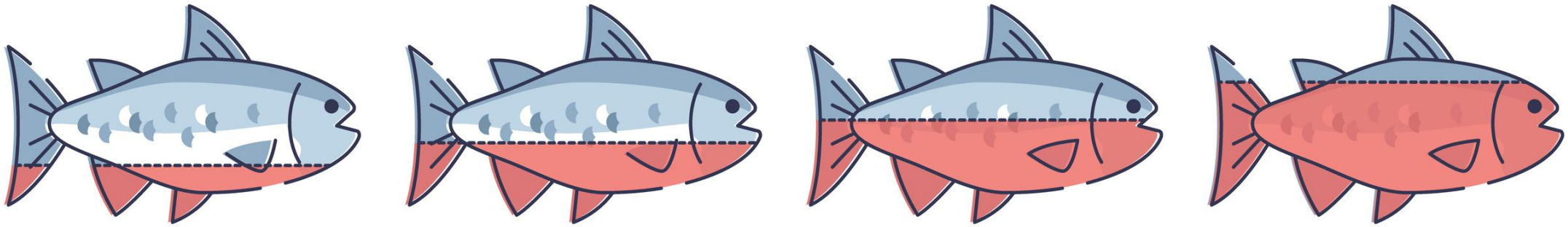
An Integrated Approach for Testing and Assessment (IATA) for Bioaccumulation



Eco-NAMs Webinar Series

10 September 2025

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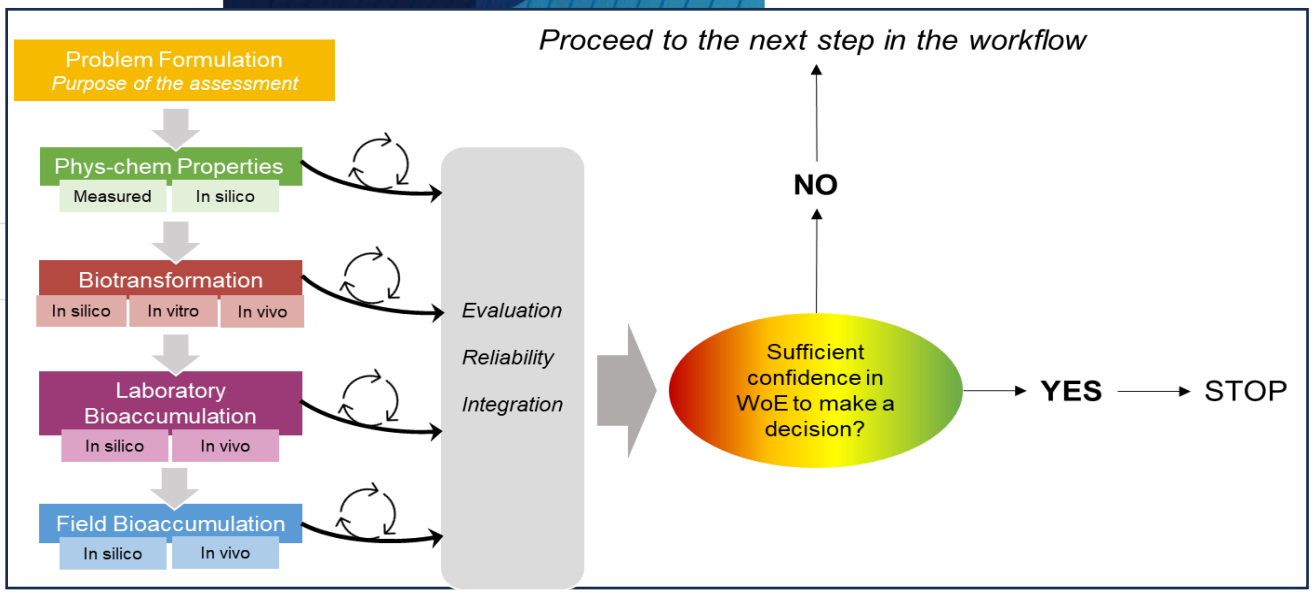
Deputy Director
Health and Environmental Sciences Institute (HESI Global)

Bioaccumulation IATA



DEVELOPED BY:

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Arnot Research & Consulting

Environment and Climate Change Canada

Givaudan

https://www.oecd.org/en/publications/case-study-on-the-use-of-integrated-approaches-for-testing-and-assessment-iata-for-bioaccumulation-ninth-review-cycle-2023_8bc8ad6f-en.html

Why a ‘B’ IATA?

Diverse Drivers & Data Requirements

Regulatory programs

REACH, TSCA/LCSA, CEPA, CSCL, Stockholm Convention

Metrics

K_{OW}, K_{OA}, lab BCF & BMF, field BAF, BMF & TMF, etc.

