BIENNIAL SCOPING MEETING

# Use of big data and AI technology to prevent occupational diseases

Eelco Kuijpers, TNO

ecetoc

We are the Centre for Chemical Safety Assessment

# Needs Challenge

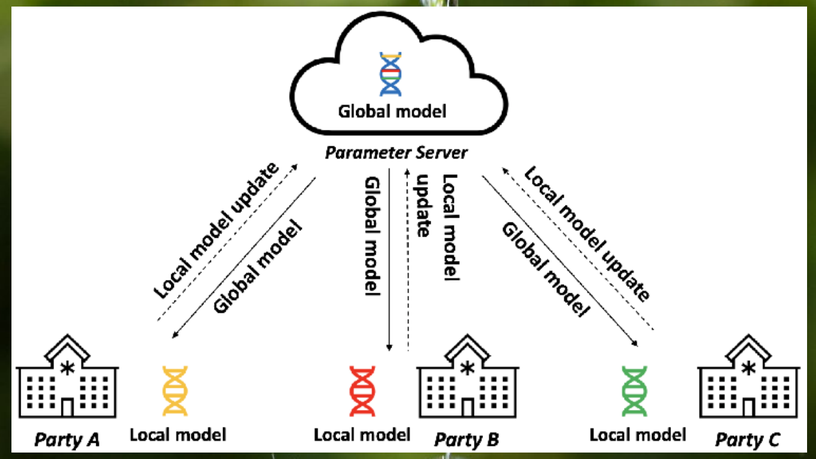
- The global burden of occupational diseases vary between 5-7% of the total mortality.
- Associated economic costs vary between 2-6% of EU countries GDP.
- **More data-driven prevention is needed.**

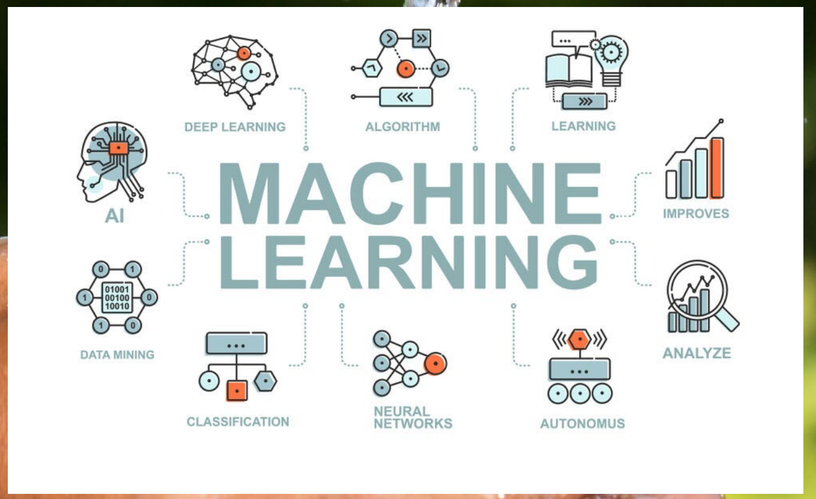



Eelco Kuijpers, TNO

# Associated knowledge/ Methodologies gaps

- High-quality data is **fragmentedly** available and often **not public** (due to e.g. GDPR and IP).
- Privacy enhanced technologies (PET) are capable of overcoming these issues, but **application** is still in its infancy.
- Machine learning models **efficiently use data**, reducing the need for data, but are largely missing for the prevention of occupational diseases.



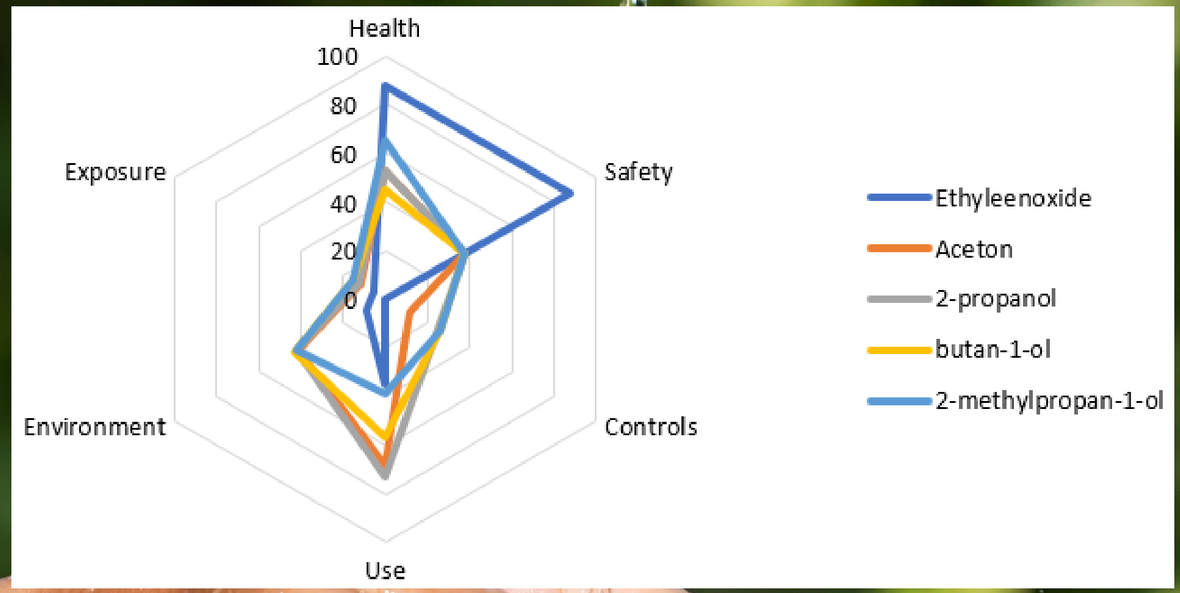



Eelco Kuijpers, TNO

# Objectives

We propose a **workshop** which includes the following aspects:

- Introduction on PET technology and machine learning;
- Some examples with the Substance Information System (SIS);
- Discussion on industries' data (sharing) needs, challenges and the added value of the aforementioned technologies;
- Defining a priority use case as a possible next step.






Eelco Kuijpers, TNO

# Expected impact

- The target audience will be trained on the possibilities of PET and machine learning technologies.
- The main expected outcome is a workshop summery with industries' identified needs, challenges and possible next steps.
- **Ultimately:**
  - More data-driven prevention becomes reality.
  - Improving worker health




Eelco Kuijpers, TNO

BIENNIAL SCOPING MEETING

# Framework to facilitate the development of Safe and sustainable by design chemicals

Neeraj Shandilya, TNO
Netherlands

ecetoc
We are the Centre for chemical safety assessment

# Needs Challenge

- EC’s Chemical Strategy for Sustainability (CSS): toxic free environment
- Safe and Sustainable by Design (SSbD) chemicals and products
- A big challenge to “successfully” implement CSS!
- SSbD chemicals development through predictive New Approach Methodologies

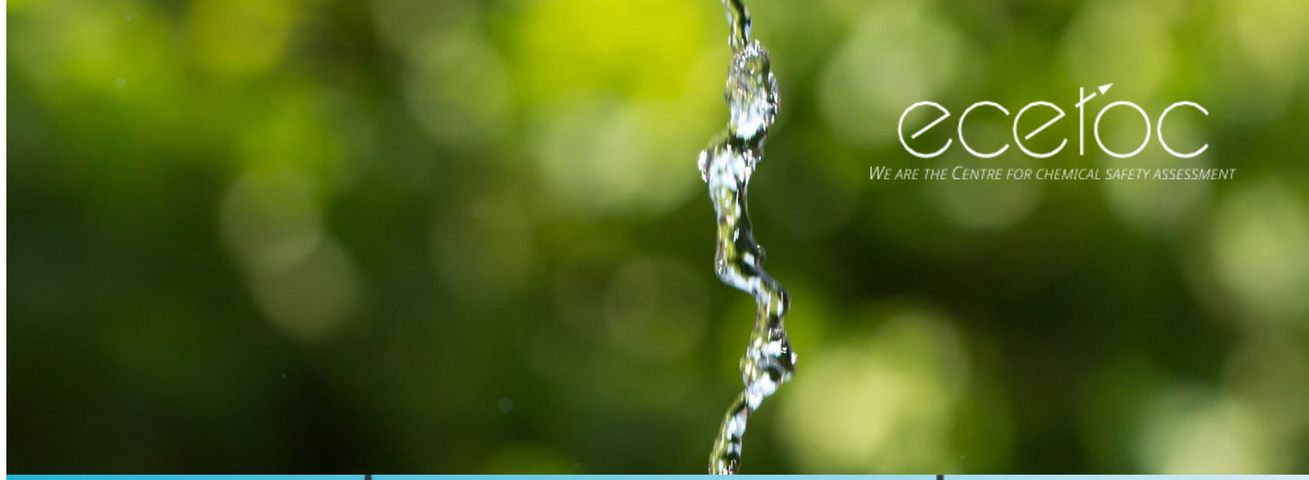
# Associated knowledge/ Methodologies gaps

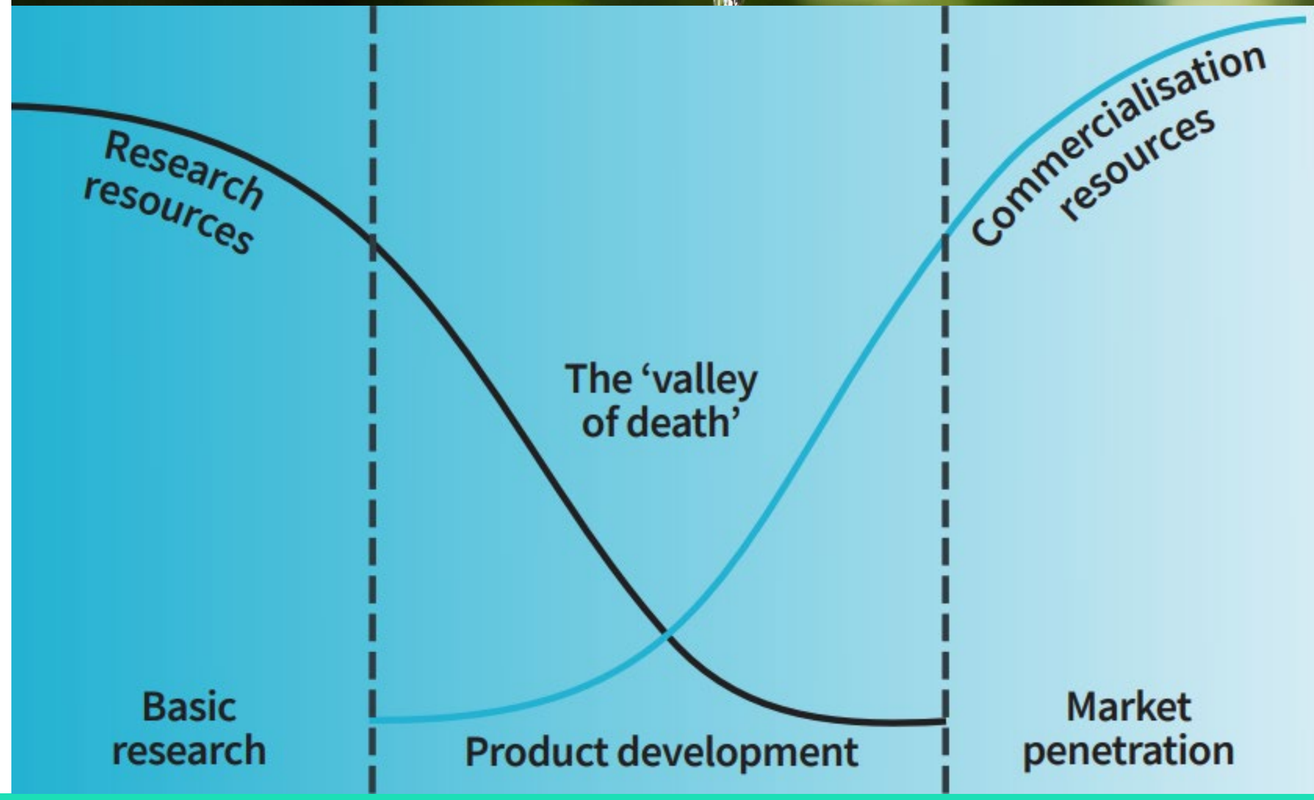
- Several NAMs: which one to use and when?
- Coupling performance properties with risk relevant data from NAMs
- An evidence-based decision making process
- Effective data use through machine learning approaches

# Objectives

**Conceptual framework** to **structure** the NAMs retrieved information and facilitate the decision making process through:

- mapping performance/functionality driving properties with safety in a Substance Information System (SIS);
- identification of potential substitutes (CRT);
- sustainability and safety screening: raising early red flags and turning them green






Neeraj Shandilya, TNO

# Expected impact

- Coherent fit of the innovative product development with the EU plans for a greener future
- Useful tool to accelerate market uptake of new and alternative chemical products and technologies
- Stable regulatory preparedness
- High economical and societal relevance to the industry


Courtesy: Royal Society of Chemistry

BIENNIAL SCOPING MEETING

# Assessing risks to biodiversity: improving our understanding and prediction through modelling

Nika Galic, Syngenta AG

ecetoc

We are the Centre for chemical safety assessment

# Needs Challenge

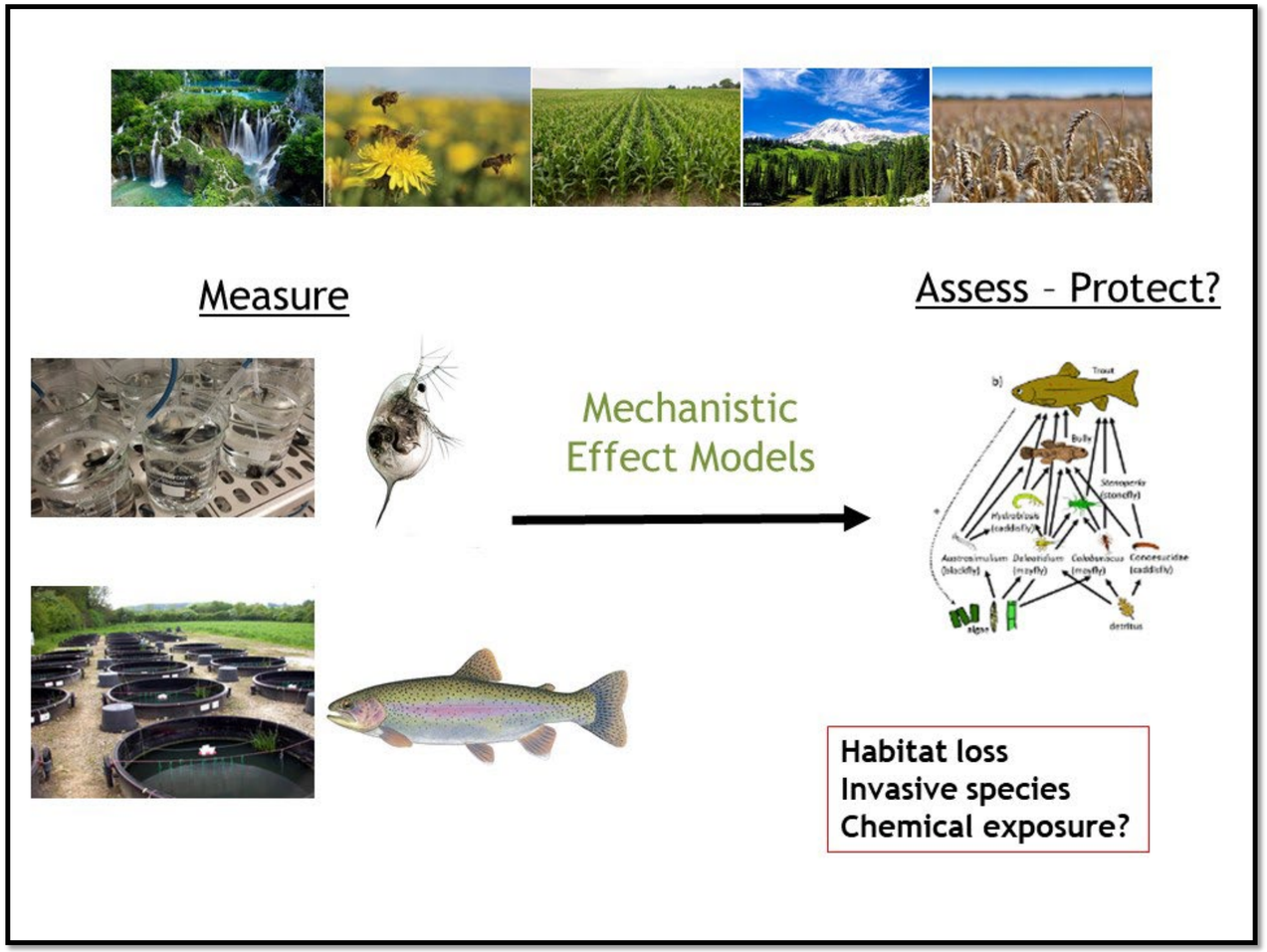
- Biodiversity loss/change – relative role of different factors
  - Various actions and strategies
- How can we better understand and assess the role and risks to biodiversity from chemicals?
  - Available tools?




