Eco-NAMs Webinar 1: State of the science for bioaccumulation: an integrated, weight of evidence approach

Regulatory and industry acceptance of New Approach Methodologies in Bioaccumulation Assessment

Dr Pippa Curtis-Jackson
Senior Specialist, Chemicals Assessment Unit
10th September 2025

Environment Agency

Overview

- Introduction to the hazard of persistence, bioaccumulation and toxicity (PBT)
- Bioaccumulation assessment
- Why do we need NAMs for bioaccumulation assessment?
- Overcoming the challenges in developing NAMs for B assessment
- NAMs as lines of evidence relevant to the B-endpoint – Research and initiatives

Persistent, Bioaccumulative & Toxic Chemicals

Persistence: Is the chemical going to hang around in the environment?

No? Organisms are only going to be exposed to the chemical briefly and locally at an emission point, so we don't worry about the chemical further in this type of assessment.

Yes? Then we need to consider if the chemical will bioaccumulate...

P

Bioaccumulation: Is the chemical going to increase in concentration within the bodies of organisms?

No? It probably isn't going to be present at levels in organisms that may cause harm, so we don't worry about the chemical further in this type of assessment.

Yes? Then we need to consider if the chemical is toxic...

B

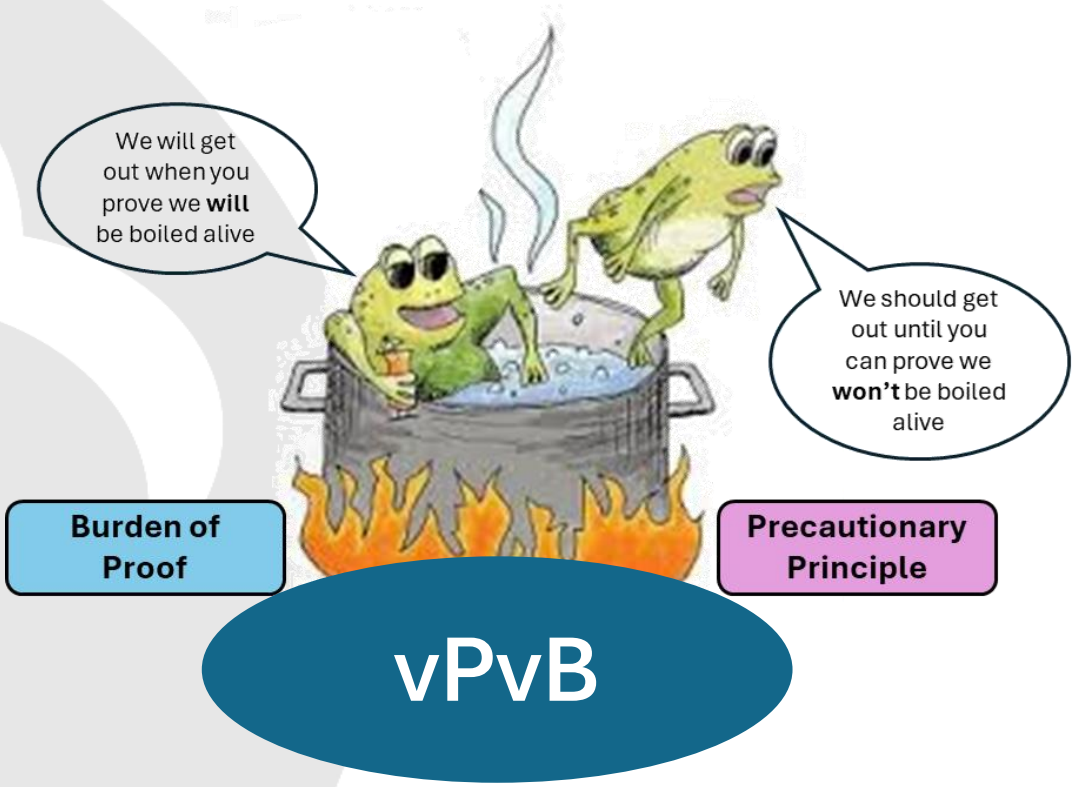
Toxicity*: Is the chemical able to cause harm?

No? *Organisms are not going to be affected by the presence of the chemical in their body, so we don't worry about it in this type of assessment.*

Yes? Then this is a cause for concern.

T

*This includes toxicity to both wildlife and people.

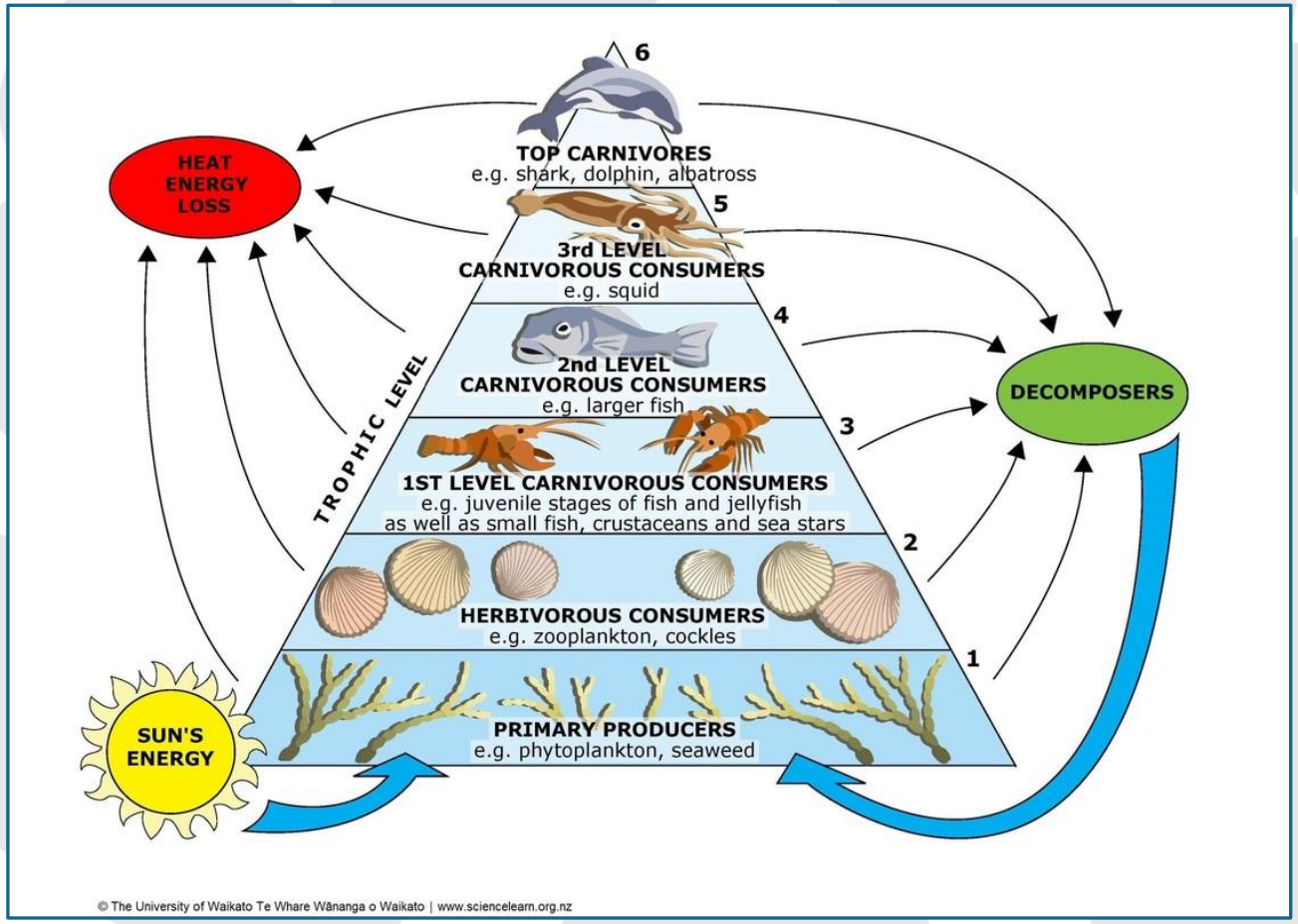


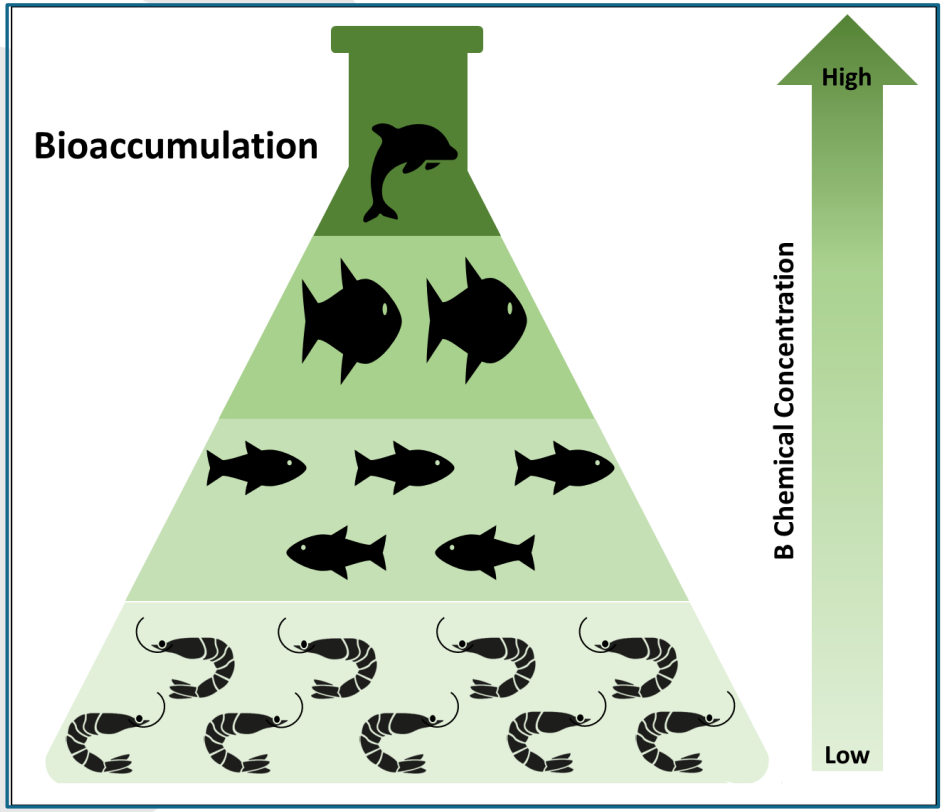
e.g. hazard relevant to EU, UK and K-REACH

