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

Dr. Bruno Campos...
and many colleagues!

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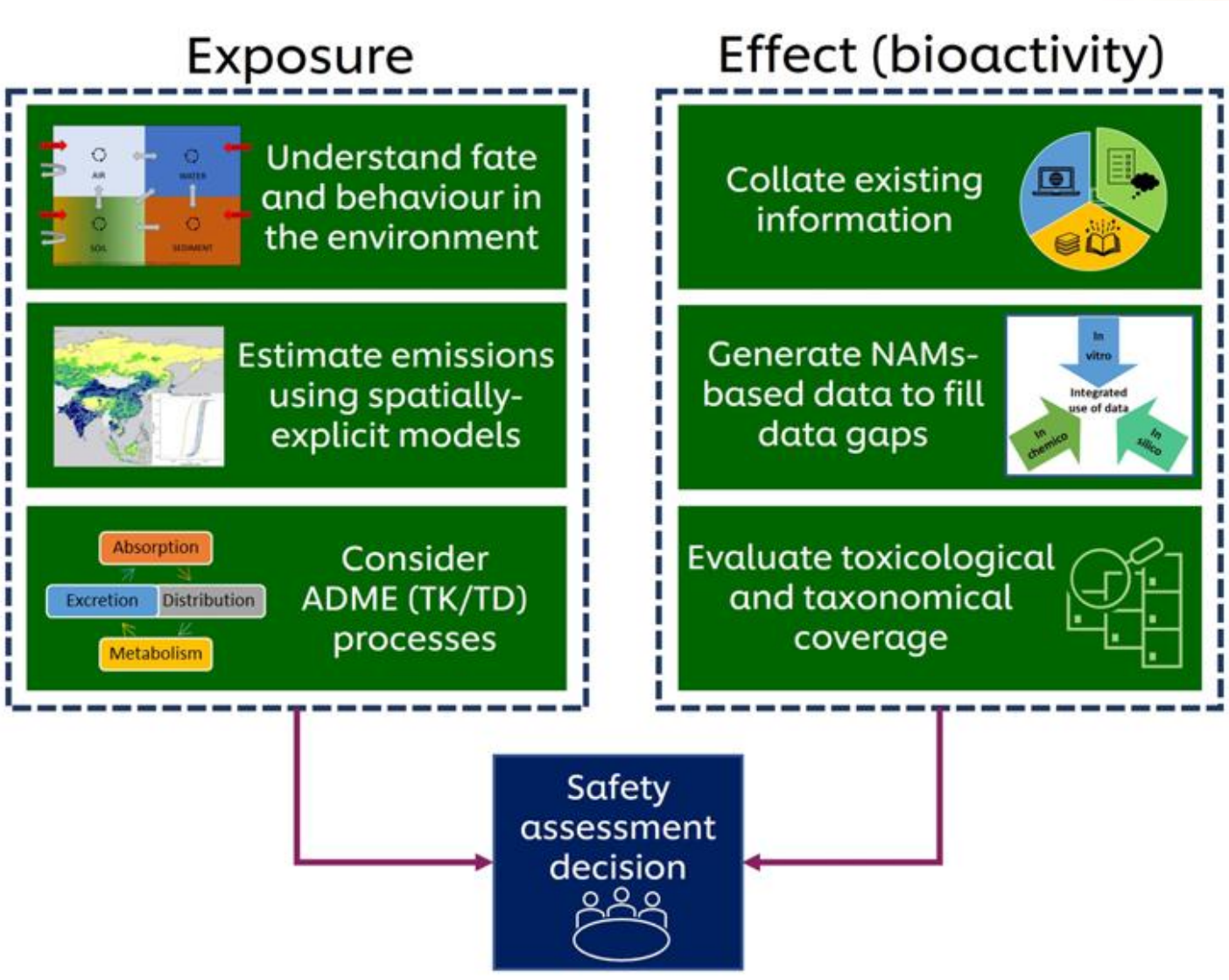





Next Generation Environmental Risk Assessment

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Establishing enhanced environmental protection through NexGen, mechanistic based environmental risk assessment.