Nika Galic, Syngenta AG

# Associated knowledge/ Methodologies gaps

- Biodiversity risk assessment – protection goals and approach undefined
- Mechanistic Effect Models (MEMs) as predictive tools in chemical risk assessment
  - Specific objectives and domains of applicability

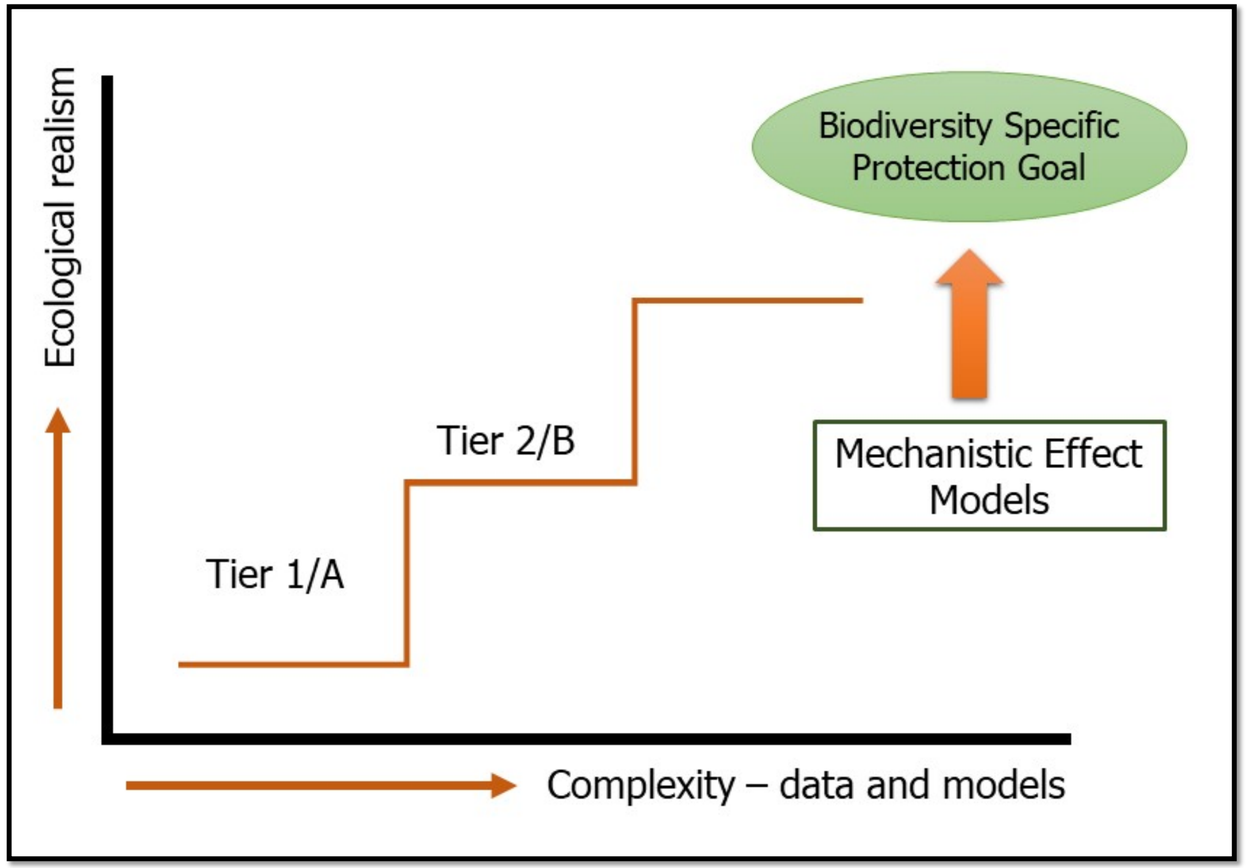


# Objectives

- Discuss and define endpoints and protection goals for biodiversity RA
- When is application of MEMs for biodiversity RA appropriate?
- Needs for future research and tool development

# Expected impact

- Multi-stakeholder agreement on the approach
- Identify appropriate modelling tools
- Define crucial next steps in approach and tool development



BIENNIAL SCOPING MEETING

# *Understanding the Environmental Hazards of Bio-based and Circular-waste Chemicals*

Sarah Hughes, Shell

ecetoc

We are the Centre for chemical safety assessment

# Needs Challenge

- We need to become carbon neutral society < 2050
- Rapid transition to circular economy
- Assumption that bio/natural = low risk
- Assumption that new feedstocks are similar risk to conventional chemicals
- Need to quickly evaluate ecorisk of novel feedstocks and products


Title

Bio- and Circular-waste Chemicals Ecorisk Taskforce

Sarah Hughes, Shell

# Associated knowledge/ Methodologies gaps

- Evaluate the landscape of waste and circular chemical products
- Uncertainty on ecohazard compared to conventional petrochemicals
- Differences in circular chemical processes “drop-in” vs novel bio-chemicals
- Need to understanding ecotoxicty risk throughout the product life cycle

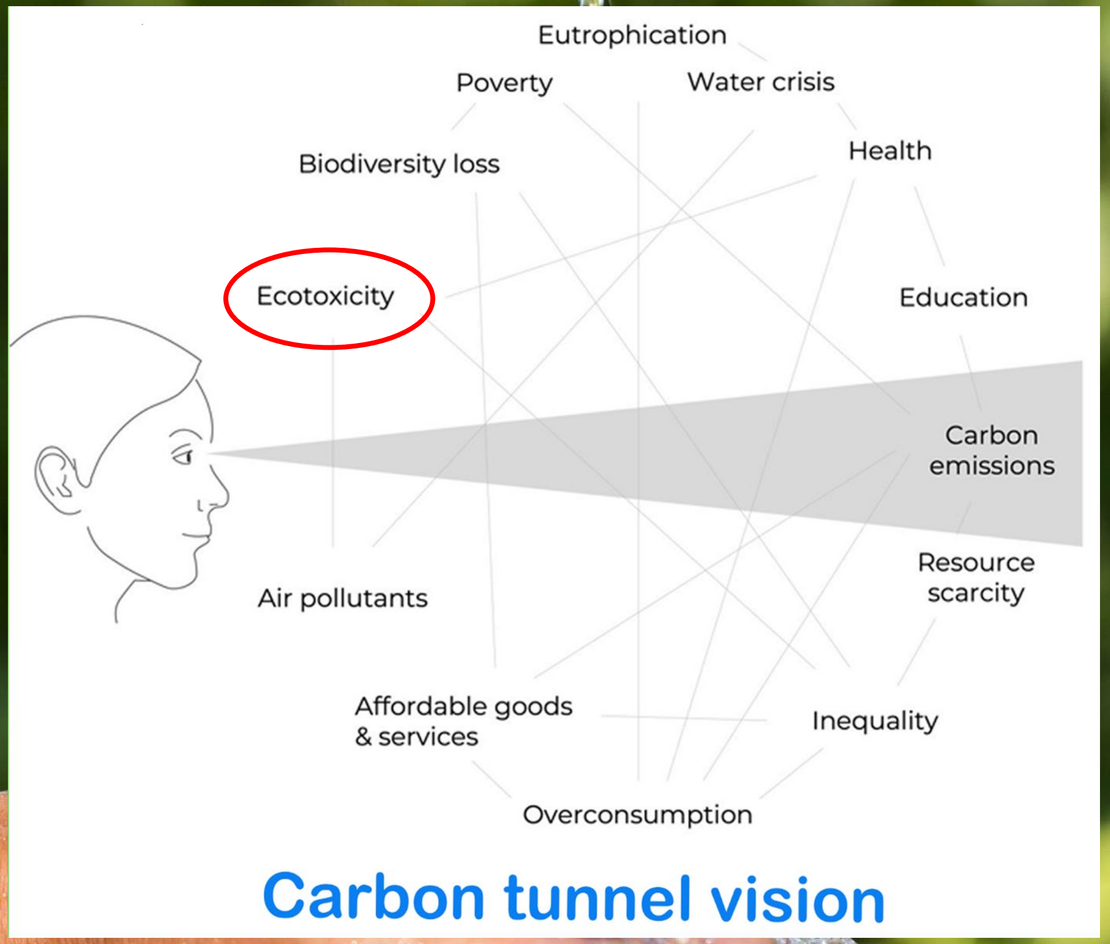



Image adapted from Jan Konietzko Source: https://digitally.cognizant.com/moving-beyond-carbon-tunnel-vision-with-a-sustainability-data-strategy-codex7121

Title

Bio- and Circular-waste Chemicals Ecorisk Taskforce

Sarah Hughes, Shell

# Objectives

- Review the state of alternative bio- and circular-based chemicals
- Evaluate environmental risks of all bio- circular feedstocks
- Identify gaps in science
- Identify where data could be read-across from conventional chemicals
- Forecast if bio and circular waste processing could alter risks conventional manufacturing processes (e.g. effluent discharges)


Title

Bio- and Circular-waste Chemicals Ecorisk Taskforce

Sarah Hughes, Shell

# Expected impact

- Safe adoption of bio- and circular-wastes
- Faster & safer transition to circular economy
- Reduce product testing
- Identify future science needs of tomorrows chemical feedstocks


Title

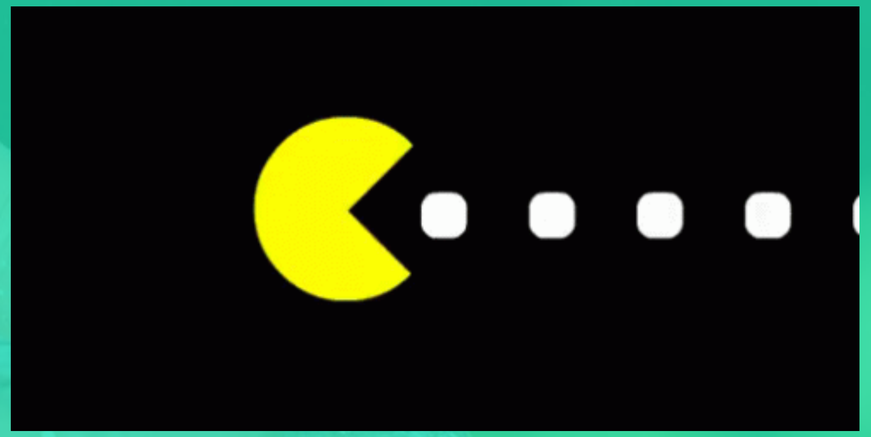
Bio- and Circular-waste Chemicals Ecorisk Taskforce

Sarah Hughes, Shell

BIENNIAL SCOPING MEETING

# Development of grouping approaches for persistence assessments

Chris Hughes, Ricardo Energy & Environment



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# Needs Challenge

- Persistence is an increasingly important property for sustainability and regulation of chemicals.
- Persistence data are very scarce, but demand is increasing rapidly.
- Testing is challenging and costly.
- Grouping approaches are needed.




Chris Hughes,
Ricardo Energy & Environment

# Associated knowledge/ Methodologies gaps

- Substance characteristics (structure and properties) that influence relevant degradation endpoints.
- Degradation at low, environmentally relevant concentrations.
- Category/read-across justifications and *in silico* methods.
- Approaches for complex (UVCB) substances.




Chris Hughes,
Ricardo Energy & Environment

# Objectives

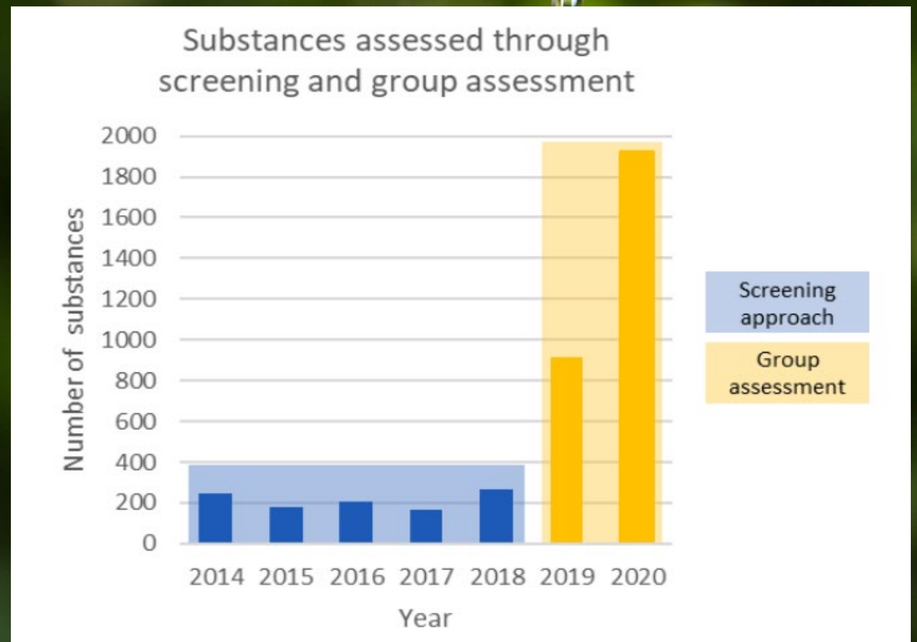
- Identify opportunities to implement grouping approaches for persistence.
- Address all key endpoints (degradation kinetics, transformation products and NER).
- Address aspects of (and barriers to) regulatory acceptance vs experimental testing.




Chris Hughes,
Ricardo Energy & Environment

# Expected impact

- Improved understanding of factors influencing persistence.
- More appropriate grouping and P assessments.
- Improved compliance with regulatory requirements and reduced testing costs.
- Fewer false positive P outcomes.
- Solutions for UVCB substances.




Integrated Regulatory Strategy Annual Report, ECHA (2021).



Chris Hughes,
Ricardo Energy & Environment

BIENNIAL SCOPING MEETING

# Leveraging available experimental data to investigate the suitability of a default Activation energy for temperature correction of biodegradation rates.

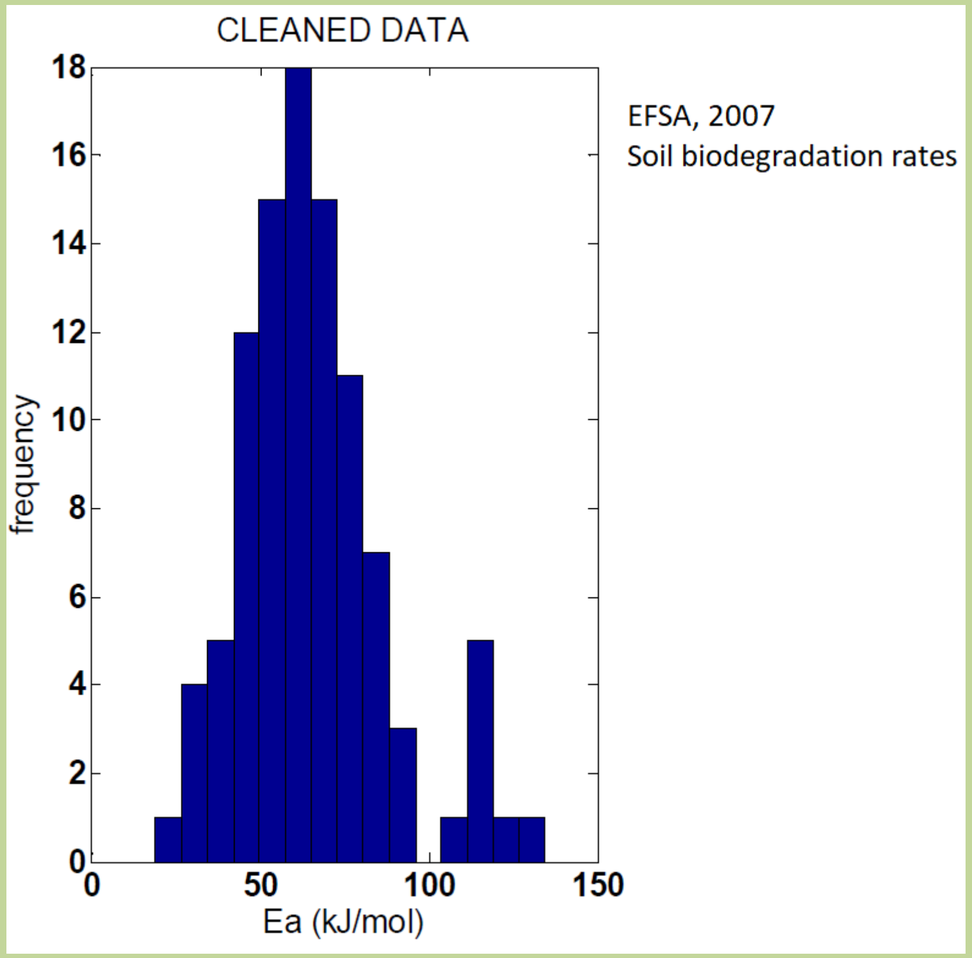
Marie Collard, Firmenich

ecetoc

We are the Centre for chemical safety assessment

# Needs Challenge

- Application of a default temperature correction by ECHA
- Default parameters applied to all situations
- Overly conservative re-calculated value overrides all other available data
- Upcoming PMT will broaden the scope of substances impacted



# Associated knowledge/ Methodologies gaps

- Relevance of practice
- Impact of temperature of collection of the inoculum
- Origin of EFSA's value
- Lack of alternative methods/values

# Objectives

- Review available literature and data to assess:
  - relevance and accuracy of the practice
  - impact of the temperature inoculum is collected at
- If possible, propose an alternative method.