Environment Agency

The protection goal of PBT

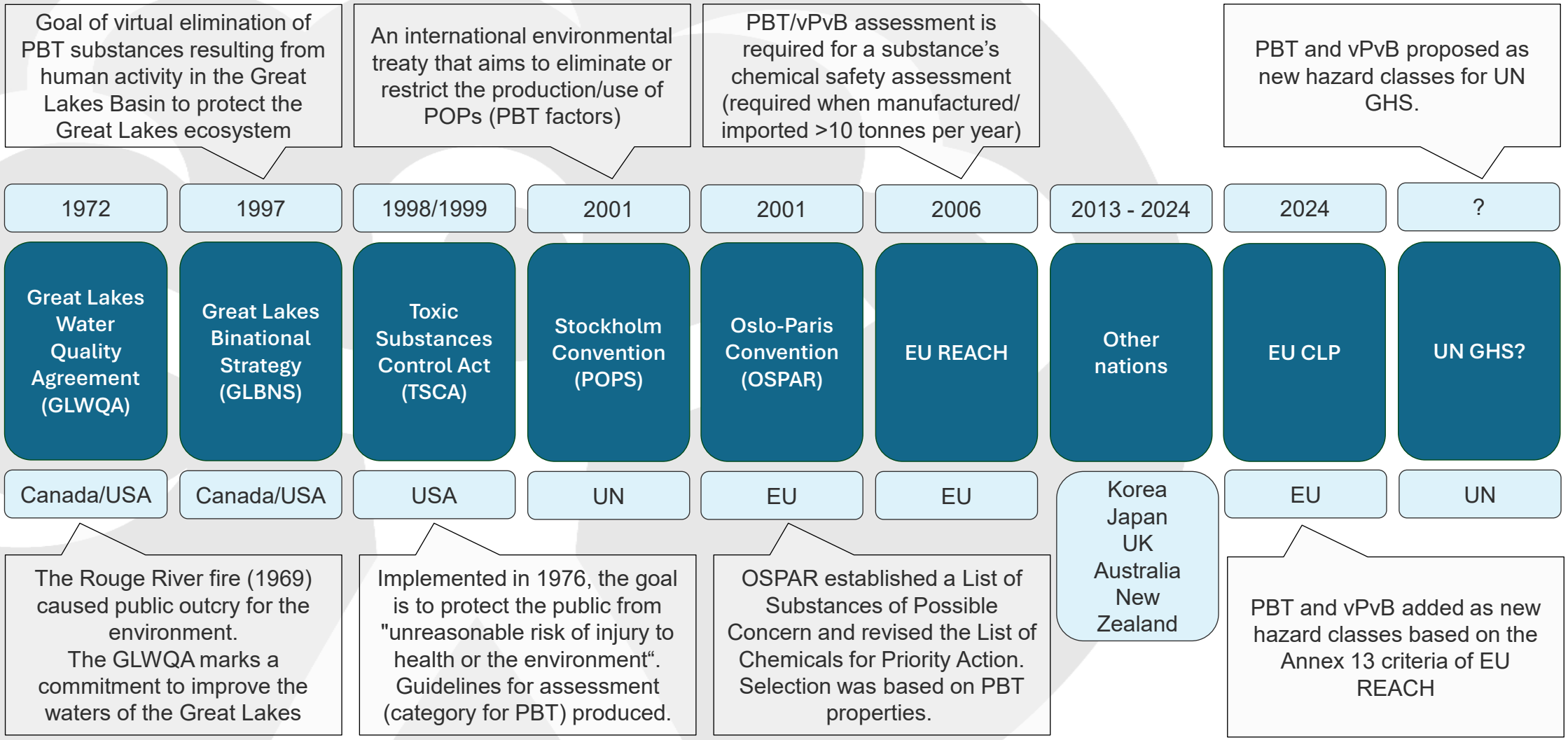
To protect the environment and humans from substances that are likely to contaminate food chains and exert toxic effects through accumulation in organisms





Environment Agency

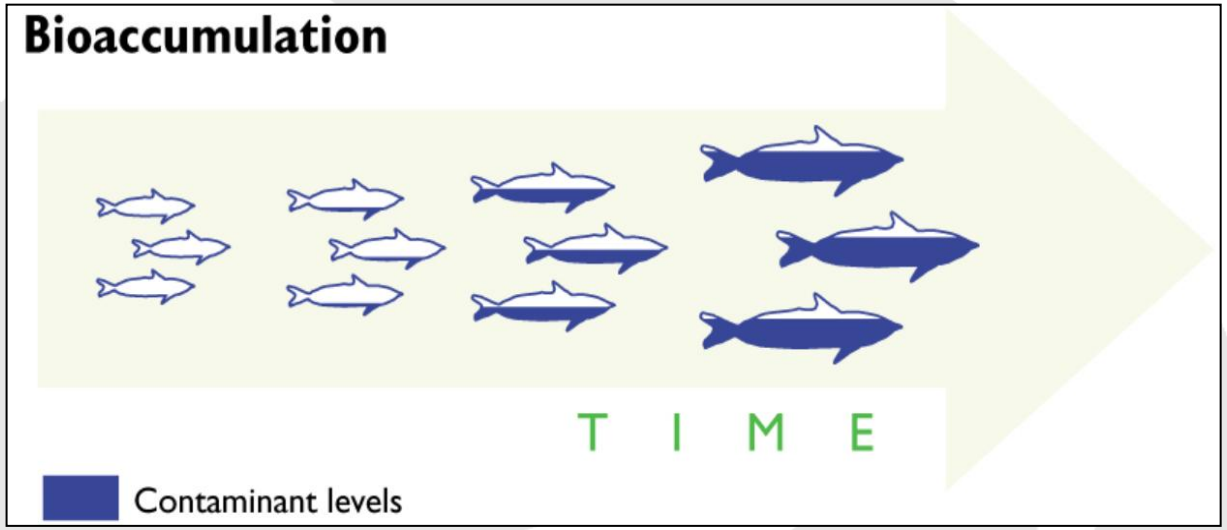
Global Evolution of Persistence Bioaccumulation & Toxicity Assessment

