Reassessing the Role of *In Vivo* Fish Testing in Chemical Risk Assessment

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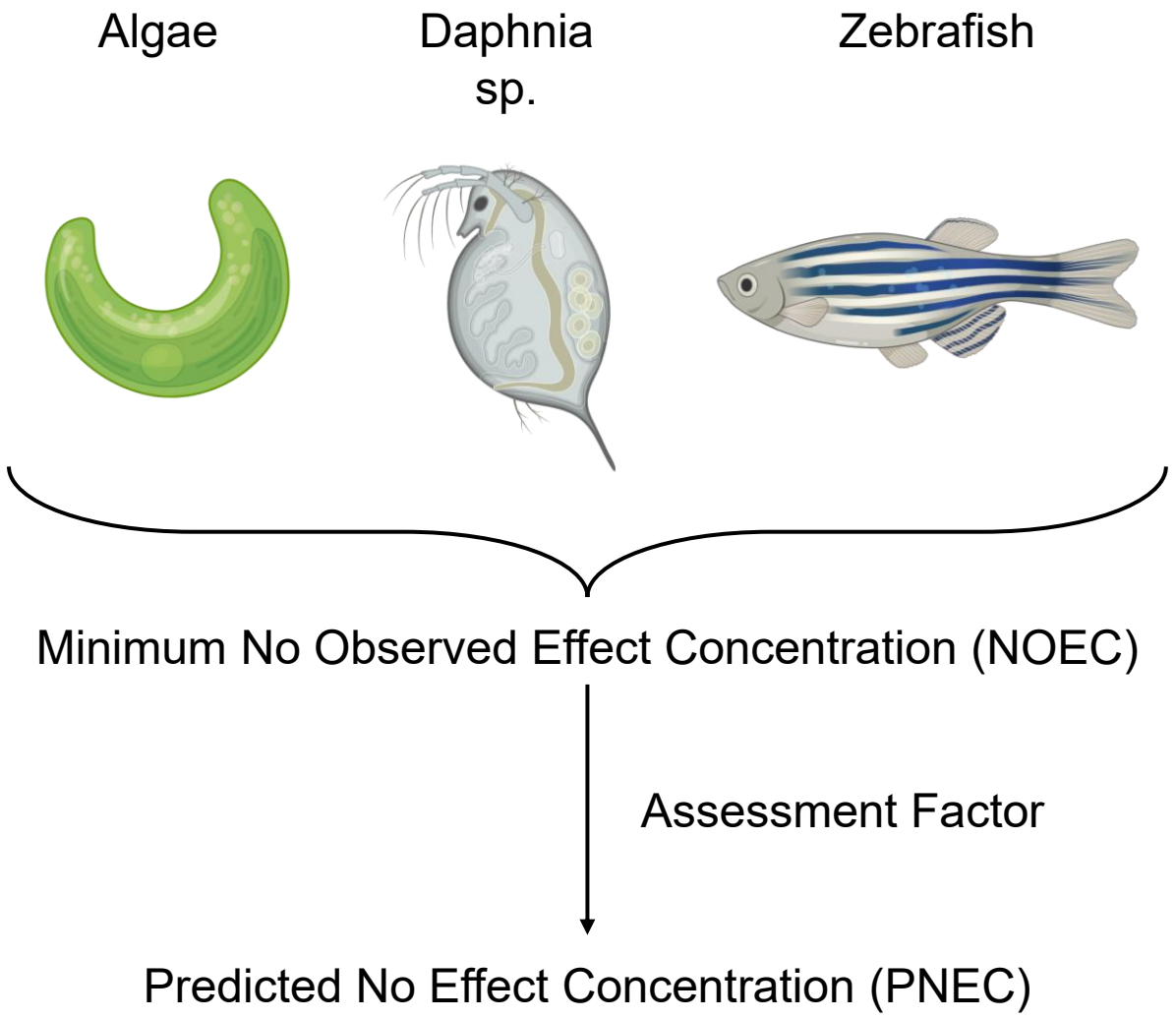
Traditional Aquatic Environmental Risk Assessment