# Expected impact

- Provide support for an alternative strategy
- Avoid mislabeling of substances as SVHCs
- Proactively provide scientific support for the update of the guidance (PMT implementation)

BIENNIAL SCOPING MEETING

# Improving exposure knowledge in human and environmental safety and sustainability assessment of chemicals – Recommendations to stakeholders

Jan Urbanus, Shell
(acknowledging contribution from Prof. Jim Bridges)

ecetoc
We are the Centre for chemical safety assessment

# Needs Challenge

- Trend towards hazard-only, not exposure – overly simplistic and regrettable
- Stakeholders do not develop exposure science capability
- Good ideas exist, need to be tailored to stakeholders and amplified – by ECETOC


**[Science and sustainable regulation]:**
**Risk = Hazard x Exposure**

**[Popular misconception]:**
**Risk = Hazard**

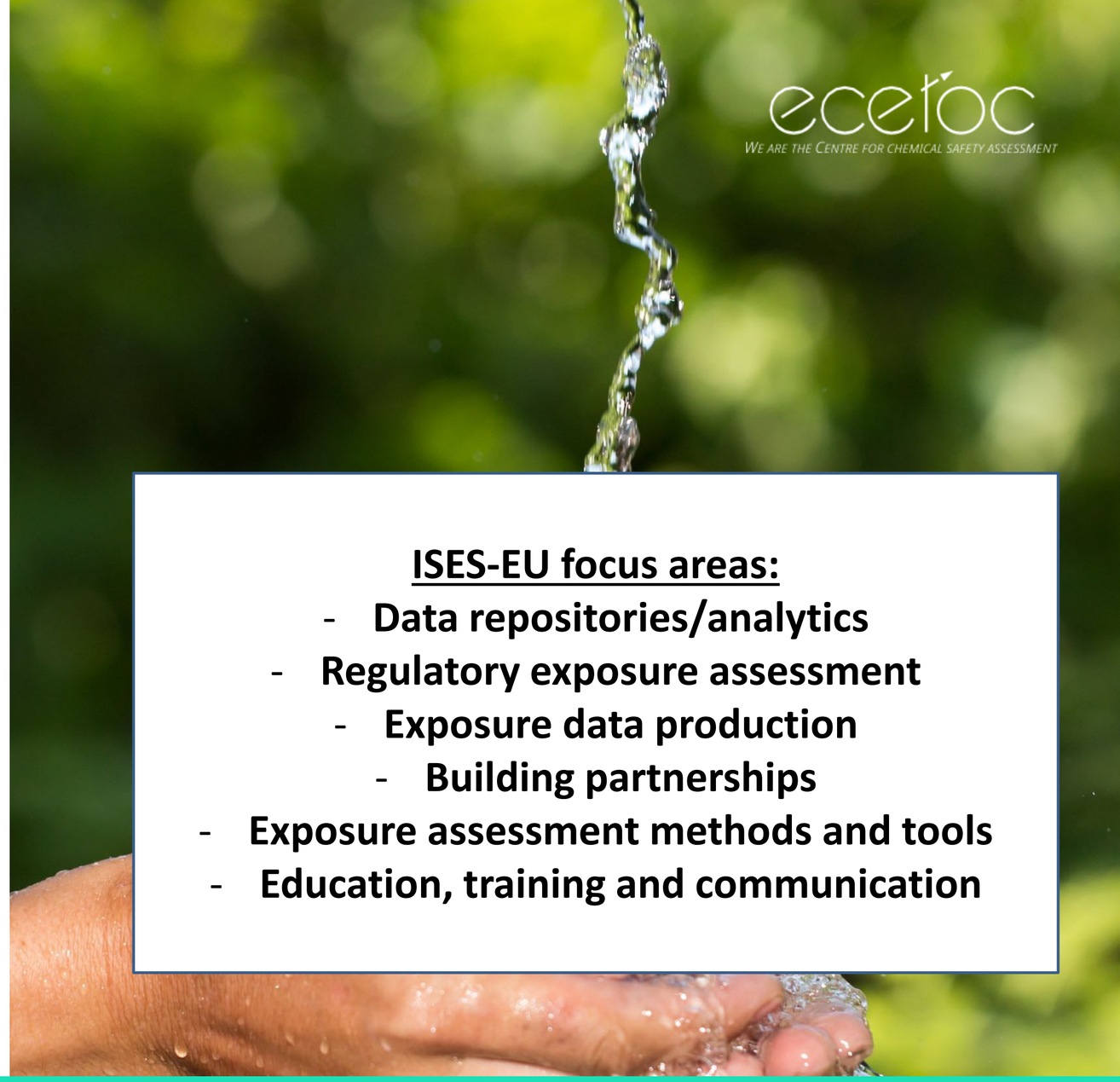
# Associated knowledge/ Methodologies gaps

- Recommendations to improve exposure science uptake not actioned by ECETOC stakeholders
- Scientific innovations not utilized; missed opportunities to improve quality of exposure knowledge
- Low potential to solve chemical management challenges through tailored exposure control


**In 2017 the International Society for Exposure Science created a European 'chapter' which produced a 2020-2030 improvement strategy for the EU**

# Objectives

- Issue ECETOC-recommendations to stakeholders to grow exposure science capability and capacity
  - Build on European Strategy of the **Int'l Soc. for Exposure Science (ISES-EU)**
  - Workshop of ISES-EU, other leading scientists and ECETOC experts
  - Identify priority actions and resource implications for ECETOC stakeholders

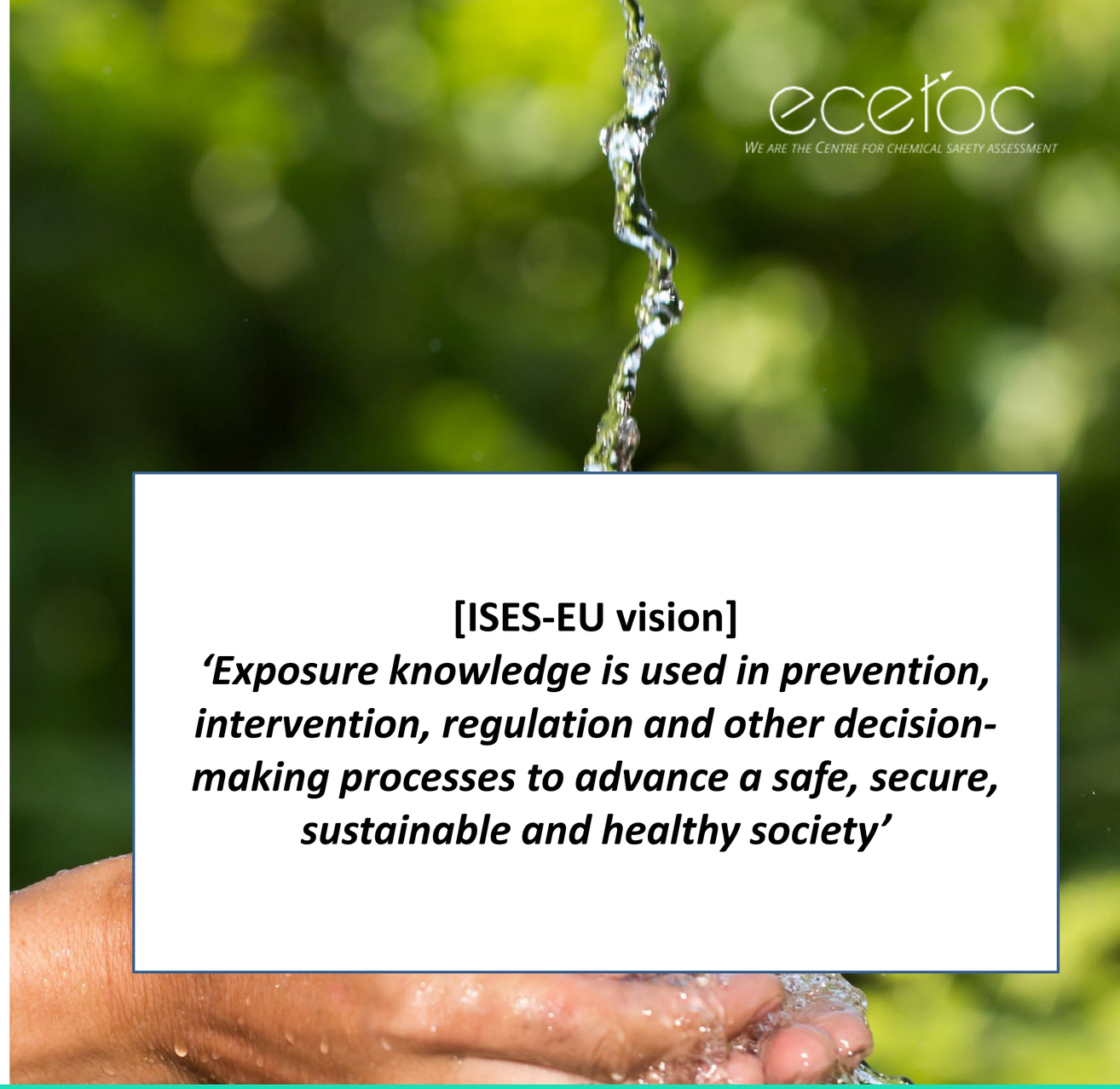



**ISES-EU focus areas:**

- **Data repositories/analytics**
- **Regulatory exposure assessment**
- **Exposure data production**
- **Building partnerships**
- **Exposure assessment methods and tools**
- **Education, training and communication**

# Expected impact

- Stakeholders implement ISES-EU recommendations based on ECETOC advice
- Increase clarity and trust between stakeholders
- Better decisions on safety and sustainability of chemicals




**[ISES-EU vision]**

***'Exposure knowledge is used in prevention, intervention, regulation and other decision-making processes to advance a safe, secure, sustainable and healthy society'***

BIENNIAL SCOPING MEETING

# Novel statistical approaches for improving exposure assessment models

Eelco Kuijpers, Remy Franken, TNO

ecetoc

We are the Centre for chemical safety assessment

# Needs Challenge

- Numerous validation studies available found performance REACH exposure models “mixed”
- Tier 1 models not always conservative enough (e.g. Van Tongeren et al., 2017; Lamb et al., 2015)
- Trends observed in ratio plots indicating conservative estimates at low concentrations and underestimates at higher (example Marquart et al., 2017)
- Schlueter and Tischer, (2020) reviewed available validation studies and concluded that (among other conclusions) tool owners need to take into account results from these studies and keep improving their tools

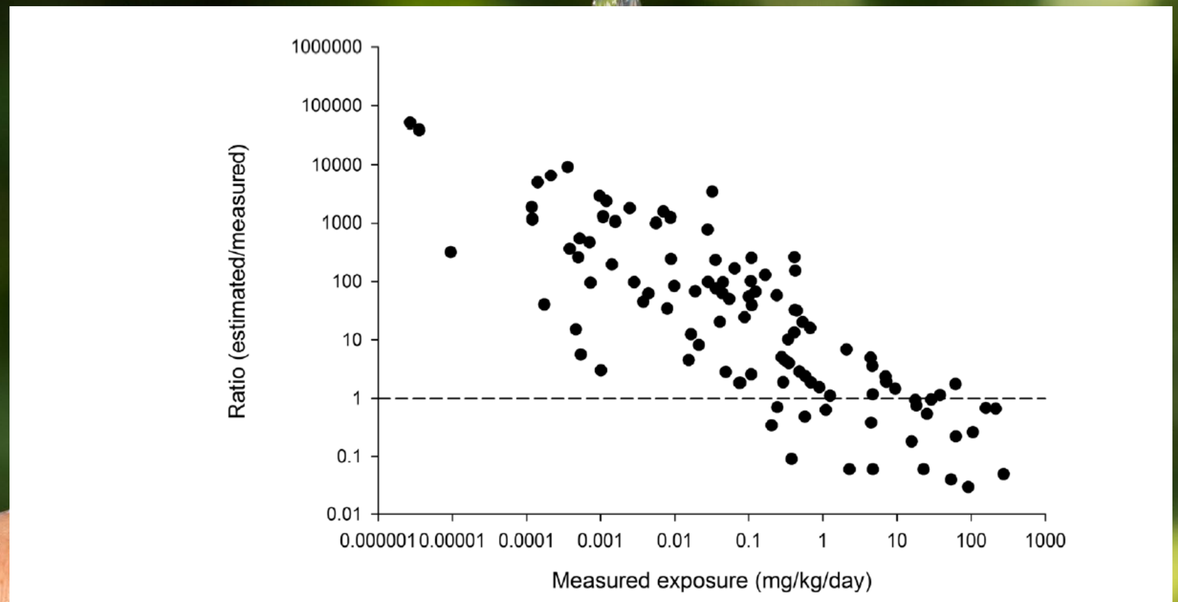


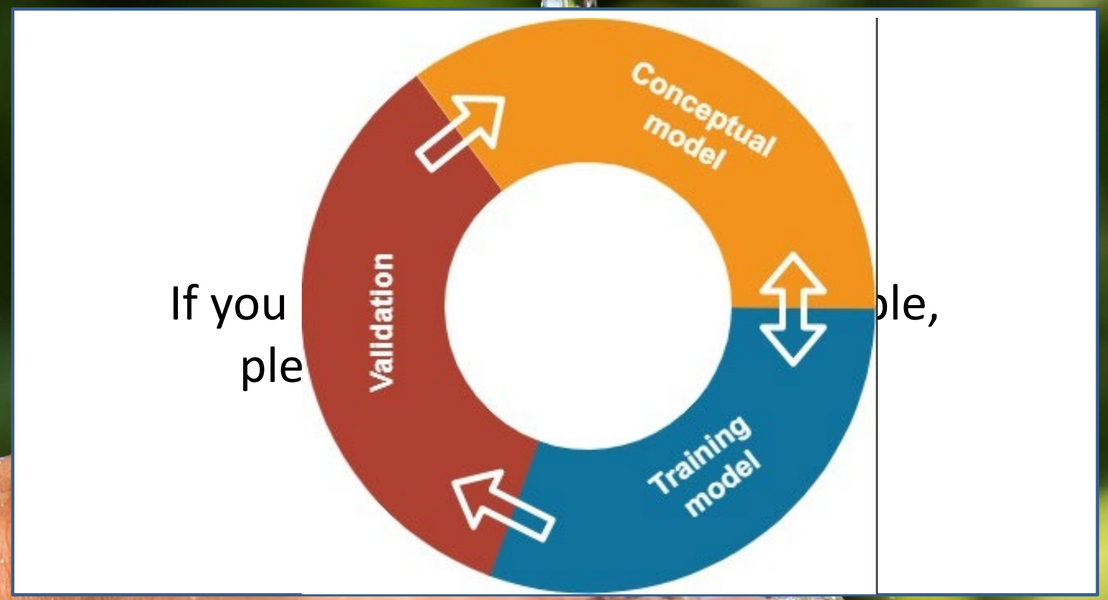

**Figure 3.** Relation between the ratio of model estimate and 75th percentile of measured values for all exposure cases.