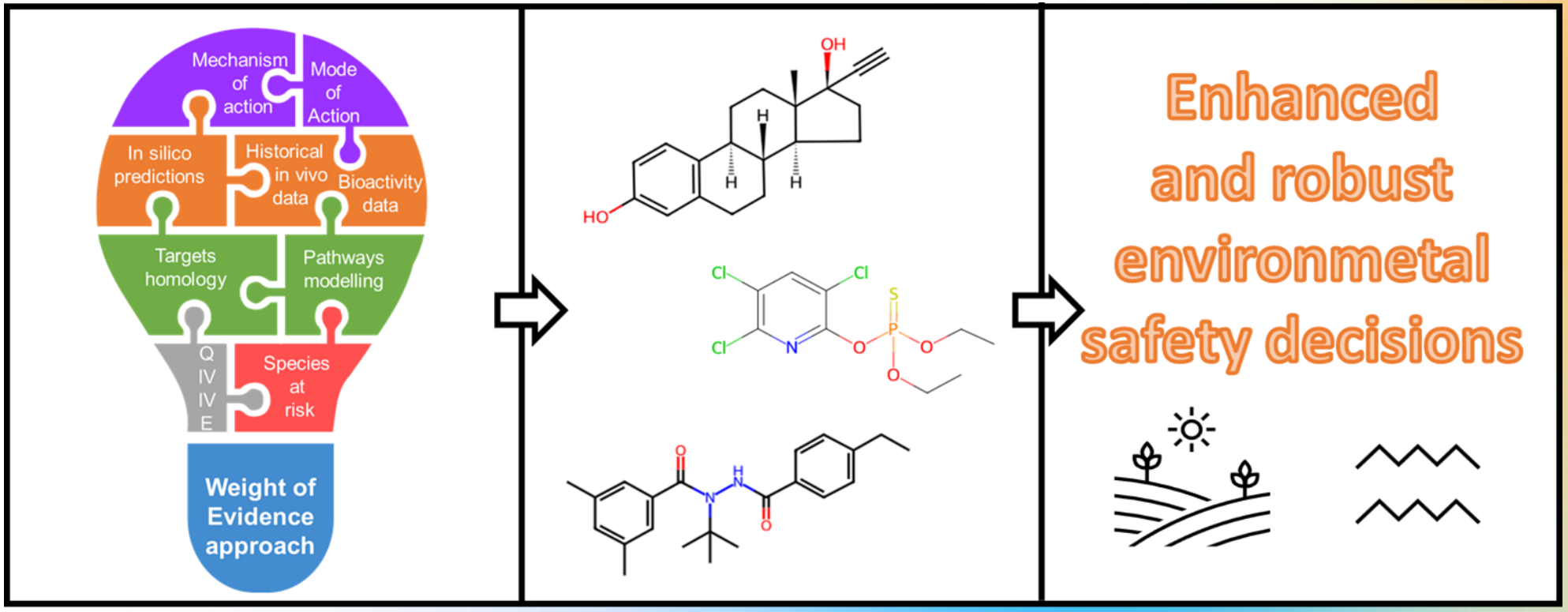
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Key Objective

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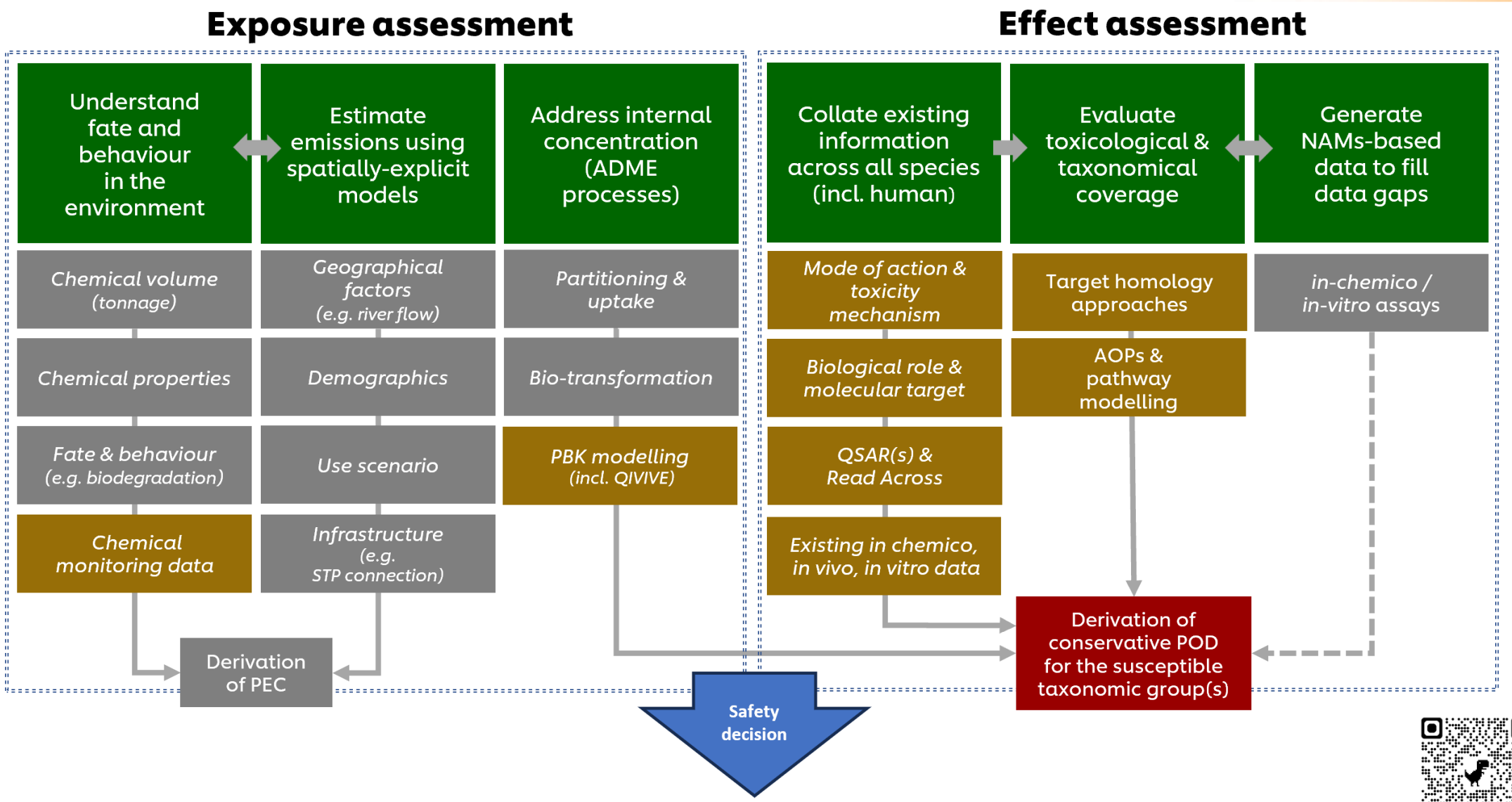
- To develop an operating framework integrating all available information within environmental safety assessment

