Development of a new framework advancing the integration of New Approach Methodologies in Environmental Risk Assessment

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SERS
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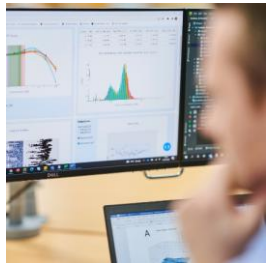

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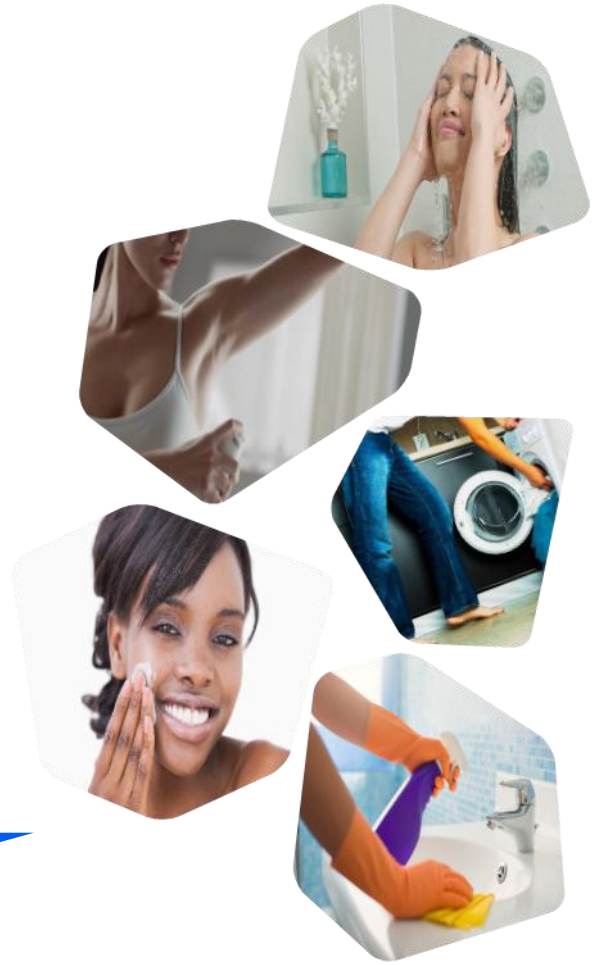
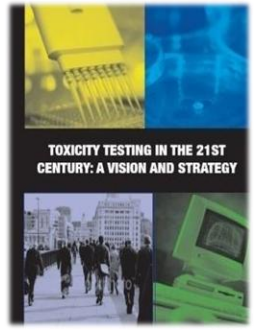
Safety science: what can we do better?

Ensuring that the use of ingredients in our products is **safe** for the receiving environment **YET…**



*NGRA is defined as **an exposure-led**, **hypothesis-driven** risk assessment approach that **integrates New Approach Methodologies (NAMs)** to assure **safety without the use of animal testing***



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New approach methodologies (NAMs)

modified *from Amelie Ott, ICCS*

NAMs are NOT
1:1 replacement to animal tests

Instead
1 NAM = 1 block

different combination can address different endpoints

- NAMs provide **mechanistic information** on the mode of action, potency, and variability of chemical effects
- NAMs **reduce ethical concerns** associated with animal testing
- NAMs can be used **in combination with, or replace existing animal data entirely**, depending on the regulatory context and the level of confidence and validation

