76th Advisory Forum meeting
Virtual meeting, 1-2 July 2020

EFSA project on New Approach Methodologies (NAMs)

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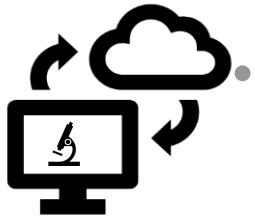
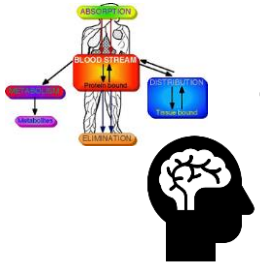
European Food Safety Authority

New Approach Methodologies

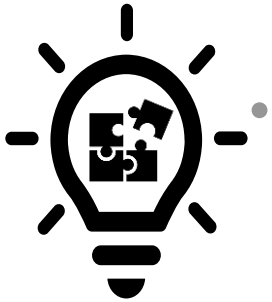
- **NAMs: more than "just" alternatives to animal testing**



- Using *in vitro* and *in silico* alternatives, but connected to modern technologies and "bigdata"
  - High-Throughput Screening (HTS) and High-Content Screening (HCS)
  - Data-models/structure facilitating harmonisation and "reuse"

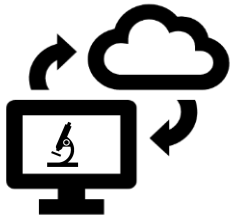


- Focusing on human relevant models
  - Human *in vitro in vivo* extrapolation (IVIVE), addressing genetic and inducted susceptibility (e.g. inter and intraspecies metabolic capacities)
  - Addressing (developmental)neurotoxicity and human unique diseases

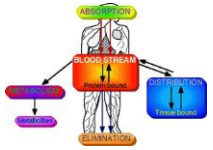


- Getting mechanistic understanding
  - Adverse Outcome Pathways (AOP)
  - Paradigm (R)evolution towards more informative risk assessments

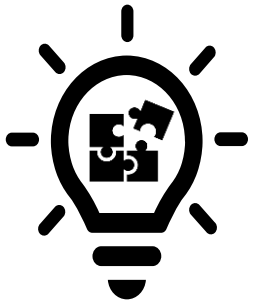
Examples of EFSA activities



- OpenFoodtox 2.0
- Quantitative Structure Activity Relationships (QSAR)
- Thresholds of Toxicological Concern (TTC)
- Read-across (new project)



- Toxicokinetic/Toxicodynamic models: Web-platform under construction
- Developmental neurotoxicity (DNT) joint project with DK
- *In vitro* models for genotoxicity, endocrine activity, comparative metabolisms, …



- Adverse Outcome Pathways (AOP) for Parkinsonian diseases, childhood leukaemia,…
- Proposal for on the ***Future of Chemical Risk Assessment***

General elements for setting the vision

- **Current situation on NAMs:**
  - Established legal framework & full incorporation in research
    - Large majority of research studies and publications on toxicity use in silico or in vitro approaches (i.e. NAMs)
    - OECD and JRC acting as links for validation/harmonisation at international/EU levels
  - Limited incorporation in regulatory chemical RA
    - Reluctancy by risk assessors (also in EFSA) and risk managers
    - Lack of paradigm/guidance for mechanistically driven toxicology
  - Dedicated networks of regulatory agencies
    - APCRA (since 2016) (International with participation and involvement of EFSA and ECHA)
    - PARERE (Preliminary Assessment of Regulatory Relevance Network) (EU MS with participation and involvement of EFSA and ECHA)

Specific elements for EFSA assessments

- ✓Information from existing animal studies is available, but frequently with limitations or deficiencies
  - ➢*Identification of data gaps and requests for additional information*

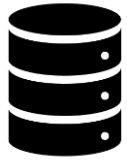
- ✓Literature searches extract NAM-based publications with *ad-hoc* protocols
  - ➢*Risk assessors do not have sufficient guidance for using mechanistic information in the risk assessment*

- ✓The mechanistic information is key for the identification of drivers for susceptibility and targeting specific population groups.
  - ➢*The identification of susceptibility drivers will produce better assessments, more informative for risk managers and society.*

Prioritisation

- **Networking:** EFSA approach for NAMs to be broadly consulted with all relevant partners and external actors