Food webs and species

Aquatic and terrestrial

Criteria

Various

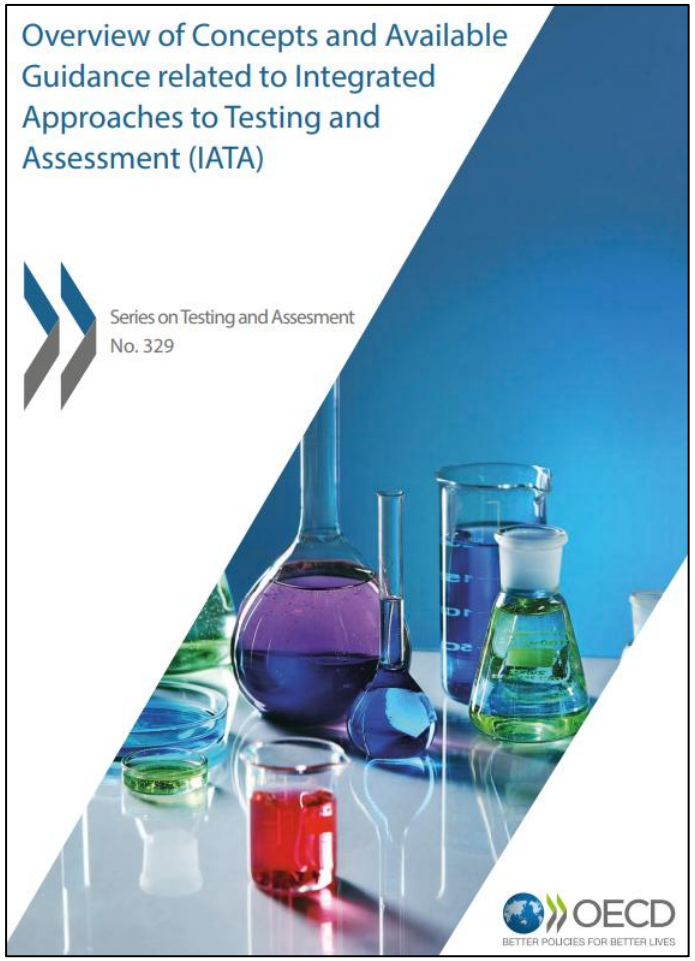
Resource limitations

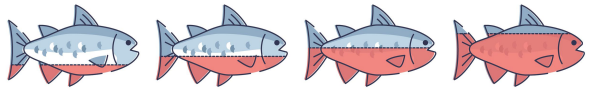
Time, animals, $$

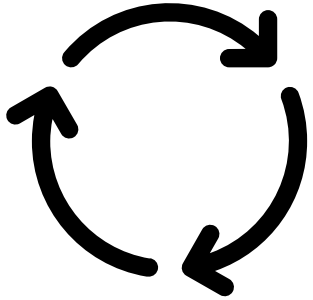
New methods and alternatives

Inherent uncertainty in measured and predicted data – need a pragmatic & transparent approach to increase confidence in decisions

Key Components of an IATA





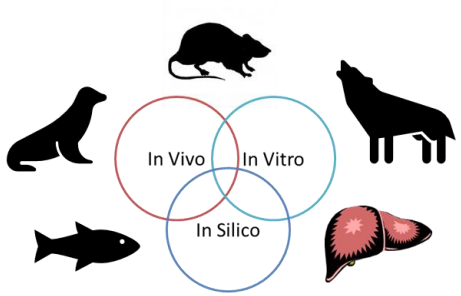


Formalized approach that:

- **Integrates and weights relevant existing evidence** (i.e., physical-chemical properties, in silico models, in vitro methods, in vivo tests and "field" data)
- **Guides the targeted generation of new data**, *when required*
- Obtains and combines sufficient information in the **most efficient way**
- Can be for **definitive conclusions** or for **screening-level assessments *to prioritize chemicals and/or methods for further testing***

Building from the Bioaccumulation Assessment Tool (BAT)

- **THE CHALLENGE:** Develop a tool that can be used to……
  - Collect, evaluate, generate, and integrate various lines of evidence relevant to B assessment
    - In vivo, in vitro, in silico TK & ADME, lab, and field B data
  - Evaluate both aquatic and terrestrial systems
  - Provide consistent and transparent results in a WoE approach
  - Guide and inform B assessment decision making
  - Guide testing strategies to address uncertainty