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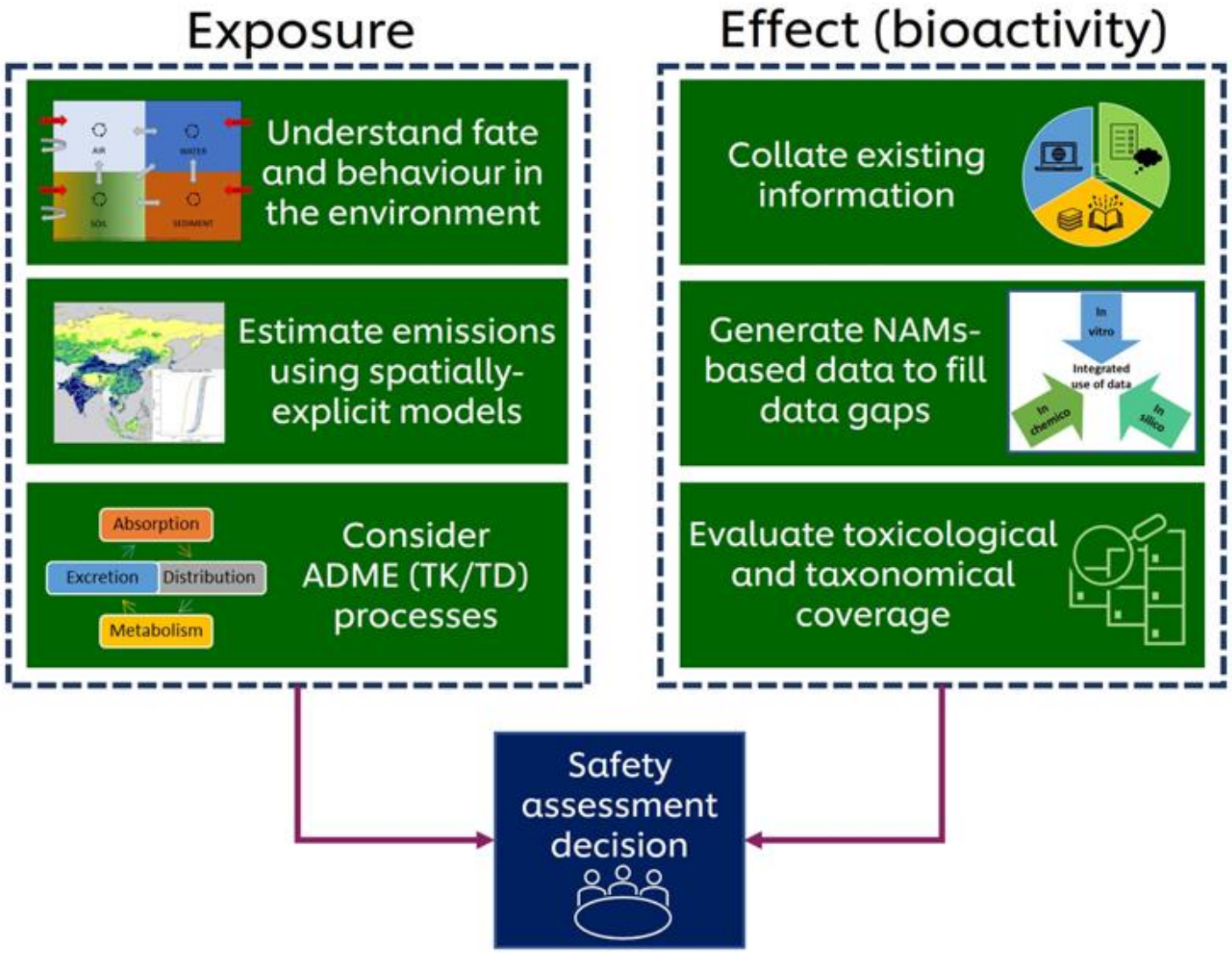
Next Generation Environmental Risk Assessment

Establishing enhanced environmental protection through NexGen, mechanistic based environmental risk assessment paradigm shift