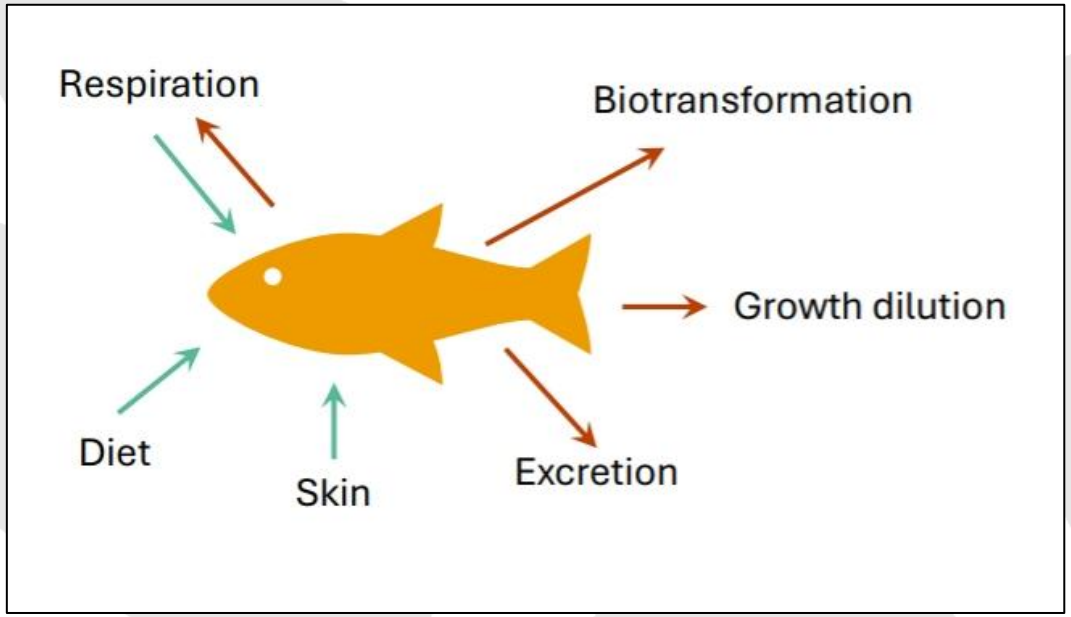


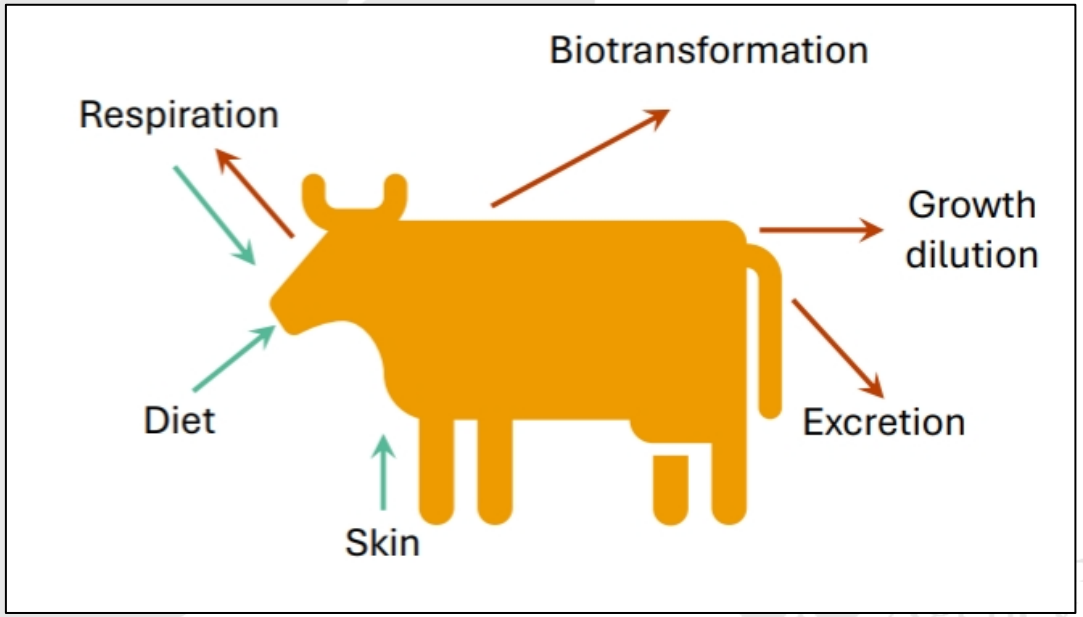
Threshold criteria and evaluation vary globally

Environment Agency

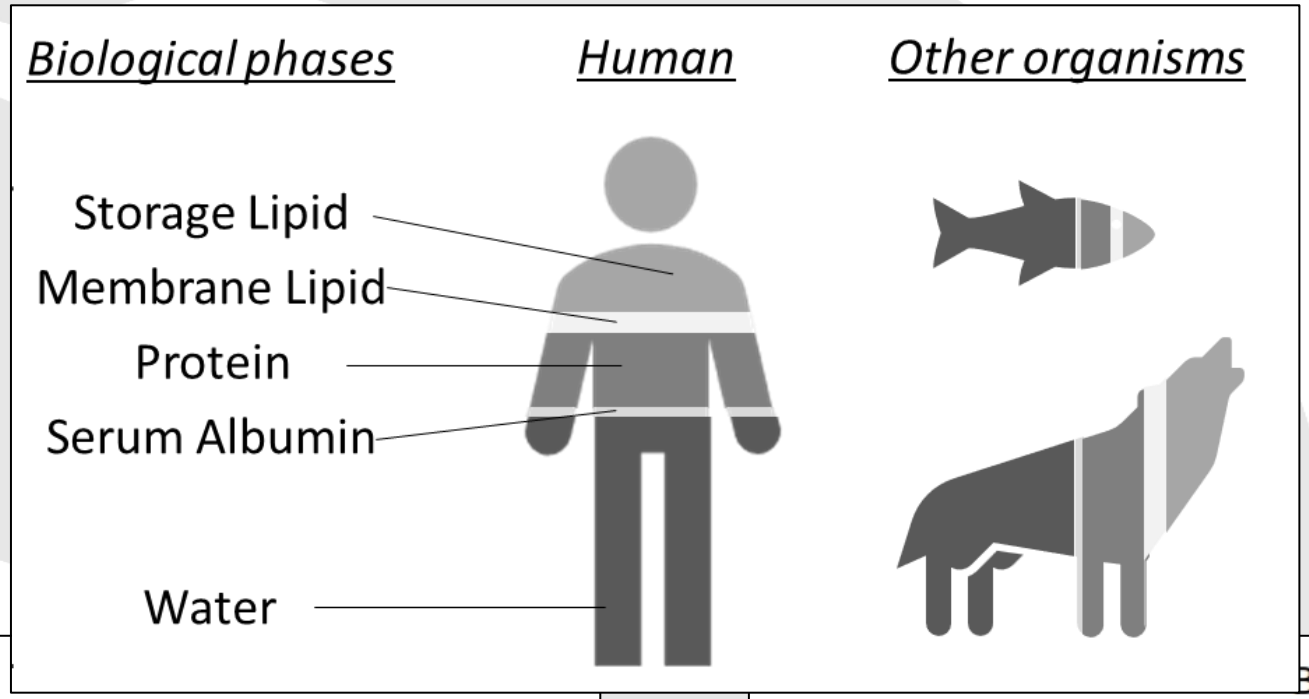
Zooming in on Bioaccumulation

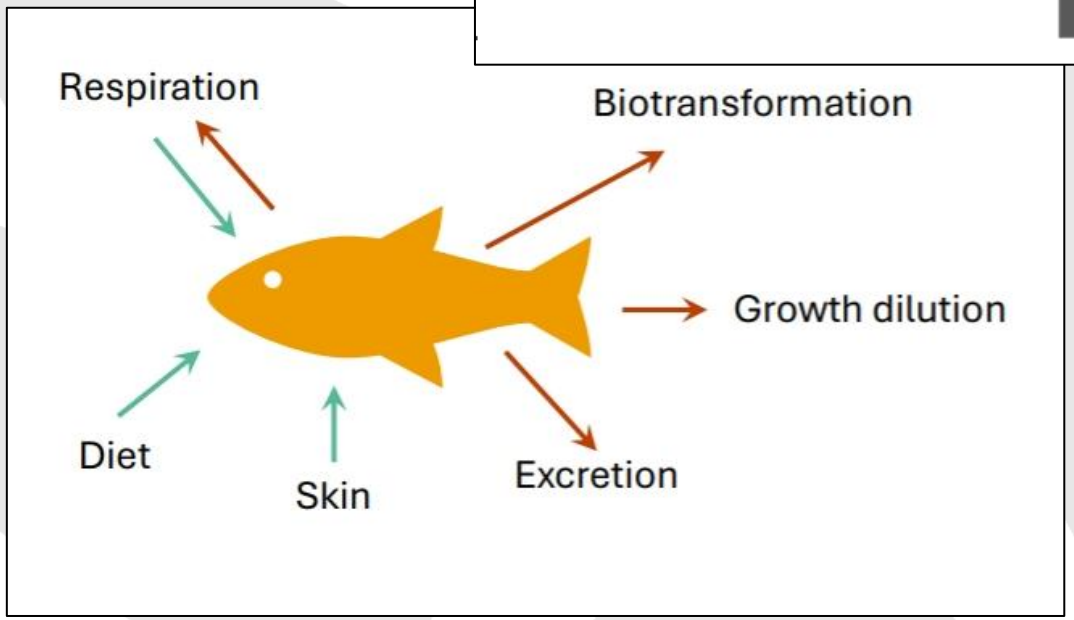


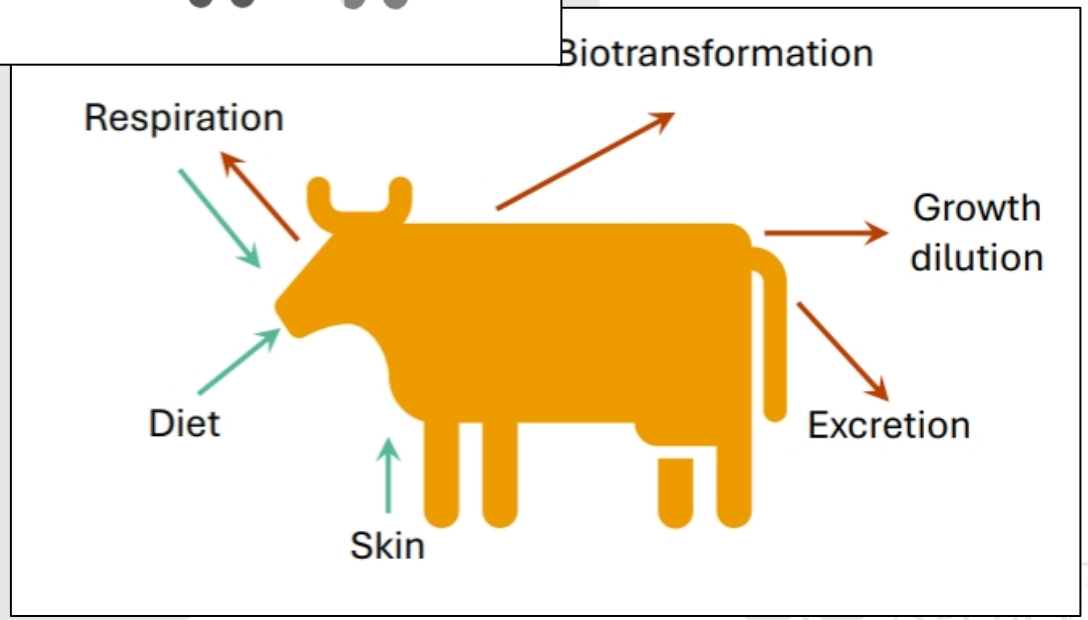




Zooming in on Bioaccumulation







Bioaccumulation assessment – UK REACH - Annex 13 criteria*

Screening criteria

Biota	Screening information		Potentially B
Aquatic organisms	n-octanol water	Log K_{OW}	≥ 4.5
Air-breathing organisms	n-octanol air n-octanol water	Log K_{OA} Log K_{OW}	≥ 5 ≥ 2