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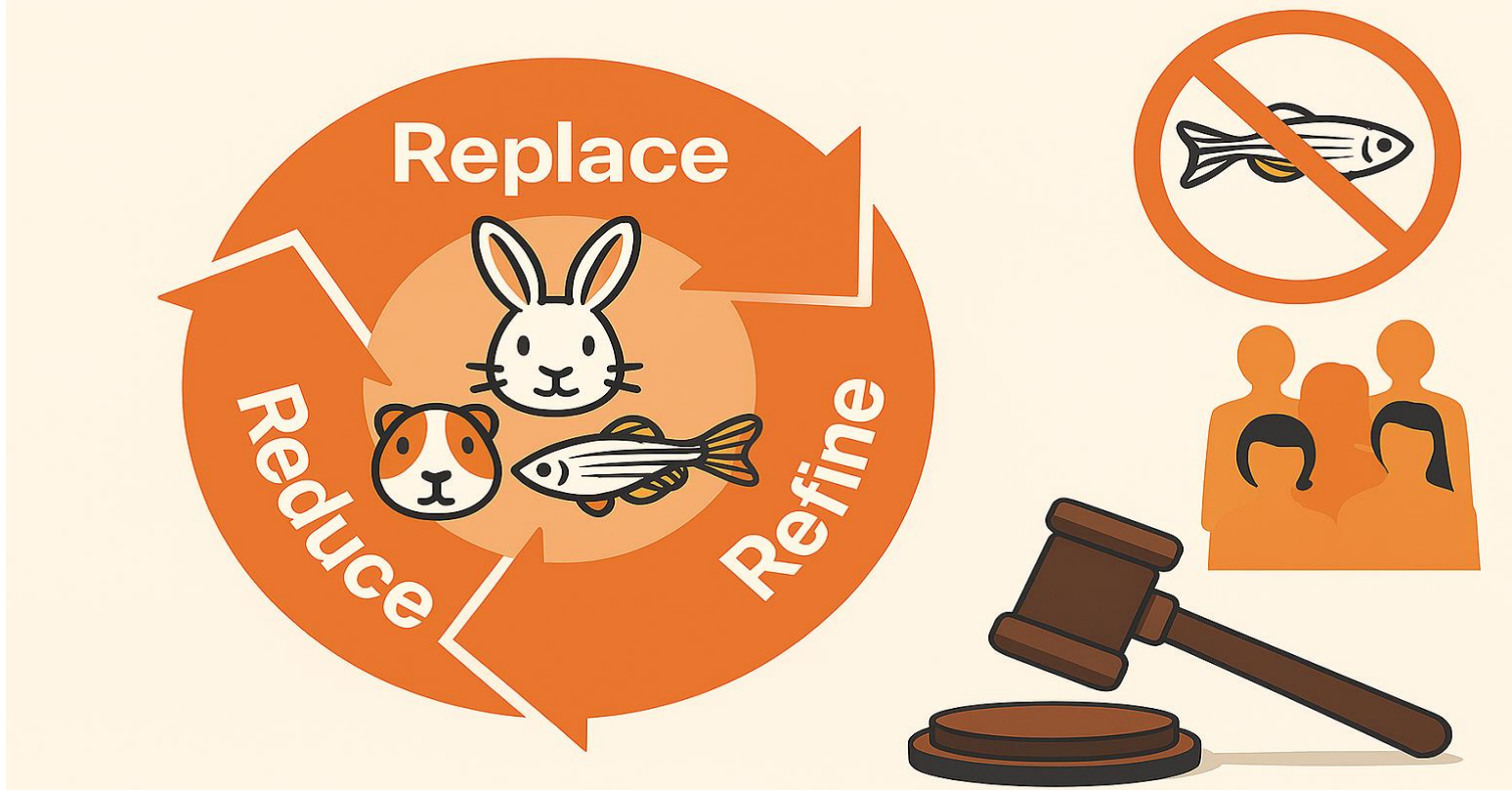
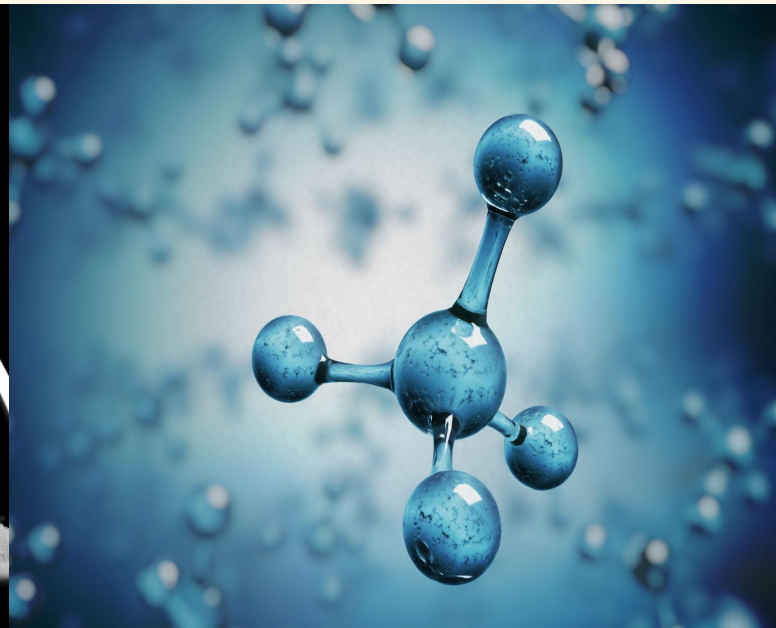
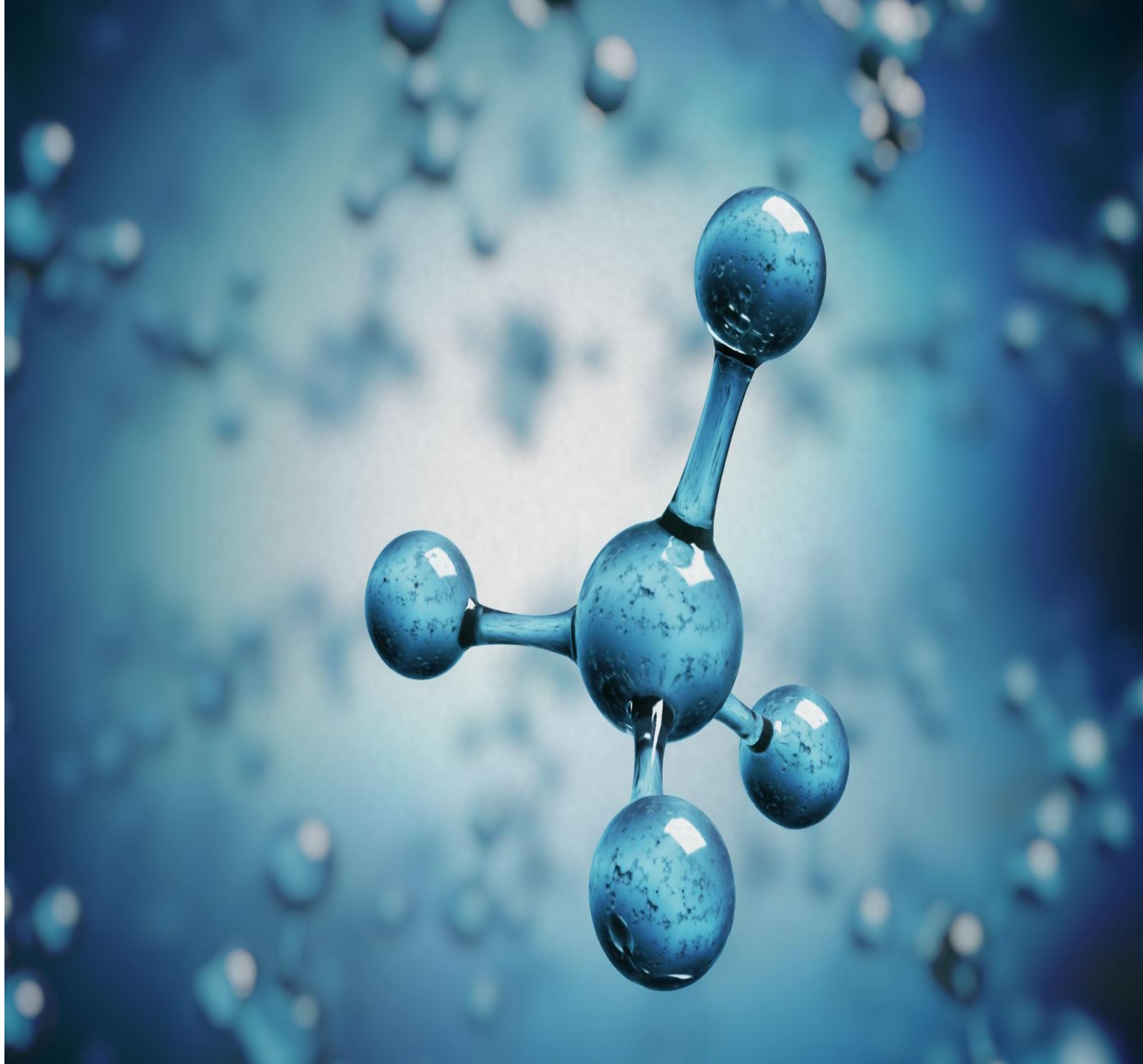
Challenges of Traditional Environmental Safety Testing of Chemicals