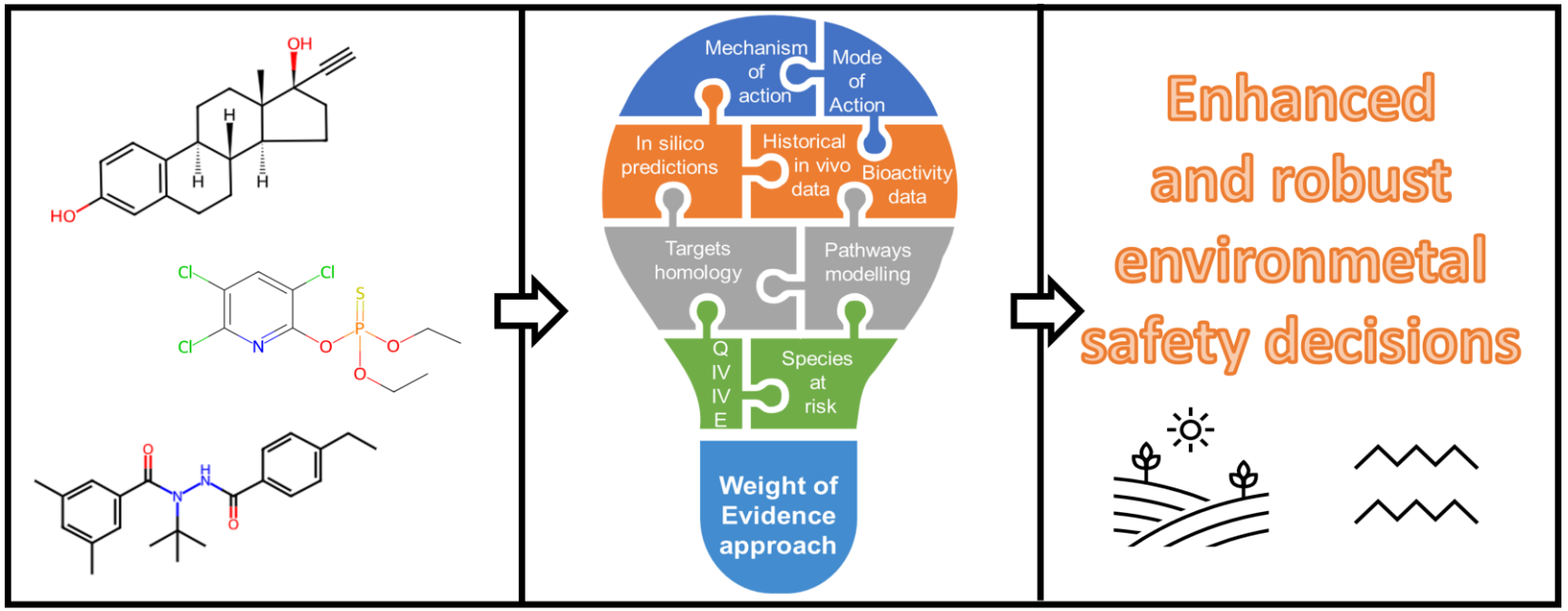


Rivetti & Campos (2023) IEAM

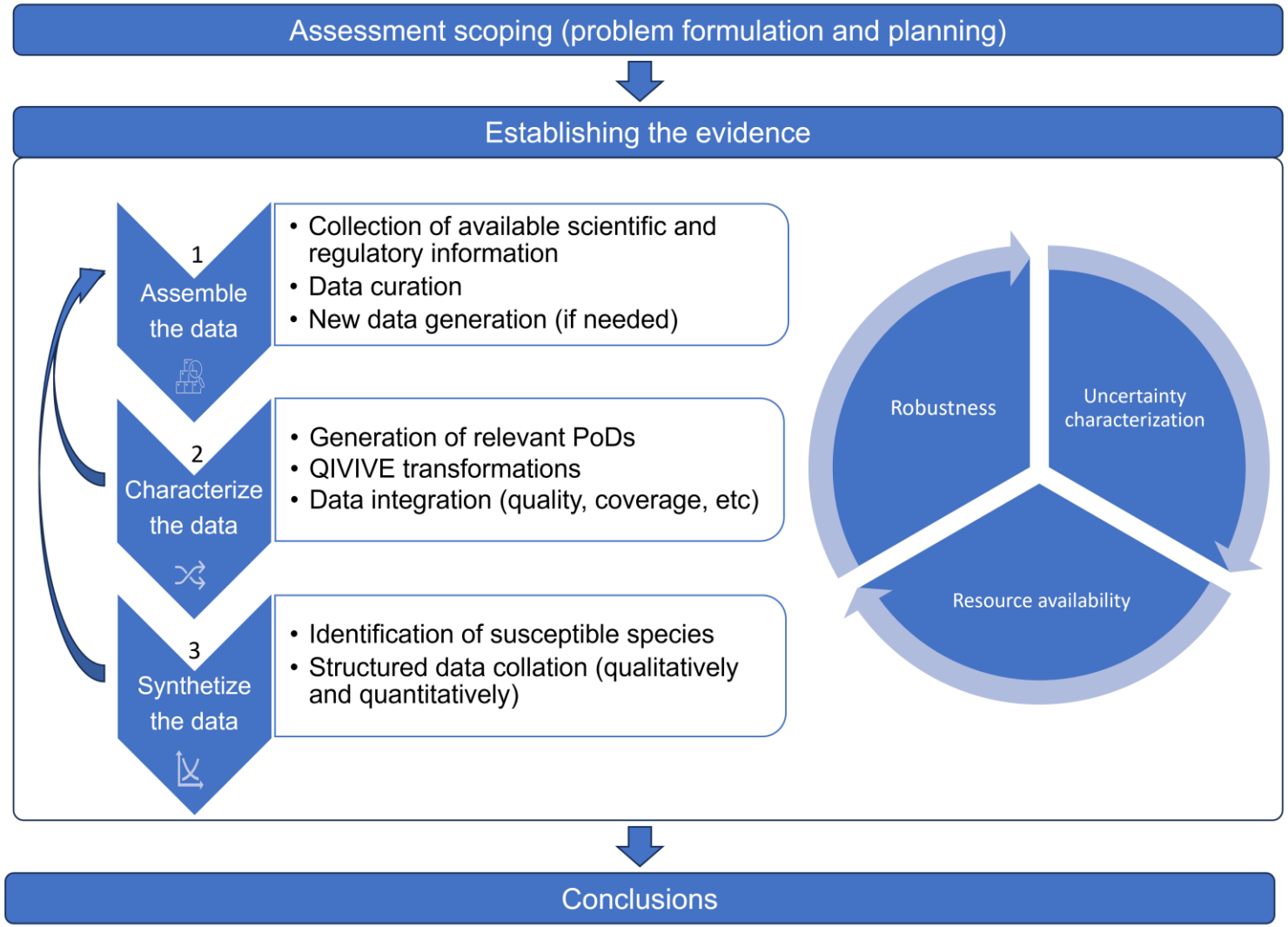
Objectives

➢ To develop an operating framework integrating all available information within environmental safety assessment