Definitive B threshold criteria for Aquatic Organisms

B Criteria	vB Criteria
BCF > 2000	BCF > 5000

Under UK REACH Annex 13 sets out the legal thresholds for identification of substances of very high concern (SVHC) – at a global and legislative level bioaccumulation screening and definitive metrics vary

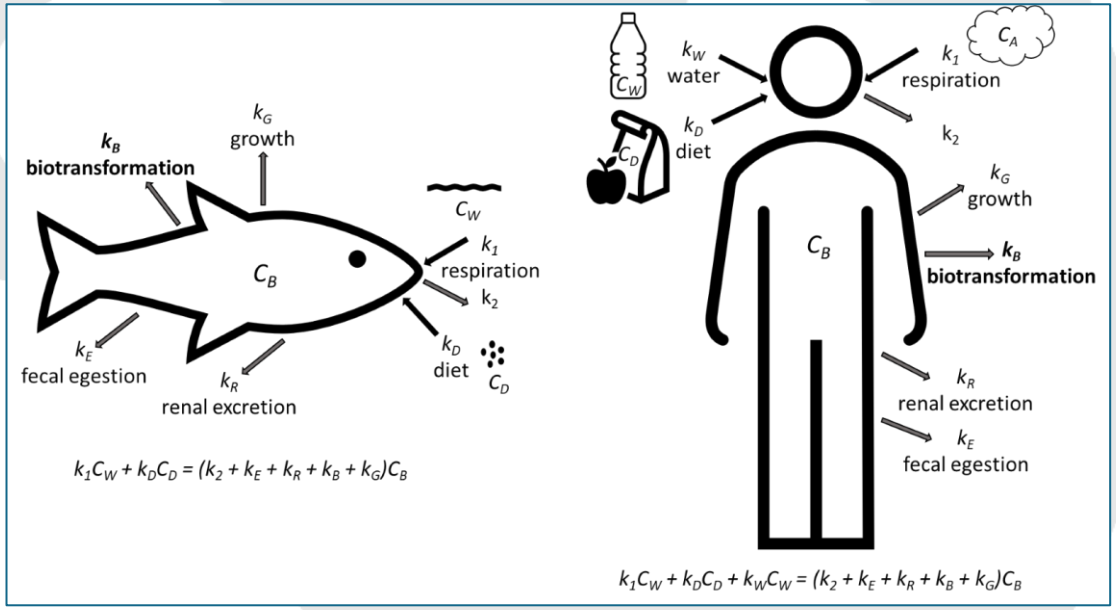
Bioaccumulation assessment – weight of evidence approach

Physico-chemical data

Laboratory data

Field data

Toxicokinetic data



Read-across data

ADME data

Estimated data (QSARs)

Non-standard study data

Environment Agency

Why do we need NAMs for bioaccumulation assessment?

Current criteria = 1970's – 1990's science of NLOCs

→ Complex chemical universe:
Applicability domain
Accumulation in different tissues

OECD 305 (Fish BCF test)

→ Ethics: Uses large number of vertebrates
Logistics: time-consuming, expensive
Representation: accumulation in air-breathers versus water-breathers

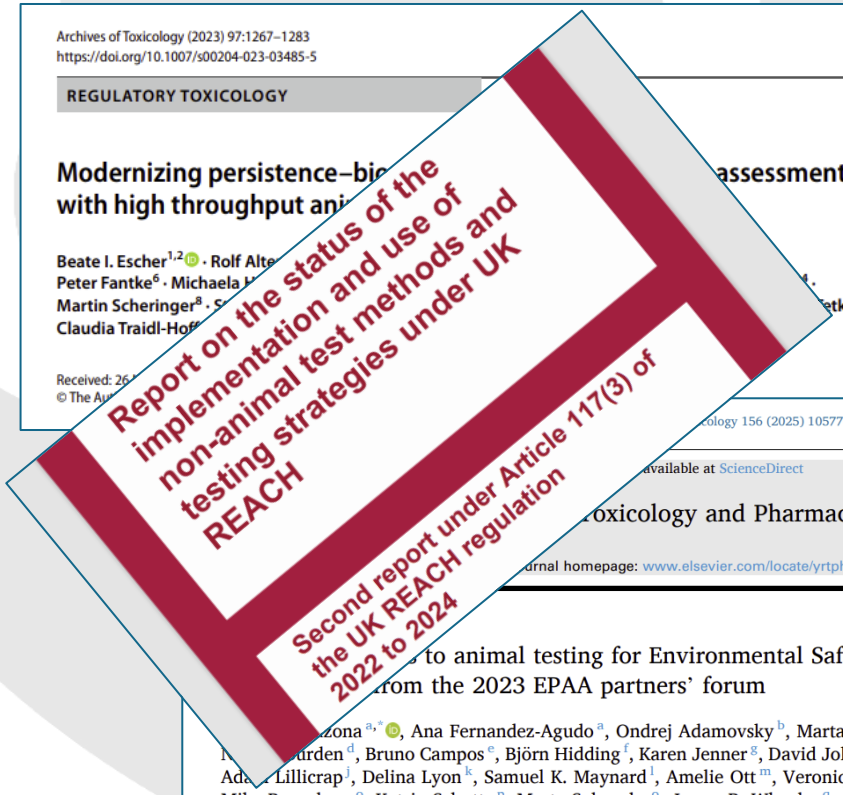
Overcoming the challenges in developing NAMs for B assessment

Regulatory and organisation barriers

Validation and standardisation

Biological complexity

Species diversity



Archives of Toxicology (2023) 97:1267–1283
https://doi.org/10.1007/s00204-023-03485-5

REGULATORY TOXICOLOGY

Modernizing persistence–bio… …assessment with high throughput ani…

Beate I. Escher[1,2] · Rolf Alte…
Peter Fantke[6] · Michaela H…
Martin Scheringer[8] · S…
Claudia Traidl-Hoff…

Received: 26…
© The Au…

…ology 156 (2025) 105774

…available at ScienceDirect

…oxicology and Pharmacology

…urnal homepage: www.elsevier.com/locate/yrtph

…to animal testing for Environmental Safety Assessment …rom the 2023 EPAA partners' forum

…zona[a,*], Ana Fernandez-Agudo[a], Ondrej Adamovsky[b], Marta Baccaro[c], …urden[d], Bruno Campos[e], Björn Hidding[f], Karen Jenner[g], David John[h], Katia Lacasse[i], …Lillicrap[j], Delina Lyon[k], Samuel K. Maynard[l], Amelie Ott[m], Veronique Poulsen[n], Mike Rasenberg[o], Katrin Schutte[p], Marta Sobanska[o], James R. Wheeler[q]

Environmental Toxicology and Chemistry

Special Series | Open Access

Big Question to Developing Solutions: A Decade of Progress in the Development of Aquatic New Approach Methodologies from 2012 to 2022

Laura M. Langan, Martin Paparella, Natalie Burden, Lisa Constantine, Luigi Margiotta-Casaluci, Thomas H. Miller, S. Jannicke Moe, Stewart F. Owen, Alexandra Schaffert, Tiina Sikanen

First published: 01 February 2023 | https://doi.org/10.1002/etc.5578 | Citations: 5

Supporting Chemical Bioaccumulation and Biotransformation Assessments With NAMs

- **Use of fish cell lines in bioaccumulation assessment:** Paloma de Oro-Carretero, Complutense University of Madrid, developed an approach using zebrafish liver cell lines on glass plates. The 72-hour in vitro assay used two moderately hydrophobic organic chemicals with well-known biotransformation product profiles. Concentrations both in the test medium and inside the cells were determined. The results were used in mass balance and kinetic approaches coupled with in vitro to in vivo extrapolation (IVIVE) models to predict bioconcentration factors (BCF). The use of fish cell lines is a promising development since it would completely remove the need for live fish, while allowing the assays to be conducted for a longer period.
- **Support of IVIVE for bioaccumulation assessment:** Aurelia Lapczynski, Research Institute for Fragrances Materials, presented a case study with a fragrance compound, showcasing how in vitrobiotransformation assays can accurately predict fish BCFs. Using rainbow trout liver S9 fractions (OECD TG 319B), the studies showed 90% depletion of the parent compound and IVIVE modelling predicted a BCF of 309 L/kg. This extrapolated BCF showed excellent agreement with the BCF measured an in vivoOECD TG 305 study for the same chemical in bluegill sunfish (412 L/kg).

…askatchewan, presented a …on in birds using in vitro …the ecological importance of …accumulation in air-breathing …onsistent intrinsic clearance …k is planned with other test …his approach lays the …ssessment frameworks.