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



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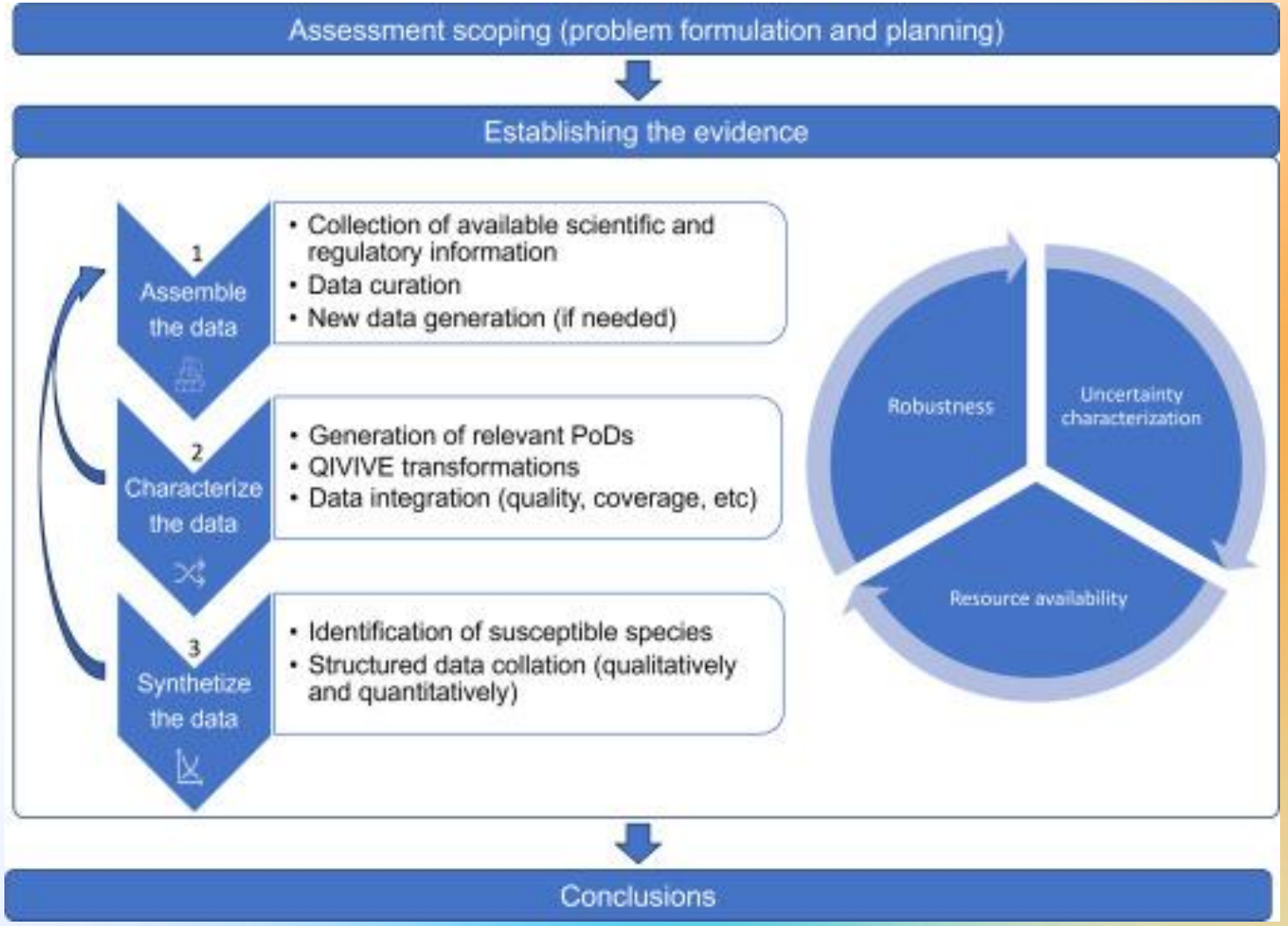
This framework aims to create a **tailored, integrated use of NAMs** and accelerate their adoption, building confidence in their validity and utility for ERA and regulatory decision-making.



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3 Case studies to test the framework