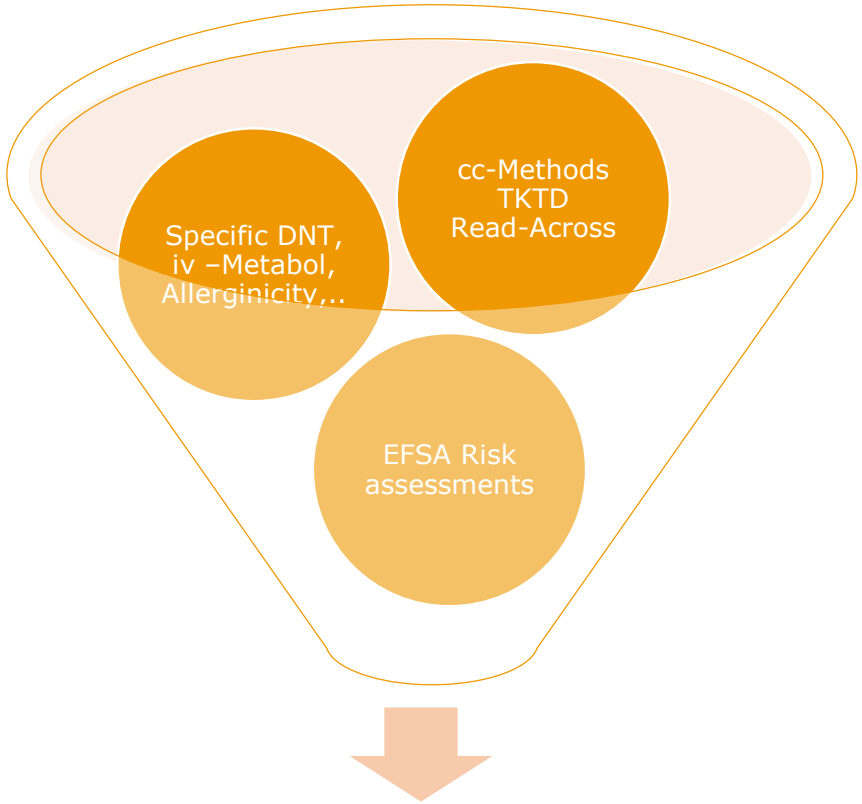
- **Methods:** Increasing EFSA efforts on developments with regulatory priority
  - Conceptual approaches: AOPs, IATAs, Read-across,…
  - Targeted developments: DNT, TKPlate, iv-Met,…



- **Data:** Facilitating connectivity and re-use of EFSA validated data
  - OPENFoodTox

- **New targeted approach**
  - Co-designing (researchers and risk assessors) NAM-based studies for addressing data-gaps identified in EFSA assessments