RESEARCH PROJECTS

New Approach Methodologies (NAMs) to Support Regulatory Decisions for Chemical Safety

Yordas Ltd, Letizia Carramusa[1], Wilfrieda Mune, Neil Hunt[1], Lorcan Browne[2], Olivia Osborne[2], Claire Potter[2]

[1] Yordas Ltd, [2] Food Standards Agency

Keywords: Chemical risks, Cutting edge regulator, Emerging challenges and opportunities, Methods, Safety assessment

https://doi.org/10.46756/001c.122591

FSA Research and Evidence

NAMs and lines of evidence relevant to the B-endpoint – UK Research

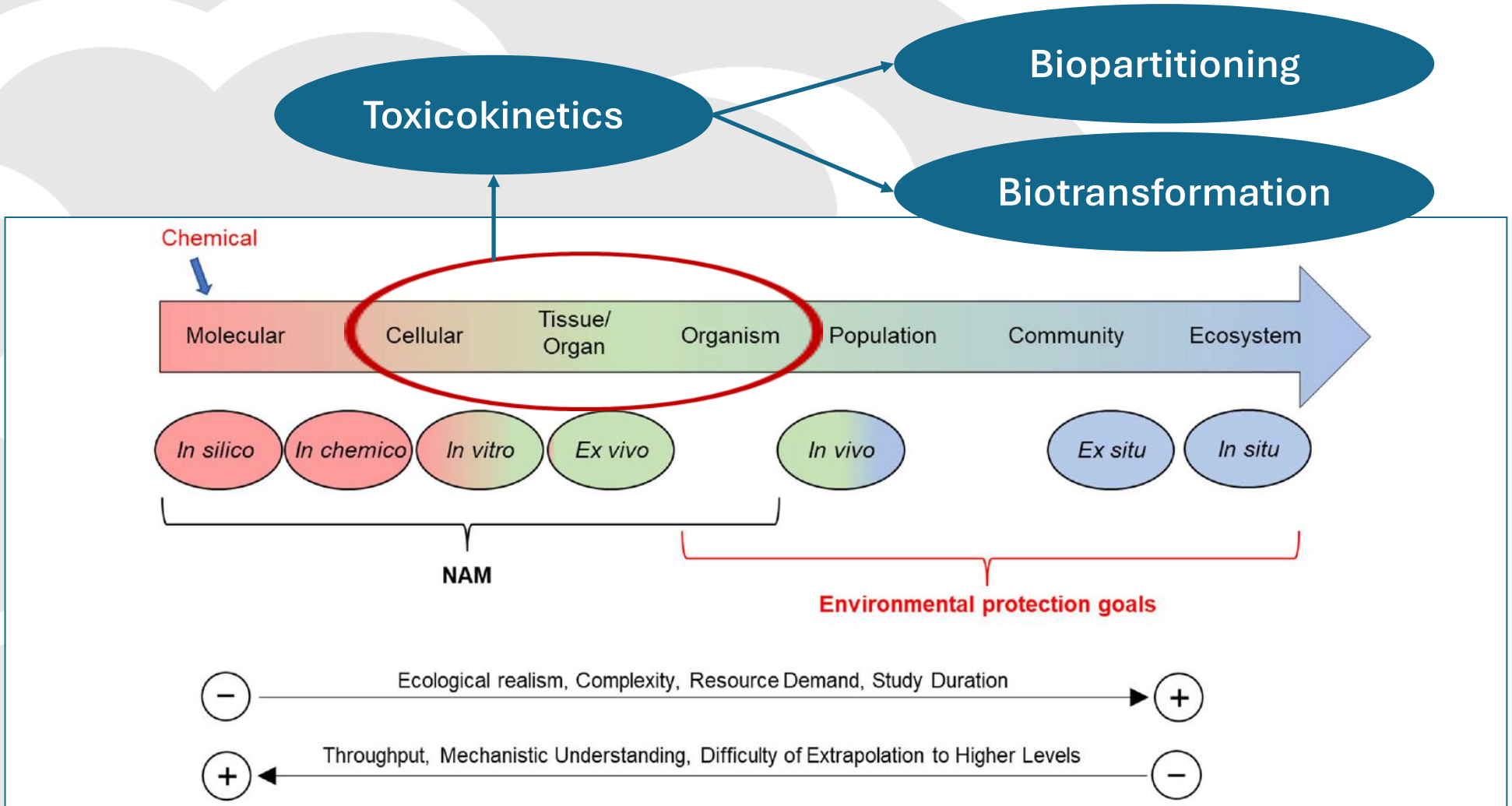


FIGURE 1: Current overview: levels of biological organization and tools in support of chemical ecological assessment. NAM = new approach methodology.

Figure adapted from - Mitchell, C.A *et al.*, (2023), New Approach Methodologies for the Endocrine Activity Toolbox: Environmental Assessment for Fish and Amphibians. Environ Toxicol Chem, 42: 757-777. https://doi.org/10.1002/etc.5584

Environment Agency

NAMs and lines of evidence relevant to the B-endpoint – UK Research

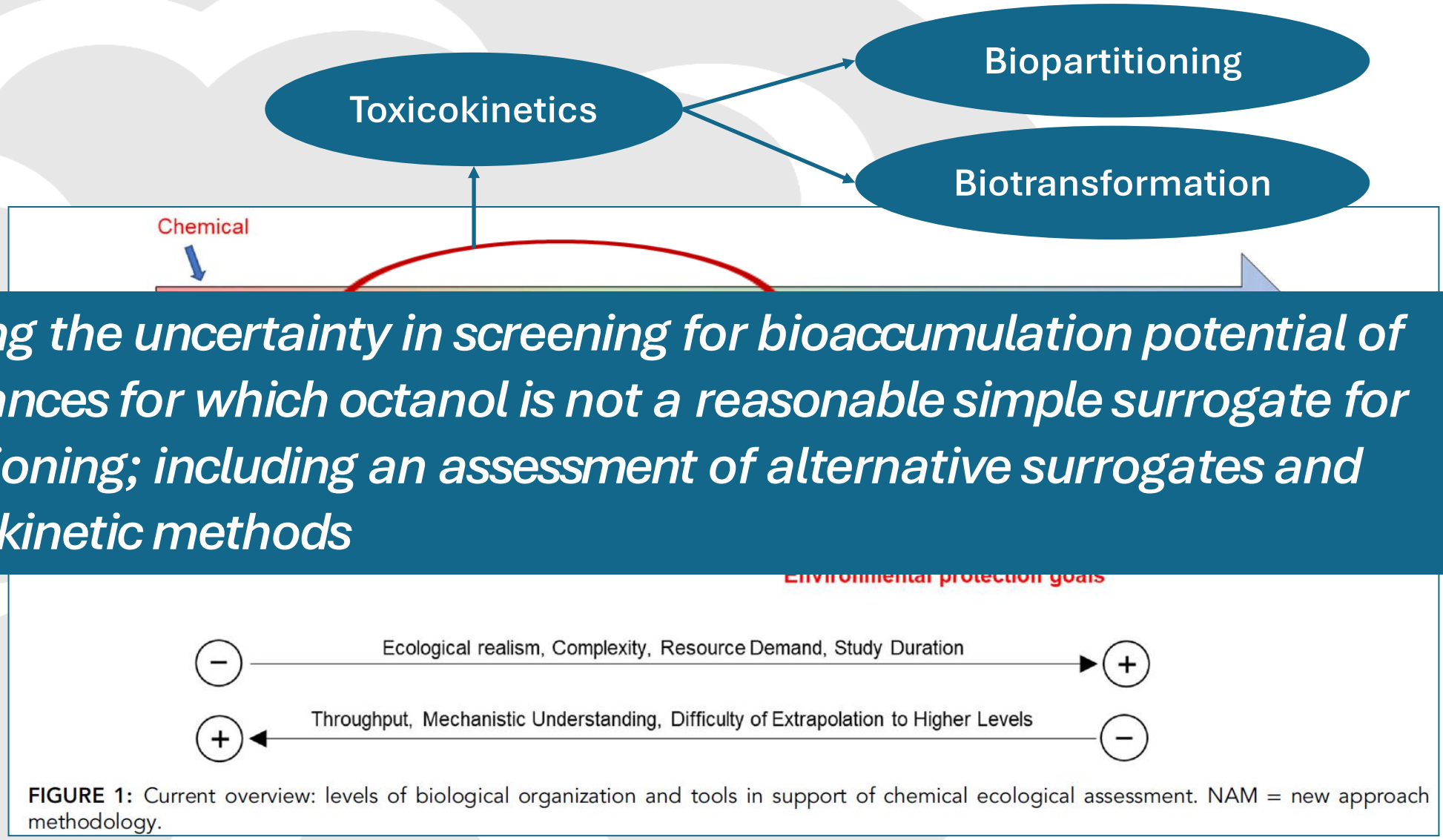


FIGURE 1: Current overview: levels of biological organization and tools in support of chemical ecological assessment. NAM = new approach methodology.