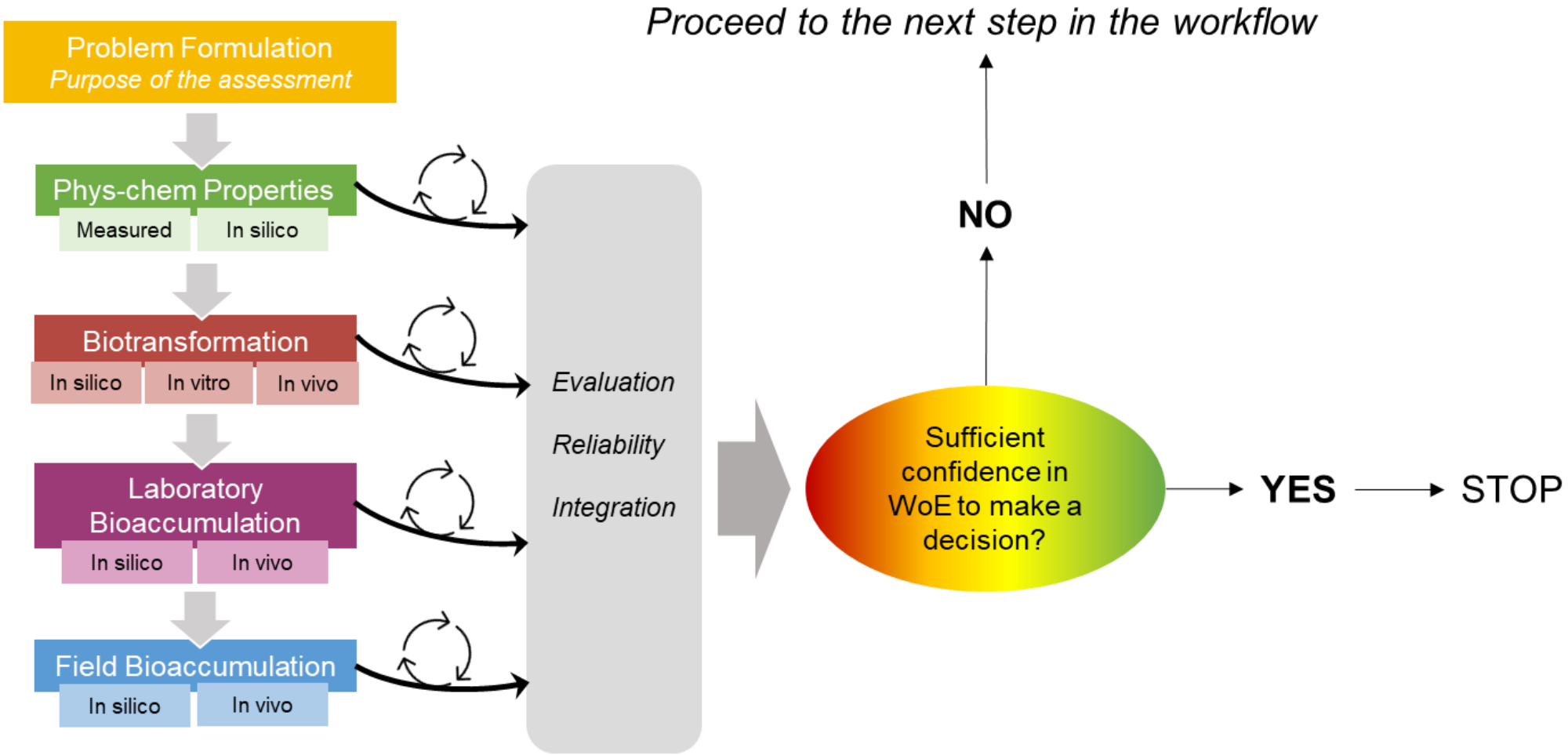
IATA leverages the foundation provided by the BAT

BIOACCUMULATION ASSESSMENT TOOL BAT Ver.2.02

Arnot Research & Consulting

https://arnotresearch.com/BAT

‘B’ IATA Workflow

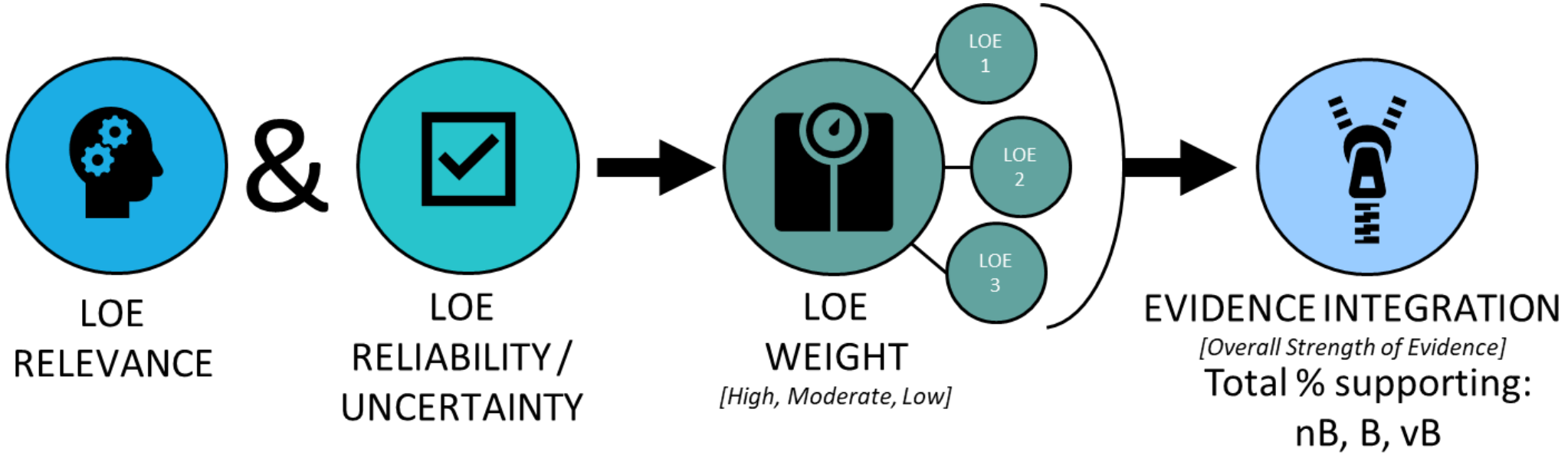


Problem Formulation

- Defines the purpose & context of the assessment
  - Regulatory prioritization & screening?
  - Application of GHS?
  - Substance registration & specifics of criteria?
- Decision context critical to understand acceptable level of uncertainty
- Includes identifying relevant lines of evidence (LoE)

- *Example problem statements:*
  - Is there sufficient evidence to conclude that a substance meets a regulatory BCF and or BAF criteria of greater than or equal to a given threshold (i.e., 5000 L/kg-ww)?
  - Is there sufficient evidence to conclude that a substance also has a BMF and/or TMF>1? (e.g., hazard assessment, monitoring, and compliance programs).