I. Chlorpyrifos
II. 17a-Ethynylestradiol (EE2)
III. Tebufenozide

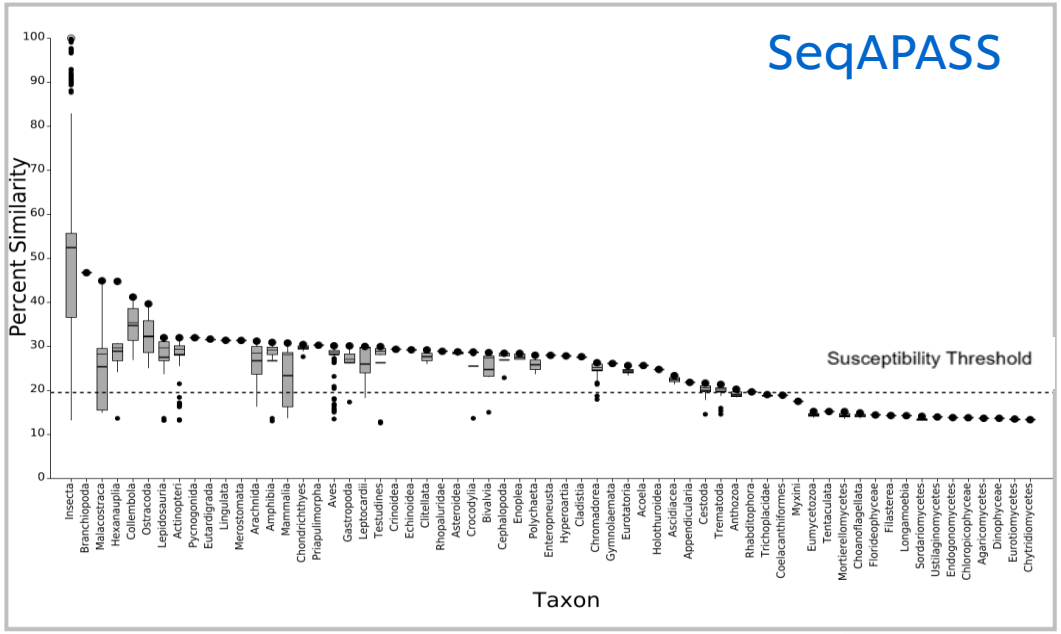


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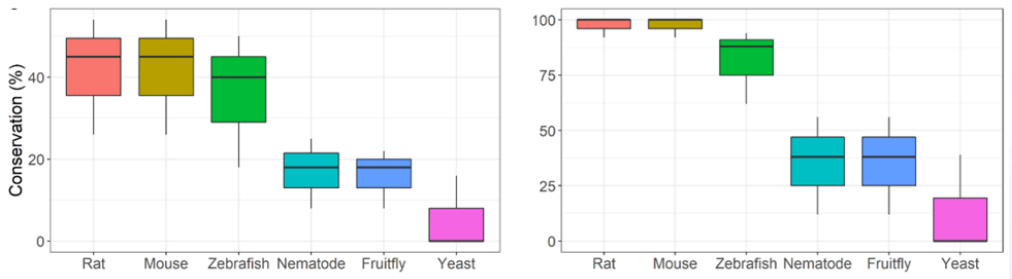
Chlorpyrifos (CPS)

✓ Phylogenetic target conservation analysis

SeqAPASS



G2P-SCAN

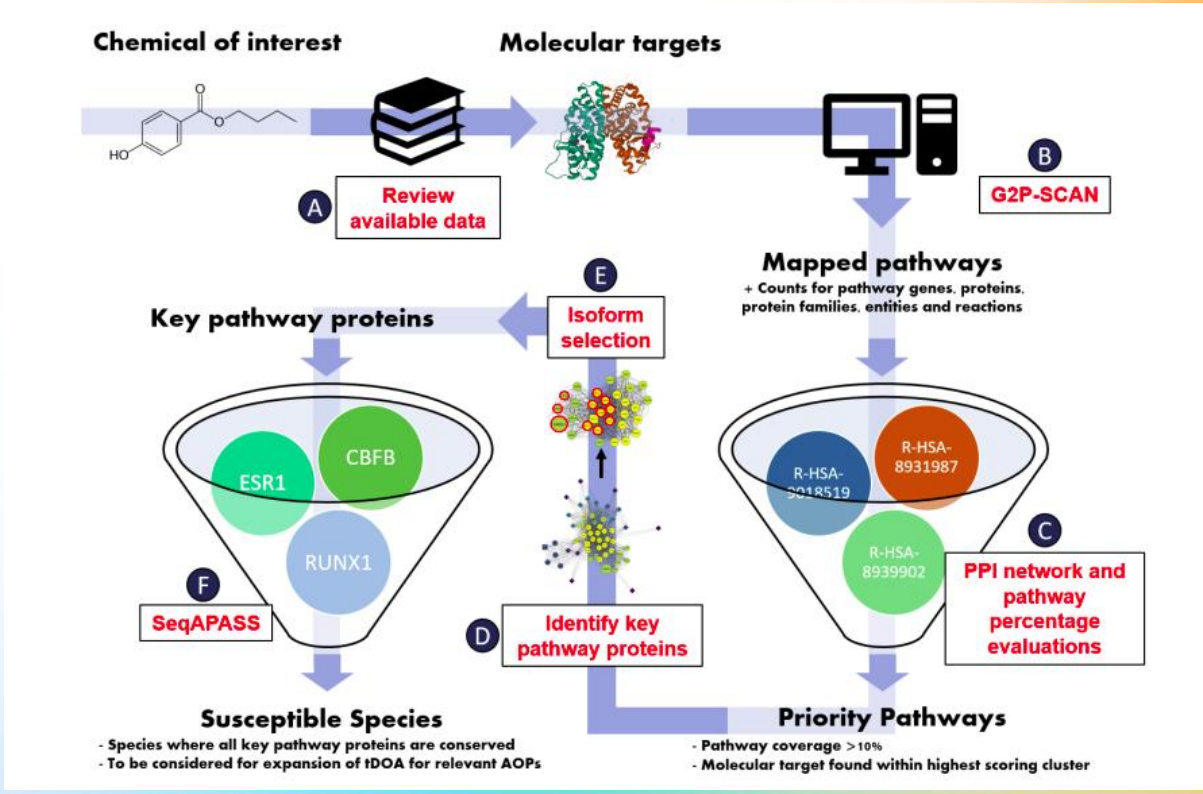


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LaLone et al., 2016
Rivetti et al., 2023