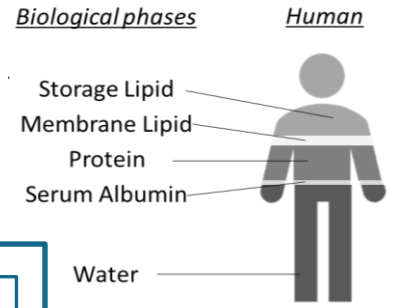
Scoping the uncertainty in screening for bioaccumulation potential of substances for which octanol is not a reasonable simple surrogate for partitioning; including an assessment of alternative surrogates and toxicokinetic methods

Figure adapted from - Mitchell, C.A *et al.*, (2023), New Approach Methodologies for the Endocrine Activity Toolbox: Environmental Assessment for Fish and Amphibians. Environ Toxicol Chem, 42: 757-777. https://doi.org/10.1002/etc.5584

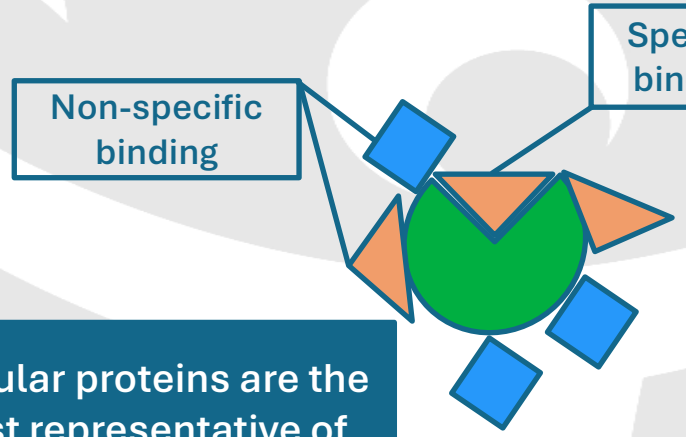
Environment Agency

Biopartitioning (surrogate screening)

Review protein and phospholipid surrogates as alternatives to octanol for partition coefficient screening



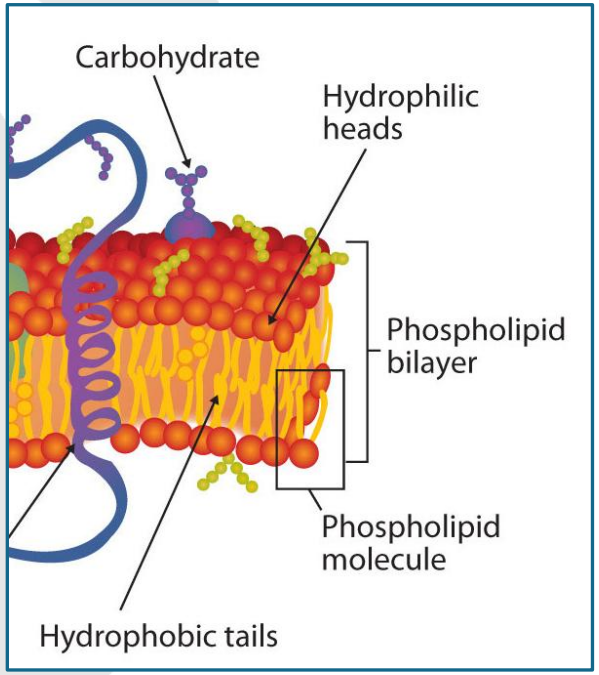
Proteins



Globular proteins are the most representative of whole-body biopartitioning and bioaccumulation potential

Galectins and carbonic anhydrase

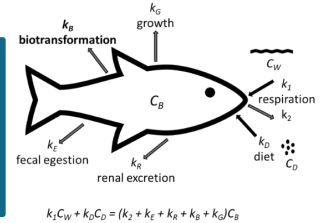
Phospholipids



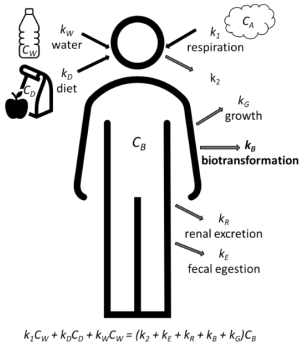
- Unilamellar liposomes
- Immobilised artificial membranes and solid supported lipid membranes

Biopartitioning (toxicokinetics)

Review toxicokinetic methods for biopartitioning and biotransformation, and their use in bioaccumulation screening



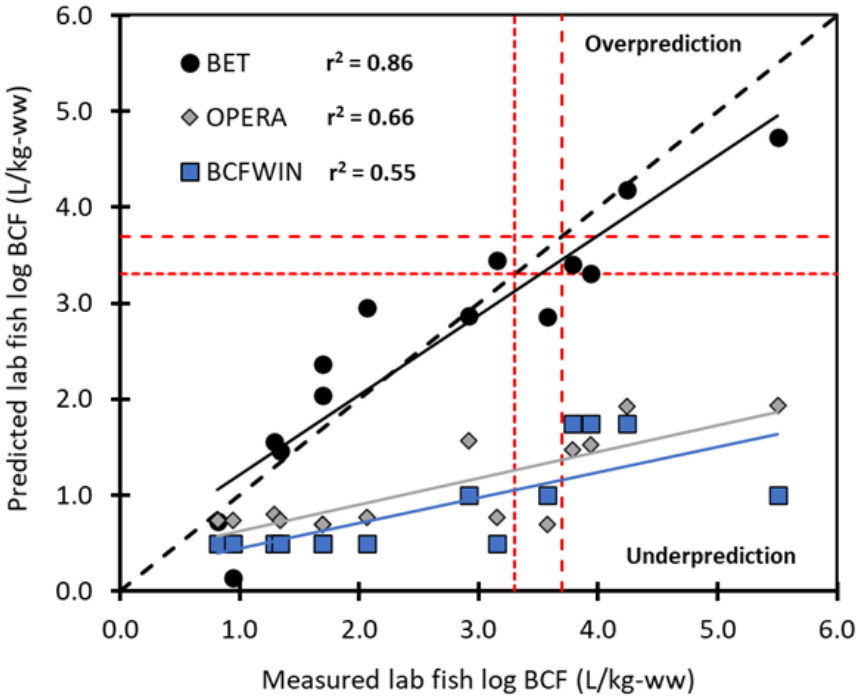
$k_1 C_W + k_D C_D = (k_2 + k_E + k_R + k_B + k_G) C_B$



$k_1 C_W + k_D C_D + k_W C_W = (k_2 + k_E + k_R + k_B + k_G) C_B$

Bioaccumulation Estimation tool (BET) versus Opera and BCFWIN in predicting laboratory BCFs shows better performance of BET.

PFAS		
Abbrev	pka	log $K_{OW,N}$
PFBA	0.4	1.43*
PFPeA	0.4	1.35
PFBS	-3.6	1.51
PFHxA	0.4	2.85*
PFHpA	0.5	2.06*
PFOA	0.5	3.1*
PFHxS	-3.3	2.20*
PFDS	-3.3	5.13
PFOS	-3.3	5.61*
PFNA	0.5	3.54*
PFDA	0.5	4.15*
PFUnDA	0.5	4.00*
PFDoDA	0.5	6.55
PFTrDA	0.5	7.15



[BAT - ARC Arnot Research & Consulting]
[Eas-E-Suite - ARC Arnot Research & Consulting]

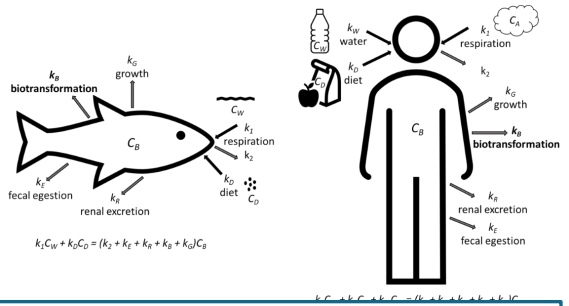
Source: Environment Agency (2026), currently under completion

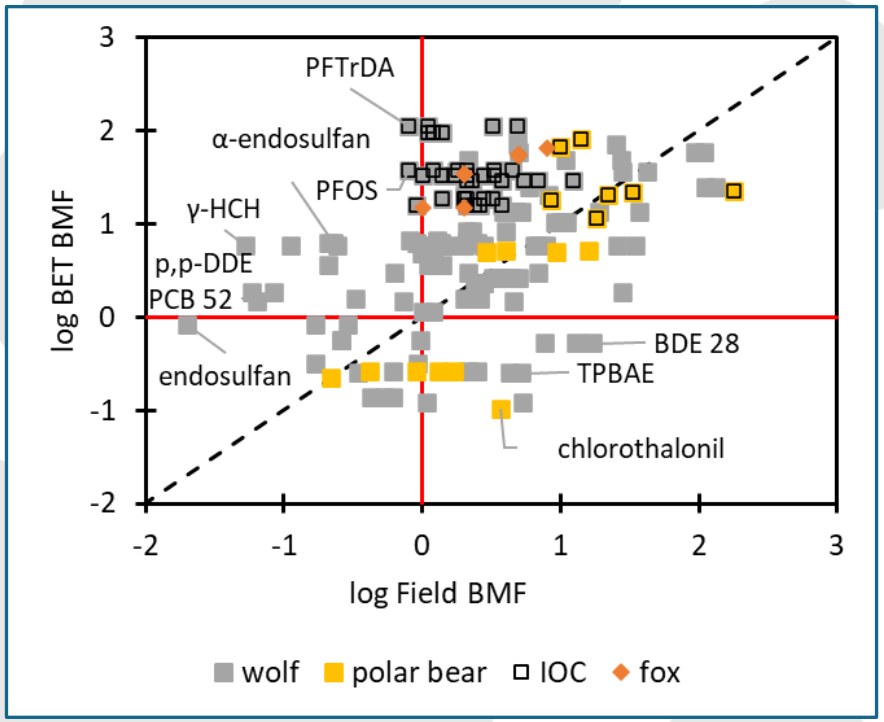
EAS-E SUITE
EXPOSURE AND SAFETY ESTIMATION SUITE

