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Model-Based Integrated Assessment of Human and Ecological Risks of Environmental Chemicals

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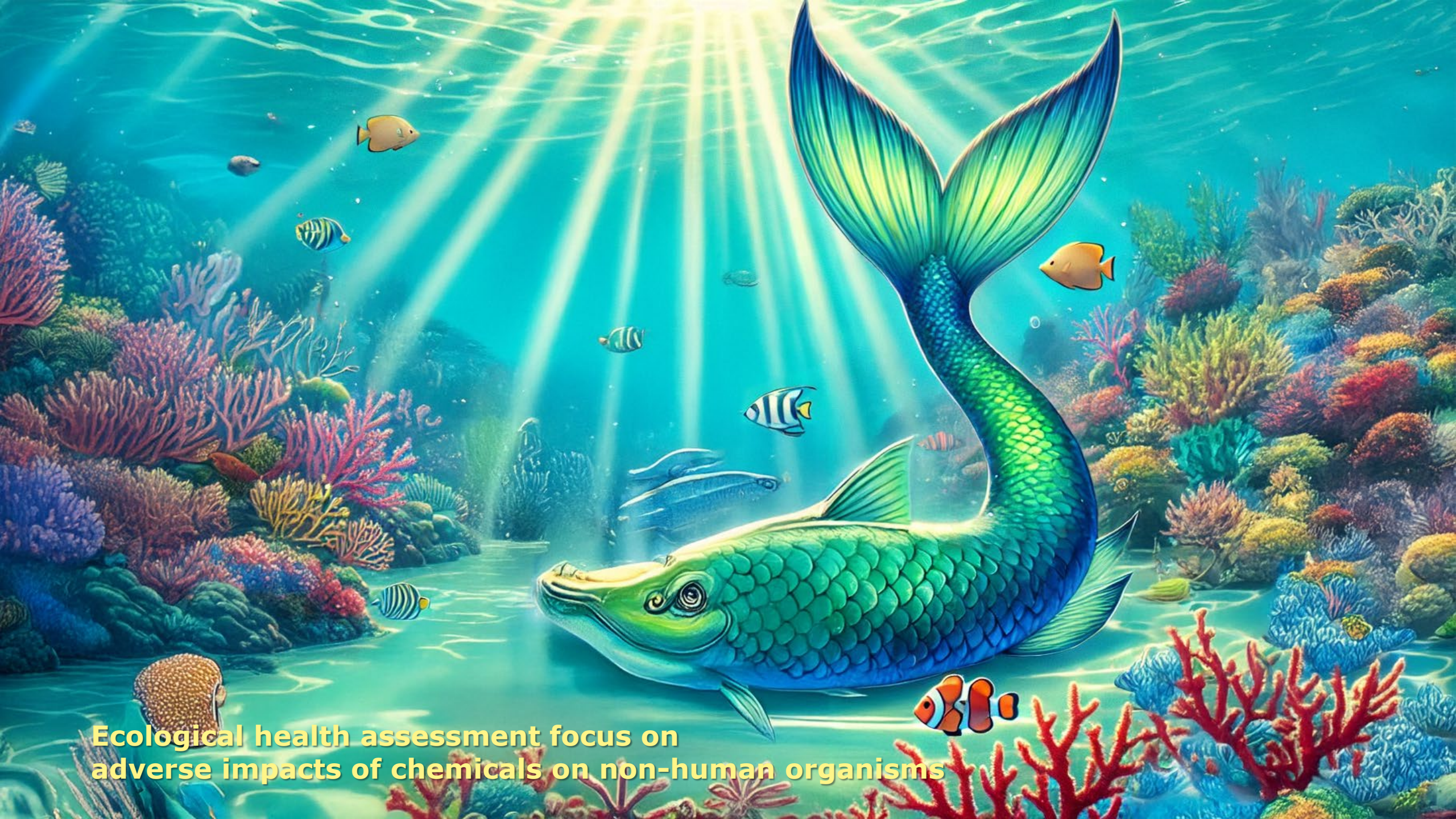
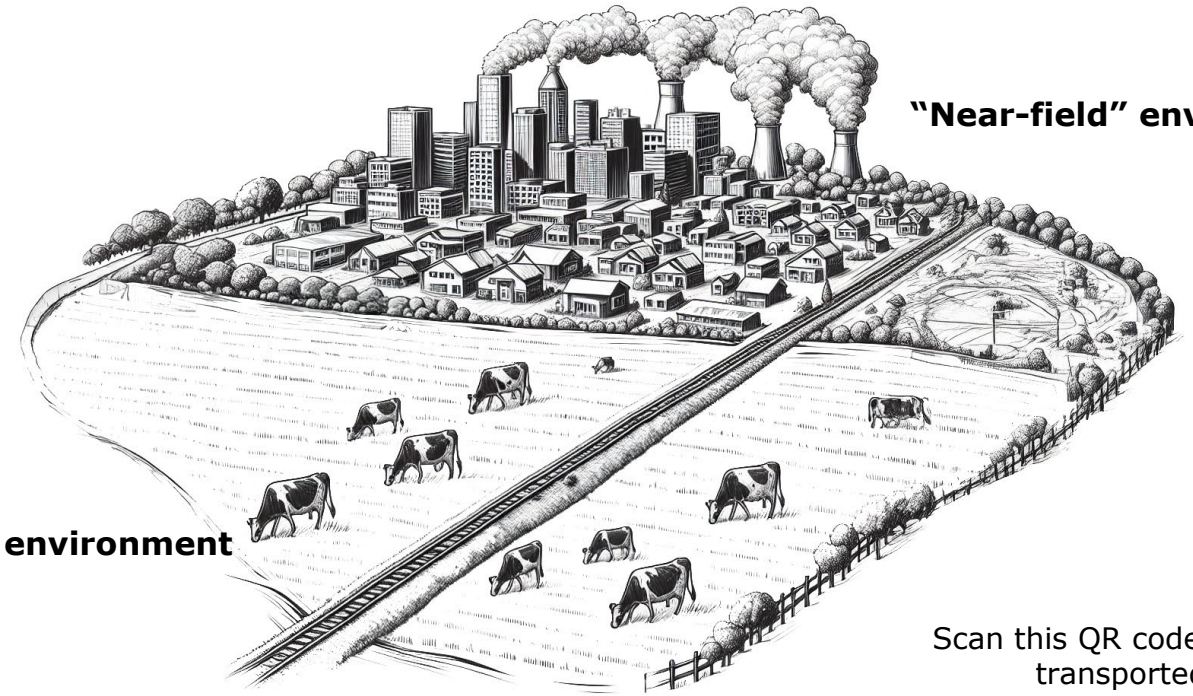