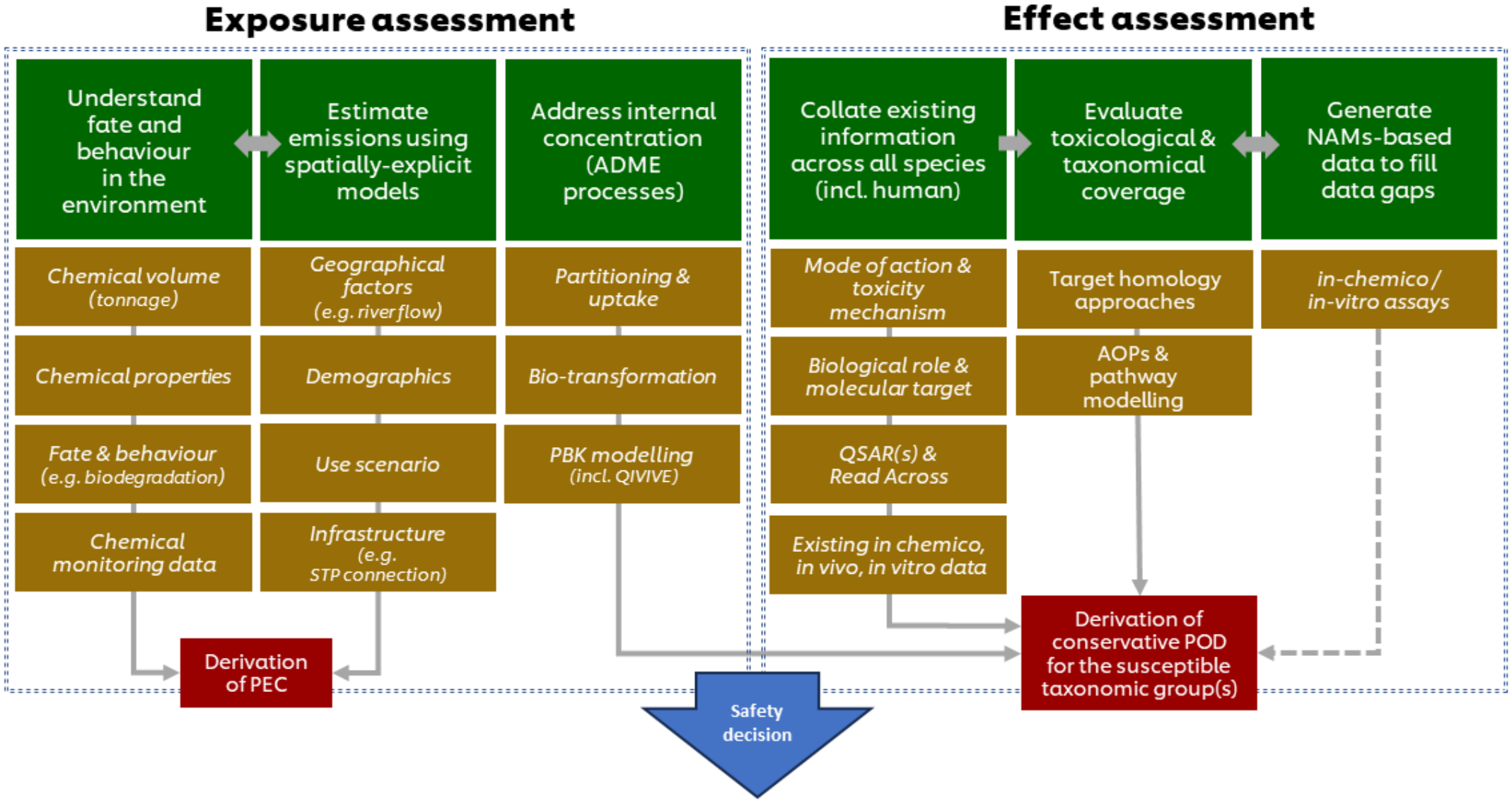
➢ To conduct case-studies to test the framework and the suitability of mechanistic-based information to support and strengthen current Environmental risk assessment practice



Development and data gathering of an environmental safety assessment



This framework aims to create a **tailored, integrated use of NAMs** and accelerate their adoption, building confidence in their validity and utility for ERA and regulatory decision-making.