Build on existing projects, networks & opportunities



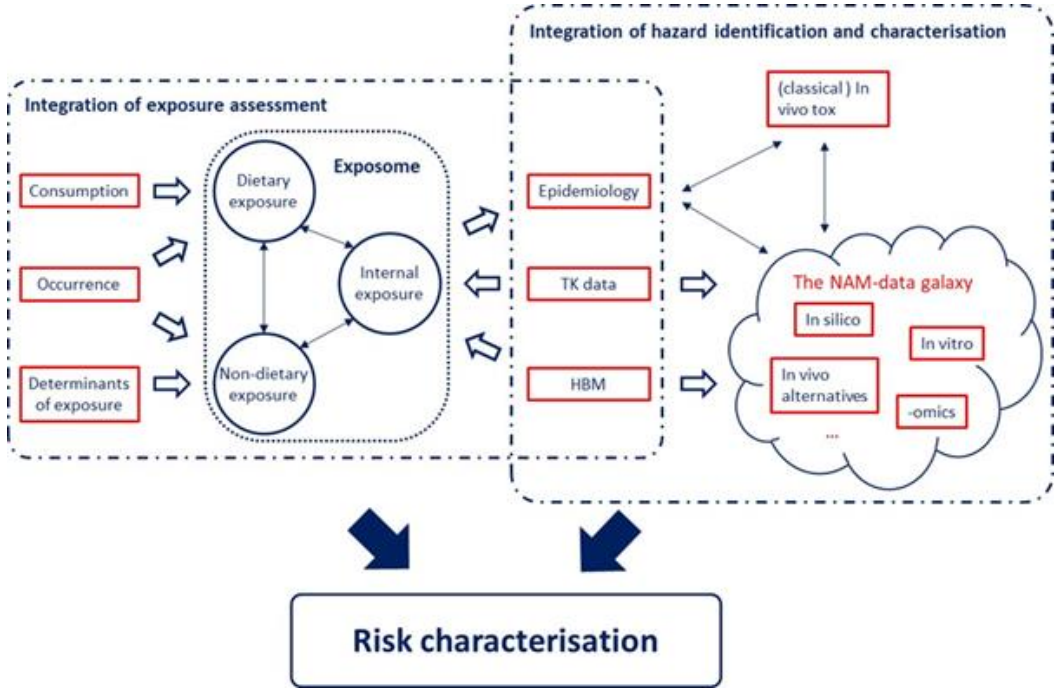
Support Panels/Units

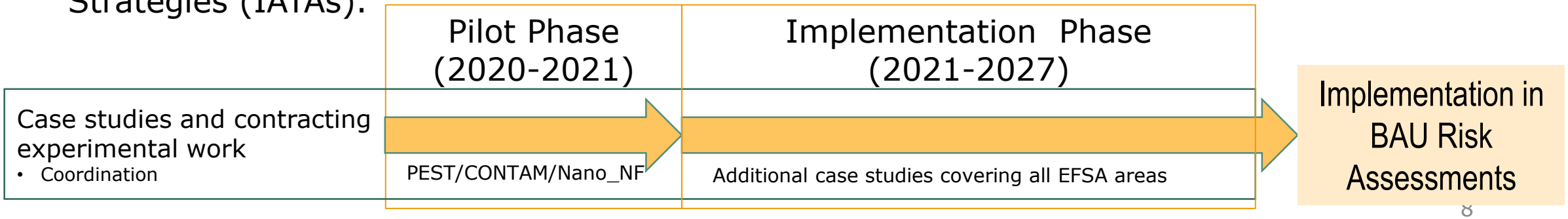
Guidance update

NAMs activities

Connected to the paradigm evolution for the:
Future of Chemical Risk Assessment

- Mechanistic-based risk assessments for chemicals in food and feed
  - Supporting risk assessors in the appraisal and integration of results from NAMs-studies
- Using NAMs for addressing data gaps in risk assessment, minimising animal testing
  - Through the design and validation of NAM-based Integrated Assessment and Testing Strategies (IATAs).





Collaborative case studies

- Real "proof of concept" cases under EFSA assessment
  - Prioritisation with MSs
    - Selection of EFSA assessments
    - Identification of data gaps
  - Co-design platform of researchers and risk assessors in EFSA, EU agencies, and MSs
    - Define the AOP or health concerns
    - Develop the IATA and test design
  - Data generation (e.g. Art. 36 organisations) and incorporation in risk assessments
    - Contract the studies
    - Validate the results from the regulatory perspective
    - Update EFSA's risk assessments with validated NAM results

Approved pilots: launching in 2020
€ 550K SCER G&P budget

- Pesticides/neurotoxicity:
  - Tebufenpyrad (mitochondrial Complex I inhibitor)/ Parkinsonian syndromes
  - IATA based on the AOP developed by EFSA
  - Cooperation with ANSES

- Nanomaterials/GIT nanofibers uptake and genotoxicity
  - Nanocellulose, Novel Food (bacterial), nano-fraction in additives, engineering nanofibers
  - Address adaptations for nanofibers in the EFSA guidance
  - Workshop with participants from OECD, JRC, IT, FI, NL, IE, BE, DK

- Contaminants/immunotoxicity
  - PFASs (epidemiological) alerts on interfering with vaccination response
  - Develop the AOP and IATA
  - To be further developed

Expected impact & Next steps

- Better and more informative risk assessments;
- Facilitate the application of NAMs in chemical risk assessment at EU level
- Demonstrates EFSAs contributions to societal needs and reduction of animal testing
- Increase researchers' interest in regulatory science

- Broad consultation on a "**Theme paper on NAMs**" with the Advisory Forum is scheduled
- Sharing experiences on NAMs and cooperation with MSs, sister agencies and international bodies is key for advancing risk assessment

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