Welcome

Webinar: Research needs for protecting human health and the environment – an EU agencies perspective

18 June 2024

Adam Elwan
Communications
European Chemicals Agency

What you can expect today

→ Understand regulatory context
→ Bridge gap toward research community
→ Update of regulatory needs
→ Get answers to your questions

Live Q&A

- → Join Q&A at: slido.com
  Event code: #science2024
- → Send questions throughout the event until 13:00 (EEST, GMT +3)
- → Question for a specific speaker? Indicate when sending your question
- → Only questions within scope
- → Question not answered? Refer to published Q&A

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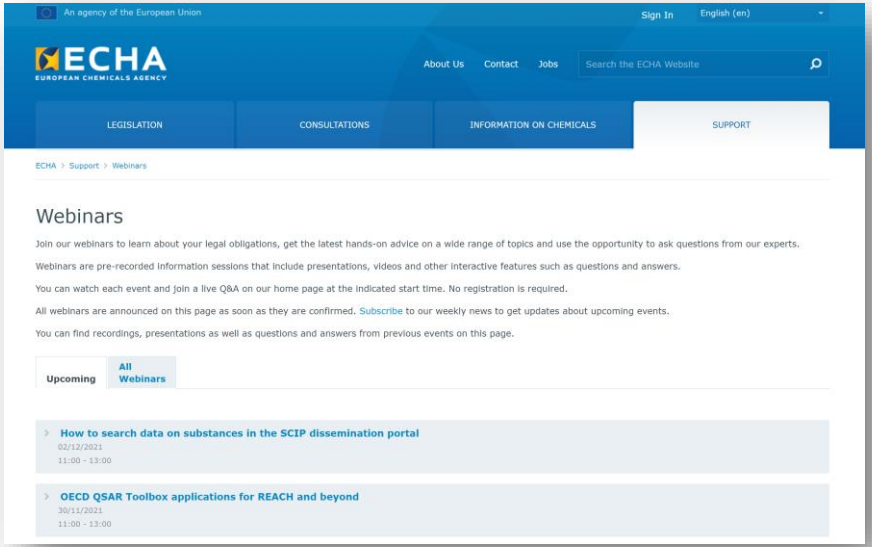
Material available

→ Video recording
→ Presentations
→ Q&A (soon after the event)



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Programme

Time	Topic	Speaker
11:00	Welcome	Adam Elwan, ECHA
11:05	Research needs for protecting human health and the environment: an EU agencies' perspective	Safia Korati, ECHA
11:15	New approach methodologies to advance EFSA's risk assessment	Jean Lou Dorne, EFSA
11:30	EEA research priorities for chemicals	Nadia Cerioli, EEA
11:45	Bioaccumulation: specific substances, air breathing animals and new approach methodologies	Jane Caley, ECHA
12:00	Conclusions	Adam Elwan, ECHA
12:05-13:00	Live Q&A panel	

Thank you

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Introduction

Webinar: Research needs for protecting human health and the environment – an EU agencies perspective

18 June 2024

Safia Korati
European Chemicals Agency

Partnership for the Assessment of Risks from Chemicals

- → EU-wide research and innovation programme to support EU and national chemical risk assessment
- → Development of data, knowledge and methods, for chemical safety challenges
- → ~80 projects ongoing (anno 2024)

7 years

€400 million (50% EU, 50% Member States)

200 institutions, 28 countries, including three European Agencies

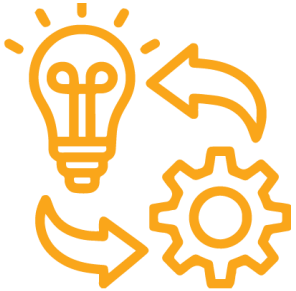
Ambition: Facilitate transition to new generation of chemical risk assessment.

- → PARC website: eu-parc.eu

efsa EUROPEAN FOOD SAFETY AUTHORITY · European Environment Agency · ECHA EUROPEAN CHEMICALS AGENCY

Our ambition

Bridge gap towards research community



Inspire and improve existing R&D projects and promote new projects

Communicate specific research needs

Identify and develop missing key elements in various scientific areas

Mind the gap – both ways

From regulatory world to academia

- → Explain how regulation works (‘regulation applies science in a specific framework’), including limitations
- → Inspire through key questions and challenges
- → Clarify need for specific data (problem formulation) with usually need for fast turn over

- → Bring data-driven solutions (while acknowledging uncertainties)
- → Generate data to address key regulatory issues
- → Provide concepts to change regulatory frameworks ➔ generate trust for policy makers

From academia to regulatory world

Regulatory research needs 2024

Update *Key Area's of Regulatory Challenge*

→ Detailing new approach methodologies section

→ Detailing needs for assessing bioaccumulation

Promote use of new approach methodologies to advance EFSA's risk assessments:

→ Integrate kinetic data and calibrate predictive kinetic and dynamic models for humans and animal species

→ Explore omics for human health risk assessment

EEA articulation of research needs:

→ Environmental monitoring data gaps

→ Human biomonitoring data gaps

Reach out to us

- → To frame research and innovation to address regulatory needs
- → To develop fit for purpose tools and methods for regulatory assessments
- → To explore opportunities to contribute to chemical hazard, exposure or risk assessment, monitoring
- → …

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NAMs TO ADVANCE EFSA'S RISK ASSESSMENTS

Jean Lou CM Dorne
Lead Expert on NAMs

efsa
EUROPEAN FOOD SAFETY AUTHORITY

NAMs IN THE EFSA STRATEGY 2027

GOALS

Develop and integrate **NAM-based approaches** for regulatory risk assessment (quality matter)

Ensure more **informative** risk assessments (target on human)