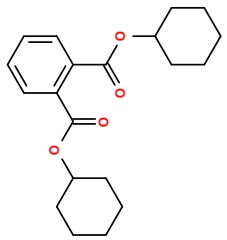
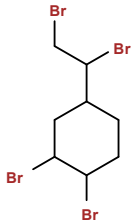
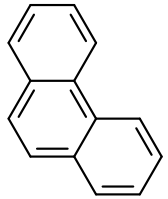
Integration of Lines of Evidence (LOE)

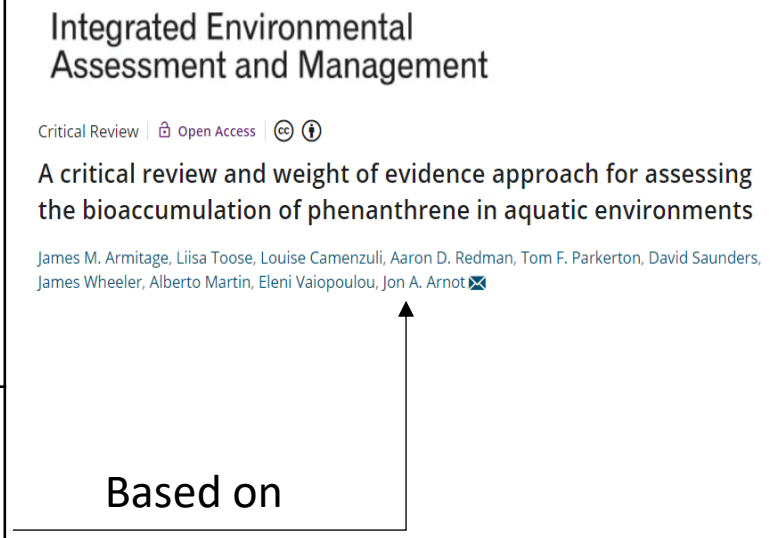


The goal of data evaluation is to be able to use the outcomes to assign a weight (or score) to the data such that an overall strength of evidence can be obtained to compare to the B hypothesis

Illustrative Case Studies

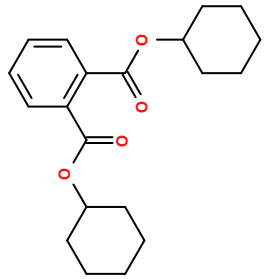
These are illustrative examples only and are not intended to reflect any specific regulatory decisions by any of the agencies involved in their development.

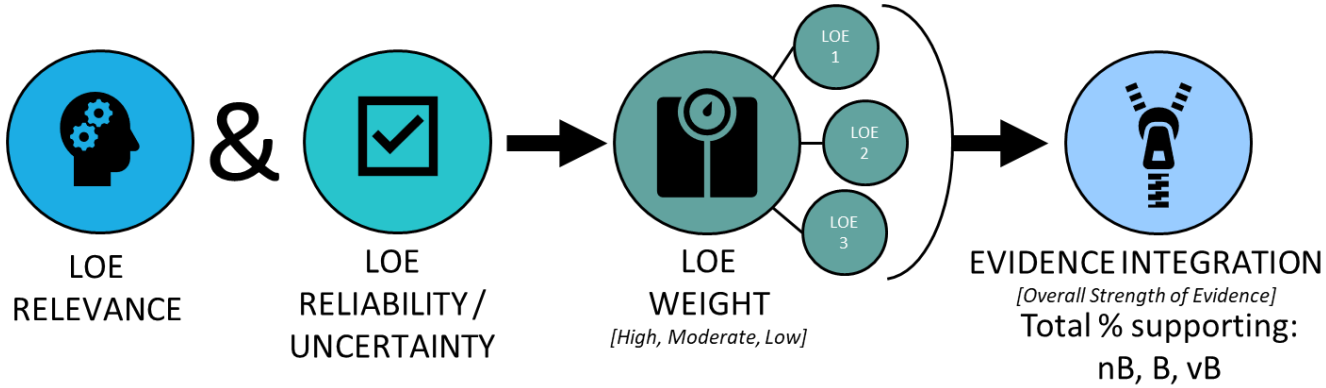
	Dicyclohexylphthalate (DCHP)	CAS 84-61-7	Log Kow = 6.18	DATA POOR
	1,2-Dibromo-4-(1,2-dibromoethyl)cyclohexane (TBECH)	CAS 3322-93-8	Log Kow = 4.33	
	Phenanthrene (PHE)	CAS 85-01-8	Log Kow = 4.47	DATA RICH



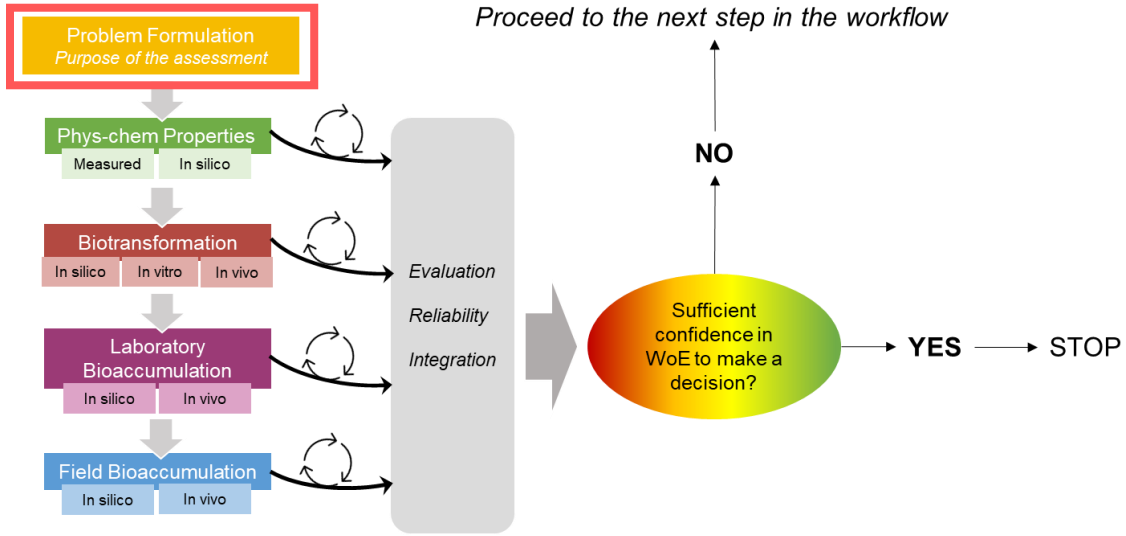
Dicyclohexylphthalate (DCHP)