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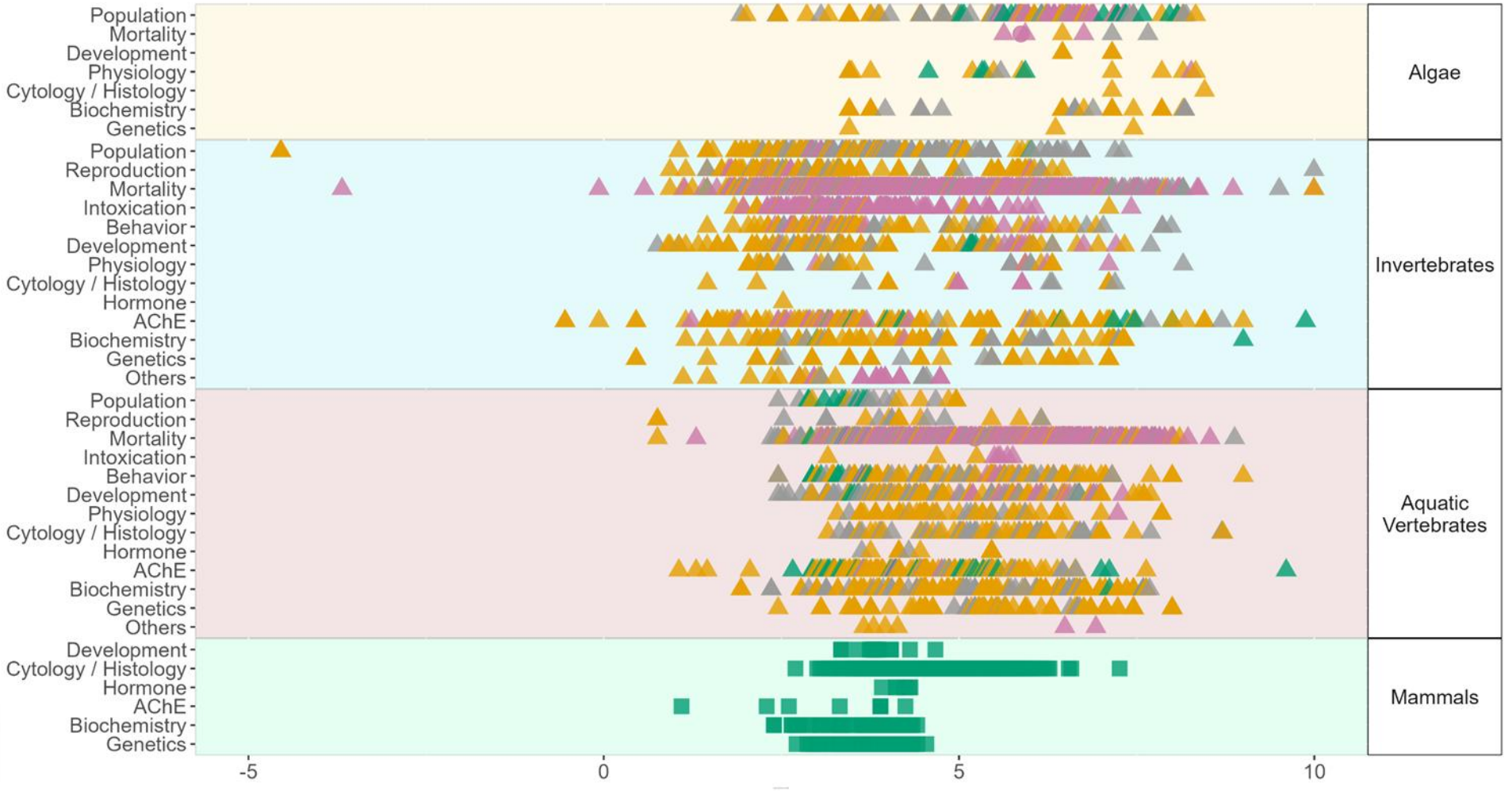
OECD Series on Testing and Assessment No. 415: Case studies for the IATA in the application of combined bioinformatics approaches for cross species extrapolation of toxicity knowledge to inform chemical safety