350,000+ chemicals

~30% tested[1]



[1] *Transforming EU chemicals regulation to better protect human health and the environment - Joint Research Centre (2023). https://joint-research-centre.ec.europa.eu/jrc-news-and-updates/transforming-eu-chemicals-regulation-better-protect-human-health-and-environment-2023-12-11_en*

Fish Acute Tests

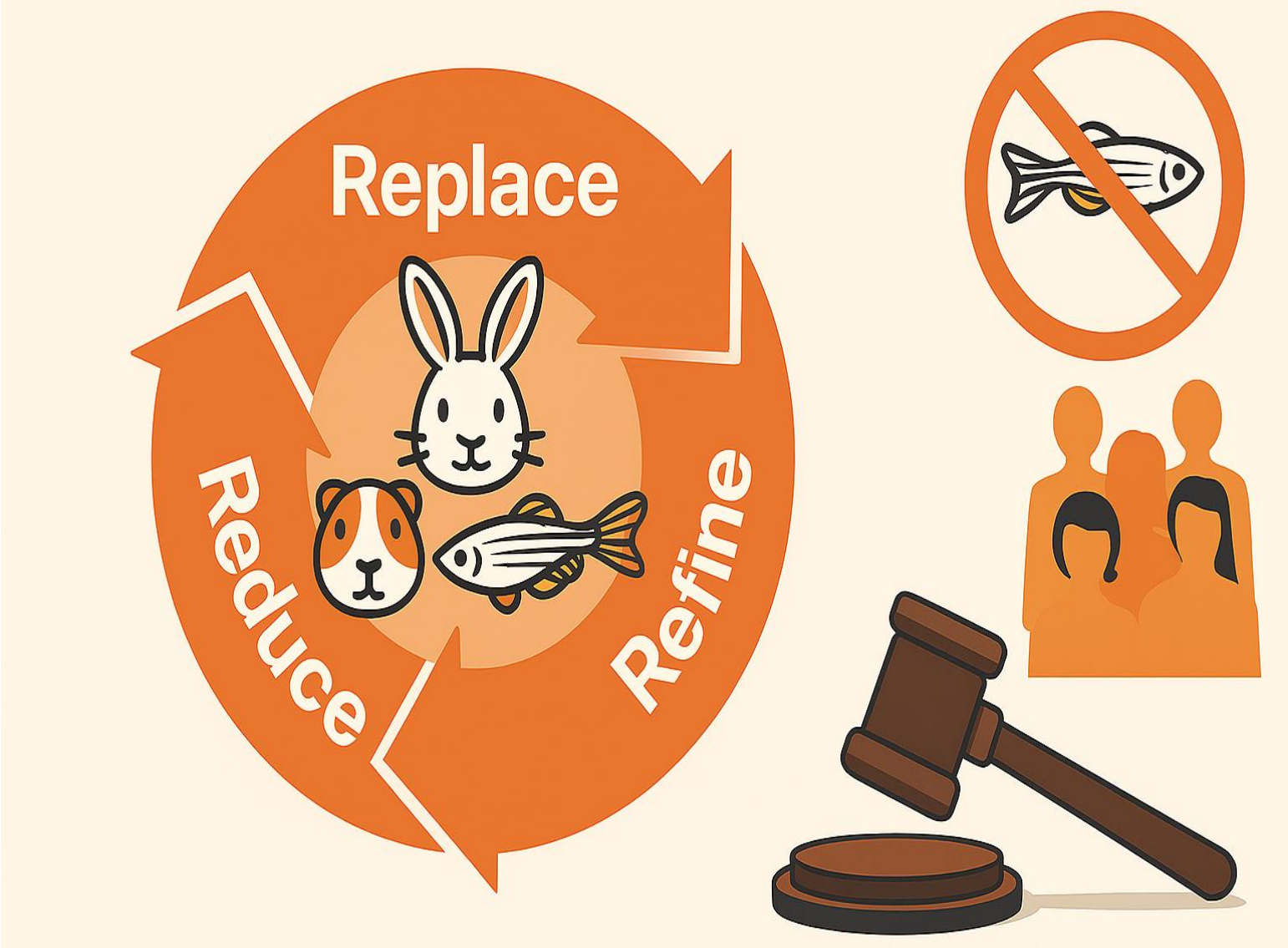
< 96 hours

Fish Chronic Tests

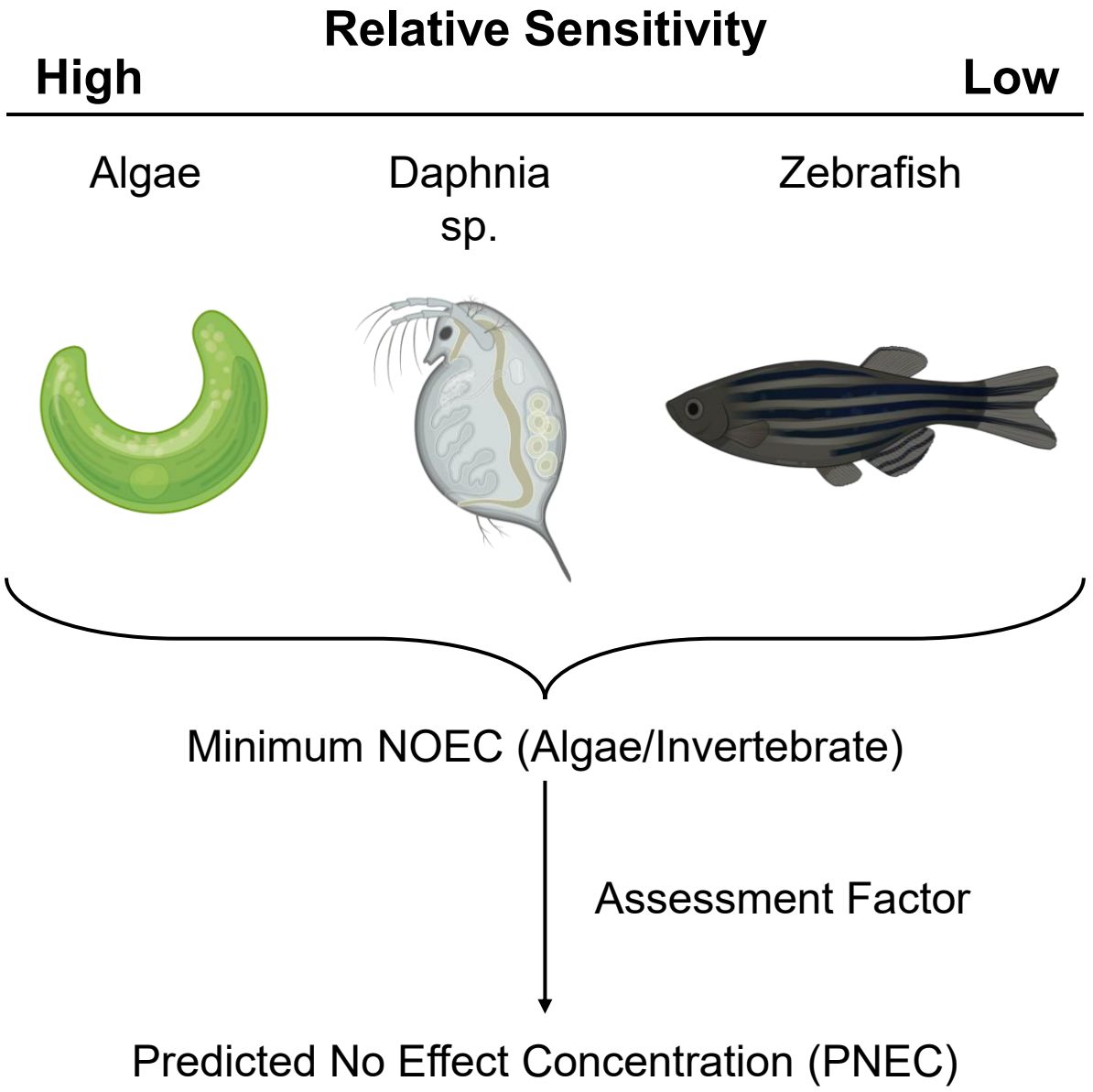
> 10 weeks

Move towards 3Rs
Reduce
Refine
Replace

Regulations for phasing out animal testing



Understanding Relative Species Sensitivity to Chemicals



Images from BioRender

Methodology

Ecotoxicity Data

ECOTOX
Aquatic species
(GNverifier, Taxoniq)

Chronic NOECs,
Acute LC50s (Lethal Concentration 50)

Lab-based in vivo studies

Gunnarsson et al.
Chronic NOECs

Taxonomic Group Comparison

Grouping by CAS, taxonomic group and endpoint: Median concentration (mg/L)

Ratios across group combinations calculated

Factor of 100 to determine relative fish sensitivity

WebApp

DASH Plotly used to create AMIRA Webapp

Animal-free
Mechanistic
Inference for species-specific chemical
Risk
Assessment

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Chemical Data

PubChem, DrugBank: Chemical molecular weight and CAS

Exposure Duration Filters

Test Type	Taxonomic Group	Exposure/ observation duration	OECD
Acute LC50s	Algae	<=72 h	Test No. 201
	Invertebrate	<=48 h	Test No. 202
	Fish	<=96 h	Test No. 203
	Amphibian	<=96 h	Test No. 231
Chronic NOECs/ NOELs	Algae	>=3 days	Test No. 201
	Invertebrate	>=21 days	Test No. 211
	Fish	>=28 days	Test No. 210
	Amphibian	>=21 days	Test No. 231

Taxonomic Group Comparison

Grouping by CAS, taxonomic group and endpoint: Median concentration (mg/L)