Make use of wider, improved and new **data streams (big data)**

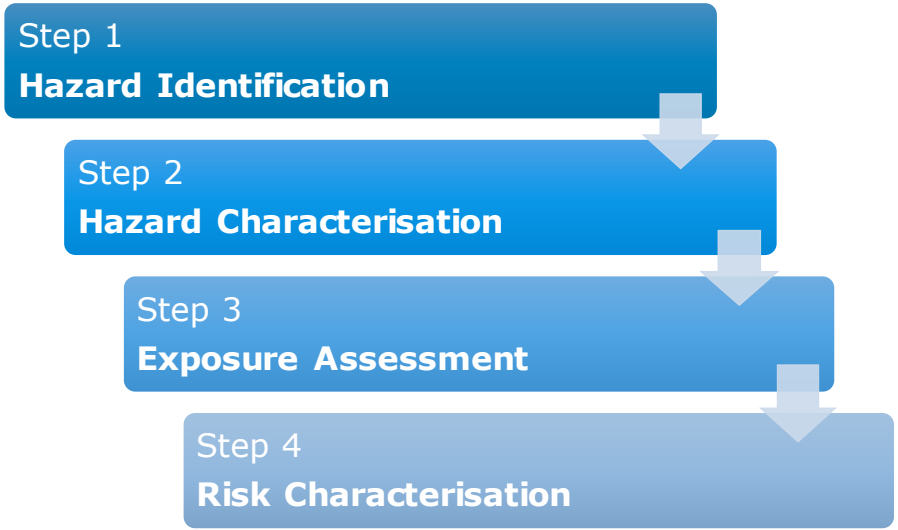
ACTIONS

Launch **experimental case studies** for filling data gaps identified in EFSA risk assessments using NAMs

Define in parallel the **mid-term strategy** (i.e., development of a Roadmap for action)

Increase **international cooperation** i.e., Sister Agencies, APCRA, and ILMERAC Working Group on NAMs, PARC, ECVAM

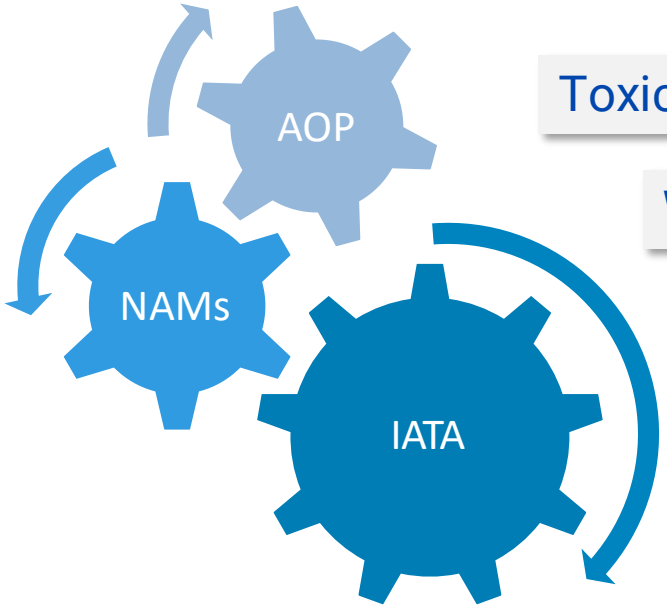
WHERE CAN NAMs BE INTEGRATED IN RISK ASSESSMENT



- **In vivo** hazard vs. NAM based hazard (e.g. **In vitro** concentration response)
- **Dose-response** (NOAEL, LOAEL, BMD,) vs. **concentration-response** (ED 50, BMC, hit specific analytical pipeline)

POINT OF DEPARTURE
Complementary information:
ADME characterisation
Biokinetic data/QIVIVE/PBK modelling

A COMMON APPROACH FOR NAMs IMPLEMENTATION IN RISK ASSESSMENT



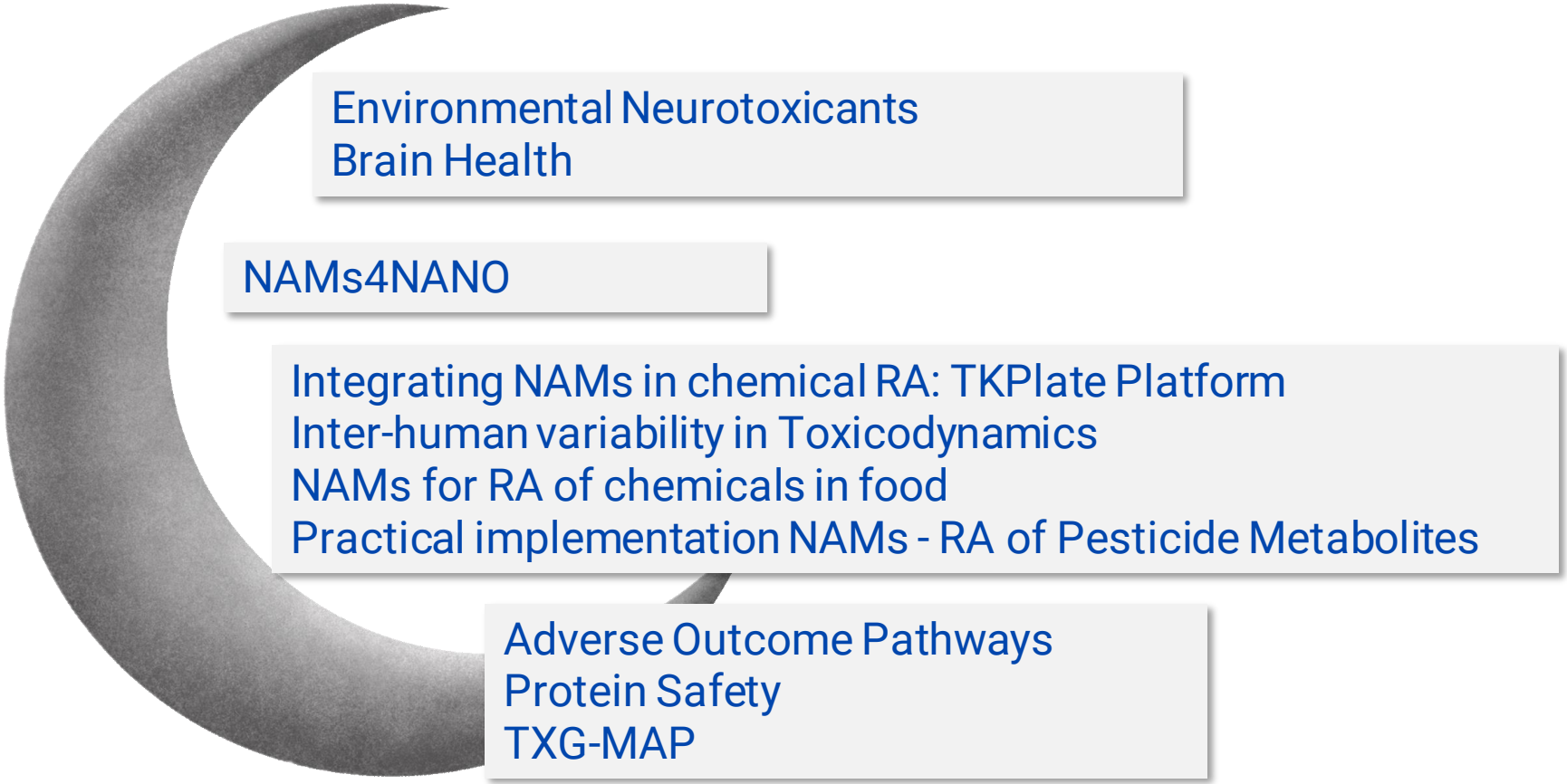
Toxicodynamics: Identify Point of Departure (PoD)