Novel statistical approaches for improving exposure assessment models
Taskforce

Eelco Kuijpers, Remy Franken
TNO

# Associated knowledge/ Methodologies gaps

- Focus currently mainly on improving user friendliness of tools (which is not wrong)
- Validation results show a need to improve accuracy / conservativeness of models
- Unclear how validation results can be translated to conceptual model changes / improvements

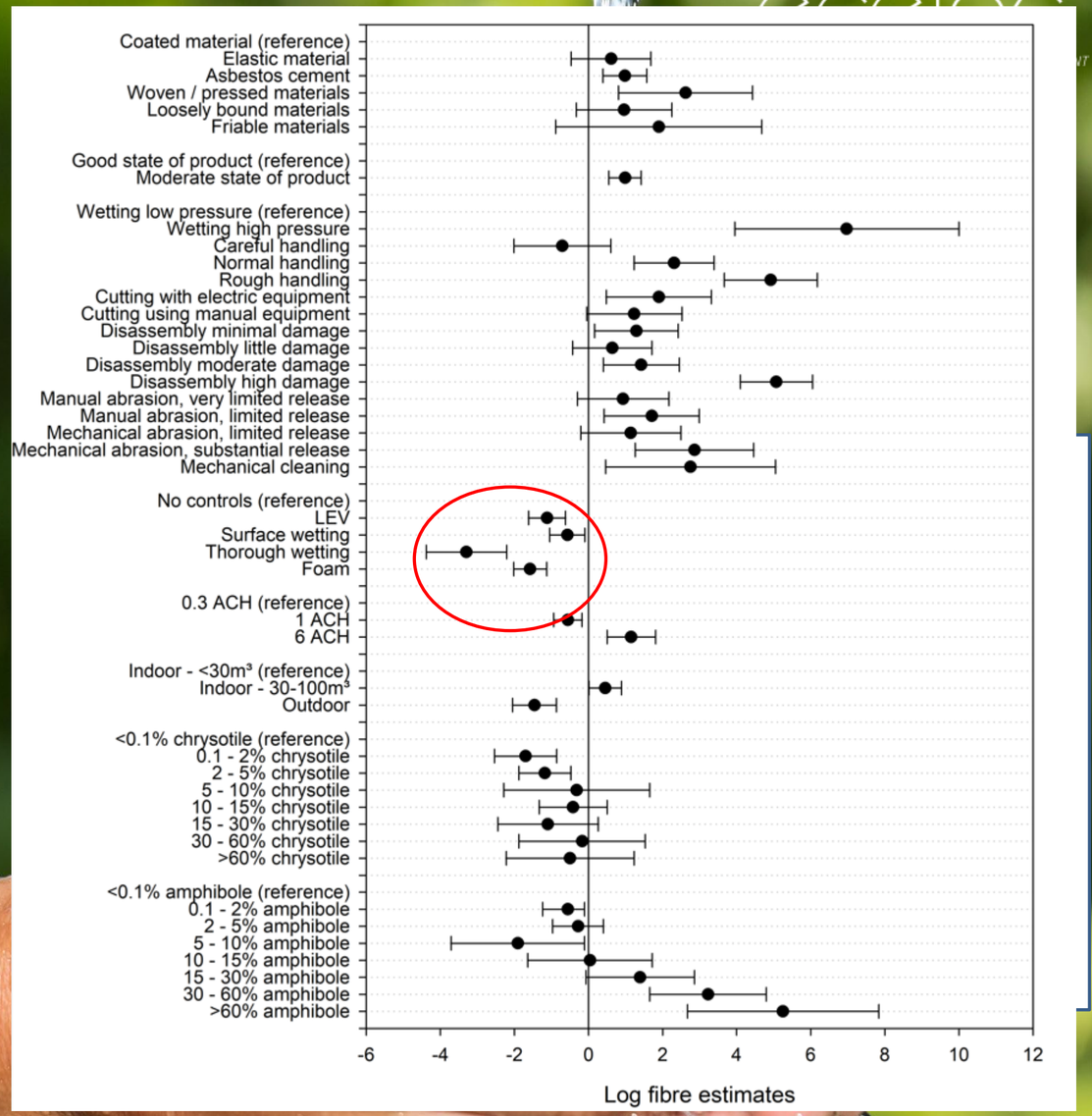



Novel statistical approaches for improving exposure assessment models
Taskforce

Eelco Kuijpers, Remy Franken
TNO

# Objectives

- Translate validation results into model improvements with use of different novel statistical approaches
- Compare impact on improvements between different approaches:
  - Linear regression (see example local controls Foam appeared less effective than original assumed);
  - Bayesian;
  - Machine learning;
- Make use of available exposure data from previous conducted validation studies
- ECETOC TRA v3.1 as case study:
  - Conservativeness, model trends, accuracy of model parameters, PROC baseline estimates, etc.




Novel statistical approaches for improving exposure assessment models Taskforce

Eelco Kuijpers, Remy Franken
TNO

# Expected impact

- Novel statistical approaches tested and compared for suitability exposure modelling in general
- New ways to translate validation results into model improvements
- Improvements made to ECETOC TRA V3.1
- Ultimately, improved worker health




Eelco Kuijpers, Remy Franken
TNO

BIENNIAL SCOPING MEETING

# Cross-species extrapolation in regulatory hazard assessment of chemicals

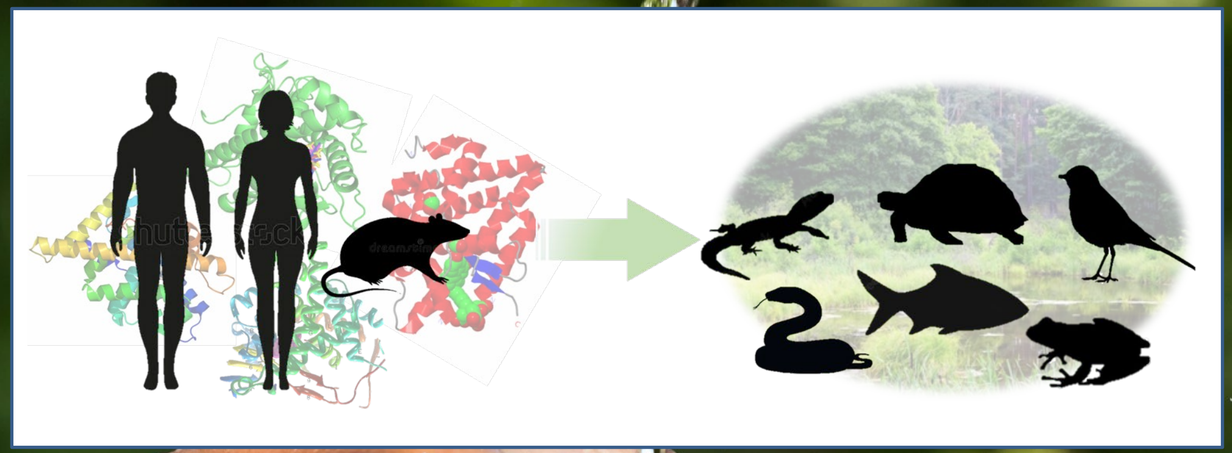
Katherine Coady & Laurent Lagadic, Bayer CropScience

ecetoc

We are the Centre for chemical safety assessment

# Needs & Challenge

- Growing interest for cross-species extrapolation in regulatory science (*e.g.*, new approach methodologies - NAMs, endocrine disruption assessment)
- Appropriately apply hazard information across species to protect ecological entities
- Understand state of the science for cross-species extrapolations

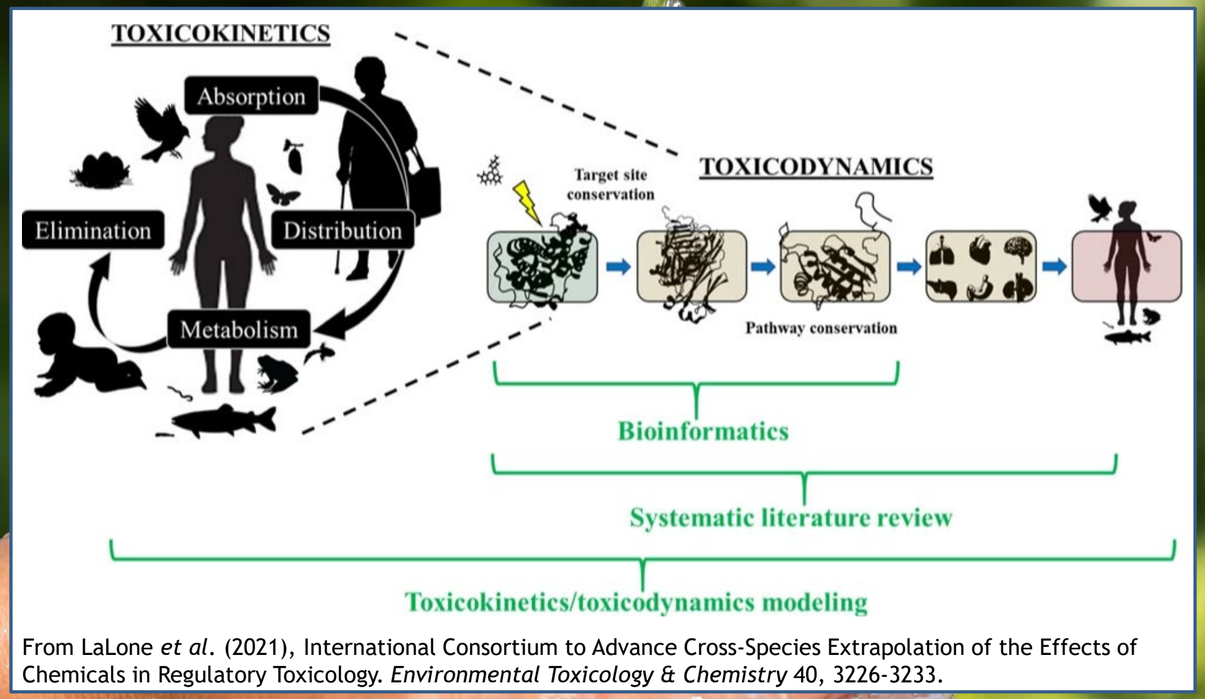


Title
Cross Species Extrapolation Taskforce

Katherine Coady & Laurent Lagadic,
Bayer CropScience

# Associated knowledge/ Methodologies gaps

- The following are important factors for cross species extrapolation: physiology, life history, toxicokinetics, toxicodynamics
- There are multiple approaches for cross species extrapolation – Which is the best for regulatory decisions?
- Data gaps exist for many ecological species (*e.g.*, metabolic capability, physiology, MoA, etc.) - Where should efforts focus to fill these gaps?



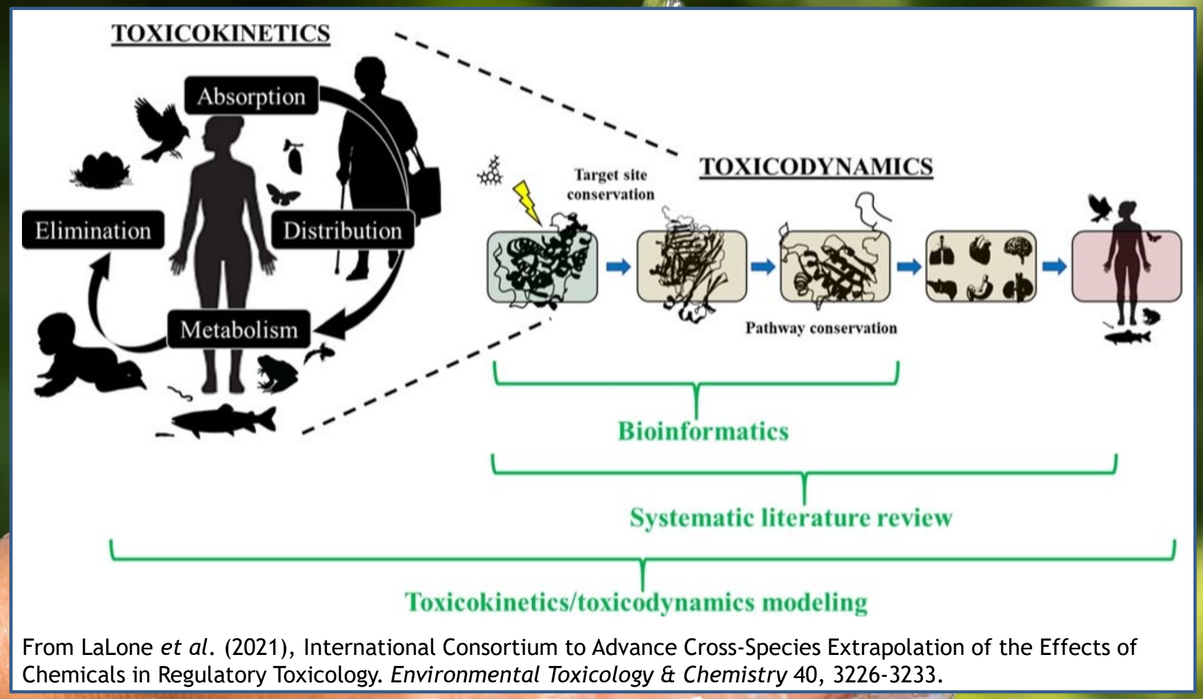

From LaLone *et al.* (2021), International Consortium to Advance Cross-Species Extrapolation of the Effects of Chemicals in Regulatory Toxicology. *Environmental Toxicology & Chemistry* 40, 3226-3233.




Katherine Coady & Laurent Lagadic, Bayer CropScience

# Objectives

- Survey methods and provide recommendations on approaches for cross-species extrapolation in regulatory scenarios
- Identify high priority research needs and advance regulatory adoption
- Integrate perspectives with other groups evaluating cross-species extrapolation (*e.g.*, ICACSER group at SETAC)

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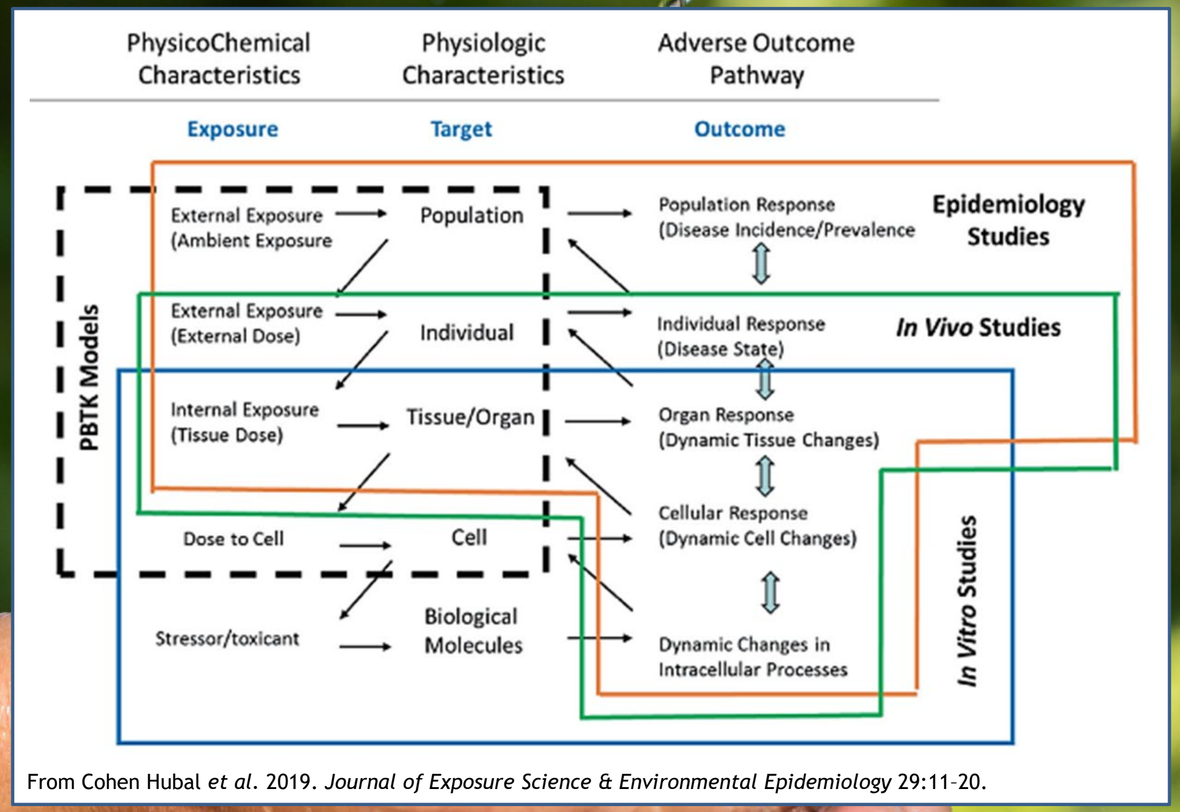
Title
Cross Species Extrapolation Taskforce

Katherine Coady & Laurent Lagadic,
Bayer CropScience

# Expected impact

- Deliverable: Guidance document / recommendations on the use of a “cross-species extrapolation toolbox” in regulatory scenarios
- Enhance coordination on cross-species extrapolation methods and data gaps with other interested parties
- Increase use & acceptance of cross-species hazard assessments; minimize animal use in hazard testing



From Cohen Hubal *et al*. 2019. *Journal of Exposure Science & Environmental Epidemiology* 29:11–20.