Environment Agency

Biopartitioning (toxicokinetics)

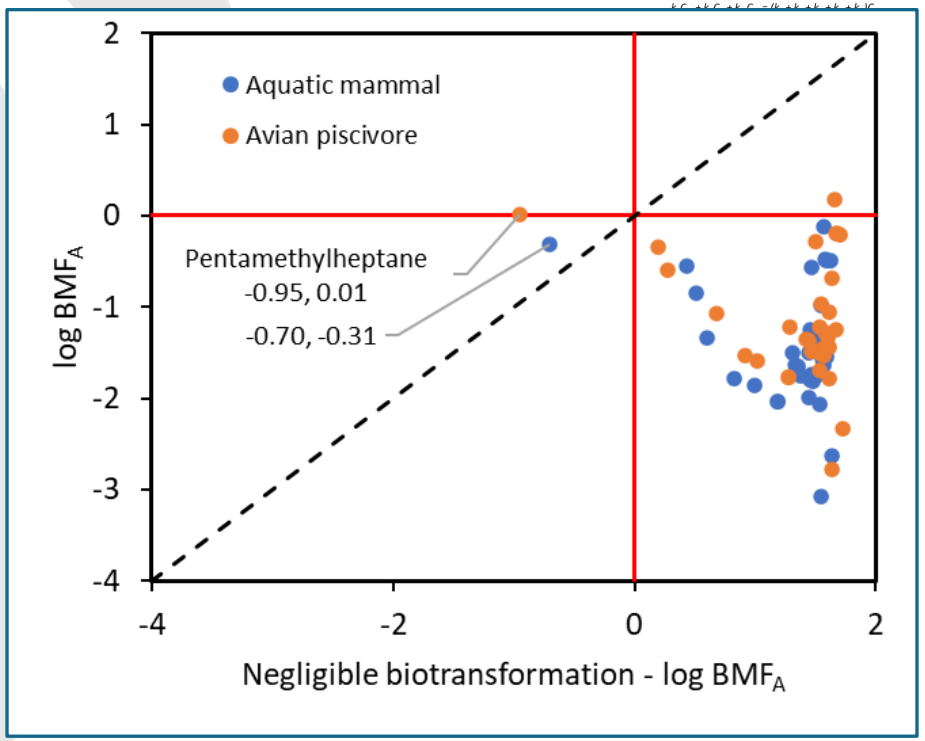
Review toxicokinetic methods for biopartitioning and biotransformation, and their use in bioaccumulation screening





Reasonable agreement between predicted and field BMF data for air-breathers (and correct categorisation).

Effect of including and excluding biotransformation on the predicted BMF data shows the importance of characterising biotransformation correctly.



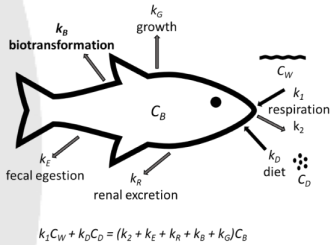
Environment Agency

Biotransformation (toxicokinetics)

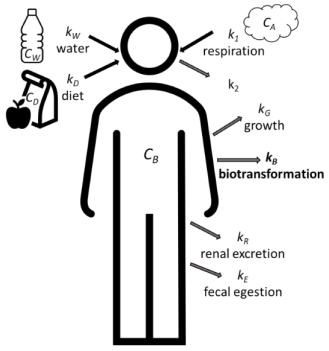
Arnot Research & Consulting

Review toxicokinetic methods for biopartitioning and biotransformation, and their use in bioaccumulation screening

- Collation and integration of biopartitioning data – proteins
- Data base integration with the EAS-E Suite Platform
- Expansion and recalibration of parameters using the integrated database
- Run predictions for ~ 80,000 chemicals replacing the octanol surrogate assumptions with the new biopartitioning predictions
- Case studies
  - in vitro (OECD 319 – IVIVE model) / in silico → model validation
  - QSAR model scoping for elimination half life in fish for > 20,000 substances



$k_1 C_W + k_D C_D = (k_2 + k_E + k_R + k_B + k_G) C_B$



$k_1 C_W + k_D C_D + k_W C_W = (k_2 + k_E + k_R + k_B + k_G) C_B$

EAS-E SUITE

EXPOSURE AND SAFETY ESTIMATION SUITE

Environment Agency

NAMs and lines of evidence relevant to the B-endpoint - UK Research

Aquatic invertebrates – can they be used to screen for bioaccumulation potential?

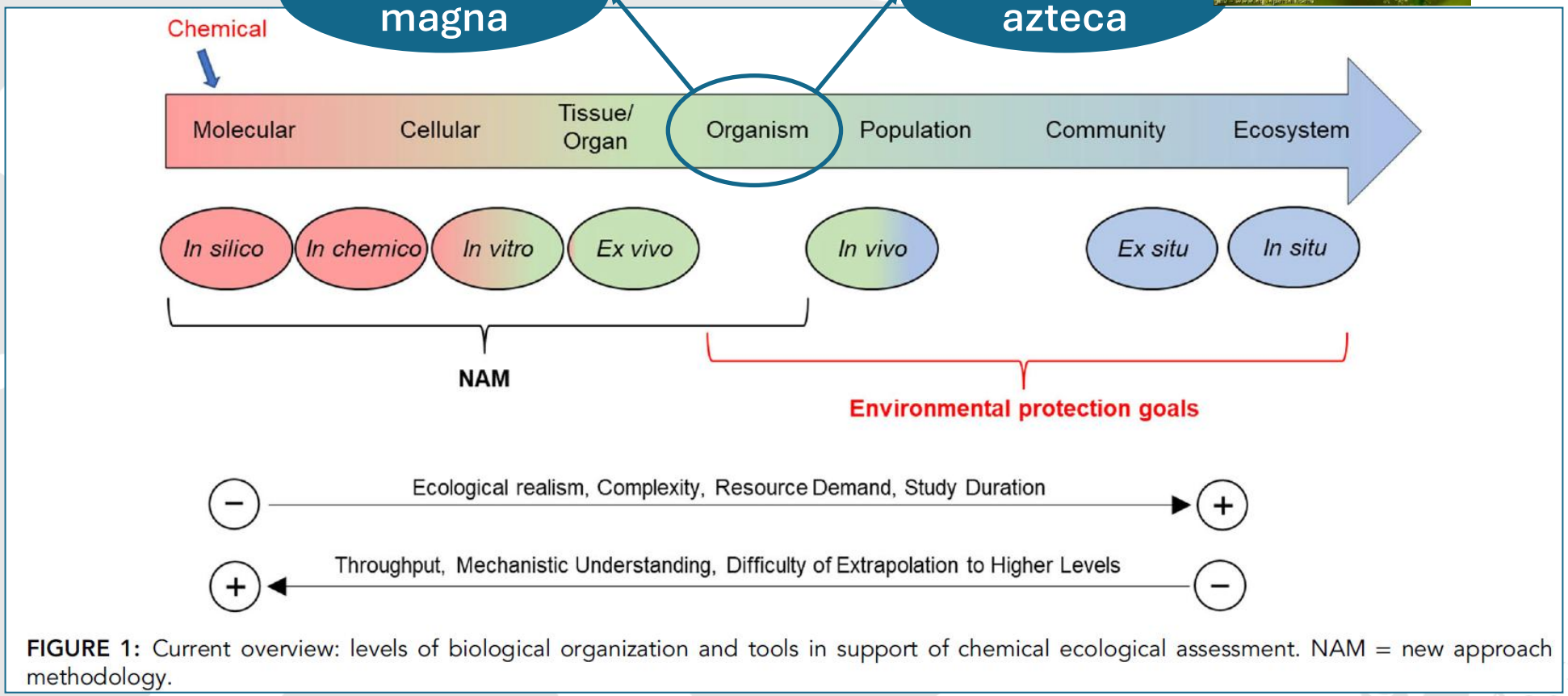


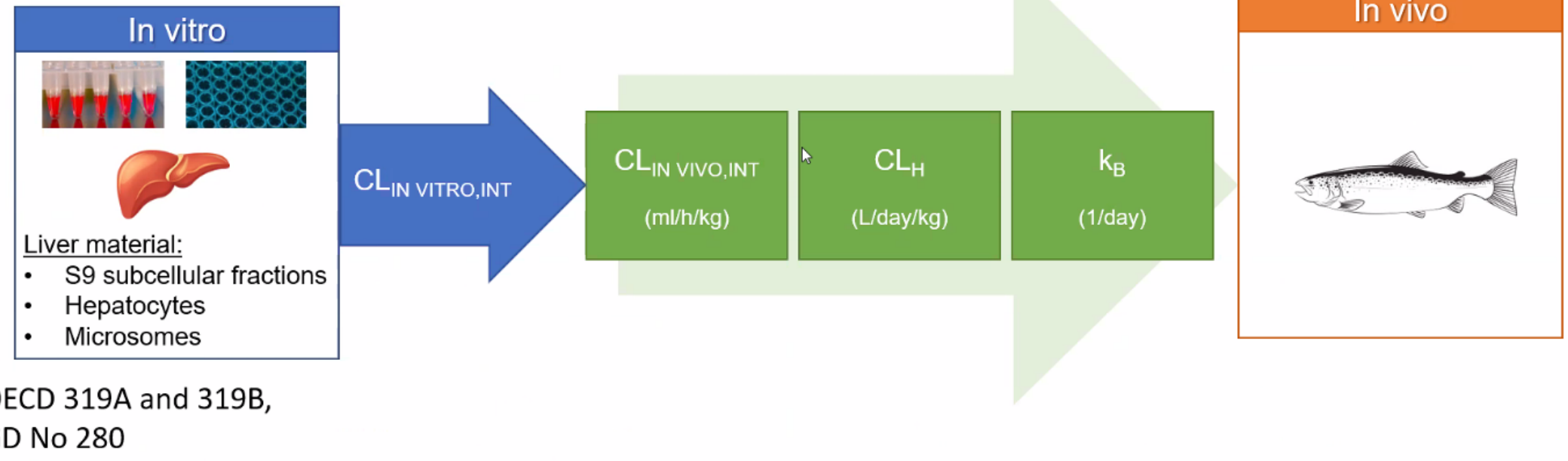
FIGURE 1: Current overview: levels of biological organization and tools in support of chemical ecological assessment. NAM = new approach methodology.