Weight of Evidence

Understanding what are you testing for

Toxicokinetics: Integrate PoD with Internal dose for risk assessment

10 NAMS PROJECTS @EFSA



Environmental Neurotoxicants
Brain Health

NAMs4NANO

Integrating NAMs in chemical RA: TKPlate Platform
Inter-human variability in Toxicodynamics
NAMs for RA of chemicals in food
Practical implementation NAMs - RA of Pesticide Metabolites

Adverse Outcome Pathways
Protein Safety
TXG-MAP

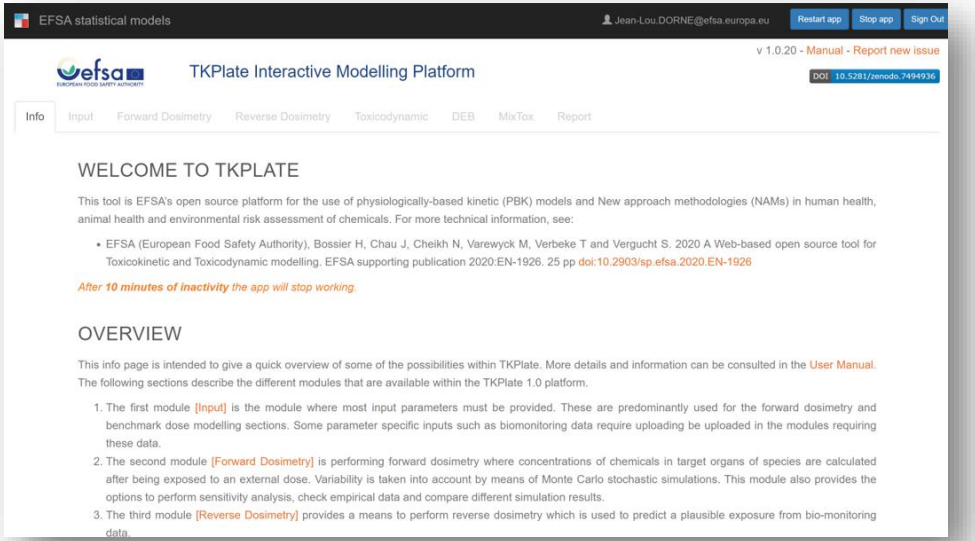
RESEARCH NEEDS AREAS

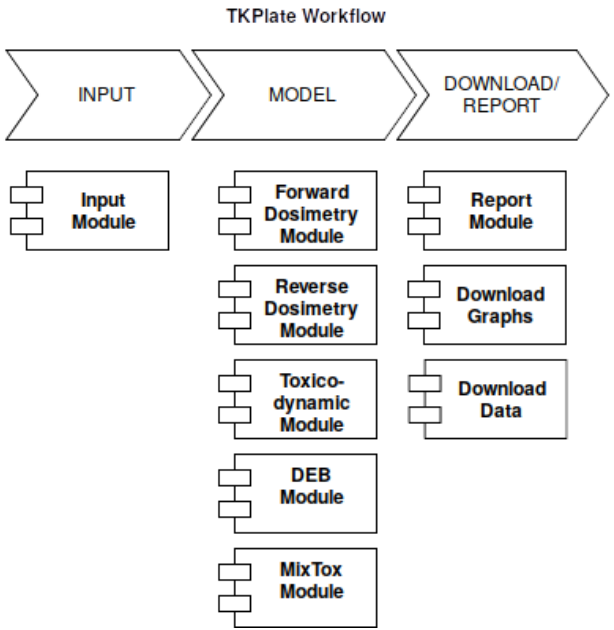
- **In vitro and In silico ADME and PBK models implementation**
- **Micro and nano-sized material**
- **Uniform approach to identify harmful chemicals**
  - Neurotoxicants
  - Immunotoxicants
  - Endocrine Disrupters
- **Phasing out animal testing**
- **Protein safety**
  - IATA case studies for read across and NAM-Based approach
  - In vitro/in silico testing battery for target organ and chronic toxicity
    - Omics based methodologies
    - In vitro and in silico testing battery for DART and other endpoints
  - GMO
- **NAM based testing framework for novel food components**
- **Implementation of analytical methods**

TKPLATE@EFSA: INTEGRATING NAMS IN RA THROUGH AUTOMATED TK AND TD MODELLING

TKPlate 1.0 allows to model in humans and animals:

- What the body does to the chemical (Toxicokinetics)
- What the chemical does to the body (Toxicodynamics)





SYNERGIES BETWEEN EFSA, ECHA AND EUROPEAN PROJECTS (PARC, ASPIS)