Title
Cross Species Extrapolation Taskforce

Katherine Coady & Laurent Lagadic,
Bayer CropScience

Pre-read

BIENNIAL SCOPING MEETING

# Cross-species extrapolation in regulatory hazard assessment of chemicals *Back-up slides*

Katherine Coady & Laurent Lagadic, Bayer CropScience

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We are the Centre for chemical safety assessment

Pre-read

# Cross-species extrapolation in regulatory hazard assessment

- **With New Approach Methods (NAMs) being developed across the globe and the increasing needs to protect threatened ecological entities, it is a key time to evaluate tools for cross-species extrapolations.**
- **Use both *exposure* (ADME) and *Adverse Outcome Pathways (AOPs)* to guide cross-species extrapolations**
- Many potential regulatory applications for cross-species extrapolations:
  - Screening and prioritization of animal testing for chemical registrations
  - Endocrine Disruptor Hazard and Risk Assessments
  - Ecological Risk Assessments (Pesticides, Industrial chemicals, Legacy contaminants)
  - Endangered Species



Katherine Coady & Laurent Lagadic,
Bayer CropScience

Pre-read

# Cross-species extrapolation in regulatory hazard assessment

- **Four proposed work-groups for the Cross-Species Extrapolation Taskforce**

1. **Toxicokinetic tools for cross-species extrapolation**
   - Understand differences/similarities in ADME and internal exposure across species
2. **Molecular homology (relatedness-based, “omics”) to inform on cross-species extrapolations**
   - Homology assessment of toxicodynamic targets: genes, proteins, docking models
3. **Comparative toxicity across species**
   - Models and databases for interspecies comparisons (both *in vitro* & *in vivo* endpoint responses)
4. **Organismal and ecological factors influencing cross-species extrapolation**
   - Trait-based comparisons related to physiology, life history, resilience, etc.



Katherine Coady & Laurent Lagadic,
Bayer CropScience

Pre-read

# Cross-species extrapolation in regulatory hazard assessment

- **References**


Celander *et al*., 2011. Species Extrapolation for the 21st Century. *Environmental Toxicology and Chemistry* 30:52-63.

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Lalone *et al*., 2018. Evidence for cross species extrapolation of mammalian-based high-throughput screening assay results. *Environmental Science and Technology* 52:13960-13971.

Thiel *et al*., 2014. A systematic evaluation of the use of physiologically based pharmacokinetic modeling for cross-species extrapolation. *Pharmacokinetics, Pharmacodynamics and Drug Transport and Metabolism* 104:191-206.

van den Berg *et al*., 2021. Cross-species extrapolation of chemical sensitivity. *Science of the Total Environment* 753:141800.





Katherine Coady & Laurent Lagadic, Bayer CropScience

BIENNIAL SCOPING MEETING

# Capacity Development in Industry and Agencies on NAMs

HM Hollnagel, Dow Europe GmbH

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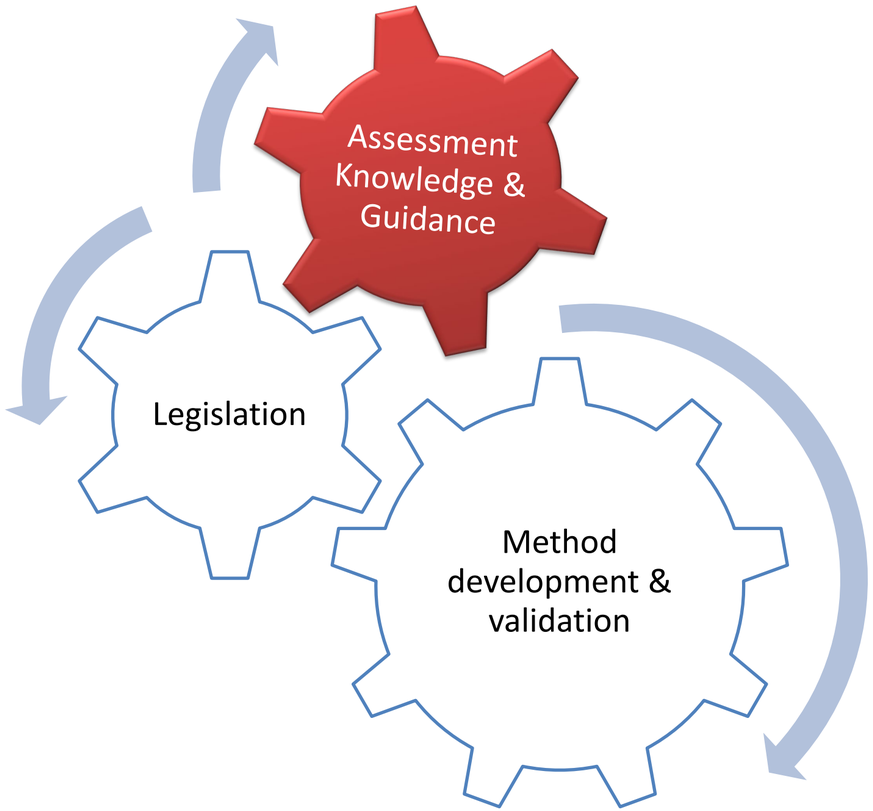
# Needs Challenge




How to avoid that additional information requirements under REACH,
envisioned by the “Chemical Strategy for Sustainability”,
will trigger an unprecedented increase in animal testing?

# Associated knowledge/ Methodologies gaps

- Regulatory (eco)toxicologists are largely trained to interpret animal studies, both in Industry & Agencies
- Lack of opportunities for continuing education of professionals on
  - novel approaches as such and
  - within assessment frameworks

# Objectives

- lower the barriers to change by building knowledge in broader stakeholder groups
- develop webinars and/or other educational materials for
    1. persons with natural sciences background but no education in toxicology
    2. persons with traditional education in toxicology

# Expected impact

**Decreased uncertainty in interpretation of NAM data**

- Increased uptake of specific NAMs in legislation
- Increased acceptance of diverse NAM data to support waiving and read-across

BIENNIAL SCOPING MEETING

# Omics data handling and analysis training program

Florian Caiment, Maastricht University

ecetoc
We are the Centre for Chemical Safety Assessment

# Needs Challenge

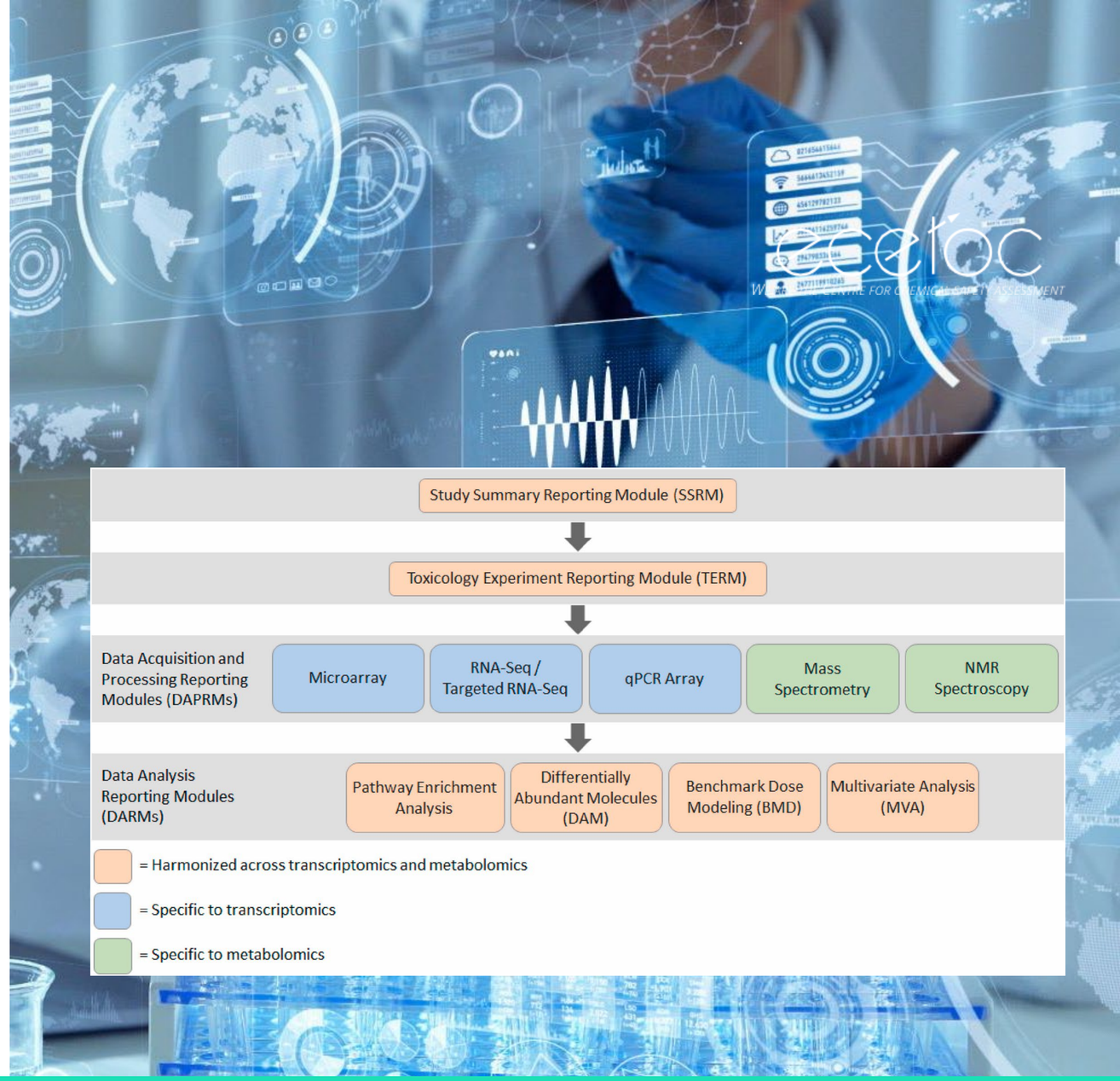
- Big data are used everywhere…
- … except is regulatory risk assessment
- Main argument was the lack of reference tools and frameworks



Florian Caiment,
Maastricht University

# Associated knowledge/ Methodologies gaps

- Tools and Framework have been recently developed and published:
  - OECD Omics Reporting Framework
  - R-ODAF : Omics Data Analysis Framework for Regulatory Applications
- The real challenge: data science and regulatory sciences speak different languages






Florian Caiment,
Maastricht University

# Objectives

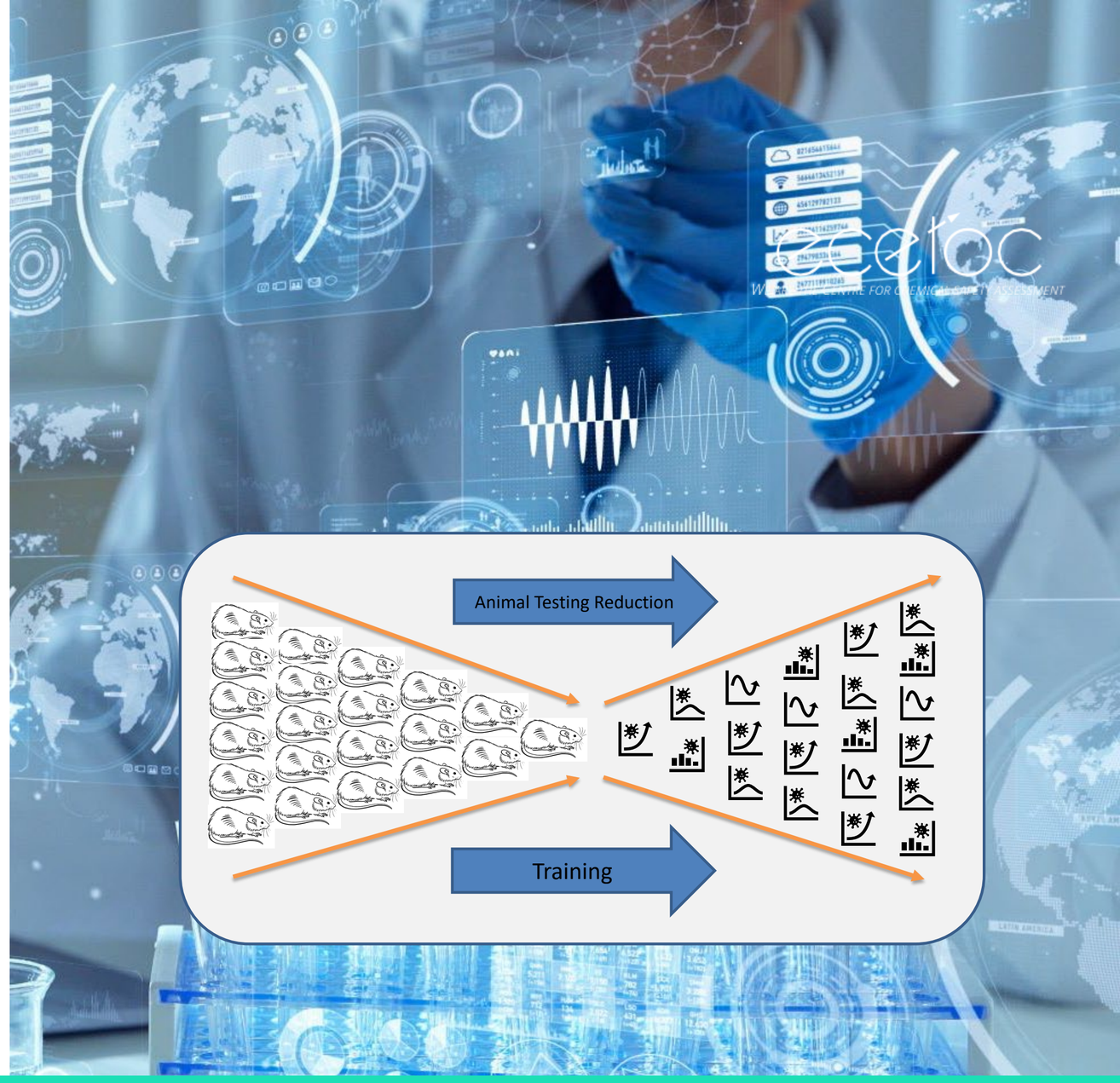
- Organize a data handling and analysis training adapted for biologist
- Training workshop
- Accessible for regulatory agency and industry staff
- Establish online support




Florian Caiment,
Maastricht University

# Expected impact

- Bridge multiple worlds:
  - Data scientist – Biologist
  - Academia / Industry / Regulators
- Make sure that previous investment are not lost
- Contribute to the transition to Next-Generation Risk Assessment






Florian Caiment,
Maastricht University

BIENNIAL SCOPING MEETING

# Enabling Regulatory USE of Omics by forming an Expert Group to Develop an Omics Data Interpretation Framework for Regulatory Application (ODIFRA) and outreach/training materials

Richard Currie, Syngenta
David Rouquie, Bayer
Tim Gant, PHE

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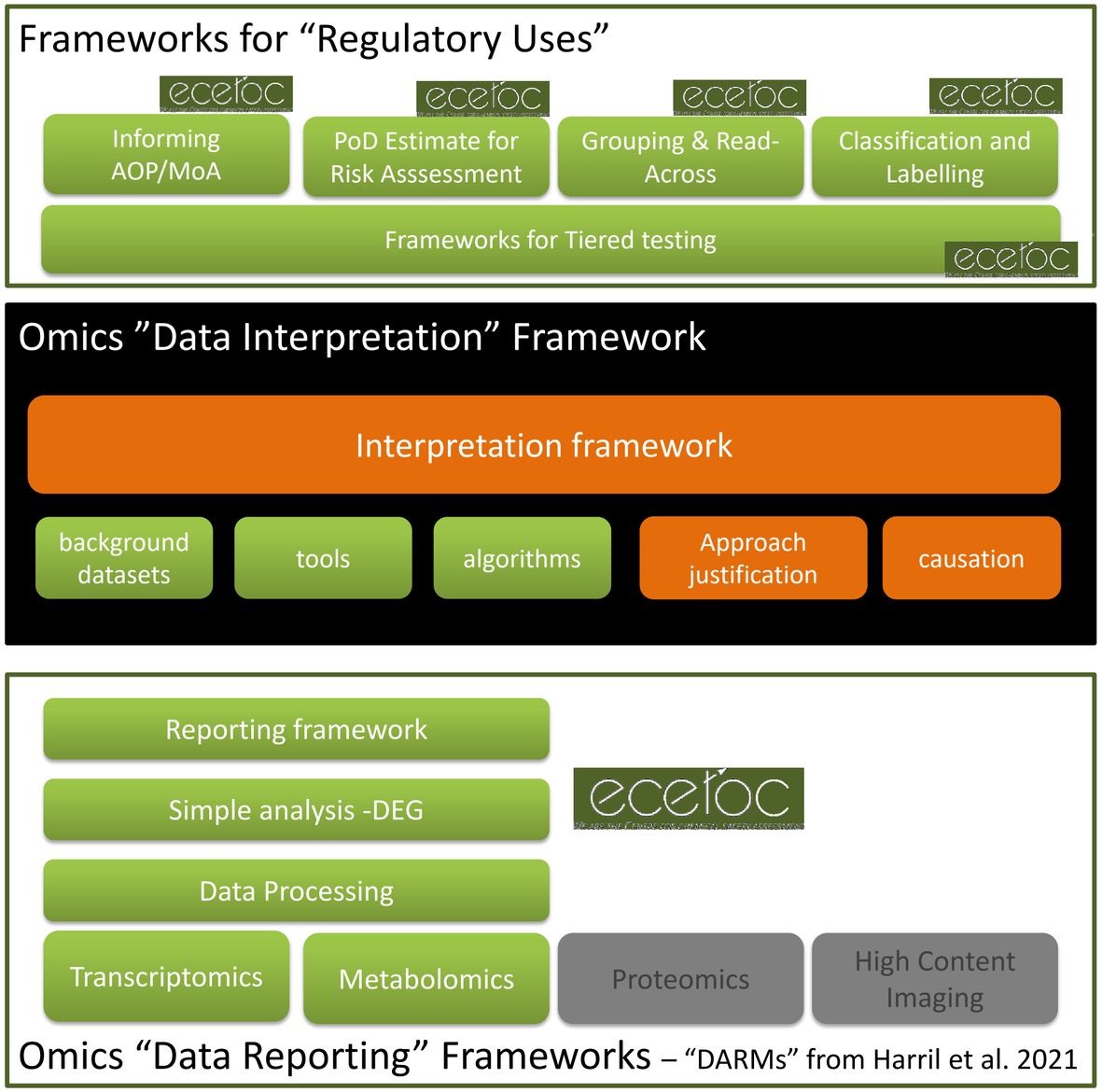
# Needs Challenge