CAS RN: 84-61-7



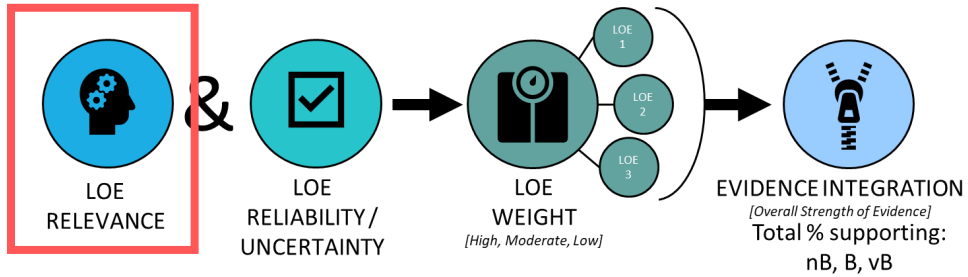


- Building a WoE: "data poor" example
- PROBLEM STATEMENT: Is there sufficient evidence to support the conclusion that DCHP is **bioaccumulative in fish** (i.e., bioaccumulation relative to water) using the "B" and "vB" criteria thresholds of 1000 and 5000, respectively?



Illustrative example only: not intended to reflect any specific regulatory decisions by any of the agencies involved in the OECD B IATA

Relevance Scores – DCHP

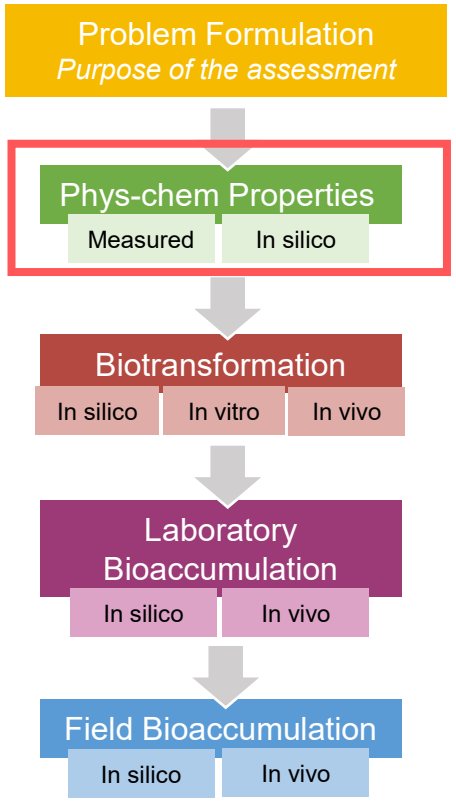


LoE description	Organism type	Relevance Score (0 = least; 5 = most)	Relevance Score Description
In silico lab BCF	Fish	4	Focus on fish; in silico lower score than in vivo
In silico BAF	Fish	4	Focus on fish; in silico lower score than in vivo
In silico BAF	Invert	0	Not relevant for this example; could be in other jurisdictions; higher uncertainty
In silico lab BMF	Fish	0	Criteria specific to BCF or BAF
In silico lab BMF	Rat	0	Focus on fish
In silico field BMF	Various	0	Criteria specific to BCF or BAF
In vivo lab BCF	Fish	5	Focus on fish; in vivo higher score than in silico
In vivo lab BCF	Invert	0	Not relevant for this example; could be in other jurisdictions; higher uncertainty
In vivo lab BMF	Fish	0	Not relevant for this example; could be in other jurisdictions; higher uncertainty
In vivo field BAF	Various	5	Focus on fish; in vivo higher score than in silico
In vivo field BMF	Various	0	Criteria specific to BCF or BAF
In vivo field TMF	Various	0	Criteria specific to BCF or BAF

Physicochemical properties - DCHP

Property (value used)	Value	Source
MW (330.42)	330.4	EAS-E Suite (www.eas-e-suite.com)
log K_{OW} (6.18)	6.18	KOWWIN_v1.69-AFC & IFSQSAR LogKOW-ppLLFER
	6.20	KOWWIN_v1.69-AFC
	6.17	IFSQSAR LogKOW-ppLLFER
	5.83	OPERA logP-KNN

- log K_{ow} > 4.5
- Although physicochemical property screening criteria are not specified, insufficient confidence to "decide"
- Proceed to next step of workflow



Experimental and estimated physical-chemical properties for DCHP. Values selected for this assessment are noted in parentheses in the first column. All values are model estimates unless otherwise noted.