Chlorpyrifos (CPS)- *AChE inhibitor (organophosphate)*

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



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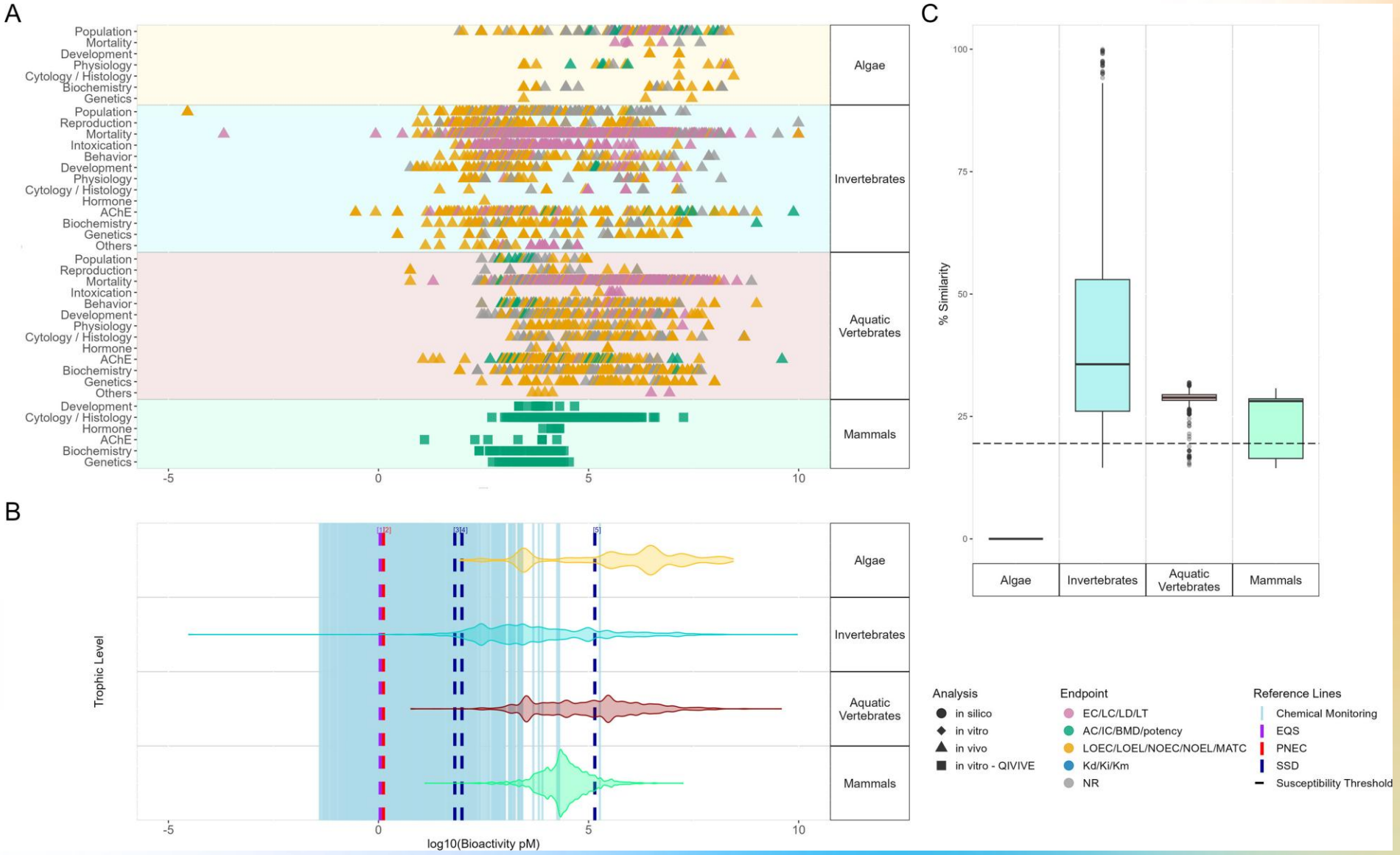
Analysis
- in silico
- in vitro
- in vivo
- in vitro - QIVIVE

Endpoint
- EC/LC/LD/LT
- AC/IC/BMD/potency
- LOEC/LOEL/NOEC/NOEL/MATC
- Kd/Ki/Km
- NR

Chlorpyrifos (CPS)- *AChE inhibitor (organophosphate)*

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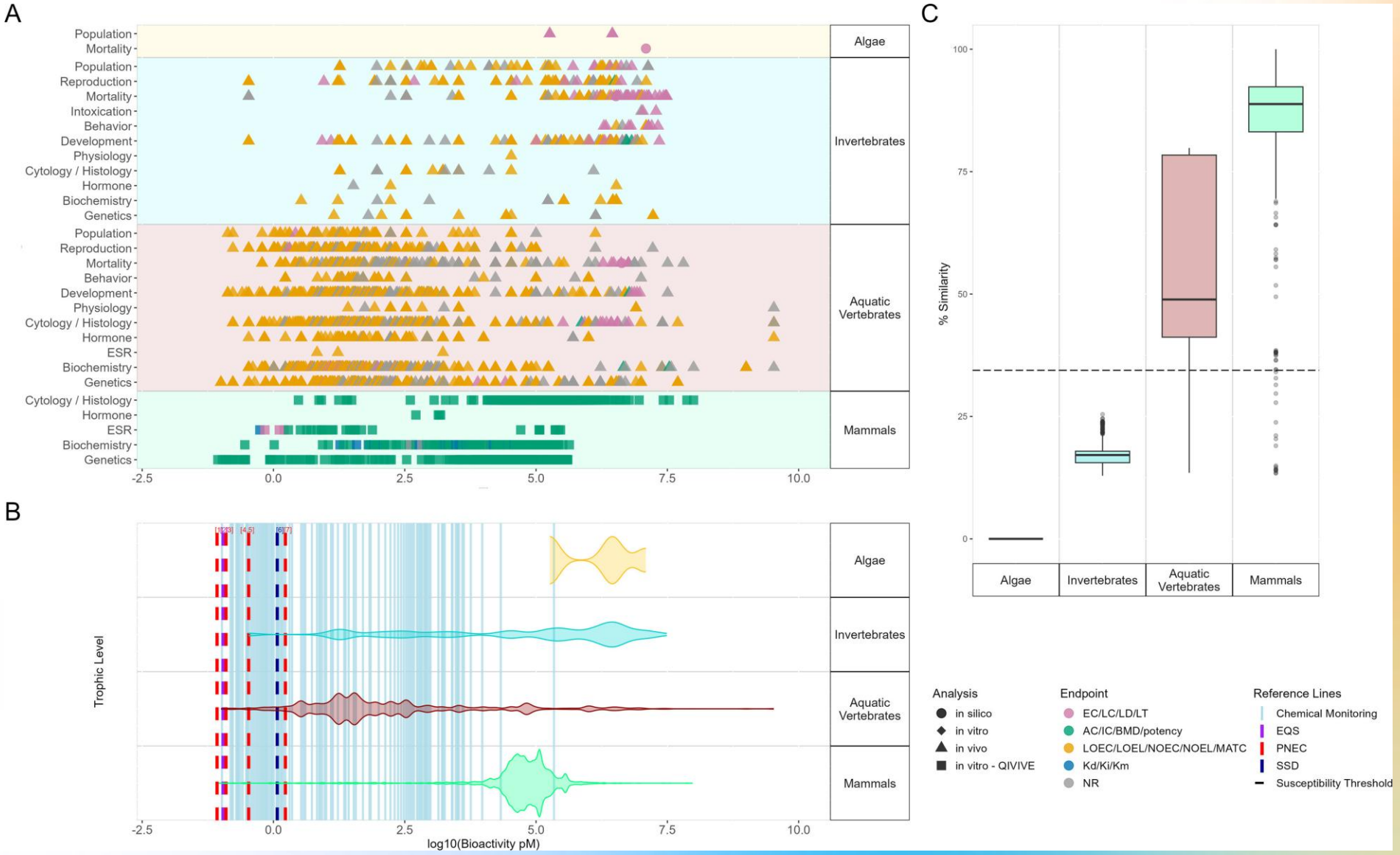
✓ A total of 10131 bioactivity data points were extracted from available sources