Research Needs

- Generate *in vitro* kinetic data to calibrate PBK/QIVIVE models (Absorption, distribution, Metabolism and transport, excretion)
- Importance of data requirements for kinetic data to integrate kinetic data and calibrating models for regulatory purposes

PBK/QIVIVE MODELLING

- In vitro parameters to calibrate/run models (EFSA-ECHA-FDA priority)
- Need mapping all models from PARC and ASPIS : ID relevance for RA
- Generic PBK models (TKPlate) : integration through synergies
- Human Biomonitoring data and reverse dosimetry: aggregate exposure
- Quantitative AOPs can be integrated in RA (e.g steatosis): Link with PB/QIVIVE and Benchmark dose modelling
- Bioaccumulation models (EFSA-ECHA priority)
- TKTD Models for ecotoxicological assessments

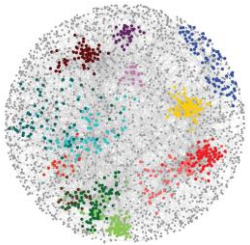
EXPLORING THE USE OF OMICS IN RISK ASSESSMENT

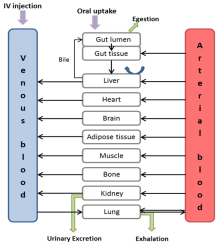
Genomic signature as toxicity surrogates in humans i.e. transcriptomics, metabolomics and epigenomics

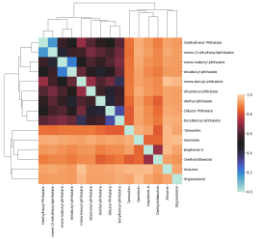
Standardisation/ validation essential for regulatory acceptance

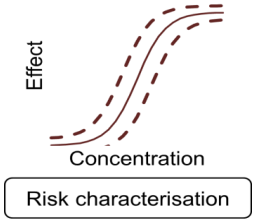
Integrating signature data with traditional tox data: improve predictive accuracy for toxicity pathways

Modelling of Dose response data using Benchmark Dose and PBK/QIVIVE Modelling









NAMs FOR ENVIRONMENTAL RISK ASSESSMENT (ERA)

EXPLORE UTILITY OF NAMS4ERA

(I.E. OPPORTUNITIES & CHALLENGES)

Provide New Data Streams

Provide Alternative Test Systems (Model Species & Endpoints)

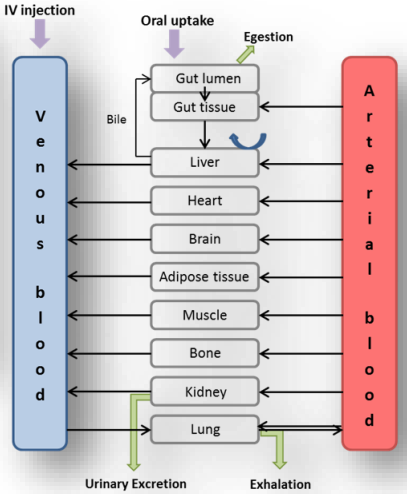
INNOVATE & MODERNISE ERA

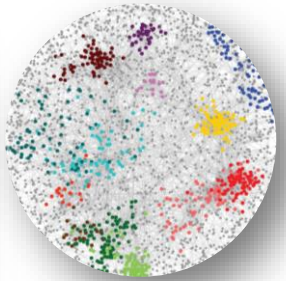
Provide improved Mechanistic Knowledge of Toxic Effects on biological systems

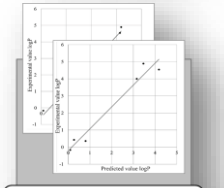
IMPROVE ERA EFFICIENCY, RELIABILITY & REALISM

Enable Prediction of Effects (from lab to field; from individuals to populations; across species)

THANK YOU FOR YOUR ATTENTION!







Chemical parameter estimation by QSAR

Risk characterisation

EEA perspective on chemicals' research needs

Monitoring:

Human health and the environment

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From ESD PT18 for household and professional uses ENV/JM/MONO(2008)14

EEA at a glimpse

- A European Agency
- Founded in 1994
- 280+ employees
- 200+ datasets
- Located in Copenhagen, Denmark

We support policies with evidence-based knowledge to help the European Union and our member countries achieve sustainability

We inform public and policy discussions on sustainability solutions and challenges

We build and maintain networks and partnerships to facilitate sharing of knowledge and expertise across Europe

We collect, quality check and disseminate data, making full use of digitalisation and latest innovative technologies

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EEA and chemicals

Not a typical regulatory agency…

But the **EEA** is:

- Assessing the state of the environment (including impacts from chemicals)
- Assessing cross-cutting and systemic challenges
- Informing on policy implementation
- Offering a network for exchange of data and knowledge

The **occurrence of chemicals** in **surface water, drinking water, soil, air, biota and in humans** is key in order to:

- Provide data on real exposure levels from multiple sources
- Estimate impacts on ecosystems and human health
- Evaluate the state of the environment
- Validate information from upstream chemical regulation (REACH, PPP, BPR, etc)
- Target policy interventions to substances that matters!

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Research needs from the EEA perspective

EEA main areas of interest for filling knowledge gaps are:

1. **Environmental monitoring**
2. **Human biomonitoring**
3. Chemicals in the circular economy
4. Safe and Sustainable by Design
5. Early warning system for emerging chemical risks
6. Chemical impacts on biodiversity loss and burden of disease
7. Indicators
8. Crosscutting topics

Environmental monitoring (1)

Antibiotics

Explore the link between Environmental Quality Standards (EQS) and Minimum Inhibitory Concentration (MIC)

Scope: implementation of Anti Microbial Resistance (AMR) standards in the environment

Coupling medicine, health and water regulatory frameworks aspects

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Environmental monitoring (2)

Waters and chemicals related climate changes

- Investigate link between climate change and chemical induced effects: rivers, lakes and groundwater (droughts and floodings)

Better understanding of the implications on water

Develop better management options for water in a changing climate

Environmental monitoring (3)