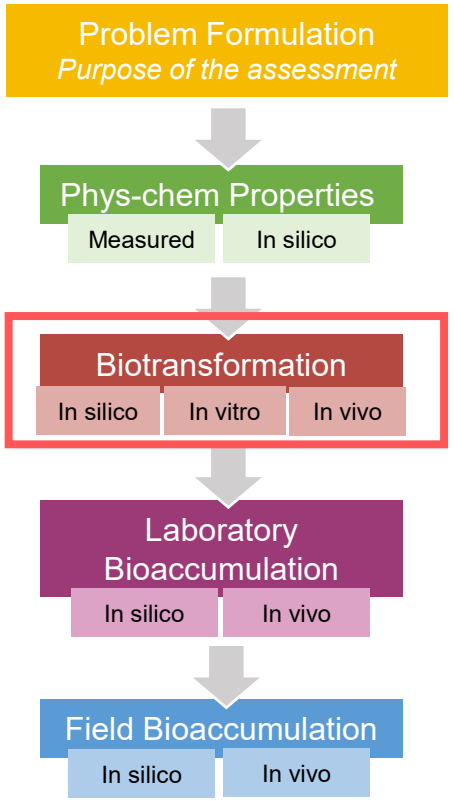
Biotransformation - DCHP

Whole-body biotransformation half-life (HL_B) predicted by OECD validated QSARs

Species	Value (h)	Source / notes
Fish (@ 0.01 kg)	**14.2**	IFSQSAR fhlb-IFS/QSARINS FishM1-Molecular descriptors/QSARINS FishM2-Molecular descriptors/QSARINS FishM3-Molecular descriptors (consensus of 4 values)
	20.4	IFSQSAR fhlb-IFS
	11.9	QSARINS FishM1-Molecular descriptors
	14.9	QSARINS FishM2-Molecular descriptors
	11.4	QSARINS FishM3-Molecular descriptors
	12.6	OPERA ver.2.6

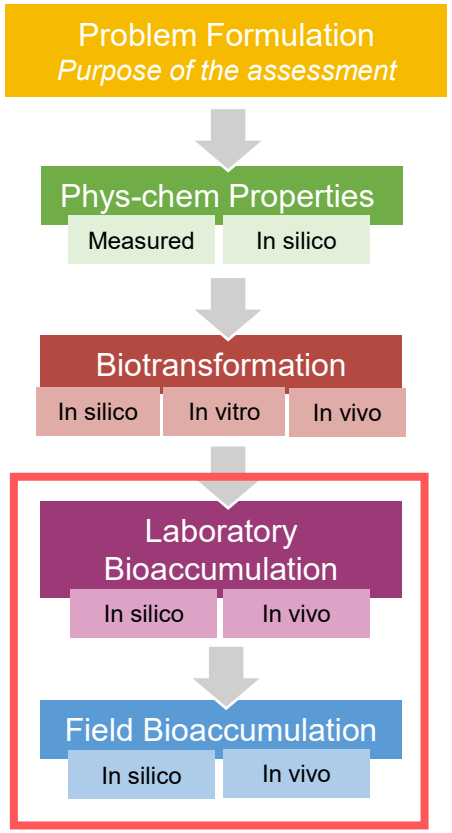
- 5 HL_B predictions very consistent
- Will use consensus of 4 modeled values (14.2 h)

***Reliability evaluation**: All half-life predictions are within the applicability domain and meet the QMRF criteria & QSAR DET*



In silico B predictions - DCHP

Metric	Value (L/kg-ww)	Model (In Silico)
In silico fish BCF 1	162	OPERA ver.2.6
In silico fish BCF 2	517	BET ver.0.9 – EAS-E Suite (representative lab fish) *
In silico fish BCF 3	**5750**	**BCFBAF – EPI Suite (regression-based estimate)**
In silico fish BCF 4	135	BCFBAF – EPI Suite (Arnot & Gobas; upper TL)
In silico fish BCF 5	185	BCFBAF – EPI Suite (Arnot & Gobas; mid TL)
In silico fish BCF 6	204	BCFBAF – EPI Suite (Arnot & Gobas; lower TL)
In silico fish BAF 1	137	BCFBAF – EPI Suite (Arnot & Gobas; upper TL)
In silico fish BAF 2	266	BCFBAF – EPI Suite (Arnot & Gobas; mid TL)
In silico fish BAF 3	795	BCFBAF – EPI Suite (Arnot & Gobas; lower TL)
In silico fish BAF 4	606	BET ver.0.9 – EAS-E Suite (planktivorous fish) *
In silico fish BAF 5	599	BET ver.0.9 – EAS-E Suite (benthic fish) *
In silico fish BAF 6	725	BET ver.0.9 – EAS-E Suite (omnivorous fish) *
In silico fish BAF 7	1010	BET ver.0.9 – EAS-E Suite (piscivorous fish) *

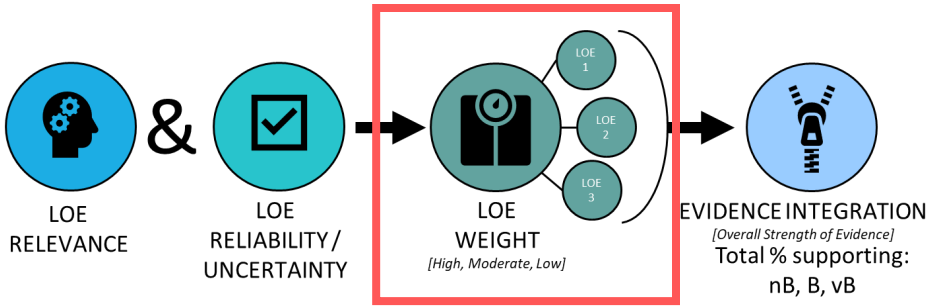


* In silico models run using consensus of 4 HL_B–QSAR predictions

Reliability evaluation: All in silico BCF and BAF predictions are within their applicability domain and meet the QMRF criteria & QSAR DET