Ratios across group combinations calculated

Factor of 100 to determine relative fish sensitivity

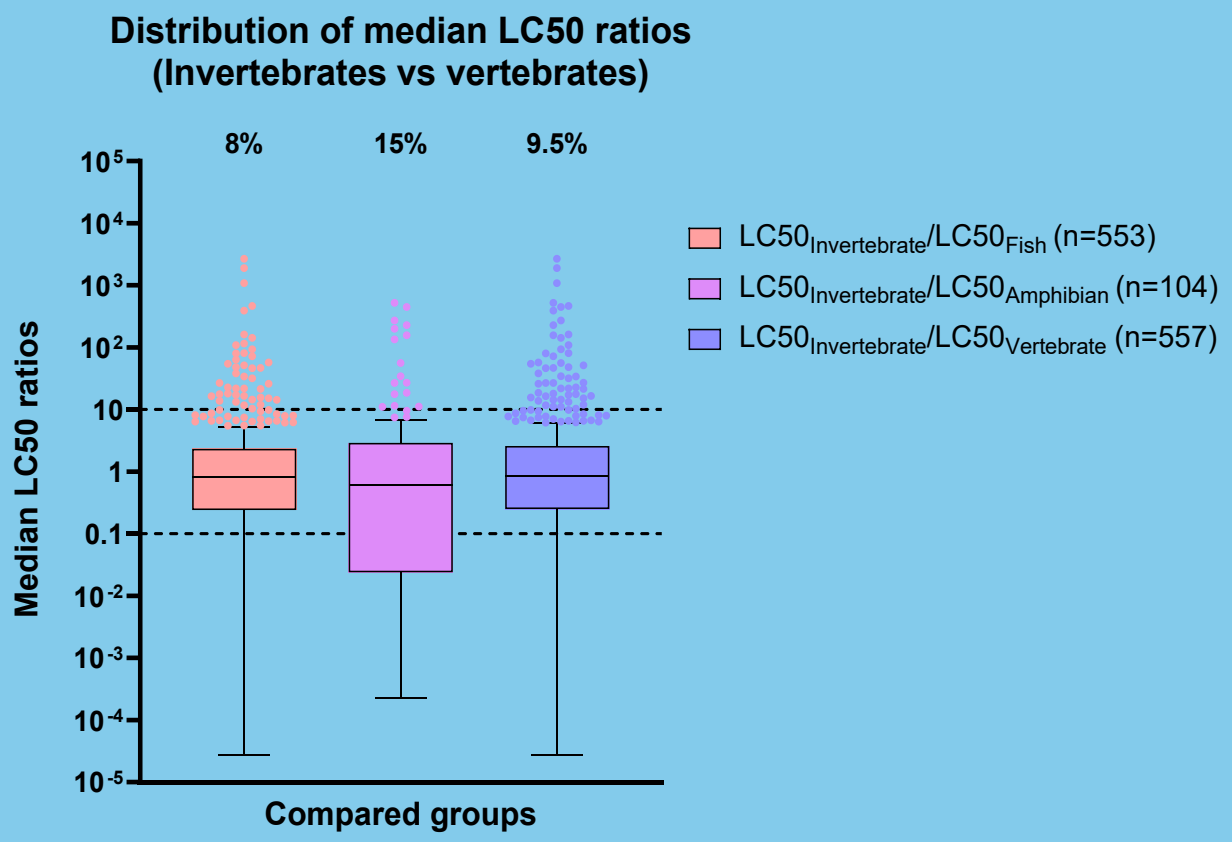
Taxonomic Group Combinations	Ratio calculation (E∈{LC50,NOEC})
Algae vs fish	$\frac{median\ E_{Algae}}{median\ E_{Fish}}$
Invertebrates vs fish	$\frac{median\ E_{Invertebrate}}{median\ E_{Fish}}$
Algae/invertebrates vs fish	$\frac{min(median\ E_{Algae}, median\ E_{Invertebrate})}{median\ E_{Fish}}$
Algae/invertebrates vs Vertebrates	$\frac{min(median\ E_{Algae}, median\ E_{Invertebrate})}{min(median\ E_{Fish}, median\ E_{Amphibian})}$

Low Fish Sensitivity
Ratio<0.1

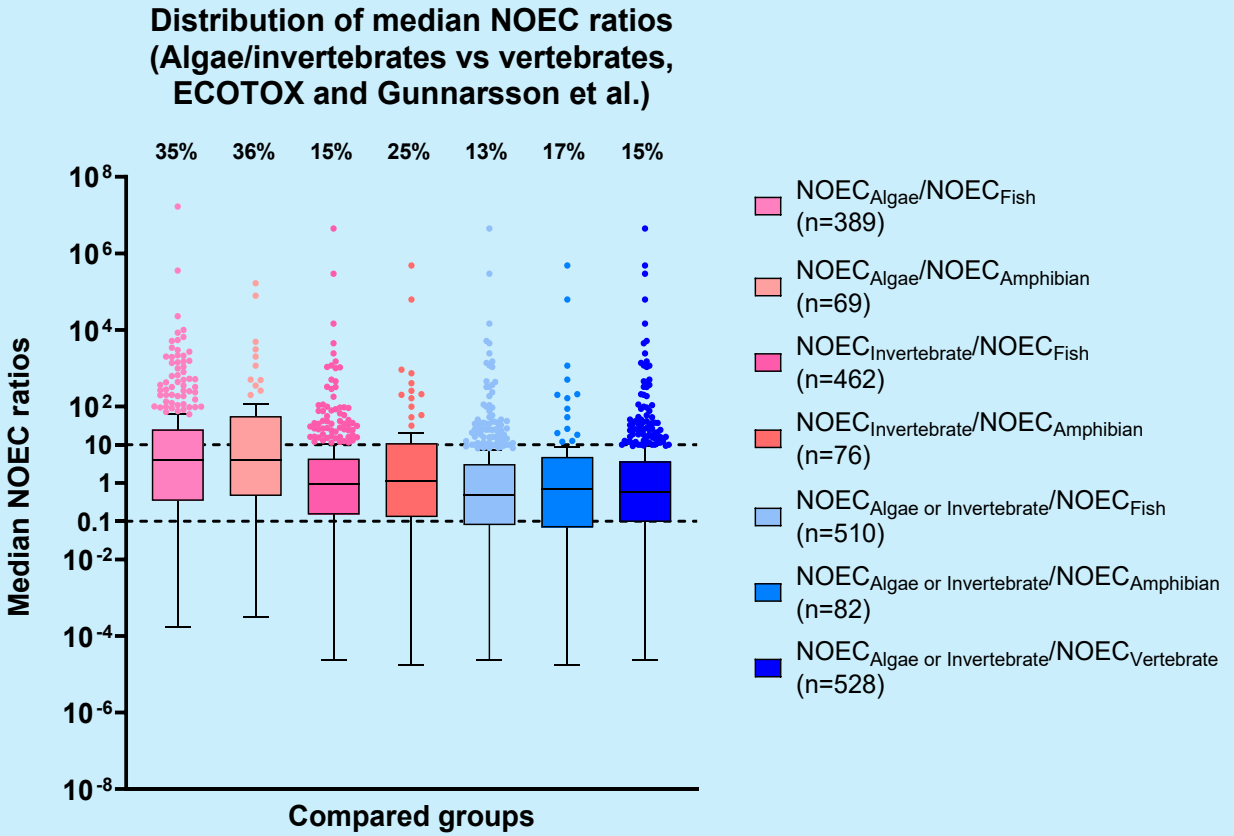
High Fish Sensitivity
Ratio>10

Results

LC50 Comparison (Acute Lethality)