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17α-Ethynylestradiol (EE2)- Oestrogen receptor agonist

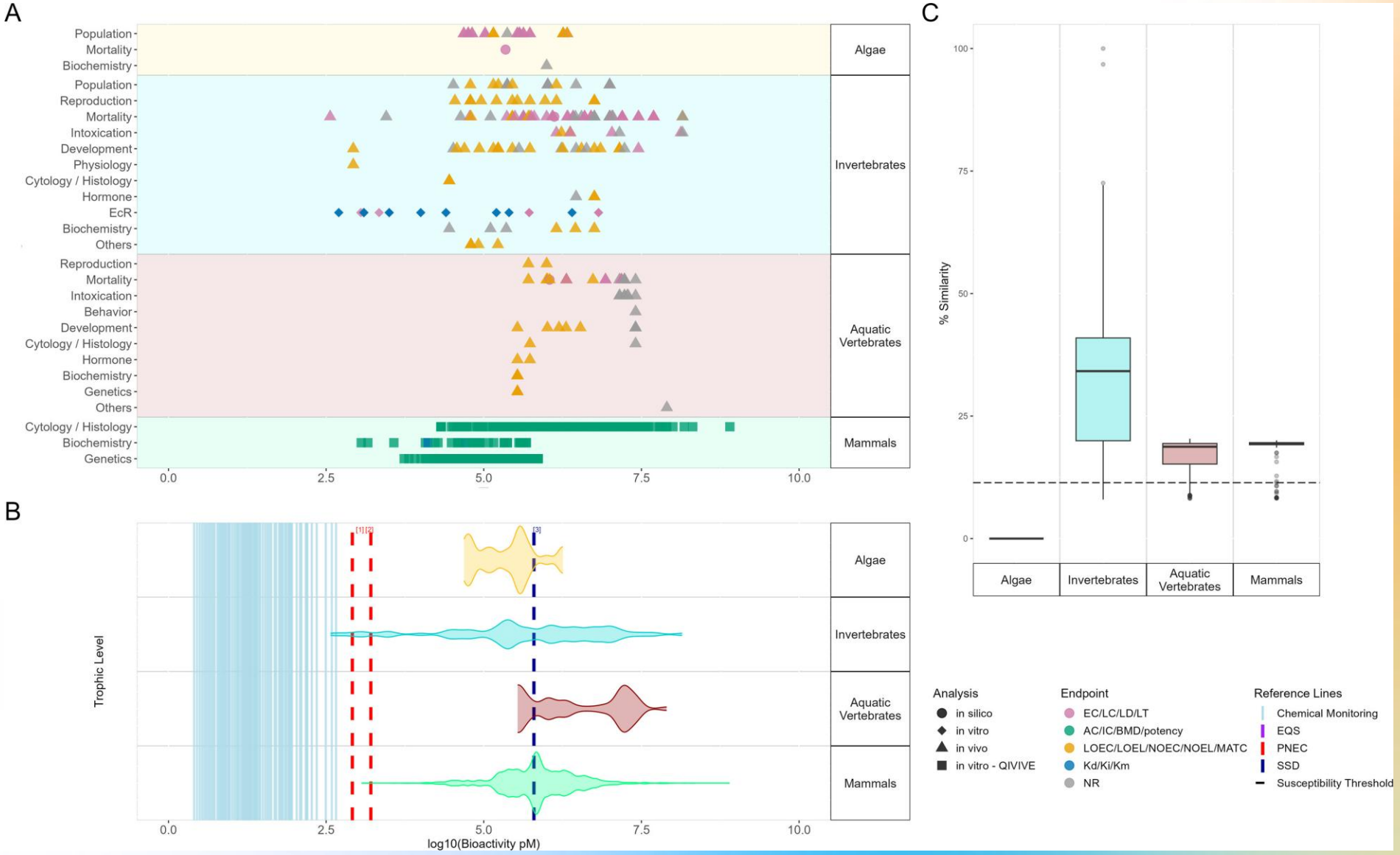
- ✓ A total of 8004 bioactivity data points were extracted from available sources