- 5/6 in silico BCF model predictions indicate that DCHP is nB in fish (below 1000)
- 6/7 in silico BAF model predictions indicate the DCHP is nB in fish (below 1000)
- 2/13 predictions are above the B threshold (1 B, 1 vB)

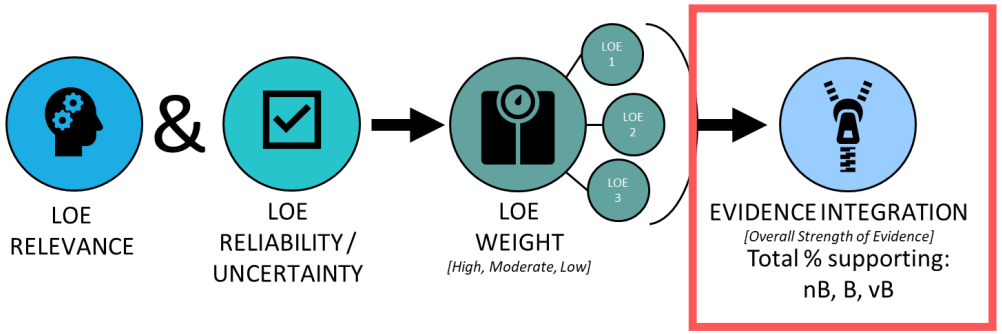
LoE Weight – DCHP



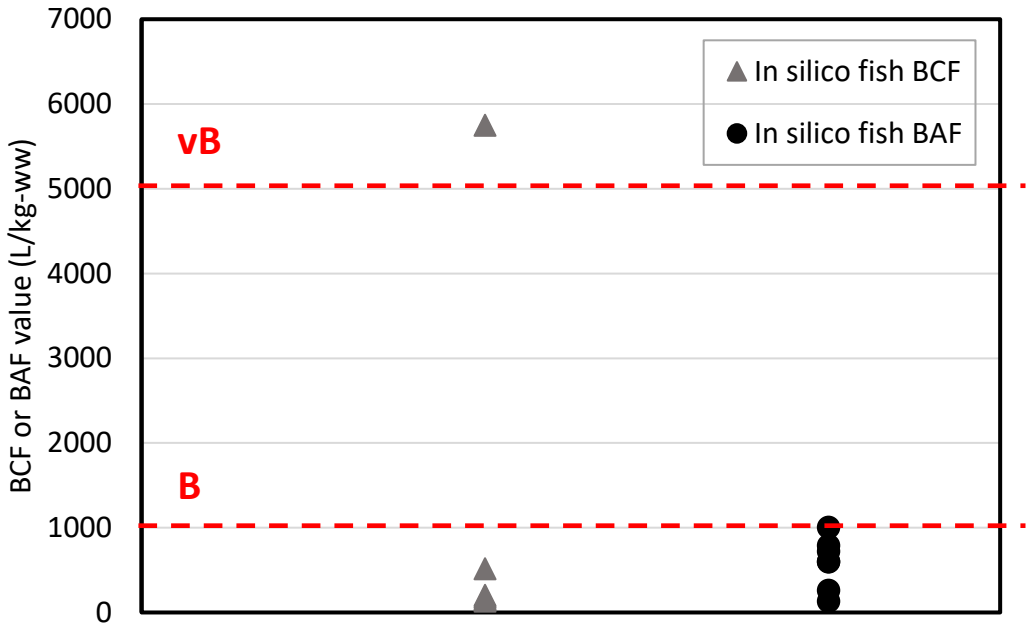
LoE	"B" cat.	Relevance	Data Reliability Score	LoE Weight
In silico fish BCF 1	nB	4	5	High
In silico fish BCF 2	nB	4	5	High
In silico fish BCF 3	vB	4	5	High
In silico fish BCF 4	nB	4	5	High
In silico fish BCF 5	nB	4	5	High
In silico fish BCF 6	nB	4	5	High
In silico fish BAF 1	nB	4	5	High
In silico fish BAF 2	nB	4	5	High
In silico fish BAF 3	nB	4	5	High
In silico fish BAF 4	nB	4	5	High
In silico fish BAF 5	nB	4	5	High
In silico fish BAF 6	nB	4	5	High
In silico fish BAF 7	B	4	5	High

Note: No in vivo or in vitro data available for this chemical

Evidence Integration - DCHP



LoE description	Organism	# LoE	Total # LoE	%nB	%B	%vB
In silico lab BCF	Fish	6	13	85%	7.5%	7.5%
In silico field BAF	Fish	7				