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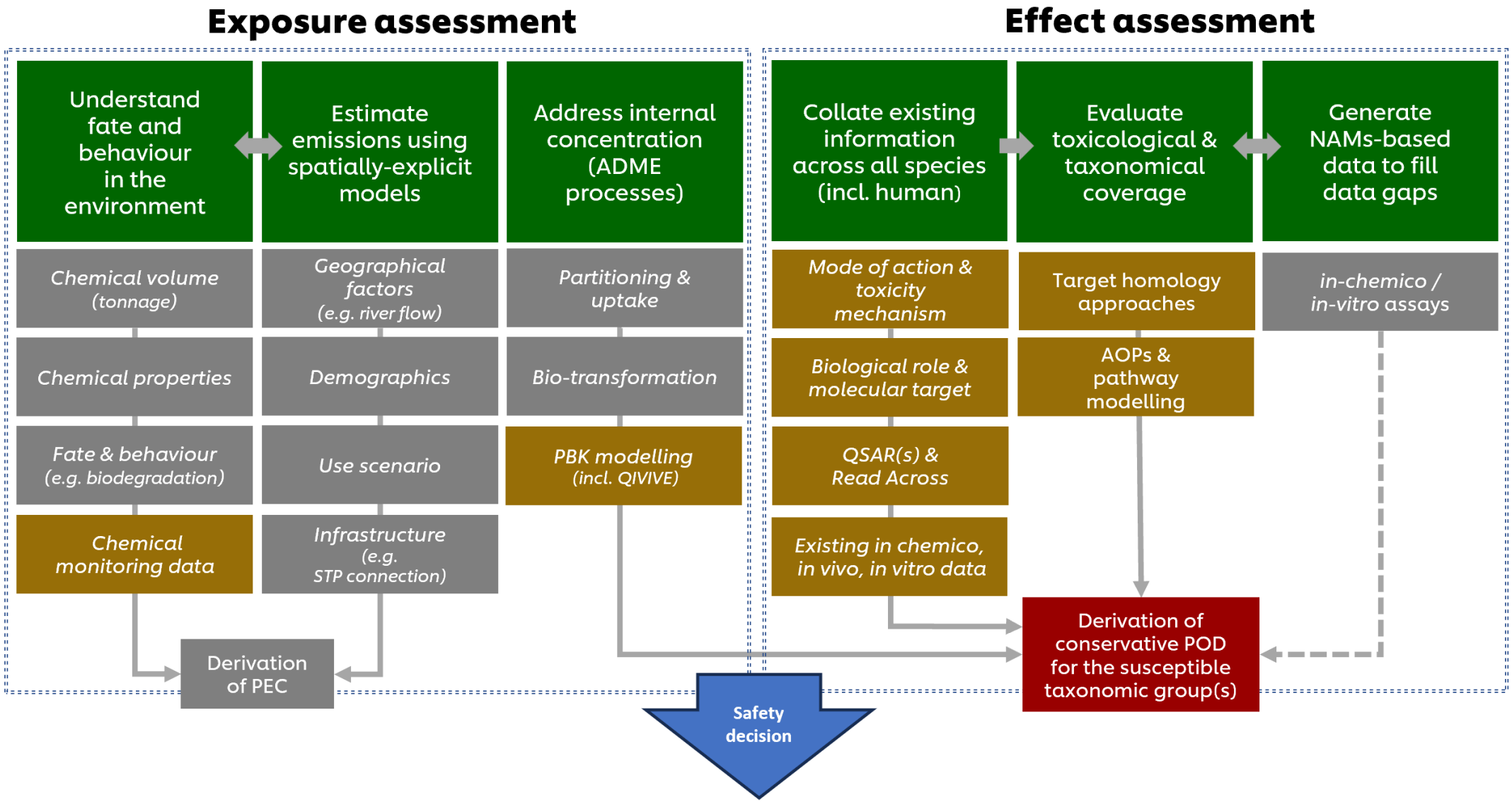
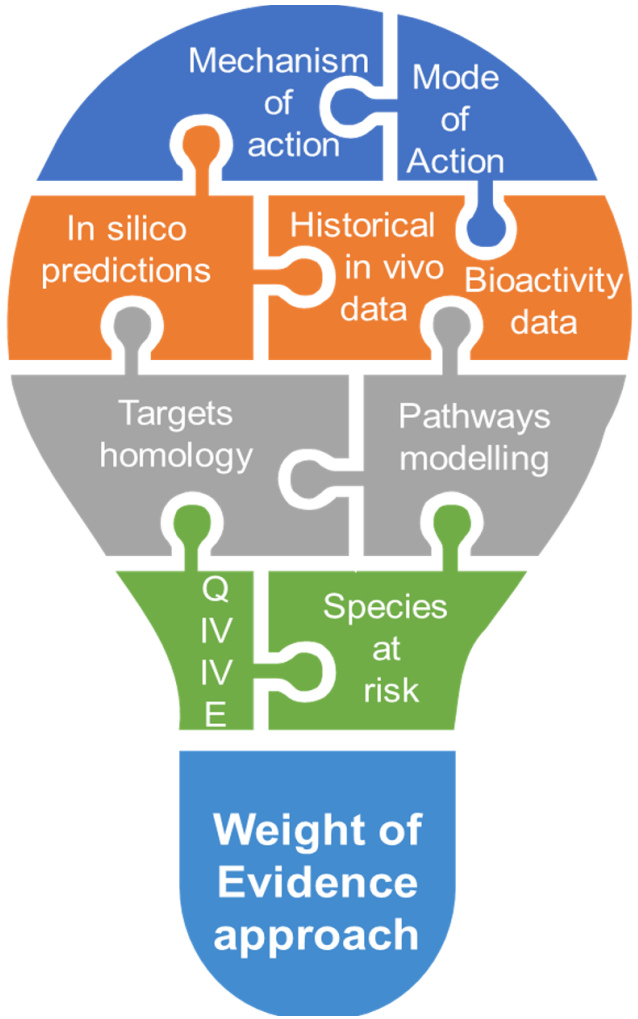


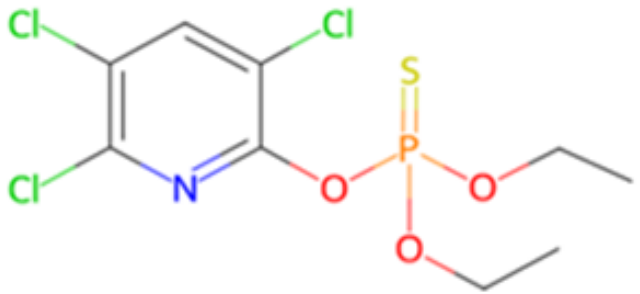
Case study for today

✓ **Chlorpyrifos (CPS)**



Data type	Scope	Data source
In silico	Mode of Action/ Toxicity mechanism	OECD Toolbox
		ChemProp
		EnviroTox
		Sapounidou-Firmin scheme
	Biological role/ molecular target	DrugBank
		ChemSpider
		ChEBI
		PubChem
	Cross-species extrapolation	EcoDrug
		SeqAPASS
		G2P-SCAN
	Adverse Outcome Pathway	AOP-WIki
	Aquatic toxicity	EpiSUite
In vitro	Bioactivity	ToxCast / Tox21
(Historical) In vivo	Aquatic toxicity	EnviroTOX
		ECOTOX db
Exposure	Chemical monitoring	NORMAN EMPODAT db

Chlorpyrifos (CPS)



MOA profilers:

- ***reactive*** - OASIS (Kienzler et al., 2019)
- ***specifically acting*** - Verhaar (Verhaar et al., 1992)
- ***related to acetylcholinesterase inhibitions*** - ASTER (Russom et al., 1991), Russom (Russom et al., 1997), and TEST (Barron et al., 2015)
- ***specifically acting*** (confidence score 3/3) - consensus MOA from EnviroTox (Kienzler et al., 2019).