Persistent Organic Pollutants in European soils

- Analysis on potential impacts of POPs on soil ecosystems
- Monitor progress towards the Zero Pollution targets
- EU Soil Strategy

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Environmental monitoring (4)

Environmental degradation pathways for polymeric PFAS

- Exempted from registration under REACH
- Limited information
- Understand the potential long-term impact on the environment
- Link with numerous EU pieces of legislation

Human biomonitoring (1)

Further EU harmonization of the approaches for HB in the EU

- High quality datasets to compare data between different countries and time periods
- Currently no regulatory requirements
- Outcome helpful for future regulatory purpose

Human biomonitoring (2)

Chemical exposure in the indoor environment

- Minimise exposure of humans and the environment to hazardous substances
- Identify substances of concern → negatively affect indoor air and dust
- Increased knowledge with monitoring

EFSA | Human bio-monitoring data

Food monitoring

vs

Human bio-monitoring

HBM data access

Prioritisation and hazard identification

Validation of modelled exposure

Integration in risk characterisation

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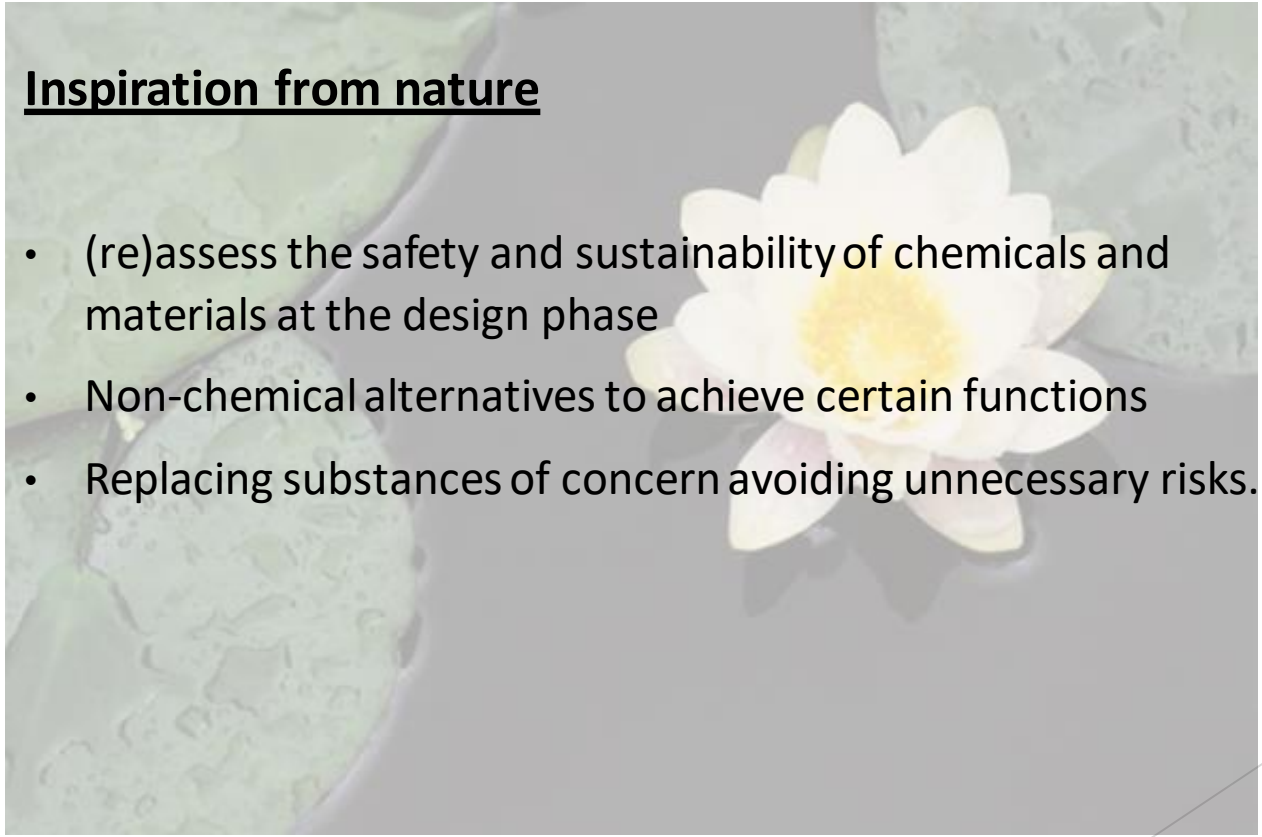
Crosscutting topic



Inspiration from nature

- (re)assess the safety and sustainability of chemicals and materials at the design phase
- Non-chemical alternatives to achieve certain functions
- Replacing substances of concern avoiding unnecessary risks.

