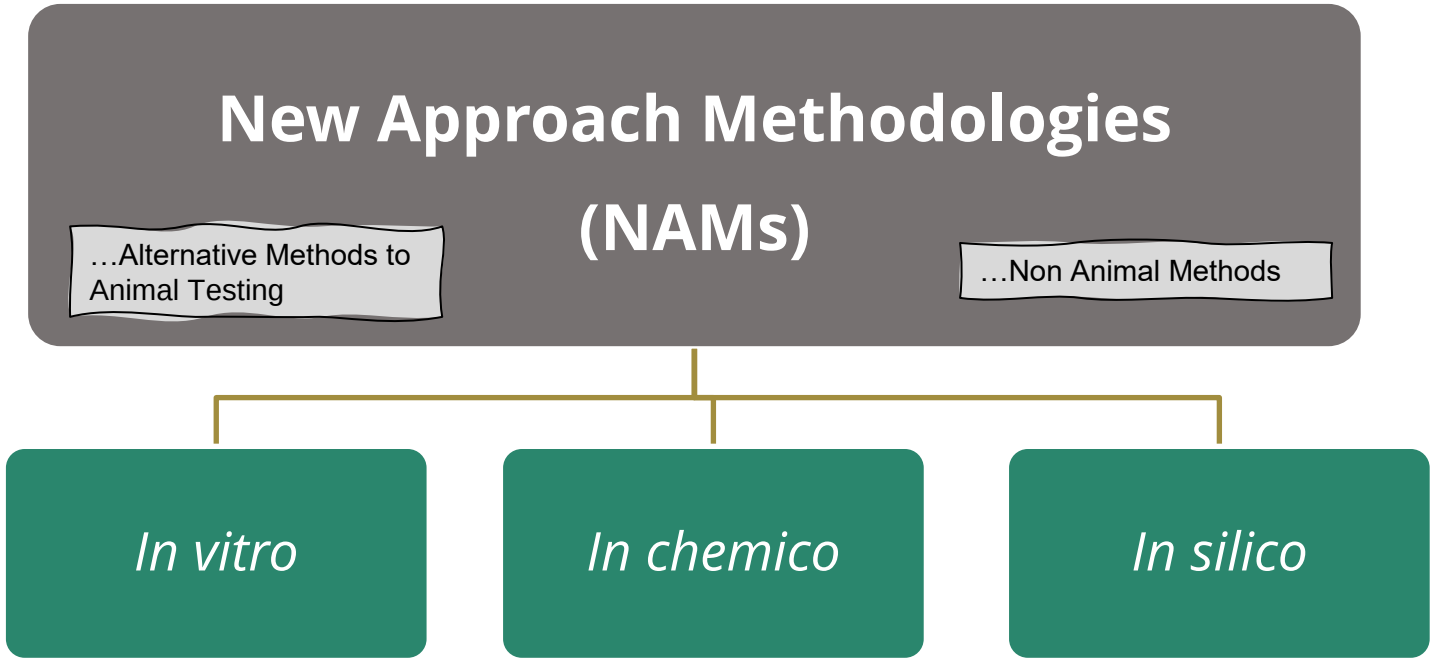
WHAT ARE NAMS ?