MechOA profilers:

- ***AChE inhibitor (organophosphate)***" - MIE tool (Firman et al., 2022; Sapounidou et al., 2021)
- ***"acetylcholinesterase inhibition for animals"*** and probable ***"other esterases inhibition for all species"*** - MechoA classification scheme (Bauer et al., 2018)

acetylcholinesterase inhibitor

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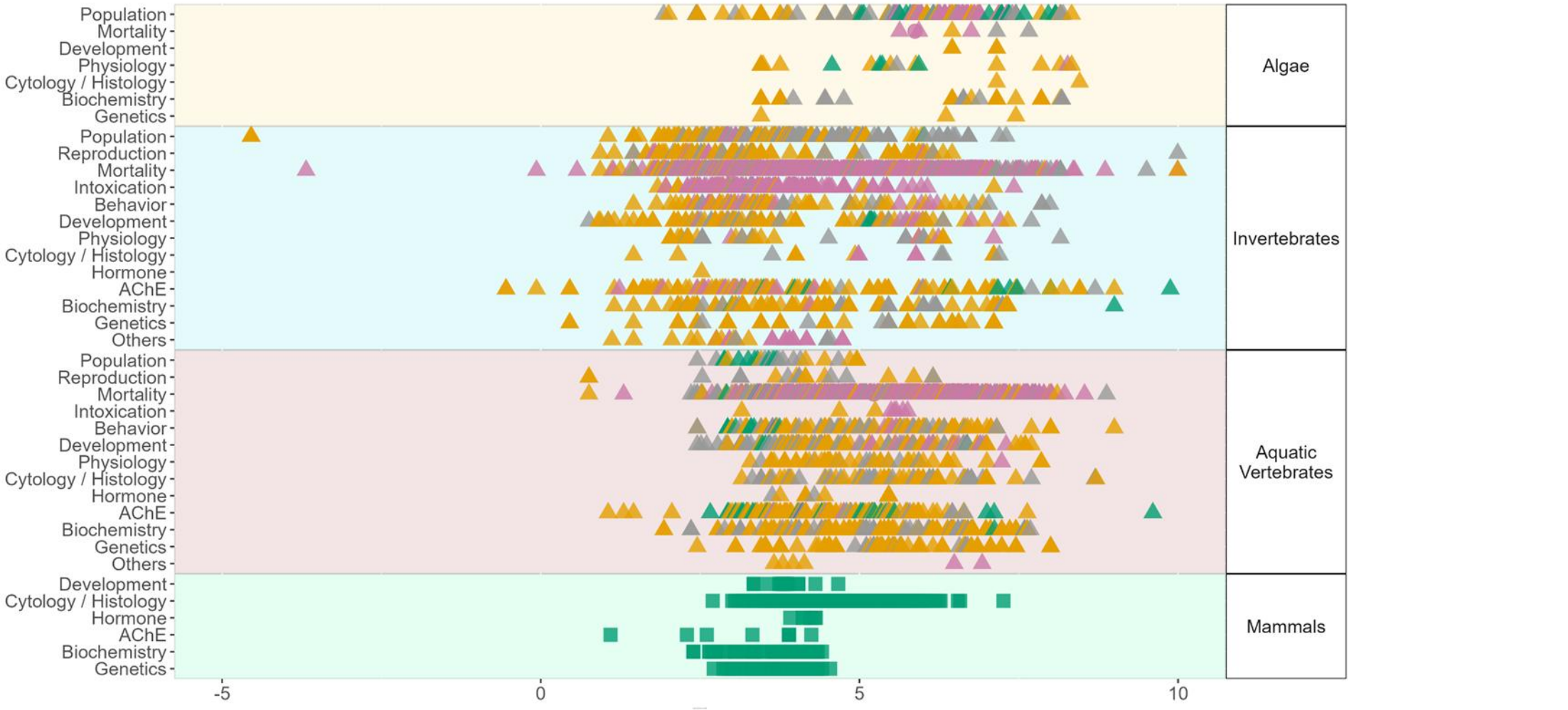
Chlorpyrifos (CPS)

- ✓ **A total of 10131 bioactivity data points were extracted from available sources**



Chlorpyrifos (CPS)