- ECETOC has explored the **use of omics data** for a variety of regulatory purposes and has driven the **creation of a technological good practice** for robustly identifying and reporting lists of altered genes/metabolites
- Now a Framework that **increases the robustness of the interpretation** of these omics data and its reporting is required
- ECETOC is well placed to **assemble an expert group to fill this gap**




Title
ODIFRA Expert Group

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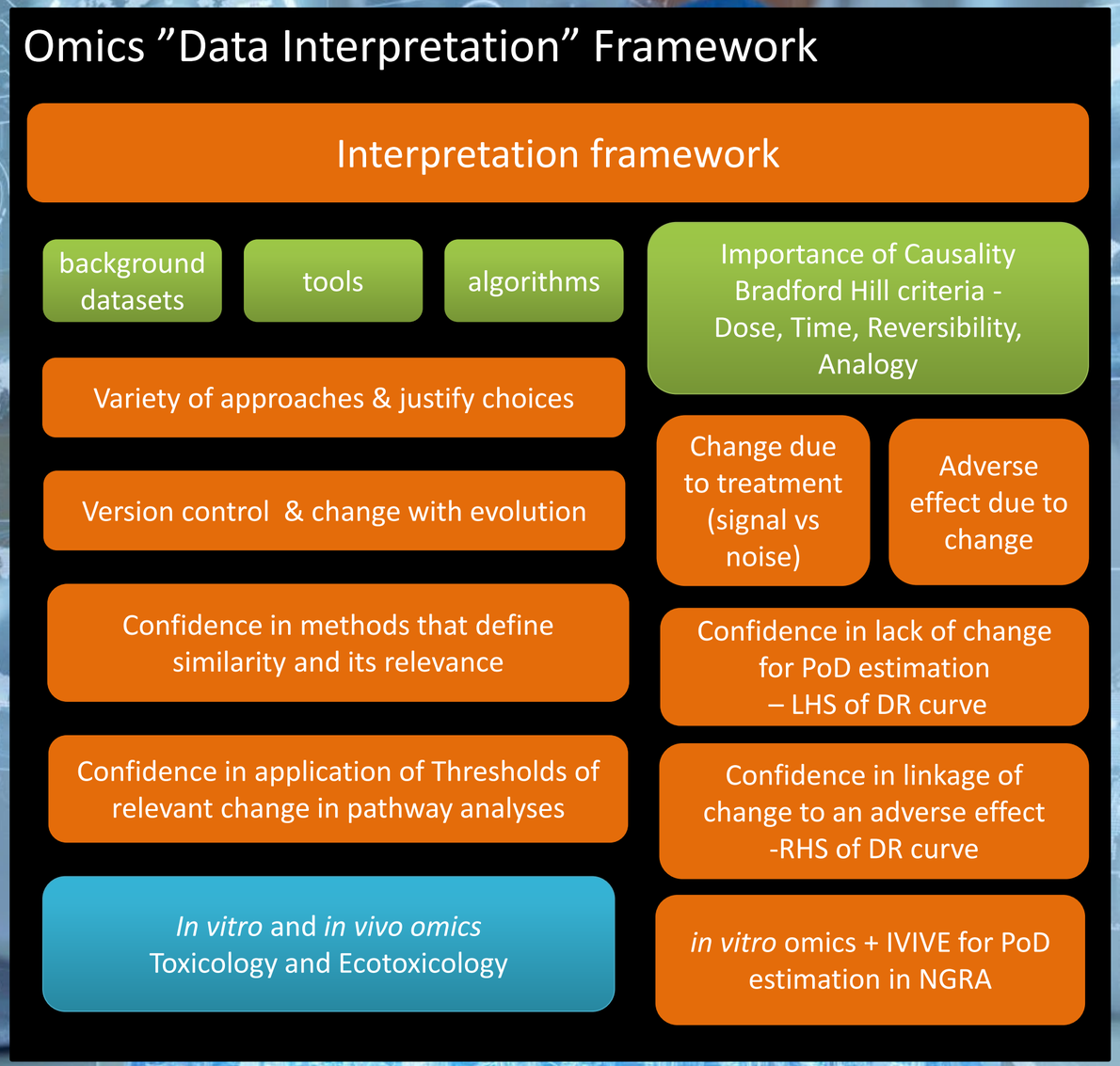
# Associated knowledge/ Methodologies gaps

- Lack of consistent reporting framework for omics data interpretation
- Justifications of analysis choices, thresholds and good practices
- Relevance of pathways and thresholds of significant pathway activation
- Quantification and amplitude of effects that drive points of adversity.
- Application of IVIVE with *in vitro* points of departure to advance risk assessment



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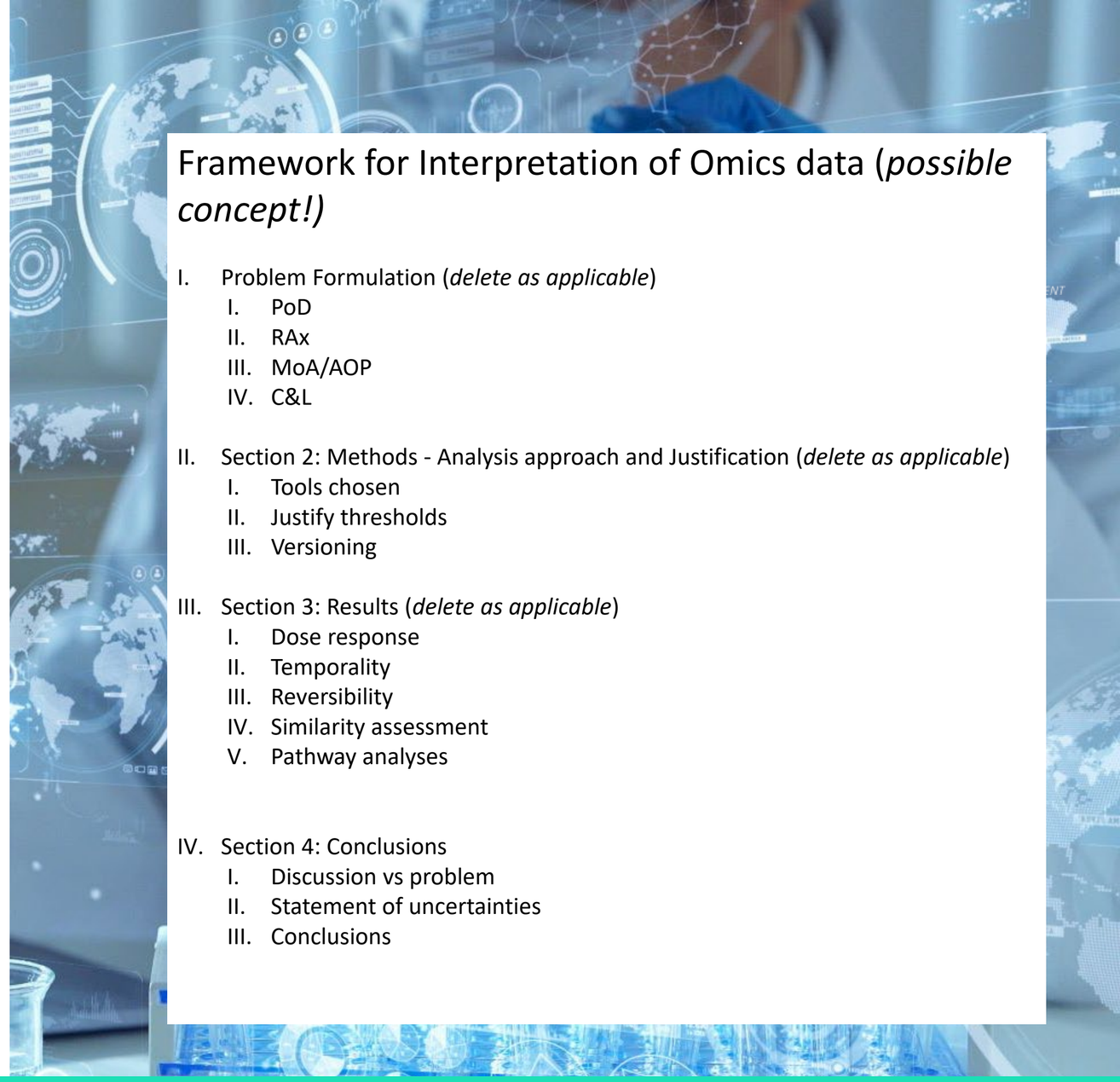
# Objectives

- Review the expected uses & technical issues to define what common/unique items need to be included in the framework
- Conduct case examples of using the framework with existing activities to identify areas for improvement
- Publication of framework and case studies
- Presentation to EAGMST and for consideration for inclusion on the workplan for a guidance document
- Generation of teaching materials and outreach activities



Framework for Interpretation of Omics data (*possible concept!)*

I. Problem Formulation (*delete as applicable*)
   I. PoD
   II. RAx
   III. MoA/AOP
   IV. C&L

II. Section 2: Methods - Analysis approach and Justification (*delete as applicable*)
   I. Tools chosen
   II. Justify thresholds
   III. Versioning

III. Section 3: Results (*delete as applicable*)
   I. Dose response
   II. Temporality
   III. Reversibility
   IV. Similarity assessment
   V. Pathway analyses

IV. Section 4: Conclusions
   I. Discussion vs problem
   II. Statement of uncertainties
   III. Conclusions

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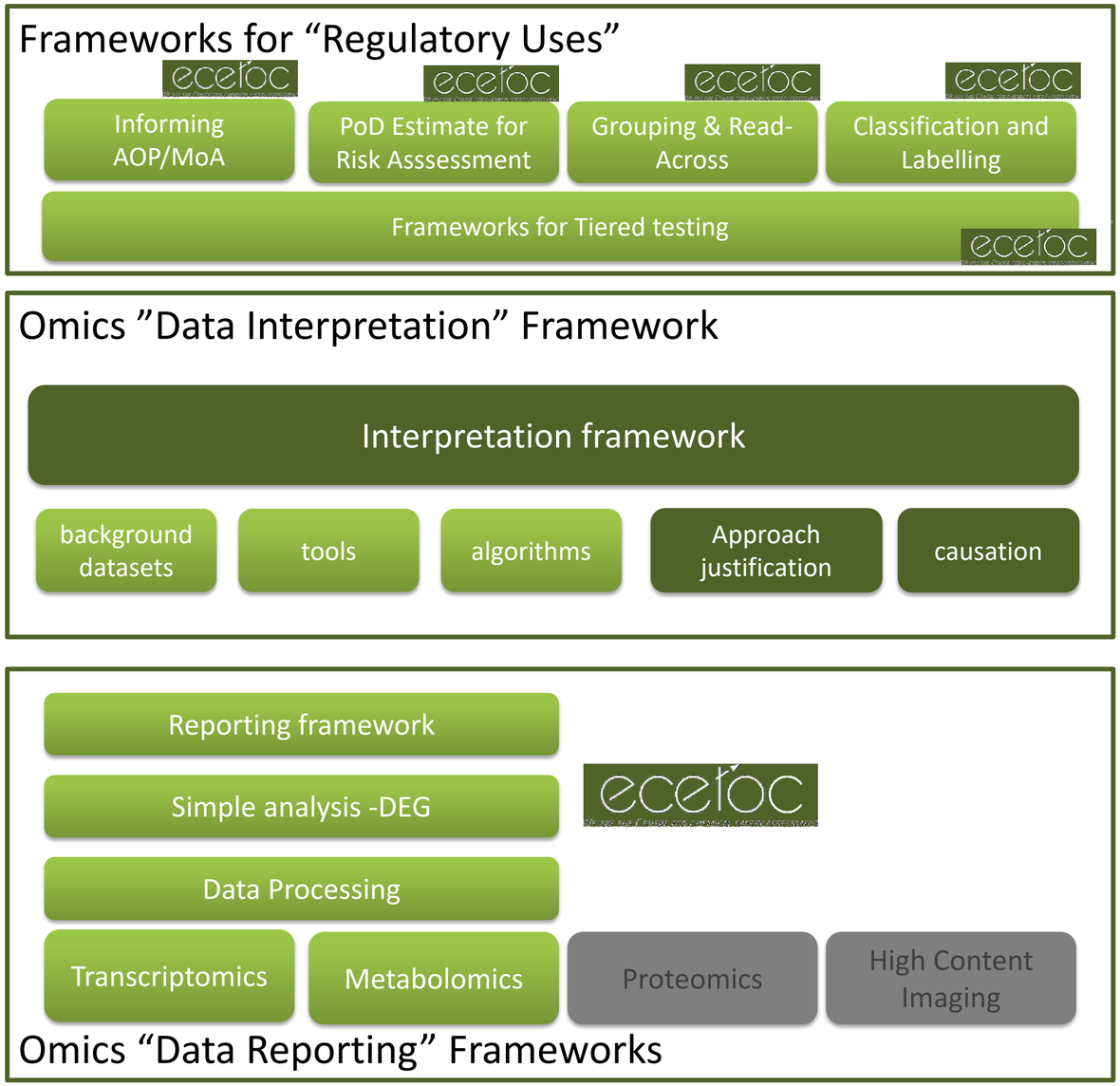
# Expected impact

- A common framework to report omics data analyses for regulatory uses
- Inclusion and development by OECD
- Uptake and use of Framework in Regulatory submissions by all potential generators or users of omics data for regulatory purposes in Industry, CROs, Consultancies and Regulatory agencies

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# Quantitative validation of New Approach Methodologies (NAMs) across interdisciplinary data domains

Neeraj Shandilya, TNO

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# Needs Challenge

- Challenge for scientific progress
- Hampered NAMs validation
- Combine in-vitro and in-silico models with AI
- Regulatory acceptance of NGRA



Neeraj Shandilya, TNO

# Associated knowledge/ Methodologies gaps

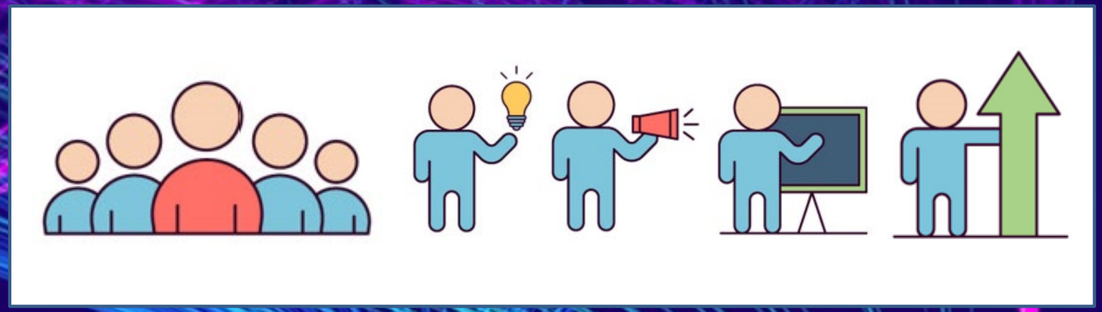
- Fragmented
- Disconnect
- Suitable models
- Human data