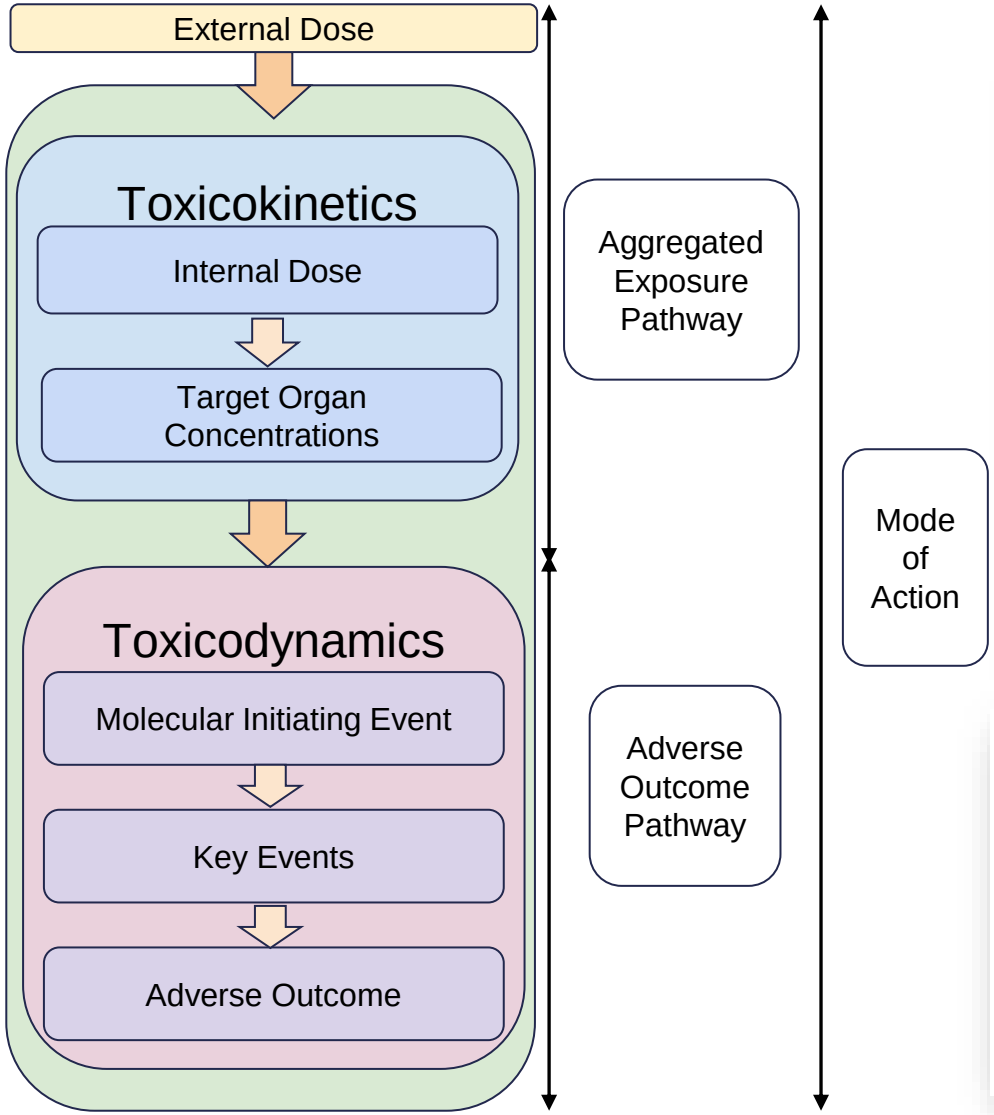


*"**NAMs** include also all the high-throughput and high-content techniques, e.g., **omics** with a focus on **metabolomics**, the use of **exposure data** in terms of volume and use etc..."*

Next Generation Risk Assessment (NGRA)

ECHA, *Proceedings of a scientific workshop* 2016
US EPA, 2014

THE SCIENTIFIC BASIS OF NAMS: TOXICOKINETIC AND TOXICODYNAMIC PROCESSES



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European Food Safety Authority
EFSA Journal 2014;12(4):3638

SCIENTIFIC REPORT OF EFSA

Modern methodologies and tools for human hazard assessment of chemicals[1]

European Food Safety Authority[2,3]

European Food Safety Authority (EFSA), Parma, Italy

*This scientific output, published on 11 July 2014, replaces the earlier version published on 24 April 2014**

ABSTRACT

This scientific report provides a review of modern methodologies and tools to depict toxicokinetic and toxicodynamic processes and their application for the human hazard assessment of chemicals. The application of these methods is illustrated with examples drawn from the literature and international efforts in the field. First, the concepts of mode of action/adverse outcome pathway are discussed together with their associated terminology and recent international developments dealing with human hazard assessment of chemicals. Then modern methodologies and tools are presented including *in vitro* systems, physiologically-based models, *in silico* tools and OMICs technologies at the level of DNA/RNA (transcriptomics), proteins (proteomics) and the whole metabolome (metabolomics). Future perspectives for the potential applications of these modern methodologies and tools in the context of prioritisation of chemicals, integrated test strategies and the future of risk assessment are discussed. The report concludes with recommendations for future work and research formulated from consultations of EFSA staff, expert Panels and other international organisations.