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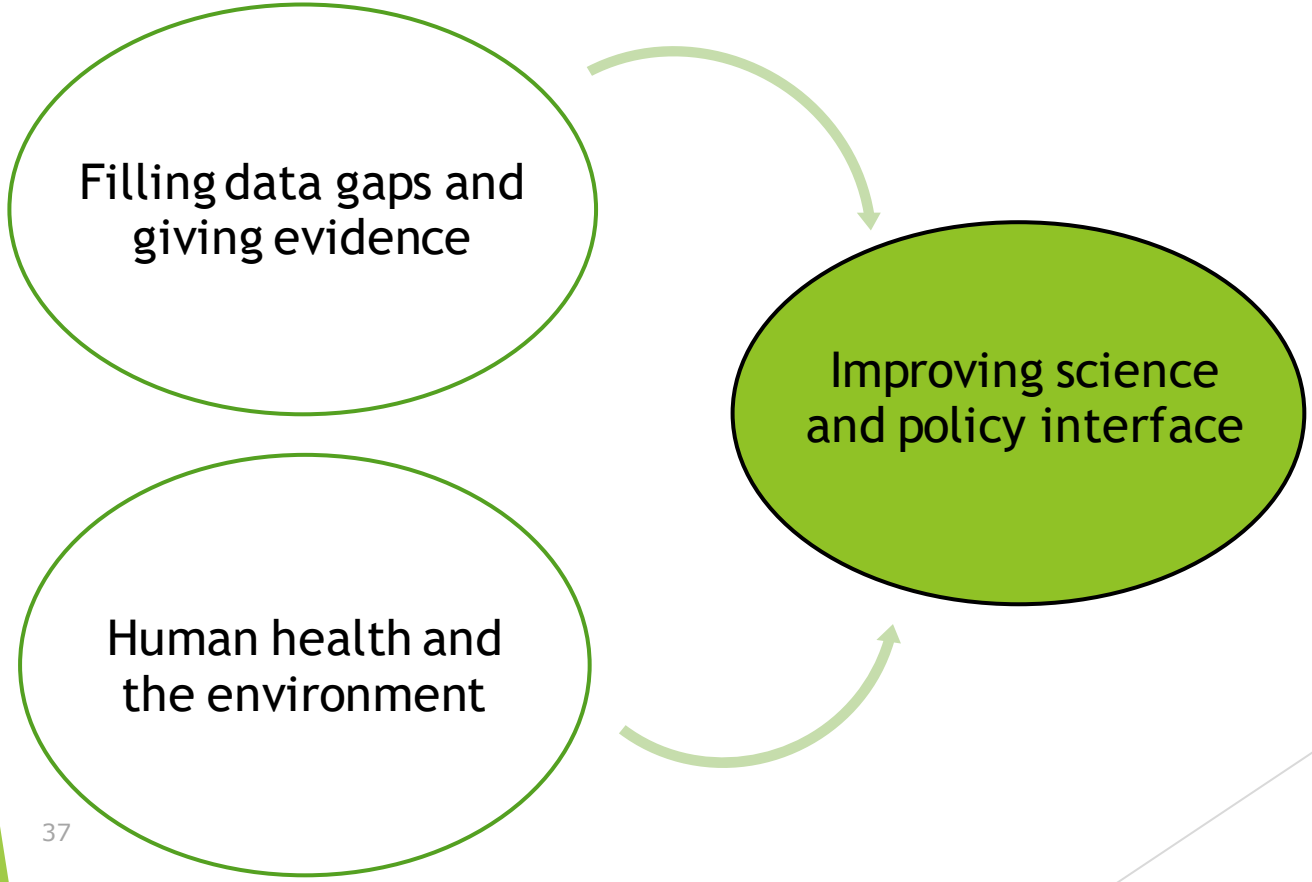
Final message from the EEA



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THANKS FOR YOUR ATTENTION!

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Bioaccumulation: research needs for air-breathers, specific substance classes and alternative methods

Webinar: Research needs for protecting human health and the environment - an EU agencies' perspective

18 June 2024

Jane Caley
European Chemicals Agency

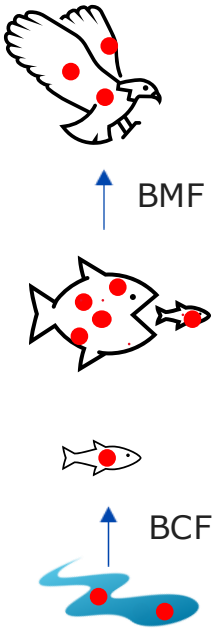
Content

- → Setting the scene
- → Key areas of regulatory challenge: Bioaccumulation
  - Bioaccumulation in air-breathing organisms
  - Bioaccumulation assessment of super-hydrophobic substances
  - Bioaccumulation potential of surfactants, ionisable substances and organo-metals
  - Alternative methods in bioaccumulation assessment

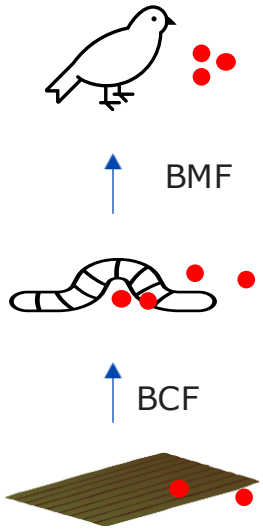
Setting the scene

Setting the scene: bioaccumulation

Aquatic food chain



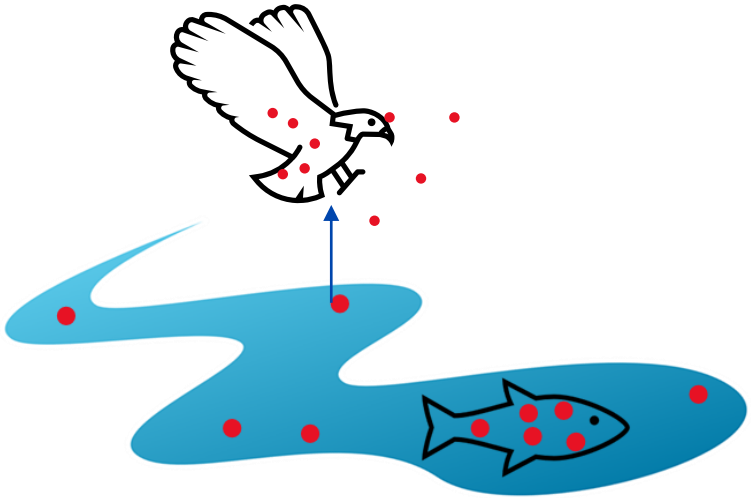
Terrestrial food chain



Bioaccumulation

- Usually driven by lipophilicity (ability to dissolve in fat)
- Predicted by octanol-water partitioning coefficient (Kow)
- Aquatic food chain: Many regulatory criteria based on bioconcentration factor (BCF) for aquatic species (fish, aquatic invertebrates)
- Terrestrial food chain (air breathers): Octanol-air partitioning coefficient (Koa) predicts substances sufficiently volatile to be readily eliminated by exhalation
- Some substances accumulate in other (biochemical) compartments than lipids, such as protein

Regulatory use



PBT/vPvB assessment or classification BCF >2000/5000 (screening log Kow ≥ 4.5 and log Kow > 2 with log Koa >5)

Classification for hazardous to the aquatic environment (BCF ≥ 500, log Kow ≥ 4.0)