NOEC Comparison (Chronic)



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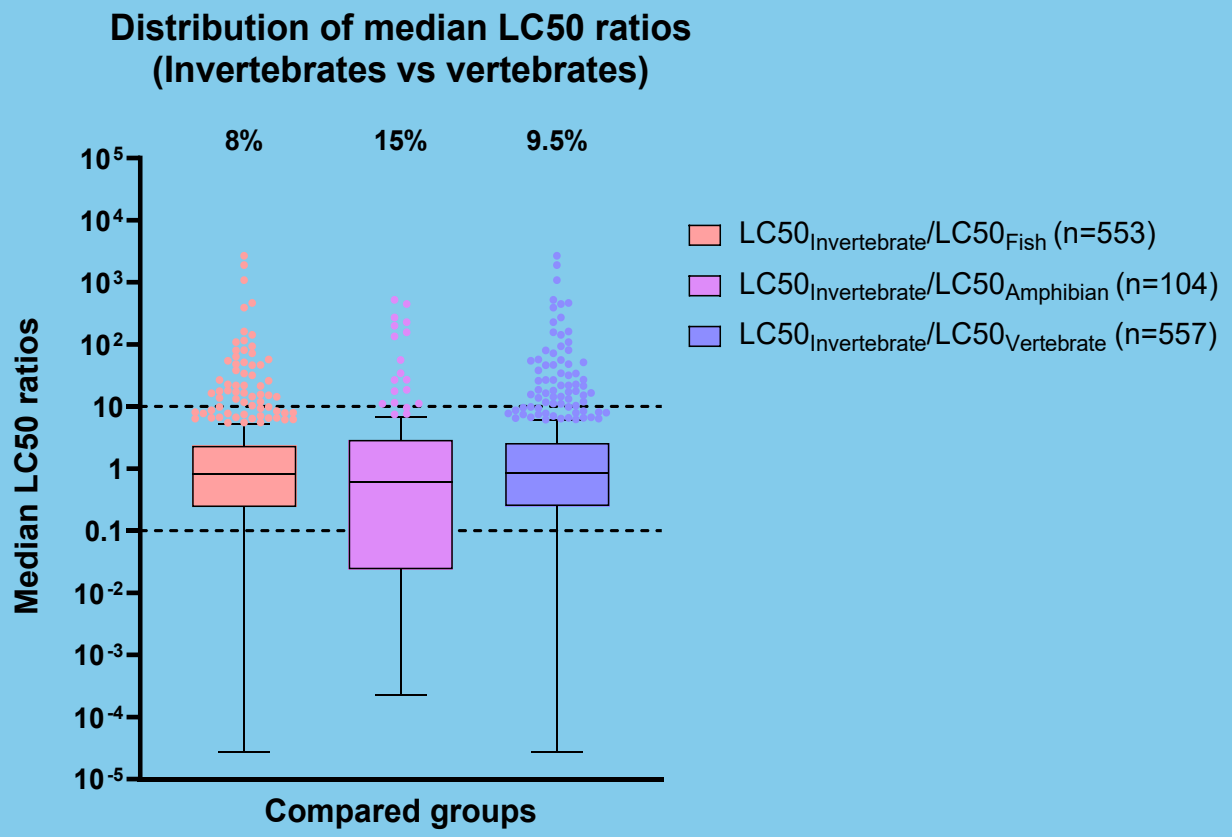
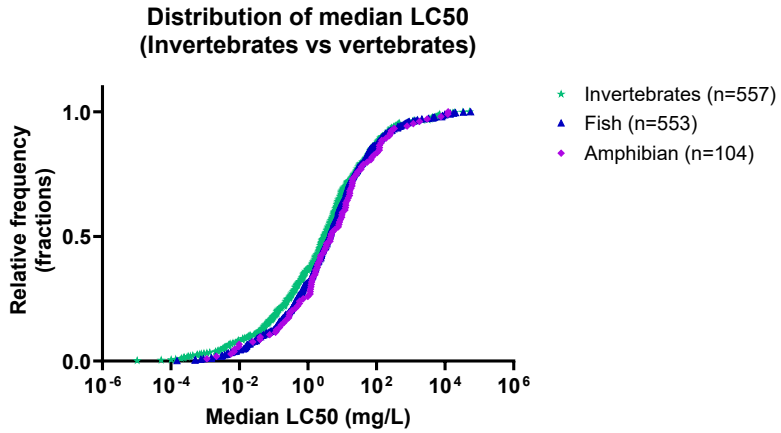