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Tebufenozide- Ecdysone receptor agonist

- ✓ A total of 2129 bioactivity data points were extracted from available sources

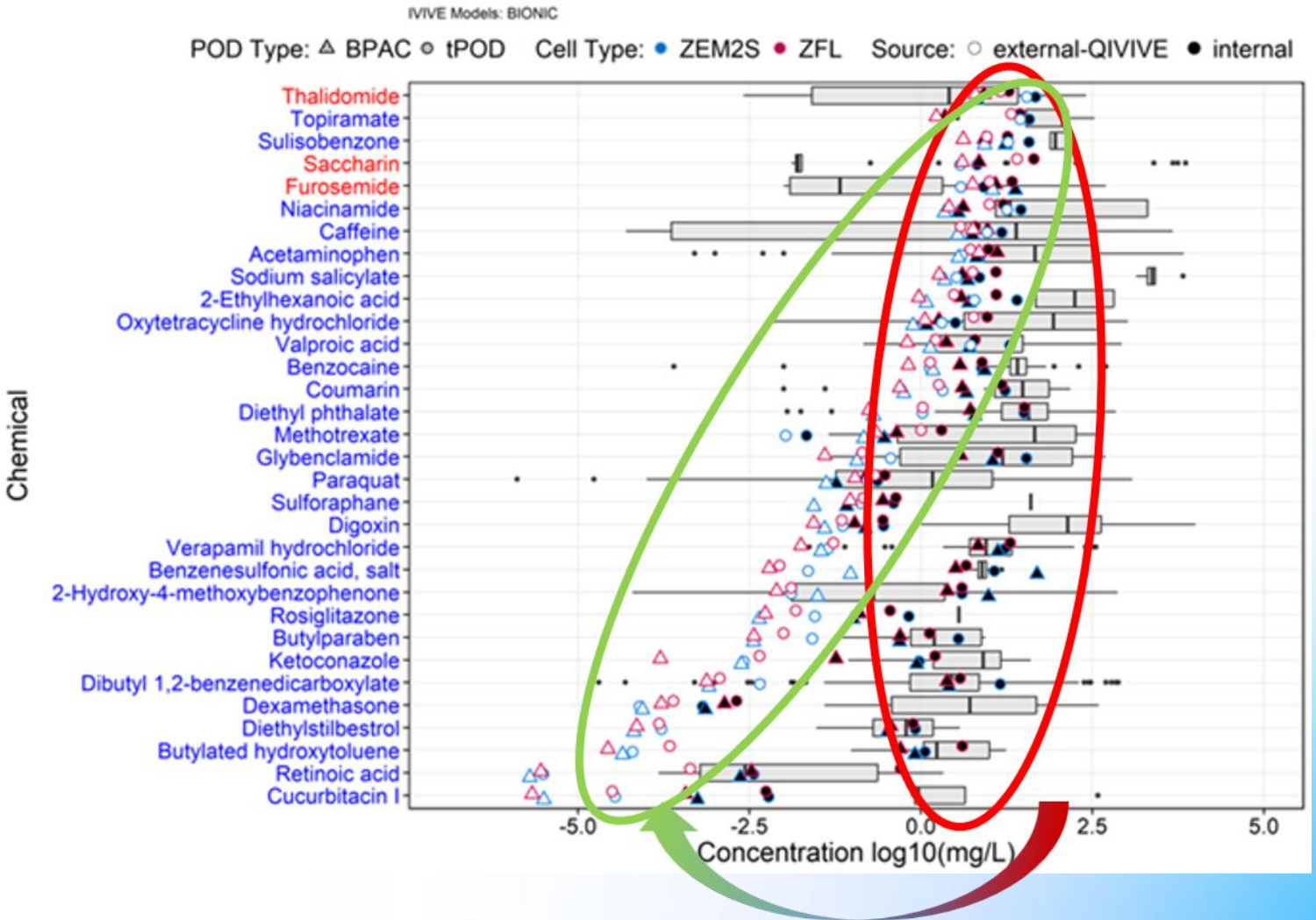


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Extra slide- related topic

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Is High-Throughput Transcriptomics protective of apical endpoints?



- ✓ Zebrafish cell line HTTr provide biologically meaningful, scalable data
- ✓ tPODs converted to predicted external water concentrations using QIVIVE models were generally protective of aquatic in vivo

Take-home messages

- Evolutionary conservation of targets and toxicological responses are (mostly!) aligned, enabling the identification of the species at risk;
- WOE approach combining conventional data with NAMs-based mechanistic information can be protective for environmental safety;
- NAM data shows protection across biology and chemical space;
- qIVIVE is a corner stone to NAM-enabled safety assessment;
- Potential for harmonizing human health and environmental safety, encouraging synergies and cross-development of NAMs for chemical assessment and regulatory decisions.

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Thank you!

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