Figure adapted from - Mitchell, C.A *et al.*, (2023), New Approach Methodologies for the Endocrine Activity Toolbox: Environmental Assessment for Fish and Amphibians. Environ Toxicol Chem, 42: 757-777. https://doi.org/10.1002/etc.5584

Environment Agency (2025) The water flea as an alternative to fish for bioaccumulation testing - GOV.UK

Update to the OECD Guidance Document 280

in vitro – in vivo extrapolation (IVIVE)



OECD 319A and 319B,
GD No 280

Arnot Research & Consulting

HESI

United States Environmental Protection Agency

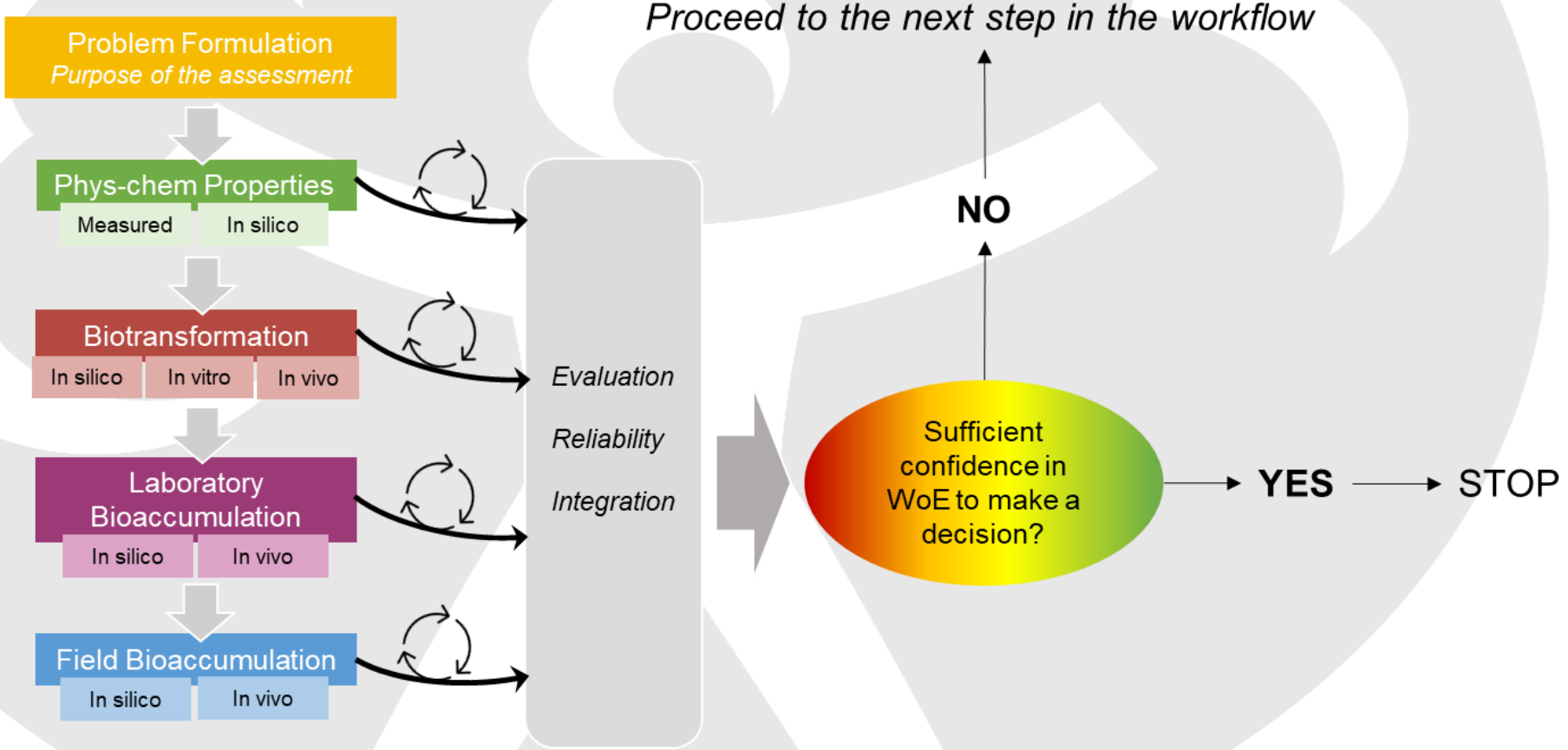
Environment and Climate Change Canada

Givaudan

Environment Agency

Bioaccumulation IATA – International projects

To bring consistency and transparency to the weight-of-evidence approach for bioaccumulation assessment.



Arnot Research & Consulting

HESI

Environment and Climate Change Canada

Givaudan

Environment Agency

What next?

- Finalisation of the biopartitioning and biotransformation (toxicokinetic) work
  - Publication in 2026
  - Commissioning of further work based on the recommendations
- Empirical data generation to support using Daphnia to screen for bioaccumulation potential
  - Development of, or amendment to existing test guidelines
- Submission to OECD VMG-ECO and WNT for the GD 280
  - Further work by the project has been proposed for additional areas of work
- Collation of laboratory derived BCF/BMF/BAF data from 2009 – current?
  - Expansion and recalibration of estimation models
  - Improvement of chemical space and applicability domain
  - Reduced uncertainty

Final thoughts.....

- To confidently move to alternative methods there are many areas of this complex subject where further understanding is needed, and tools need to be improved and updated
  - Leveraging knowledge and data from different industries

- With the increase in substance complexity - any improvements should go back to first principles and protection goals. This cannot be done without examining the foundations

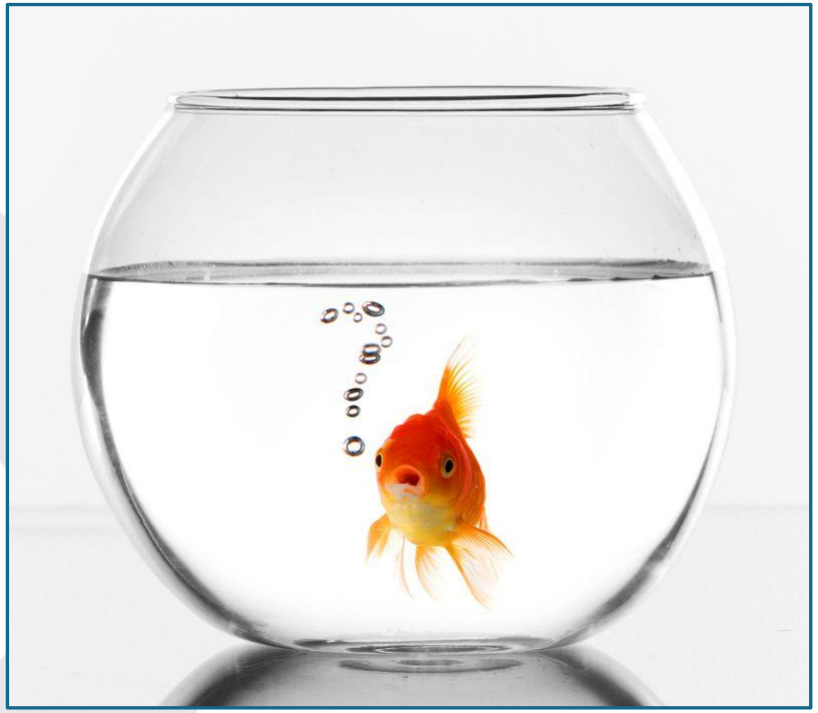
- For example, updating in silico tools
  - Collate laboratory BCF/BMF/BAF data from 2009 – current
  - Expand and recalibrate of established estimation models
  - Improve chemical space and applicability domains
  - Reduced uncertainty in outputs
  - Improve regulatory confidence?

Environment Agency

Thank you.....

- Steph Jones, Richard Gibson & Steve Dungey (Chemical Assessment Unit)
- Defra CPHW for funding the research work
- Michelle Embry (Health and Environmental Sciences Institute, Washington D.C., USA)
- Mark Bonnell (retired, Environment and Climate Change Canada)
- Jon Arnot (ARC Arnot Research & Consulting, Toronto, Canada)
- Kellie Fay (US EPA, Washington D.C., USA)
- Heike Laue (Givaudan, Switzerland)
- Alessandro Sangion (ARC Arnot Research & Consulting, Toronto, Canada)
- Trevor Brown (ARC Arnot Research & Consulting, Toronto, Canada)
- HESI Bioaccumulation Team

Environment Agency



Thank you for listening!

Do you have any questions?

Environment Agency