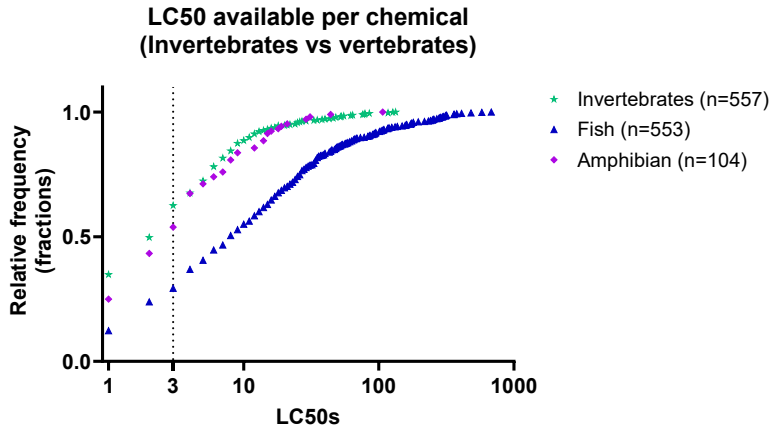
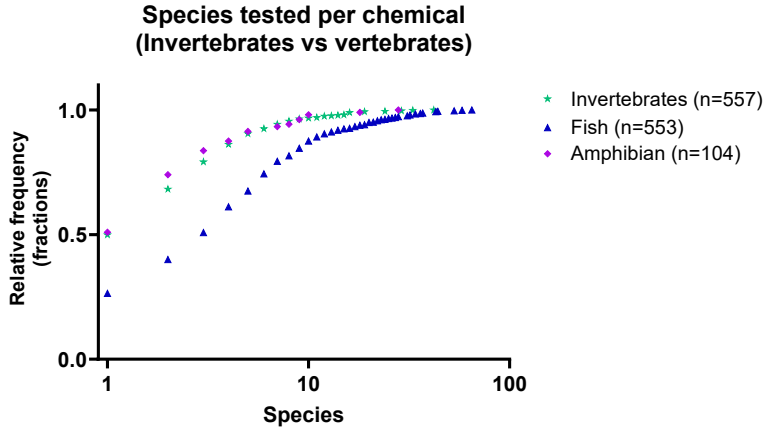
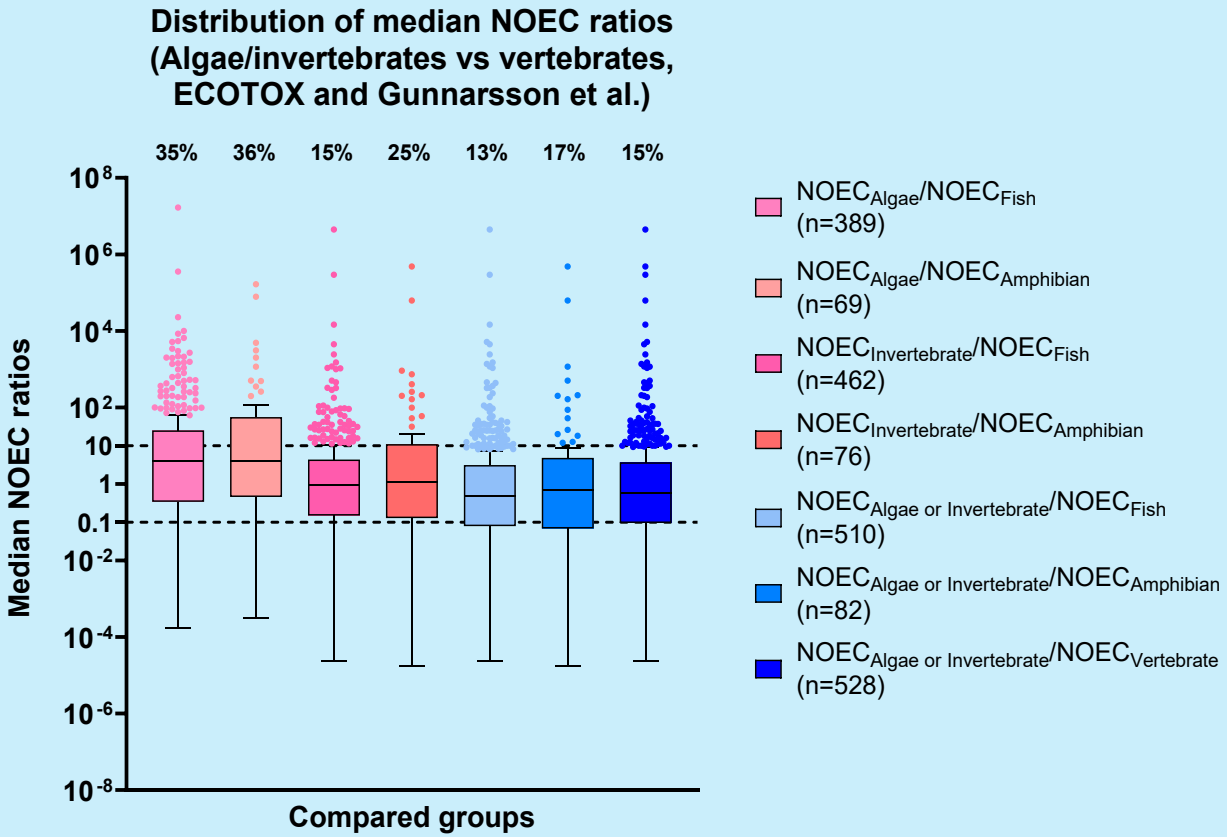