KEY WORDS

mode of action, adverse outcome pathway, integrated testing strategy, physiologically-based models, *in silico*, OMICs

GUIDANCE

EFSA Journal

ADOPTED: 17 November 2021

doi: 10.2903/j.efsa.2021.7033

Guidance Document on Scientific criteria for grouping chemicals into assessment groups for human risk assessment of combined exposure to multiple chemicals

EFSA Scientific Committee,
Simon John More, Vasileios Bampidis, Diane Benford, Claude Bragard, Antonio Hernandez-Jerez, Susanne Hougaard Bennekou, Thorhallur Ingi Halldorsson, Konstantinos Panagiotis Koutsoumanis, Claude Lambré, Kyriaki Machera, Hanspeter Naegeli, Søren Saxmose Nielsen, Josef Rudolf Schlatter, Dieter Schrenk, Vittorio Silano, Dominique Turck, Maged Younes, Emilio Benfenati, Amélie Crépet, Jan Dirk Te Biesebeek, Emanuela Testai, Bruno Dujardin, Jean Lou CM Dorne and Christer Hogstrand

- **What the body does to the chemical: Toxicokinetics**
- **What the chemical does to the body: Toxicodynamics**

HOW AND WHERE CAN NAMS BE INTEGRATED IN NEXT GENERATION CHEMICAL RISK ASSESSMENT ?

Step 1
Hazard Identification

Step 2
Hazard Characterisation

Step 3
Exposure Assessment

Step 4
Risk Characterisation

- ***From*** *In vivo* animal data (Dose response)
- ***To*** NAM-based dose response data (i.e *in vitro/ in silico*)

Point of departure and safe levels of chemicals

Complementary information:

- ADME characterisation
- Biokinetic data/*in vitro* to *in vivo*/kinetic modelling

EFSA ROADMAP ON NAMS: 6 PRIORITISED AREAS

EXTERNAL SCIENTIFIC REPORT

APPROVED: 2 May 2022

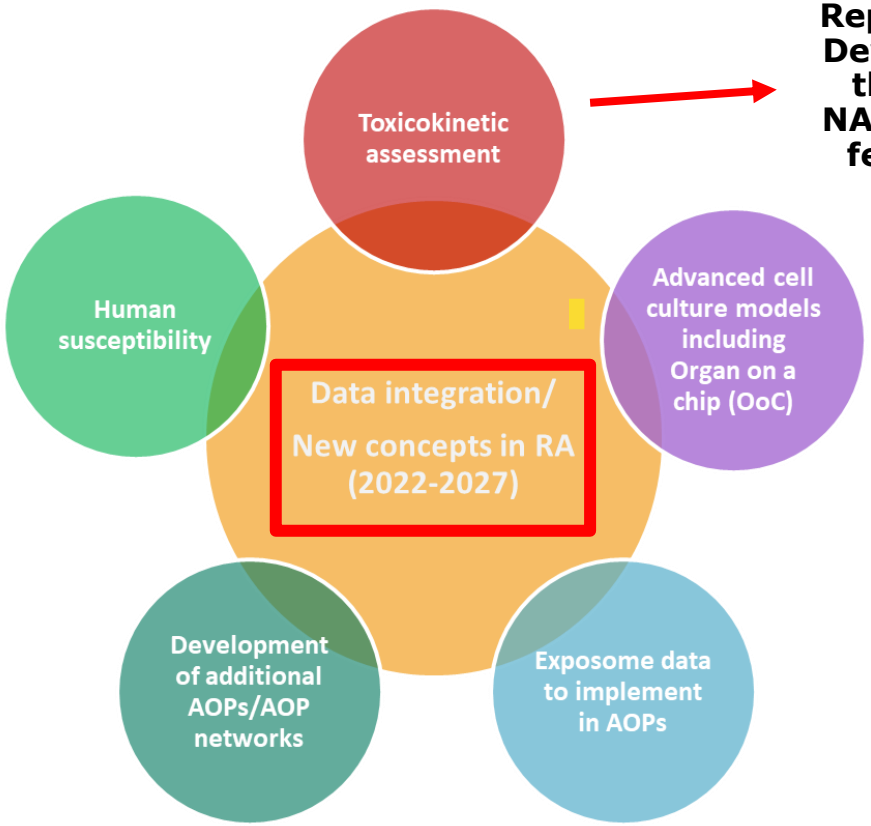
doi:10.2903/sp.efsa.2022.EN-7341

Development of a Roadmap for Action on

New Approach Methodologies in Risk Assessment

Sylvia E. Escher[1], Falko Partosch[1], Sebastian Konzok[1], Paul Jennings[2], Mirjam Luijten[3], Anne Kienhuis[3], Victoria de Leeuw[3], Rosmarie Reuss[4], Katrina-Magdalena Lindemann[4], Susanne Hougaard Bennekou[5]