Neeraj Shandilya, TNO

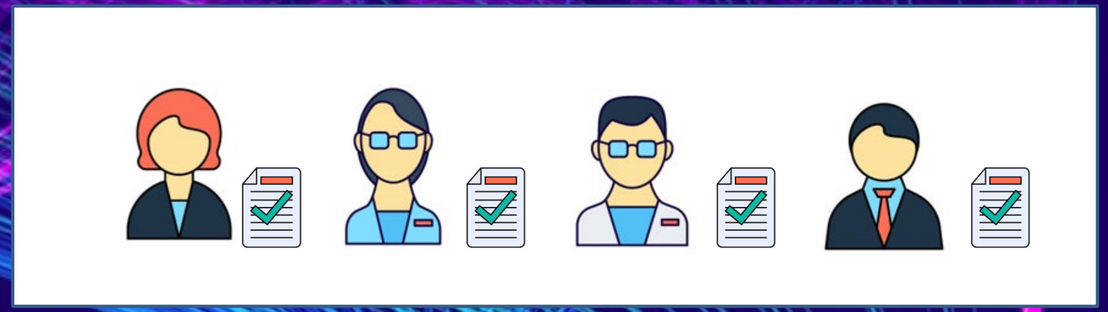
# Objectives

- Integrate expertise
- Provide guidance



# Expected impact

- Balance in what is
  - needed
  - possible
  - reliable
  - cost-efficient



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# Rethinking validation of NAMs

Susanne Kolle and Carolin Bischoff
BASF SE

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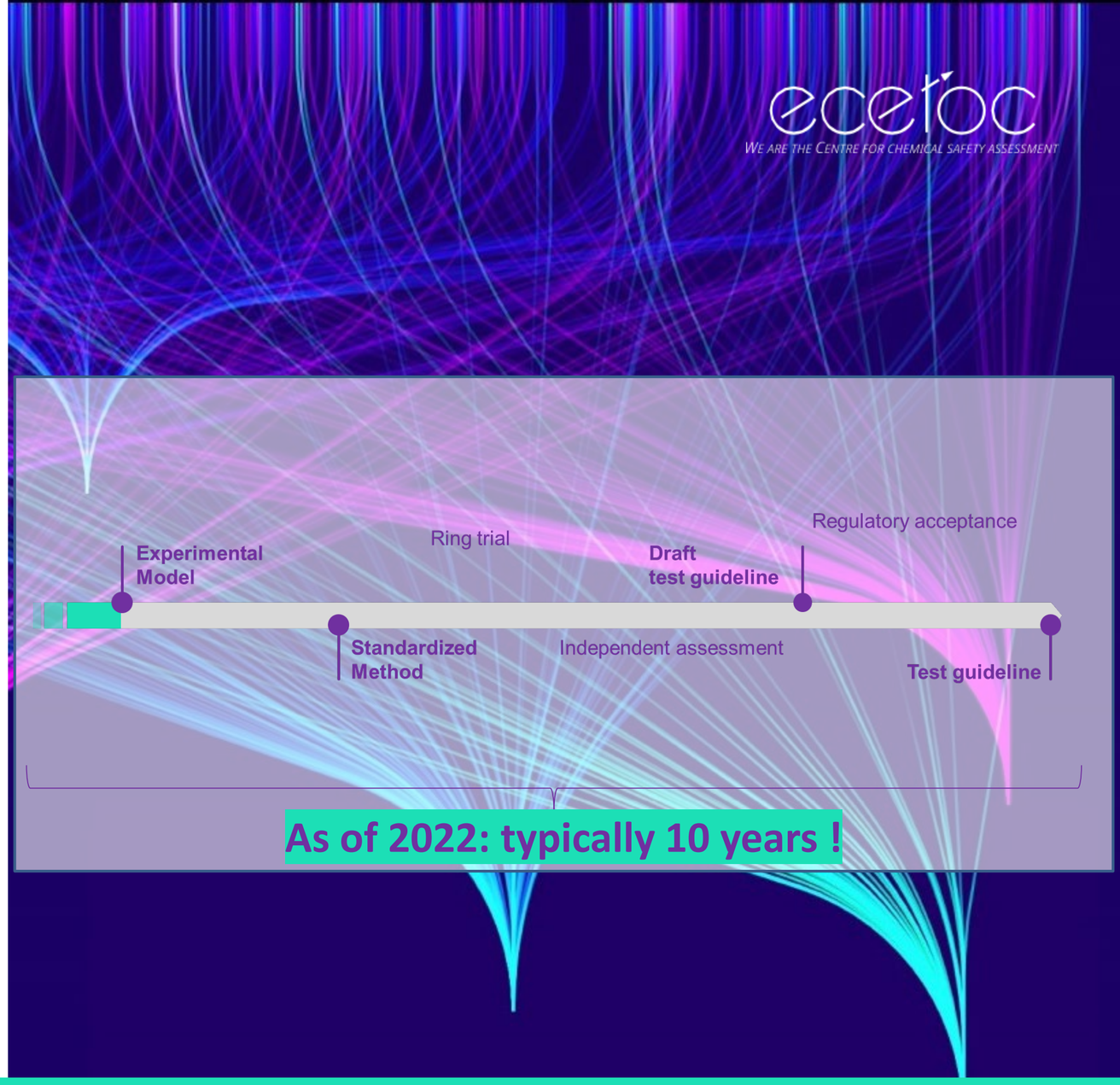
# Needs Challenge

- More and more NAMs are being developed
- New regulations add testing requirements for more and more substances and endpoints
- Validation is an indispensable prerequisite for NAM use in a regulatory context

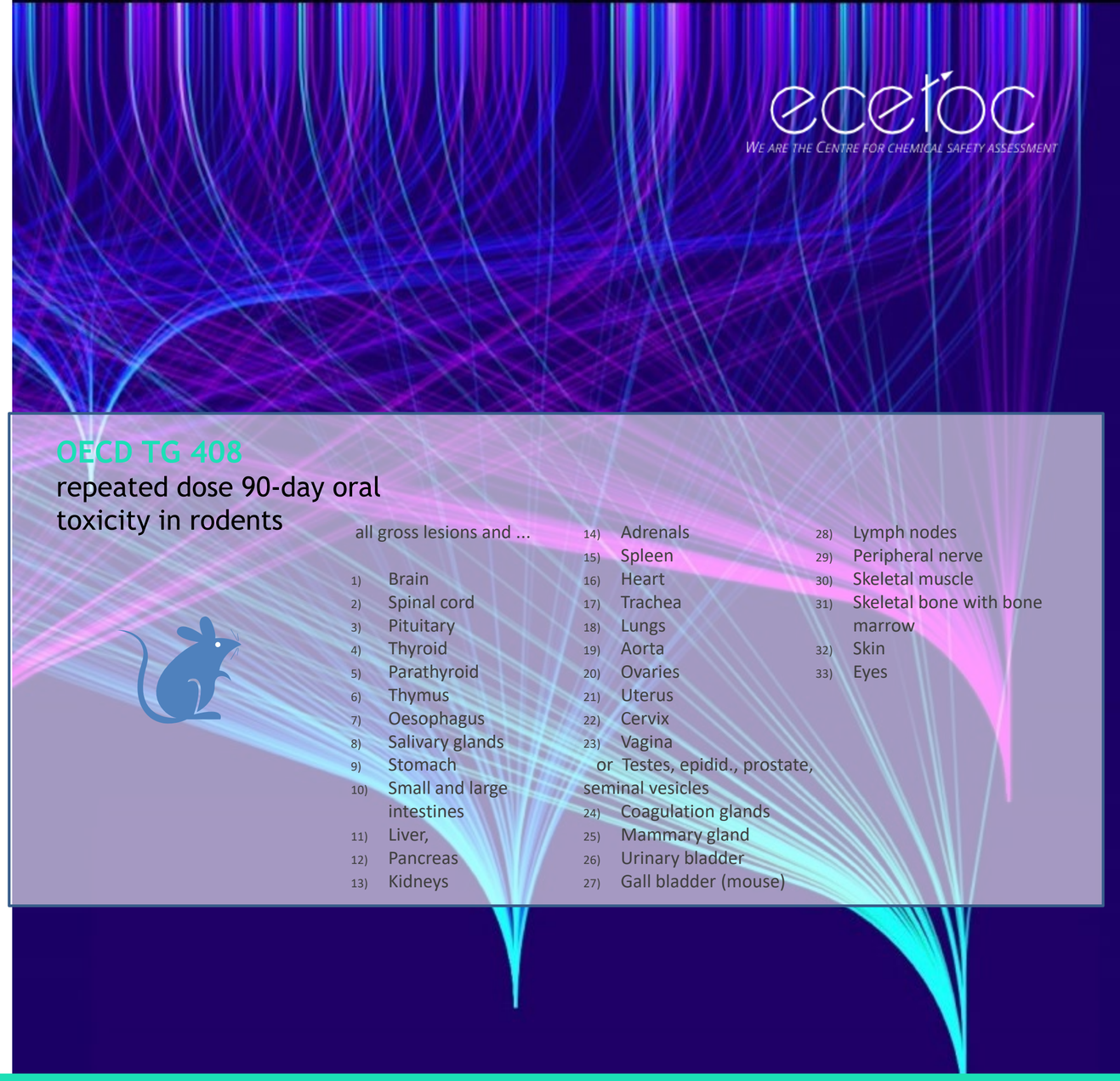





Kolle & Bischoff, BASF SE

# Associated knowledge/ Methodologies gaps

- As of 2022: validation for regulatory acceptance of NAMs takes approximately 10 years
- It will take decades to fully replace animal testing
- E.g., approximately 30 organs examined in OECD TG 408. If each is assessed by 5 NAMs and OECD adopts 5 methods per annum it will take 30 years to replace animal testing

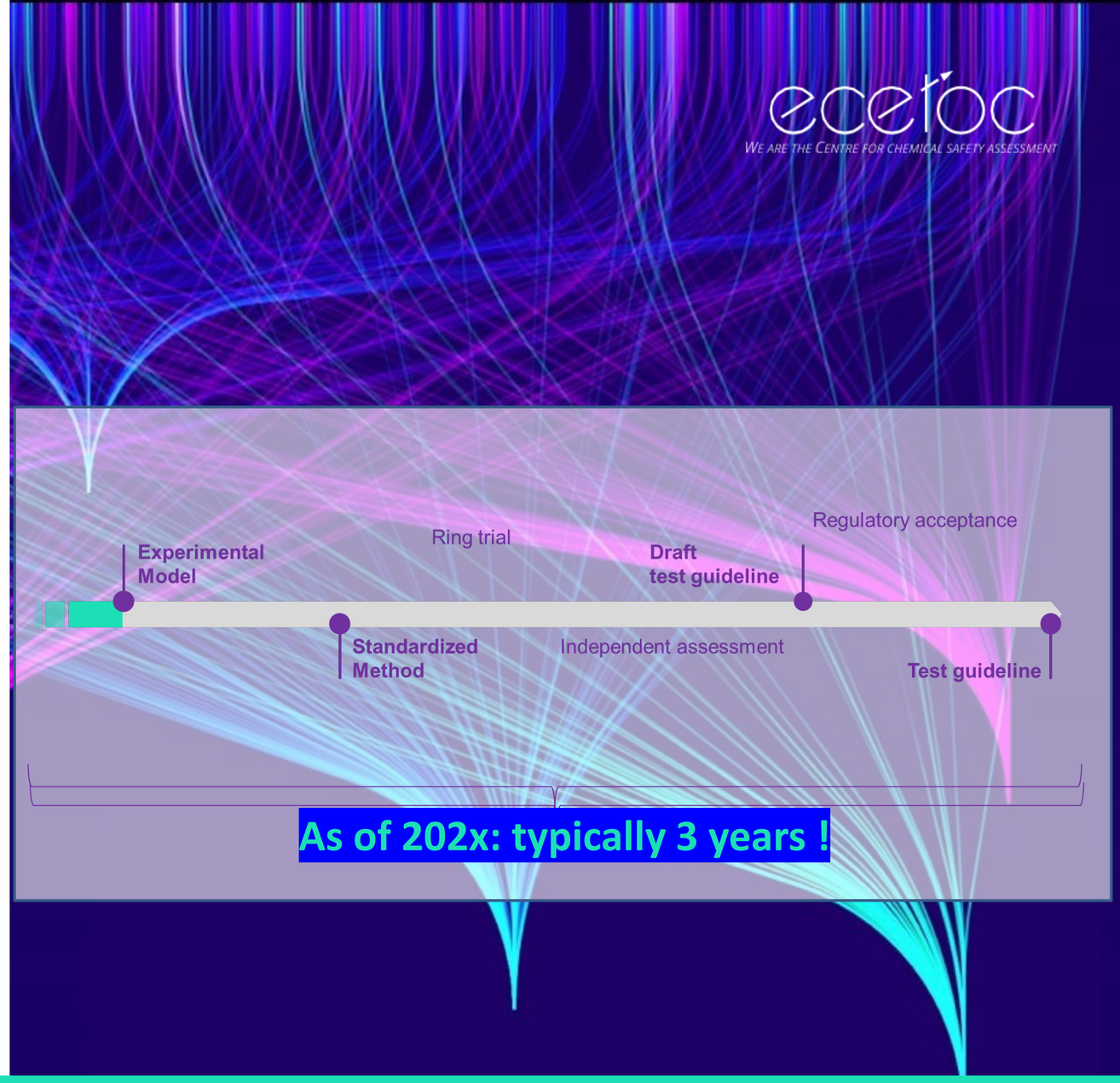





Kolle & Bischoff, BASF SE

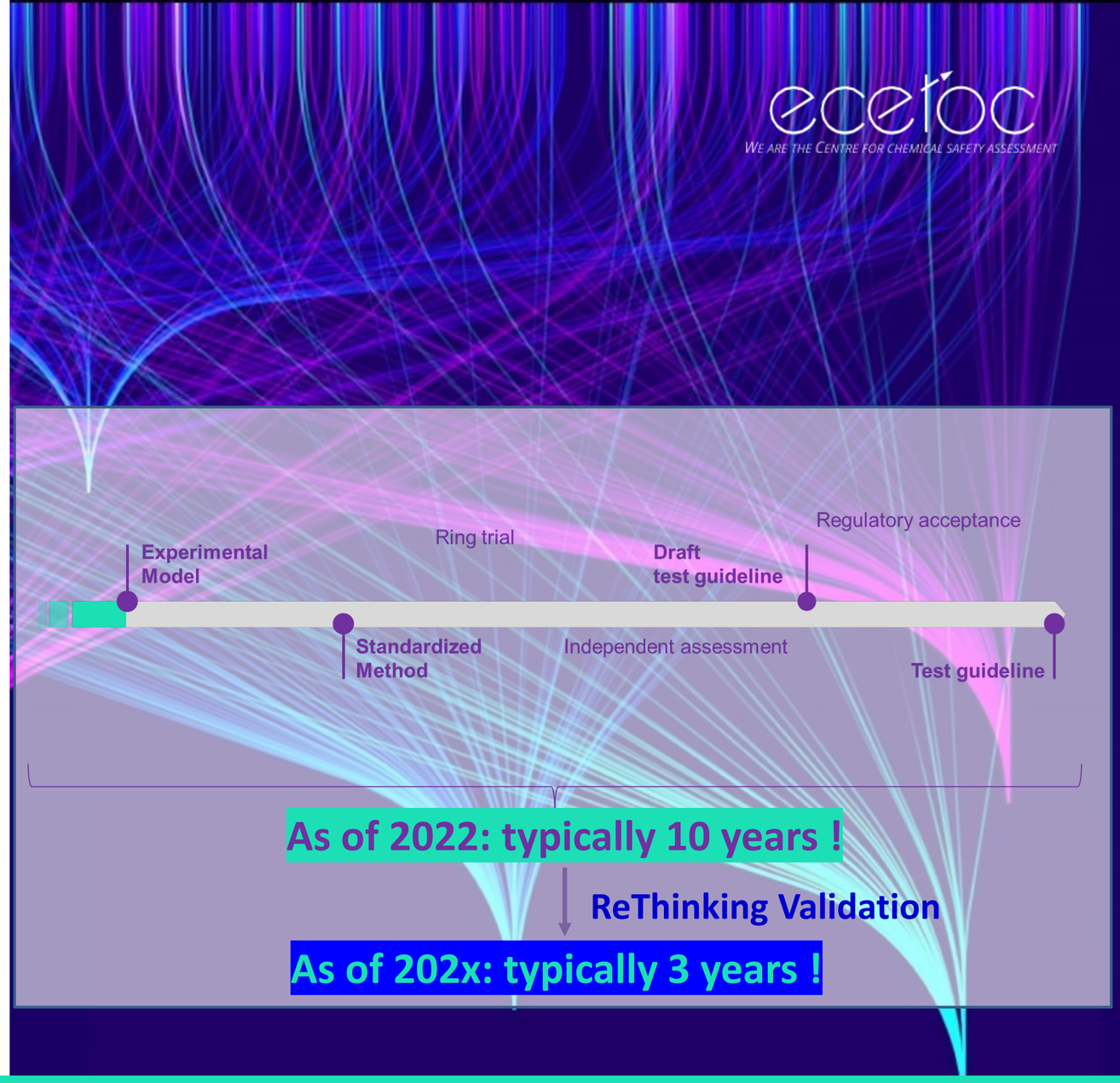
# Objectives

- To develop a validation concept for mechanistic NAMs for which there is no straightforward reference data (unlike e.g. for skin sensitization)
- Validation concept needs to be effective, efficient and accelerated