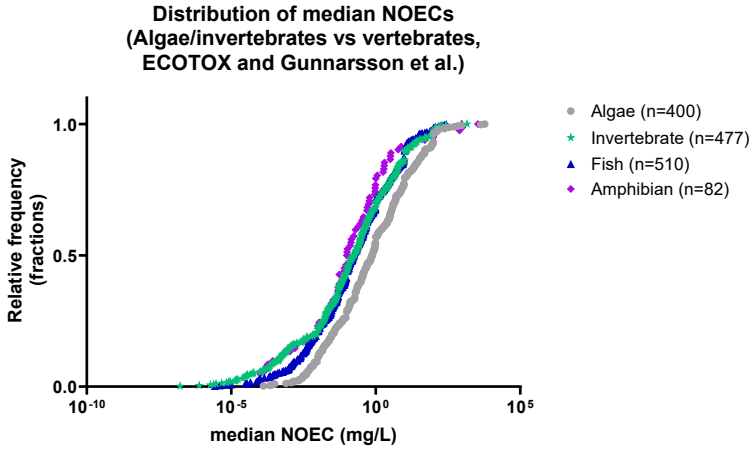


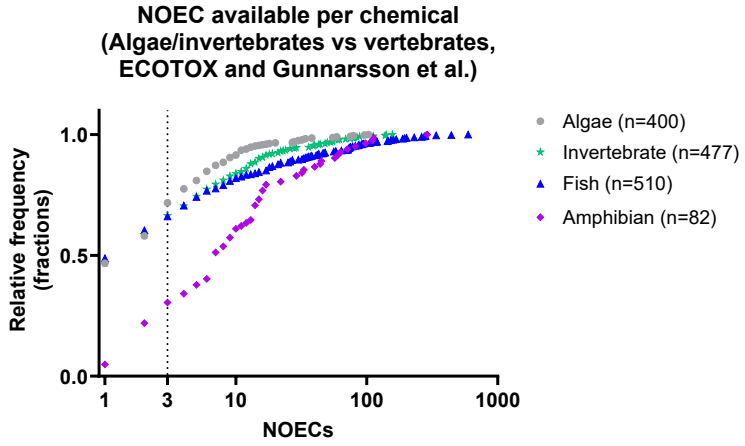


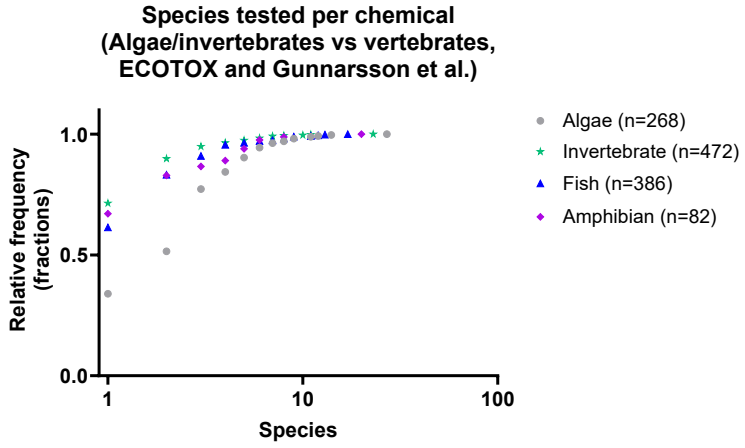


NOEC Comparison (Chronic)









Conclusion

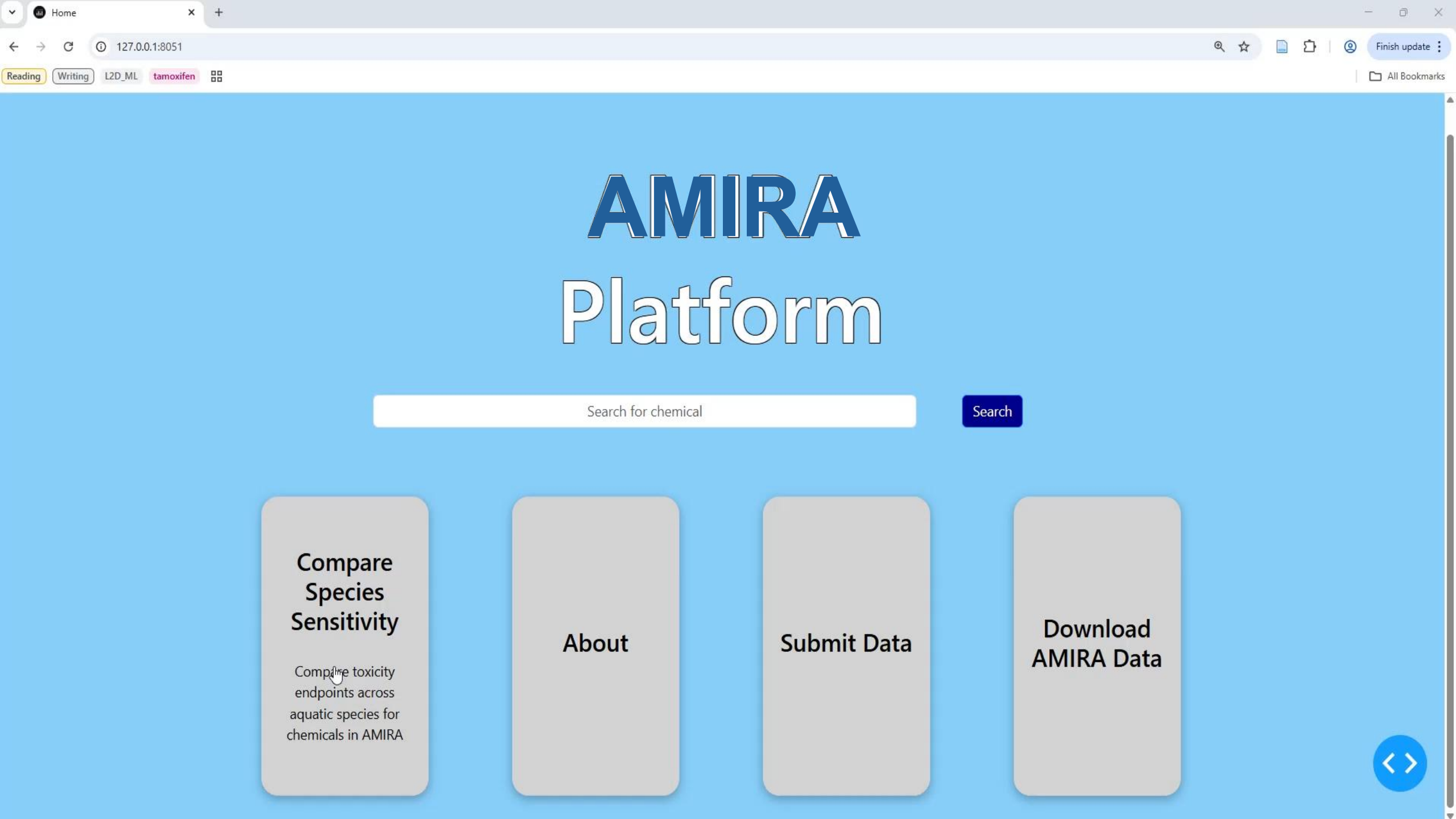
Vertebrates were found to be tenfold more sensitive than algae/invertebrates for only **9.5%** and **15%** chemicals, respectively, when comparing LC50s and NOECs.

Where fish are the most sensitive, available *in silico* and *in vitro* tools would support such a safety assessment.

Understanding the chemical structures and mechanisms of action underlying species-specific sensitivity would enable predictive modelling to classify when fish will be highly sensitive to a new chemical.

This is possible using chemical molecular fingerprints and transcriptomic changes observed in species from chemical exposure.

Animal-free
Mechanistic
Inference for species-specific chemical
Risk
Assessment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Finish update
Reading
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L2D_ML
tamoxifen
All Bookmarks
AMIRA
Platform
Search for chemical
Search
Compare Species Sensitivity
Compare toxicity endpoints across aquatic species for chemicals in AMIRA
About
Submit Data
Download AMIRA Data

Acknowledgements

Supervisory Team

Prof Christer Hogstrand

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Prof Charles Tyler

Office and Lab mates