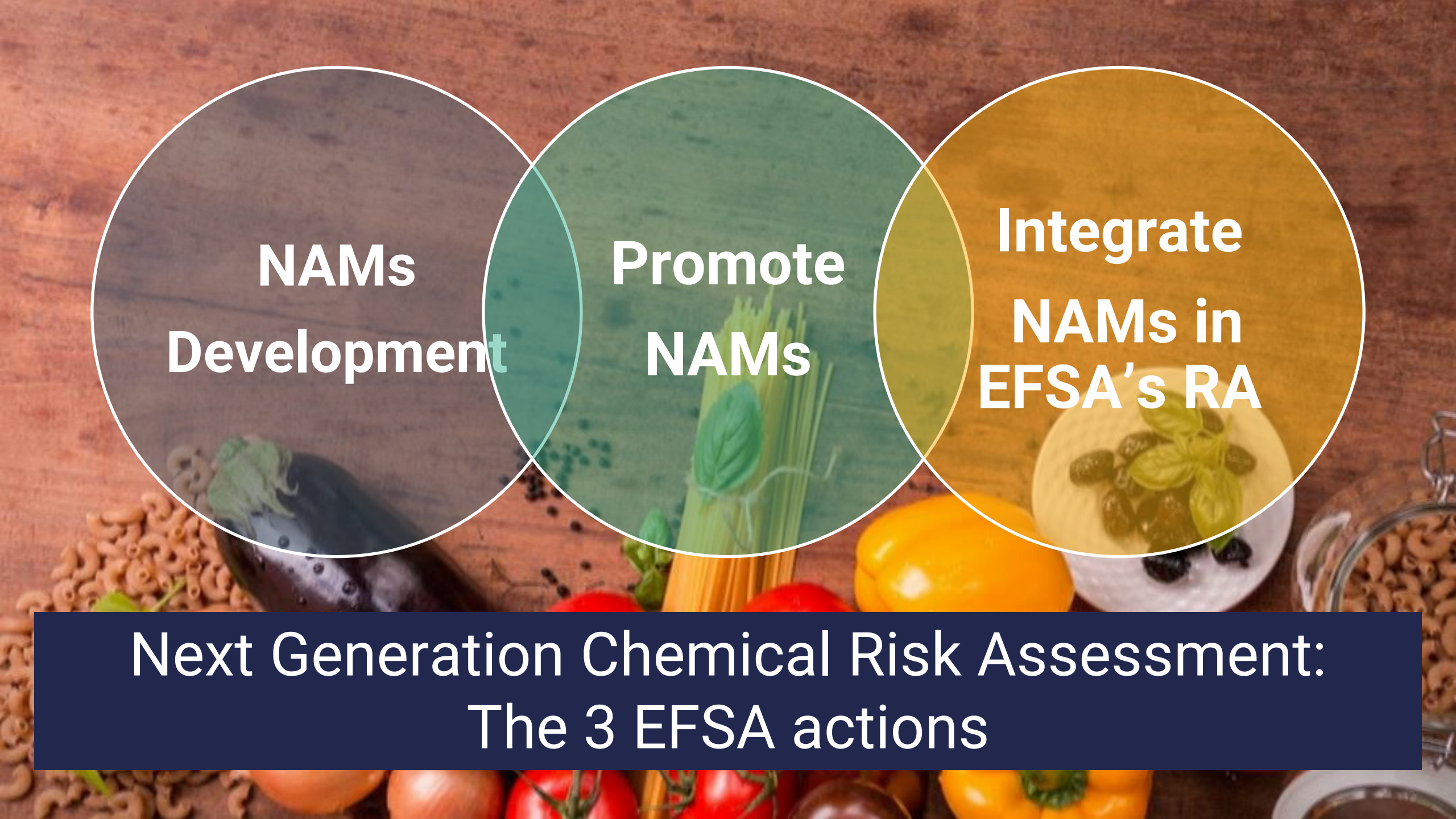
[1] Fraunhofer ITEM, [2] Vrije Universiteit Amsterdam, [3] National Institute for Public Health and the Environment, [4] Eura AG, [5] The National Food Institute Denmark



Reporting templates; Develop guidance on the integration of NAM-based data into feed and food risk assessment

Data integration approaches was considered critical for the successful application of Next Generation Risk Assessment (NGRA) through the use of NAMs.