# Expected impact

- Towards a smart, effective, and efficient validation process for NAMs
- Reliable NAM results
- Stakeholder involvement
- Fulfilling regulatory needs regarding hazard identification and risk assessment



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# In silico/QSAR Tools - comprehensive review of applicability and applicability domains of the different tools

Carolin Bischoff and Caroline Gomes, BASF SE

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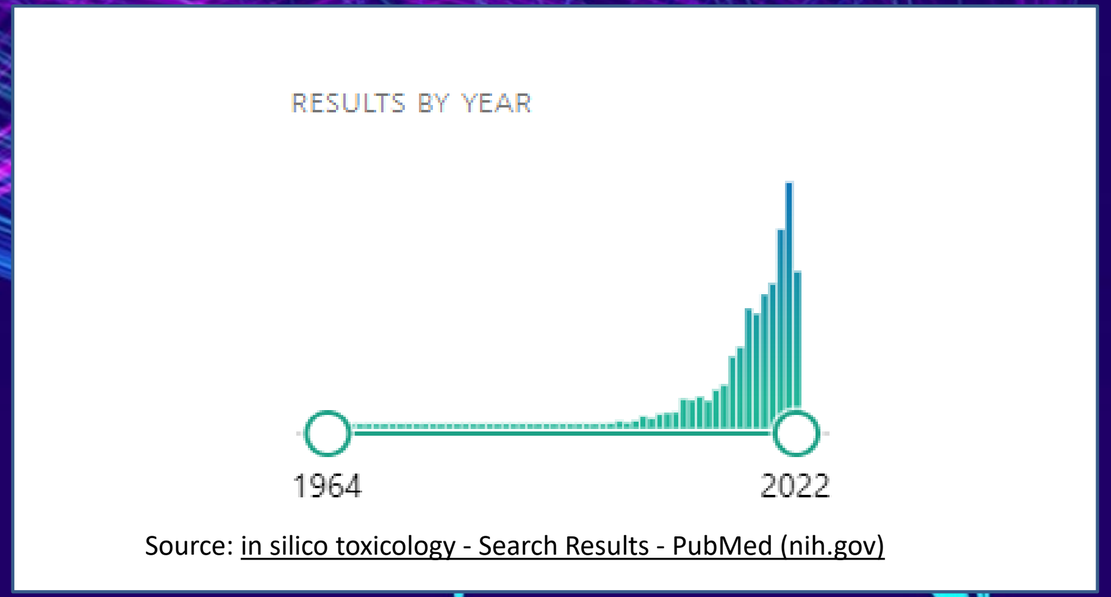
# Needs Challenge

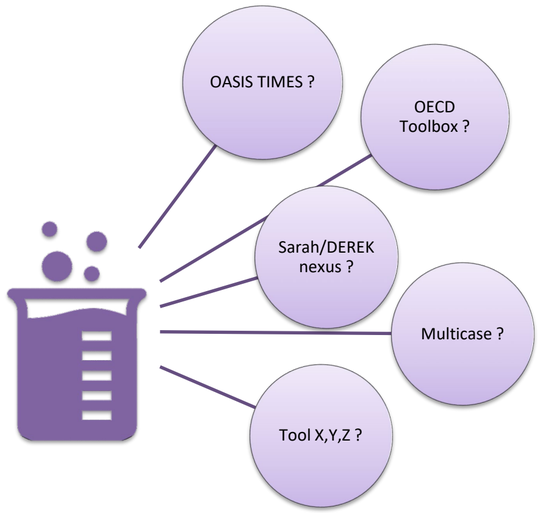
- Too many in silico tools
- Not so many endpoints
- Too difficult algorithms, applicability domains…
- How to find the right tool ?




Source: in silico toxicology - Search Results - PubMed (nih.gov)

# Associated knowledge/ Methodologies gaps

- It´s all in the graph!
- Not seeing the wood for the trees, too ?




- Knowledge based/expert system?
- Read-across or QSAR?
- Interpolation/extrapolation?
- Similarity properties?
- Choice of similar chemicals?
- Quantitative/qualitative?
- Applicability domain?
- Similarity measures?
  - Tanimoto?
  - Hamming?

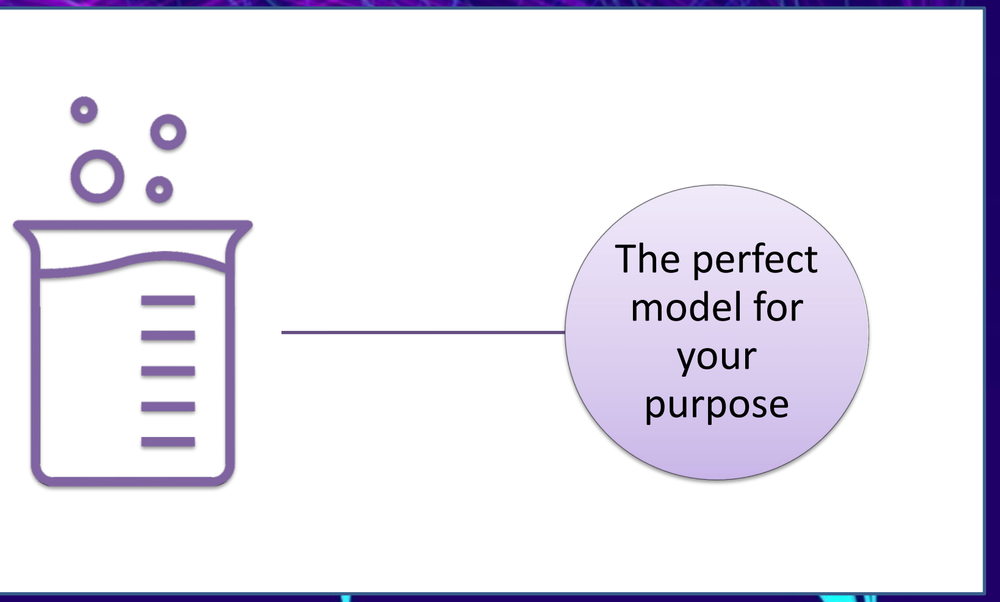
# Objectives

- Seeing the wood, not the trees ☺
- Guidance for users of in silico tools
- Guidance for developers
- Regulatory acceptance

Photo by Paul Summers on Unsplash

# Expected impact

- Consistent use between all stakeholders
- Broader regulatory acceptance
- Reduction of animal testing
- Better screening for chemicals which are safe and sustainable by design



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# Towards a formal incorporation of predictive models in chemical hazard evaluation

Adriana C. Bejarano, Shell Global Solutions US Inc.

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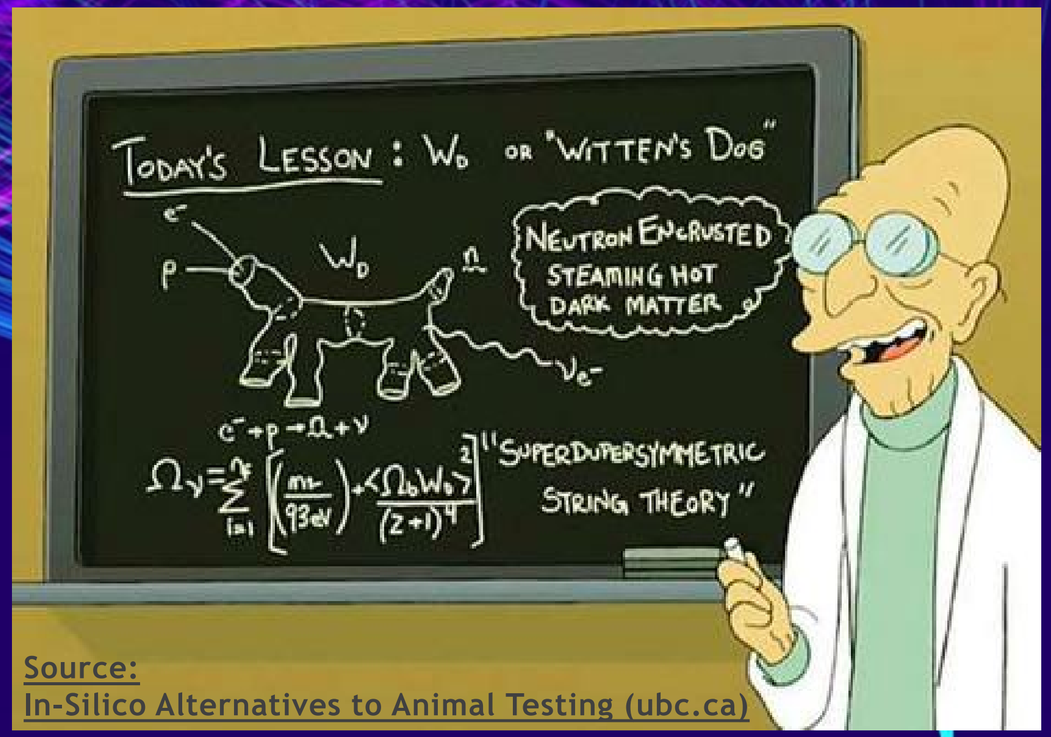
# Needs Challenge

- Predictive models can fulfil regulatory requirements and support chemical evaluations
- A formal process for their incorporation into practice is needed
- Increased confidence can be achieved through a clear strategy for their evaluation



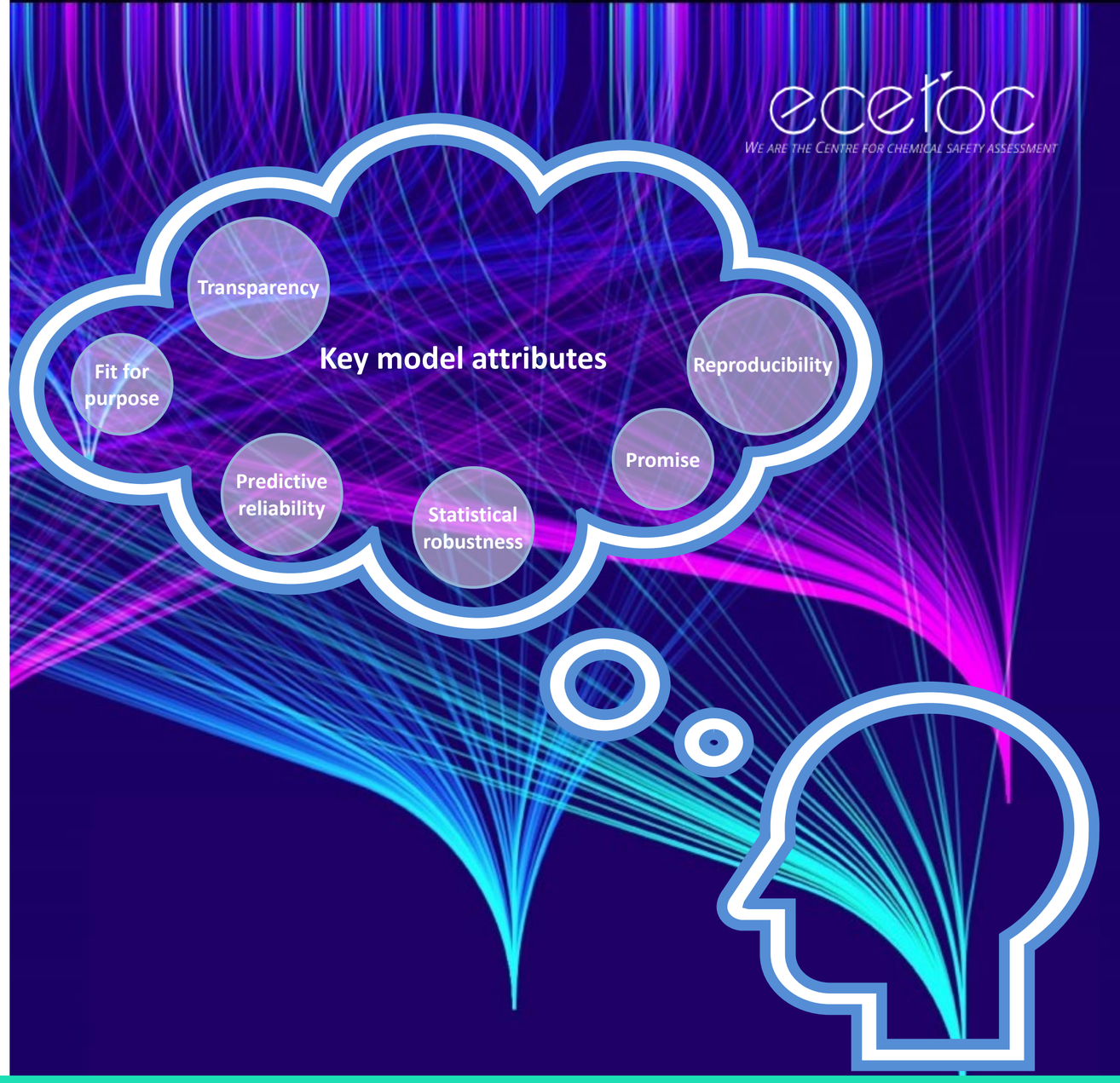

Source:
In-Silico Alternatives to Animal Testing (ubc.ca)

Towards a formal incorporation of predictive models in chemical hazard evaluation
Expert Group

Adriana C. Bejarano, Shell Global Solutions US Inc.

# Associated knowledge/ Methodologies gaps

- Fit-for-purpose models leverage existing data
- Knowledge gaps and factors impeding broader use need to be identified
- Addressing challenges would increase confidence in model performance, transparency and use




Towards a formal incorporation of predictive models in chemical hazard evaluation
Expert Group

Adriana C. Bejarano, Shell Global Solutions US Inc.

# Objectives

- Multisector **Expert Group**
- Achieve regulatory acceptance and implementation through an **evaluation** of factors, including:
  - Limitations
  - Data requirements
  - Acceptability criteria (e.g., endpoint; applicability domain; goodness-of-fit, robustness, etc.)

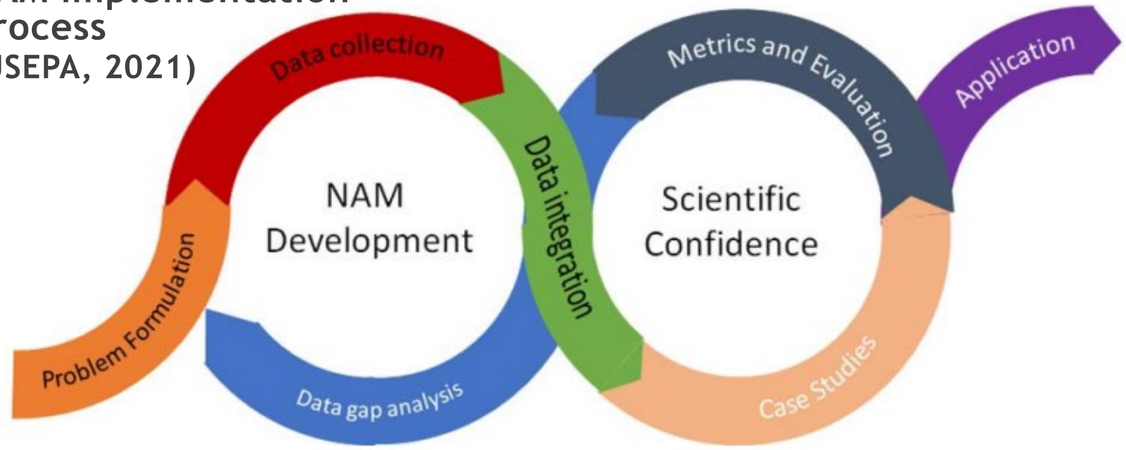



Adriana C. Bejarano, Shell Global Solutions US Inc.

# Expected impact

- Formulate a clear and globally harmonized strategy for regulatory consideration:
  - General principles and guidelines
  - Minimum acceptability requirements
  - **Case studies** for select predictive models
- **Strategic roadmap** for establishing scientific confidence

NAM implementation process (USEPA, 2021)



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