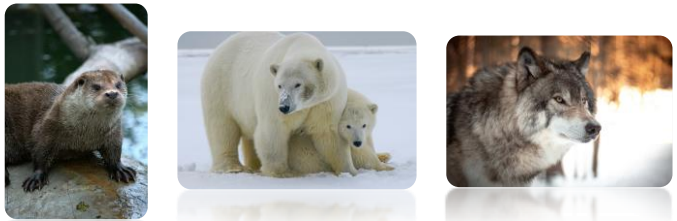
Stockholm Convention on Persistent Organic Pollutants (BCF >5000, log Kow > 5)

Secondary poisoning and humans via environment (assessment needed if log Kow > 3)

Bioaccumulation in air-breathing organisms

Bioaccumulation in air-breathing organisms

Certain types of substances do not bioaccumulate in fish (BCF below regulatory threshold) but have potential to bioaccumulate in air-breathing organisms.



Photos: © Unsplash\ Mateusz Bajdak, Hans-Jurgen Mager, Milo Weiler

Example:

Bis(4-chlorophenyl) sulphone (BCPS)

→ log Kow 3.9, fish BCF=82

→ Screening criteria for air-breathers fulfilled (log Kow > 2 and log Koa > 5)

→ Very long terminal half-life of 12 days in rats

→ Field BMFs > 1 (fish – seabirds, fish – seals food chains)

Air-breathers: research needs

Screening criteria

→ Recent research: screening criterion log Koa > 5 may not be protective for animals with lower rates of respiration (e.g. manatees, sloths), those with high-lipid diets (e.g. polar bears, birds of prey) and temperate reptiles

→ Investigate adequacy of screening criteria

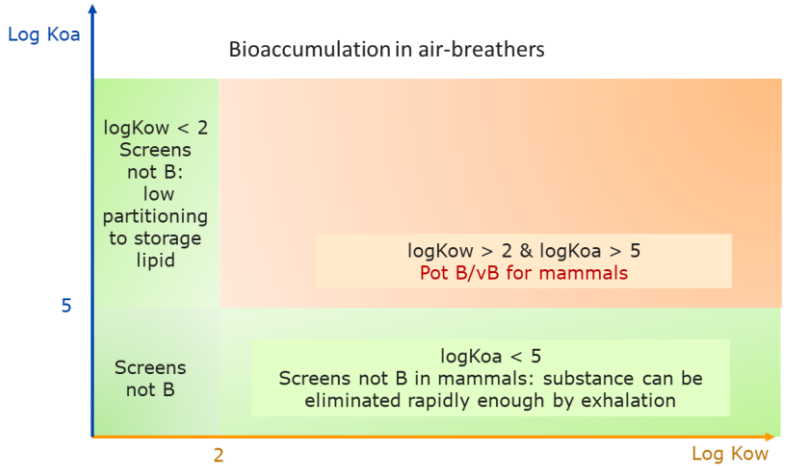



Photos: © Unsplash/US National Oceanic and Atmospheric Administration, Javier Mazzeo, Hans -Jurgen Mager, Craig Hughes

Air-breathers: research needs

Biotransformation assessment

→ Further develop *in-vitro* clearance methods and QSAR models to estimate biotransformation potential



Other research needs

→ Determination of hindered uptake for air-breathing species

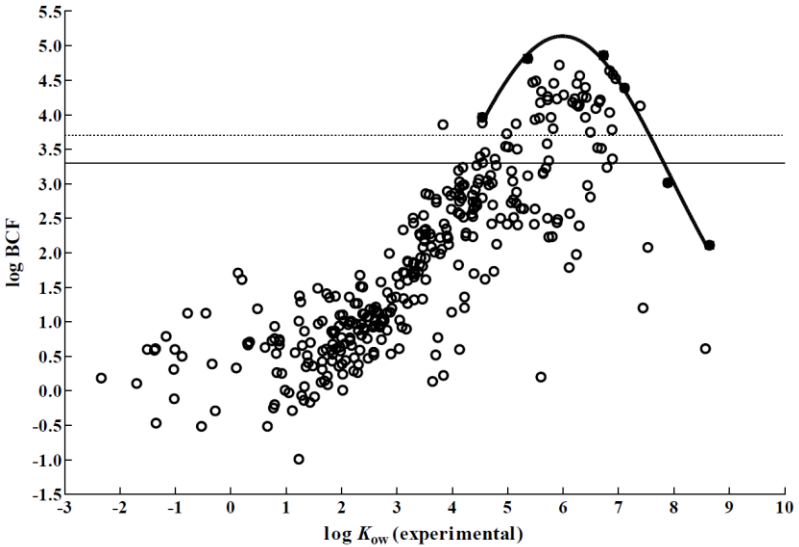
→ Expanding concept to other air-breathers such as birds

→ Generation and assessment of monitoring data

Bioaccumulation of super-hydrophobic substances

Super-hydrophobic substances

- → Substances with log Kow > 8 considered to have low bioavailability
- → Several still found to bioaccumulate e.g. Dechlorane Plus™
- → Such substances are taken up and eliminated very slowly
- → Difficult to handle in the laboratory, difficult to test over usual timeframe of laboratory tests