OECD - Integrated Approaches to Testing and Assessment (IATA)



Next Generation Chemical Risk Assessment: The 3 EFSA actions

NAMS PROJECTS UNDER EFSA IRMA PROGRAMME

NAMS4NANO

Exploring NAM integration in RA for nanomaterials in food with specific case studies

Practical implementation NAMs-RA of Pesticide Metabolites

Promote NAMs in the toxicological assessment of pesticides using in-silico models

Environmental Neurotoxicants

Assessing chemical impact on development of nervous system by providing NAM neurotoxicity data

Adverse Outcome Pathway

Developing AOPs relevant to mammalian reproductive toxicity

New approach methodologies for RA of chemicals in food

NAM-based hazard assessment in EFSA's RA through case studies

Inter-human variability in toxicodynamics

Human variability toxicodynamics to allow testing of endpoints and tools in RA

Integrating new approaches in chemical RA

Development of in silico NAMs tools for food and feed safety: TKPlate Platform

Protein Safety

Novel strategies to assess allergenicity and toxicity of proteins,

TXG-MAP

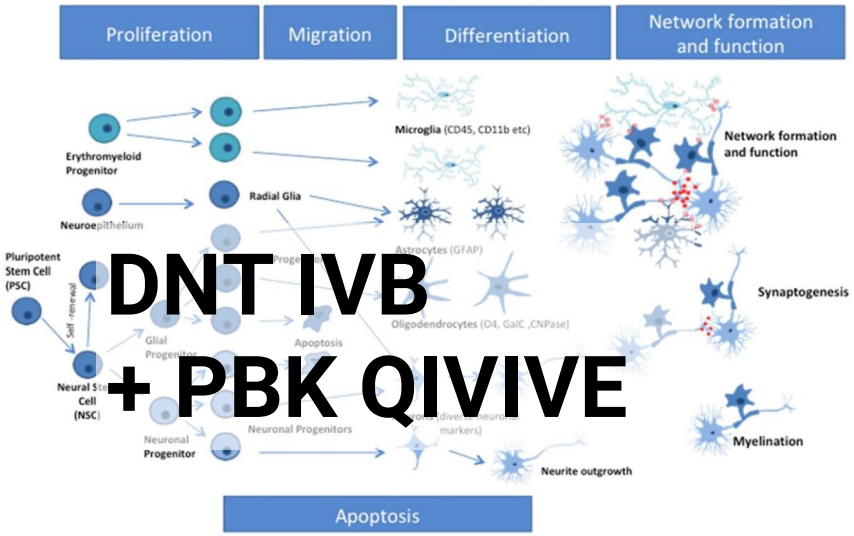
Framework for transcriptomics *in vitro* data, developing prototype/tool for data interpretation

Brain Health

Advance understanding how chemical exposures impacts brain health during development, expanding DNT in-vitro test battery

(SUPPORT) DEVELOPMENT OF NAMS

NAMs Development



DNT IVB + PBK QIVIVE

Practical implementation NAMs - RA of pesticide metabolites

QSARs

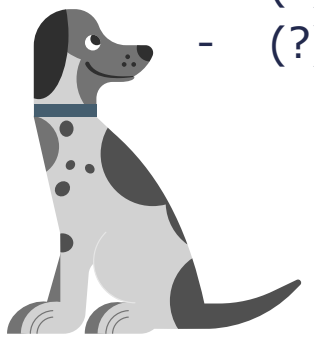
OECD Toolbox

IUCLID: Toxicity studies

MetaPath: Metabolism studies

RE-EVALUATE THE NECESSARY STUDIES - PHASING OUT OF ANIMAL STUDIES CONSIDERED REDUNDANT OR NOT USEFUL FOR THE RISK ASSESSMENT

Promote NAMs



- **Chronic toxicity study in dogs for PPP**
- (?) 90-day study for GMOs – whole food
- (?) 90-day study for enzymes
- (?) 2-year Mouse carcinogenicity study
- (?) combine ED studies to address both mammtox and eco-tox