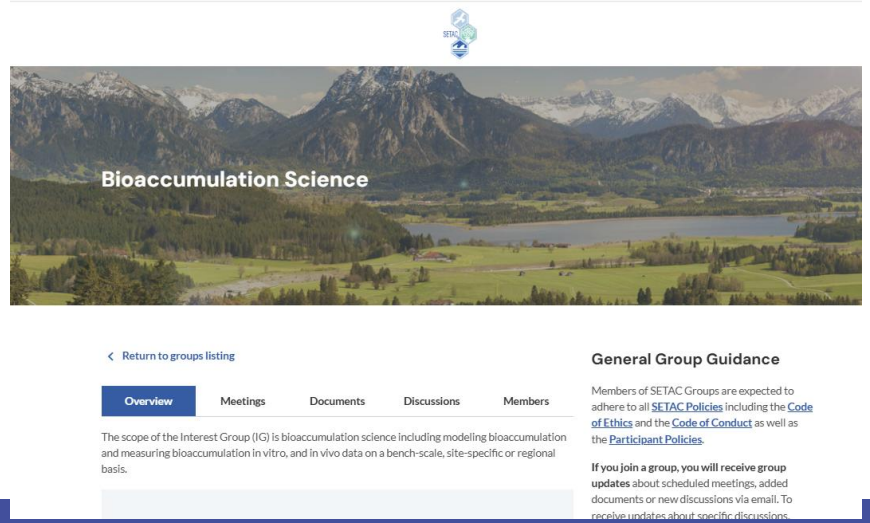
DCHP Summary

- DCHP is a very “data poor” chemical
- B assessment is limited to information from *in silico* modeling approaches
- Despite lack of empirical data, *in silico* predictions are relevant, high quality, and relatively consistent across multiple LoE
- Because no further data for this chemical are available, the decision could be made to utilize the general concordance of the various *in silico* model estimates to make a conclusion
- Alternatively, additional data could be collected…

Case study on the Use of Integrated Approaches for Testing and Assessment (IATA) for Bioaccumulation - Ninth Review Cycle (2023)

Additional related work

- **Ongoing work (via HESI Global and other partners):**
  - Case studies / applications of the IATA
  - IVIVE model for fish in vitro biotransformation methods (neutrals and IOCs)
  - Proposed revision of OECD GD280
  - *In vitro* fish biotransformation data collection
  - Evaluation / discussion of HYBIT (*Hyalella* BCF method)
  - Avian *in vitro* biotransformation method development (U of Saskatchewan)
  - Outreach and coordination via the SETAC Bioaccumulation Interest Group (BSIG)



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ICCS INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

NC 3Rs National Centre for the Replacement Refinement & Reduction of Animals in Research

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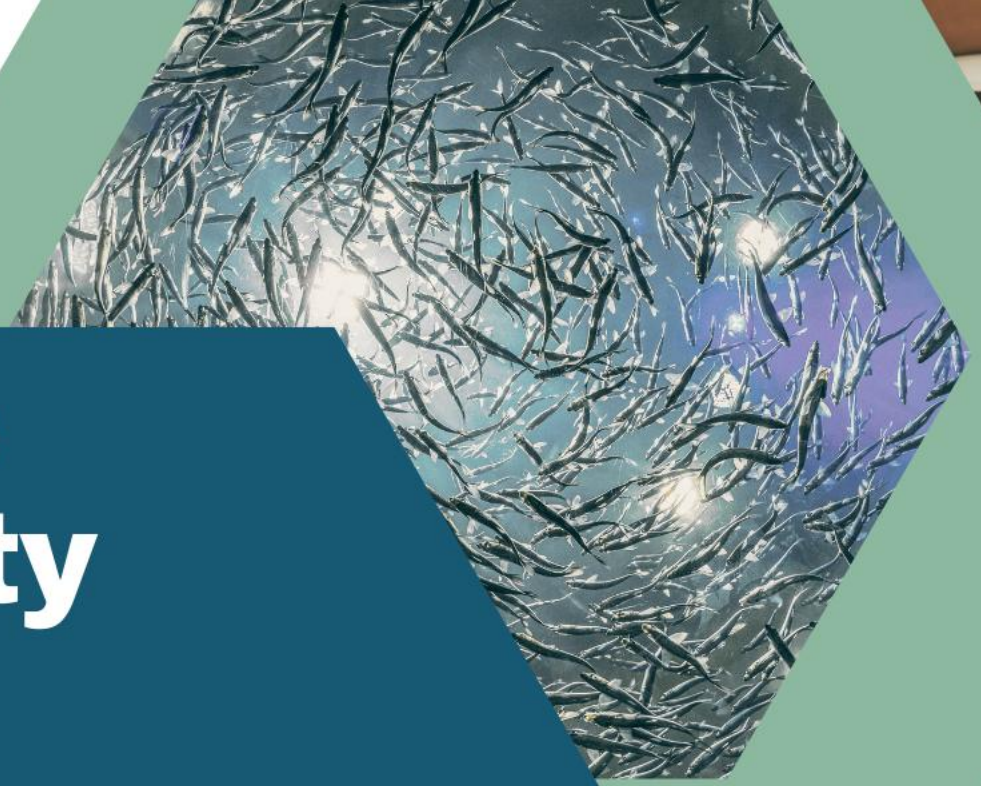

Innovate EcoSafety Summit

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THEMES

The End is Near: Replacing Acute *in vivo* Fish Testing

Endocrine Testing for Fish and Amphibians: Application of NAMs in ED Assessment

Thank you!

Acknowledgements:

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- Kellie Fay (US EPA, USA)
- Heike Laue (Givaudan, Switzerland)
- Alessandro Sangion (ARC Arnot Research & Consulting, Canada)
- HESI Next Generation Risk Assessment Committee
- OECD IATA Commenters!

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