EFSA project on New Approach Methodologies (NAMs)

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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

EFSA, JRC, ECHA, EU MS

APCRA, OECD, USEPA, FDA, HC, ...

Support Panels/Units
Guidance update

cc-Methods TKTD Read-Across
Specific DNT, iv – Metabol, Allergenicity...
EFSA Risk assessments
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).

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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
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

Approved pilots: launching in 2020
€ 550K SCER G&P budget
Expected impact & Next steps

• Better and more informative risk assessments;
• Facilitate the application of NAMs in chemical risk assessment at EU level
• Demonstrates EFSA’s 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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