EDITORIAL

EFSA Journal

APPROVED: 4 August 2022

doi: 10.2903/j.efsa.2022.e200923

Editorial: Relevance of dog studies for the derivation of health-based guidance values for plant protection products approval

Martina Panzarea, Andrea Terron, Tamara Coja and Olavi Pelkonen

The current project aims to continue contributing to the debate by reviewing/updating existing data to develop a tiered testing strategy, recommending the possible waiving of dog studies in the regulatory process when deemed scientifically justifiable. In fact, from the retrospective analysis (EFSA, 2022)[5], for the 95% of cases, in a database of 101 substances, the dog was not the most sensitive species used for setting the HBGVs. However, this project aims to go into the details of the previous analysis and explain the relevance of the dog for the cases where this species was the most sensitive one.

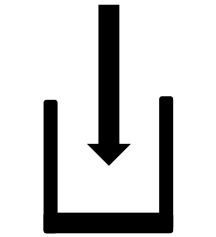
EFSA Journal 2022;20(9):e200923

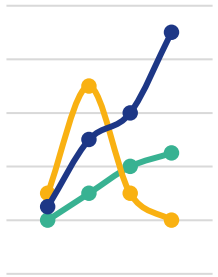
TKPLATE 1.0: IMPLEMENTING TK AND TD MODELLING IN EFSA'S RA

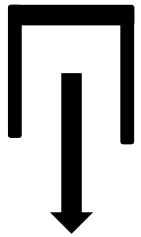
NAMs Implementation in EFSA's RA


Approved: 12 October 2023
DOI: 10.2903/j.efsa.2023.e211101
EDITORIAL
efsa JOURNAL
TKPlate 1.0: An Open-access platform for toxicokinetic and toxicodynamic modelling of chemicals to implement new approach methodologies in chemical risk assessment


Technical Report
efsa SUPPORTING PUBLICATIONS
APPROVED: 8 November 2023
doi: 10.2903/sp.efsa.2023.EN-8440
Applications of TKPlate 1.0 for toxicokinetic and toxicodynamic modelling of chemicals: Case Studies
European Food Safety Authority (EFSA),
Han Bossier, Fotis Spyropoulos, Keyvin Darney, Leonie S Lautz, Pierre André Billat, Rémy Beaudouin, Florence Zeman, Cléo Bodin, José Cortiñas-Abrahantes, Jean Lou CM Dorne







INPUT

- Select Model and Species
- Select Chemical and Data
- Set Exposure Settings and Time scale

MODELS

- Forward Dosimetry
- Reverse Dosimetry
- Toxicodynamic Modelling
- Dynamic Energy Budget
- MixTox Calculator