Super-hydrophobics: research needs

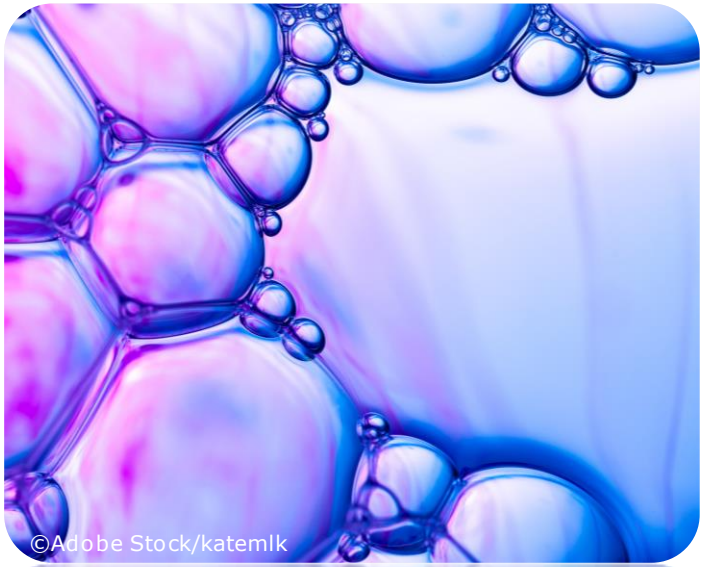
Assessment and testing strategies

- → When does standard assessment approach not apply?
- → How to predict whether they bioaccumulate or not?
- → E.g. what parameters, what test methods and for what duration?
- → What tools can be used to predict their bioaccumulation at steady state?
- → Are there suitable laboratory tests?
- → Approach needed to screen and assess bioaccumulation potential of super-hydrophobics

Bioaccumulation of surfactants, ionisable substances and organo-metals

Surfactants, ionisable substances and organo-metals

- → Log Kow not a good predictor of bioaccumulation potential
- → REACH standard data requirement may not be waived based on low log Kow alone if substance is surface active or ionisable at environmental pH (pH 4 – 9)
- → Such substances may have specific binding interactions e.g. with proteins
- → Some have specific transport mechanisms across cell membranes
- → Behaviour of cationic substances difficult to predict



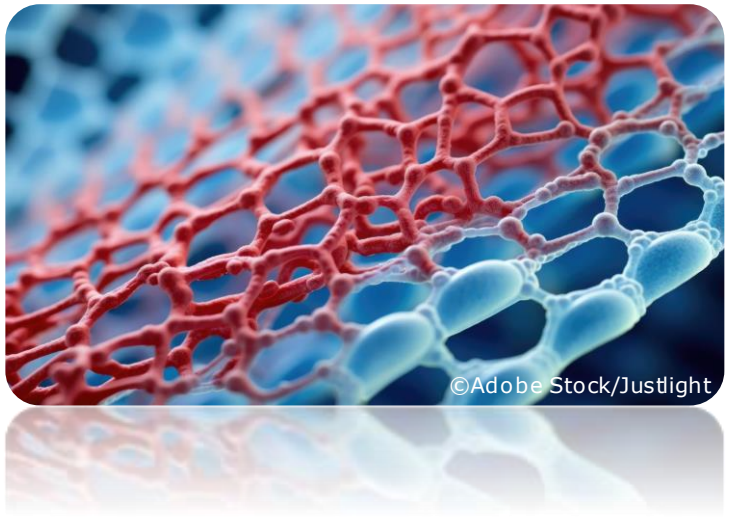
Surfactants, ionisables, organo-metals: research needs

Screening criteria

→ How to predict if such substances bioaccumulate?

→ E.g., could fish-water partition coefficient or membrane lipid-water coefficient be useful?

→ What thresholds to use?



Other research needs

→ By what mechanisms do such substances bioaccumulate?

Alternative methods in bioaccumulation assessment

Alternative methods to fish BCF

- → OECD 319A/B fish clearance rates can be extrapolated to a BCF using *in vitro-in vivo* extrapolation (IVIVE) methods
- → Fish clearance rates could support read-across and grouping approaches
- → New OECD invertebrate test guideline: *Hyalella azteca* Bioconcentration Test (HYBIT)

Photo: draft OECD HYBIT test guideline

Alternative methods – research needs

Indicators of bioaccumulation

- → Alternatives to log Kow for ionisable, surface-active and organo-metal substances
- → Improved screening criteria for air breathers

In *vitro* clearance assays

- → What types of substances does OECD TG 319A/B assay work for?
- → Why sometimes a mis-match between *in vitro* and fish BCFs?
- → Improve IVIVE models to predict BCF
- → Use of rat/bird *in vitro* clearance assays to predict bioaccumulation in air breathers

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Information sources

- ECHA Guidance on Information Requirements and Chemical Safety Assessment - Chapter R.7c: Endpoint specific guidance Version 4.0 December 2023, IR_CSA_R7c_v4.0_202312_en (europa.eu)
- ECHA Guidance on Information Requirements and Chemical Safety Assessment - Chapter R.11 PBT/vPvB assessment Version 4.0 December 2023, IR_CSA_R11_v4.0_202312_en (europa.eu)
- Saunders, L.J. and Wania F. (2023). Cross-Species Evaluation of Bioaccumulation Thresholds for Air-Breathing Animals. Environmental Science & Technology 2023 57 (29), 10491-10500.
- Mammalian toxicokinetic database (MamTKDB) 1.0, with elimination half-lives (mainly rat and human) for around 1400 substances
- Hofer T., Myhre O., Peltola-Thies J., Hirmann D. (2021). Analysis of elimination half-lives in MamTKDB 1.0 related to bioaccumulation: Requirement of repeated administration and blood plasma values underrepresent tissues. Environment International, Volume 155, 106592
- Bioaccumulation assessment of air-breathing mammals: a discussion paper, 2022 bioaccumulation_assessment_of_air_breathing_mammals_en.pdf (europa.eu)

Conclusions

Webinar: Research needs for protecting human health and the environment – an EU agencies perspective

18 June 2024

Adam Elwan
Communications
European Chemicals Agency

Key takeaways

- → Bridging research and regulation with PARC
- → Promoting new methodologies and data integration
- → Advancing risk assessments with new approach methodologies
- → Reducing animal testing, improving accuracy
- → Environmental and human biomonitoring focus
- → Addressing antimicrobial resistance, POPs, climate change
- → Refining screening criteria, developing in vitro assays
- → Enhancing predictive models
- → Collaboration and innovation
  - Cross-agency and international partnerships
  - Leveraging synergies for better chemical safety

Live Q&A

- → Join Q&A at: slido.com
  Event code: **#science2024**
  or with the QR code
- → Panellists reply until 13:00 Helsinki time (EEST, GMT+3)
- → Q&A document with replies to all questions soon after the event

Thank you

adam.elwan@echa.europa.eu

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