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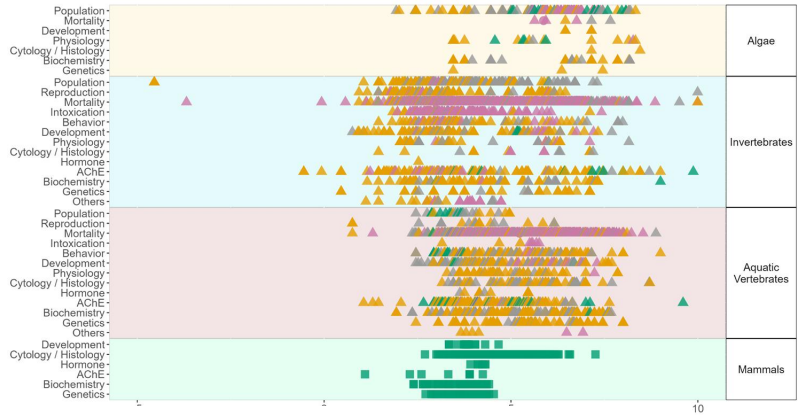
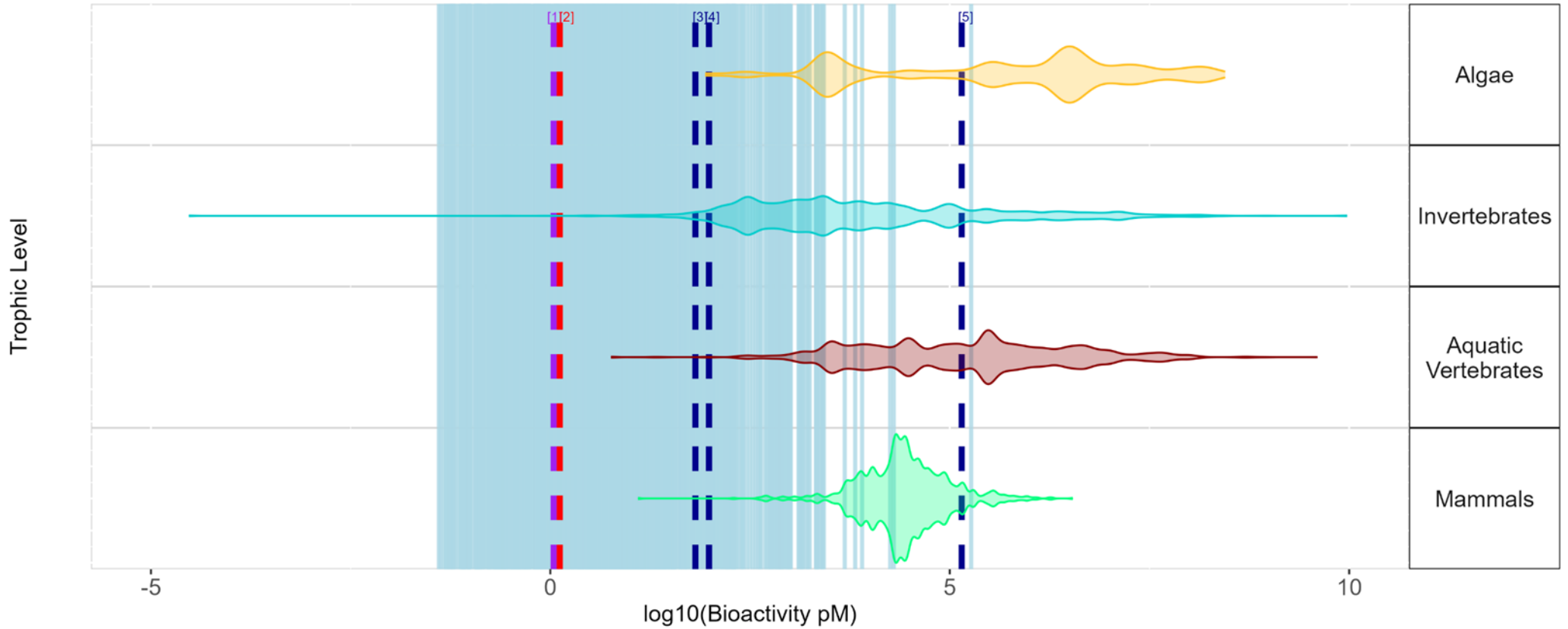