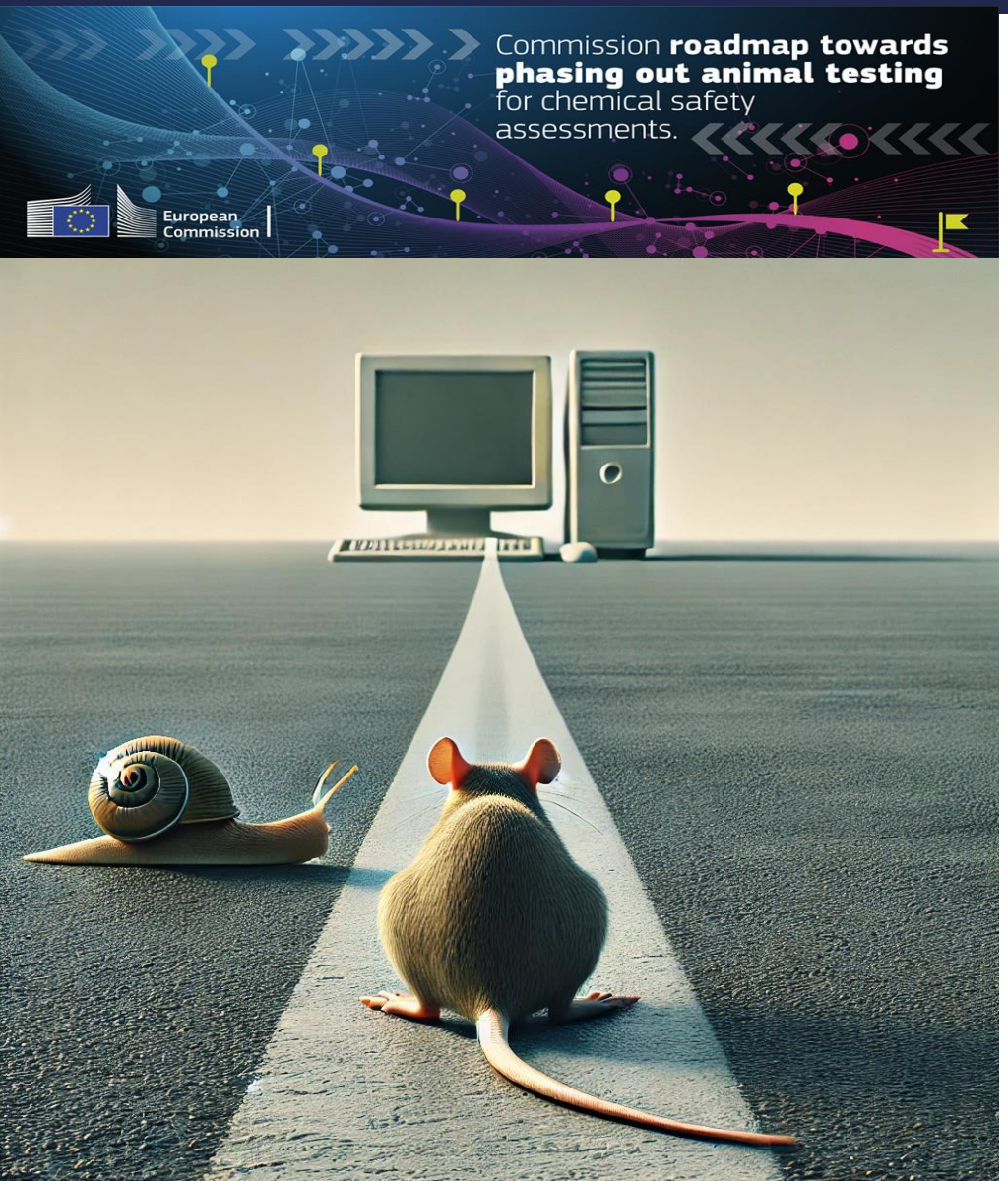
OUTPUT

- Download Automated Report
- Summary Inputs and Outputs
- Download Data and Graphs

Current implementation of TKPlate 1.0 in EFSA's BAU:

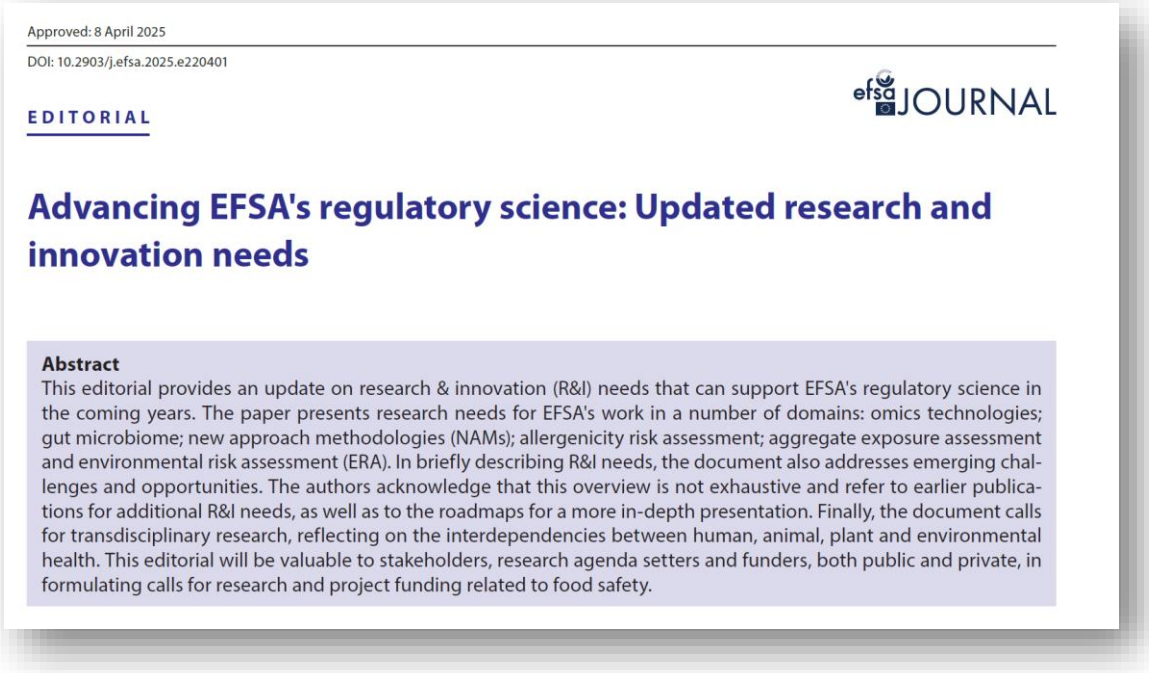
- DNT : modelling form in vitro to in vivo
- Contaminants and novel foods: THC, mycotoxins
- Integrate PARC NAM results and models in EFSA's RA

THE EUROPEAN COMMISSION ROAD MAP FOR THE PHASING OUT OF ANIMAL STUDIES



- **Road map** to accelerate reaching the goal of phasing out animal testing with short-term, mid-term and long-term visions
- To be **finalised latest in Q1 2026** after public consultation in Q2 2025
- **Implementation phase** – long-term undertaking
- Applicable to **all relevant pieces of EU chemical legislation** involving animal testing for **chemical RA**
  – 15 legislative areas identified many relevant to food and feed safety
- **EFSA** participation : Steering and Working groups

RESEARCH AND INNOVATION NEEDS



Approved: 8 April 2025

DOI: 10.2903/j.efsa.2025.e220401

EDITORIAL

efsa JOURNAL

Advancing EFSA's regulatory science: Updated research and innovation needs

Abstract

This editorial provides an update on research & innovation (R&I) needs that can support EFSA's regulatory science in the coming years. The paper presents research needs for EFSA's work in a number of domains: omics technologies; gut microbiome; new approach methodologies (NAMs); allergenicity risk assessment; aggregate exposure assessment and environmental risk assessment (ERA). In briefly describing R&I needs, the document also addresses emerging challenges and opportunities. The authors acknowledge that this overview is not exhaustive and refer to earlier publications for additional R&I needs, as well as to the roadmaps for a more in-depth presentation. Finally, the document calls for transdisciplinary research, reflecting on the interdependencies between human, animal, plant and environmental health. This editorial will be valuable to stakeholders, research agenda setters and funders, both public and private, in formulating calls for research and project funding related to food safety.

https://www.efsa.europa.eu/en/efsajournal/pub/e220401

- **EFSA Editorial**
  - ✓ OMICs
  - ✓ **NAMs**
  - ✓ Allergenicity RA
  - ✓ Aggregate Exposure Assessment
  - ✓ Environmental RA

- **NAMs**
  - ✓ In vitro models: NAM-based safe levels of chemicals
  - ✓ In silico models for safe levels of chemicals
  - ✓ Workflow to integrate in vitro/in silico using WoE and practical case studies

TAKE HOME MESSAGES: NAM@EFSA

- **NAMs@ EFSA :** 12 NAM projects (Budget >30 M Euros)

✓ NAMs Integration@ EFSA for pesticides and contaminants

✓ EC-roadmap: Identifying priority NAMs 4 EFSA

- **Research and Innovation : funding opportunities**

✓ NAM-based RA and workflow using in vitro/in silico models

- **Moving towards application of NAMs in EFSA and beyond**

✓ EFSA Knowledge and Innovation community NAMs: support integration@EFSA

✓ Training: EFSA Staff/Experts and beyond (i.e. OECD, WHO)

✓ Change management: Data requirements from in vivo to NAMs

STRONGER TOGETHER TO IMPLEMENT NAMS

EU MS Food Safety Agencies

食品安全委員会
Food Safety Commission of Japan
内閣府
Cabinet Office

European Commission

PARC

Global Coalition for Regulatory Science Research

EFSA Stakeholders

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

epaa
The European Partnership for Alternative Approaches to Animal Testing

CFSA 国家食品安全风险评估中心
China National Center for Food Safety Risk Assessment

efsa
EUROPEAN FOOD SAFETY AUTHORITY

ECHA
EUROPEAN CHEMICALS AGENCY

FDA

ASPIS

EUTOXRISK

OECD
BETTER POLICIES FOR BETTER LIVES

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

World Health Organization

APCRA
ACCELERATING THE PACE OF CHEMICAL RISK ASSESSMENT

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