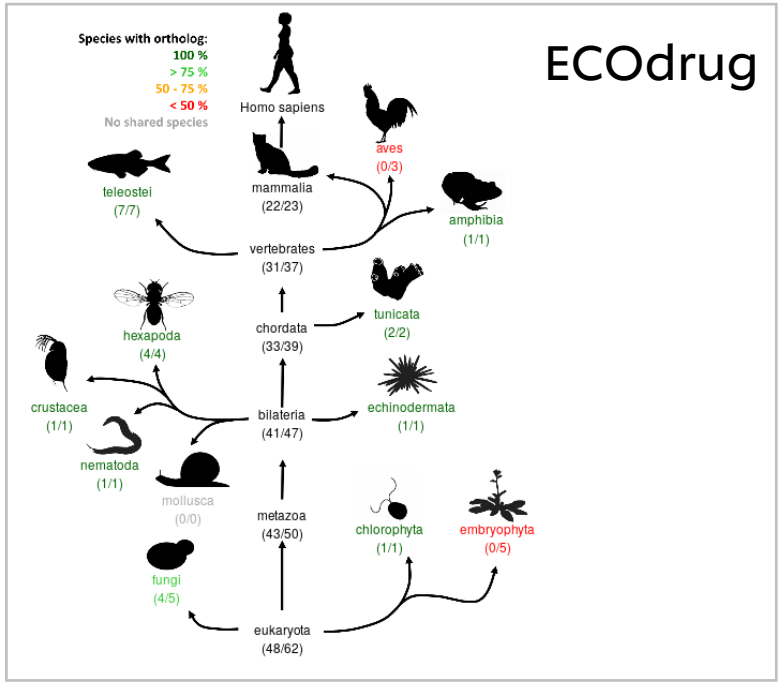
Reference Lines

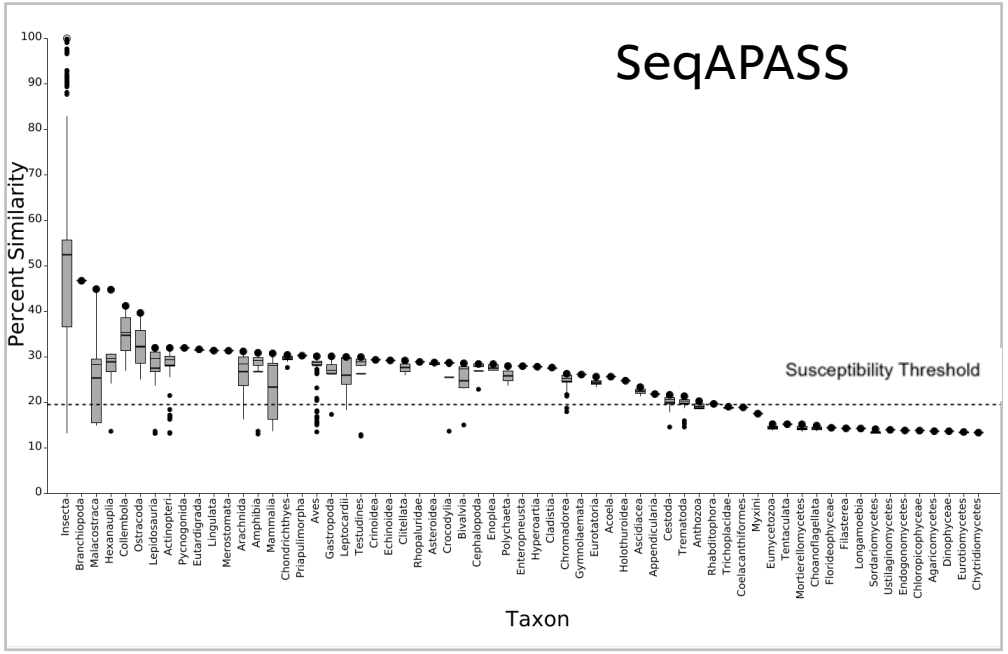
- Chemical Monitoring
- PNEC
- SSD
- EQS

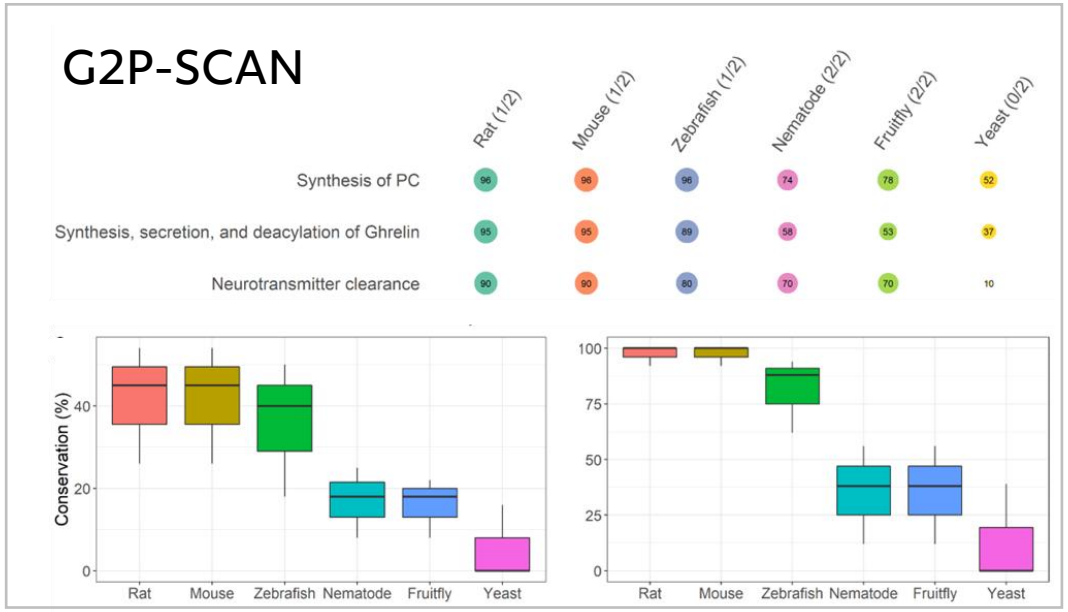


Chlorpyrifos (CPS)

- ✓ **Phylogenetic target conservation analysis**







LaLone et al., 2016
Rivetti et al., 2023
Verbruggen et al., 2018

Take-home messages

Overall, we demonstrated that:

☺ evolutionary conservation of targets and toxicological responses are aligned, identifying the biological space at risk;

☺ a WOE approach combining conventional data with NAMs-based mechanistic information can be protective for environmental safety;

☺ there is potential for harmonizing human health and environmental safety, encouraging synergies and cross-development of NAMs for chemical assessment and regulatory decisions.

Benefits

- ✓ reduce / replace animal testing
- ✓ increase the efficiency and reliability of chemical safety assessment
- ✓ address the complexity and diversity of environmental effects and exposures

Challenges

- ✓ ensure the relevance and applicability of NAMs to ecological endpoints and species
- ✓ validate and standardize NAMs for regulatory acceptance and harmonization
- ✓ integrate and interpret NAMs data in a weight-of-evidence approach

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Thank You

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