Ecological health assessment focus on
adverse impacts of chemicals on non-human organisms

Humans vs. Non-human Organisms

- Connected exposure and toxicity patterns
  - Contamination in urban habitats is interconnected with contamination in wildlife habitats. However, this interconnection is often overlooked in current separate human and ecological risk assessments.



Scan this QR code for more info about how chemicals are transported across different scales of environment

Humans vs. Non-human Organisms

- Differentiated exposure and toxicity patterns
  - Humans have distinct exposure and toxicokinetic pathways that are not shared by wildlife, esp. aquatic organisms. Humans and non-human organisms may exhibit different levels of toxicological susceptibilities and different modes of action of toxicity.

Air-breathing

High exposure from the "near-field" environment of using personal care products and cosmetics

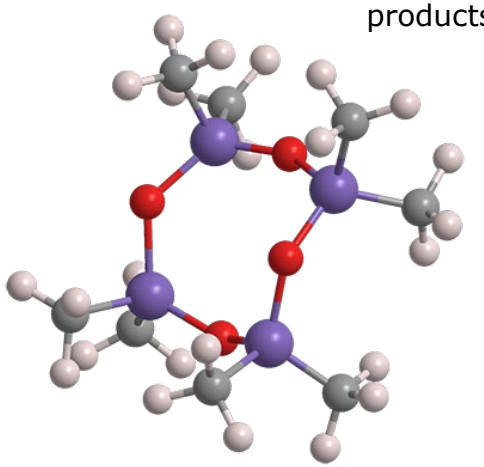
Low bioaccumulation due to efficient exhalation elimination

Water-breathing

Low exposure from the aquatic environment

High bioaccumulation due to inefficient exhalation elimination

Octamethylcyclotetrasiloxane (D4)
Volatile solvent in personal care products and cosmetics



Scan this QR code for more info about differences in human and non-human organism exposures to D4

Mechanistic Integration of Humans and Non-human Organisms

- Although the need for integrated assessments is evident, such an integrated approach has not been widely implemented.

"Patchwork"
Separate human and ecological risk assessments based on separate datasets derived from disconnected artificial and natural environments.

Pioneering attempts

PROTEX: From the **PRO**duction Line **T**o the **EX**posure Levels

Scan this QR code for more info

Production/Use

Lifecycle substance flow modeling

Emissions

Environmental fate & transport modeling

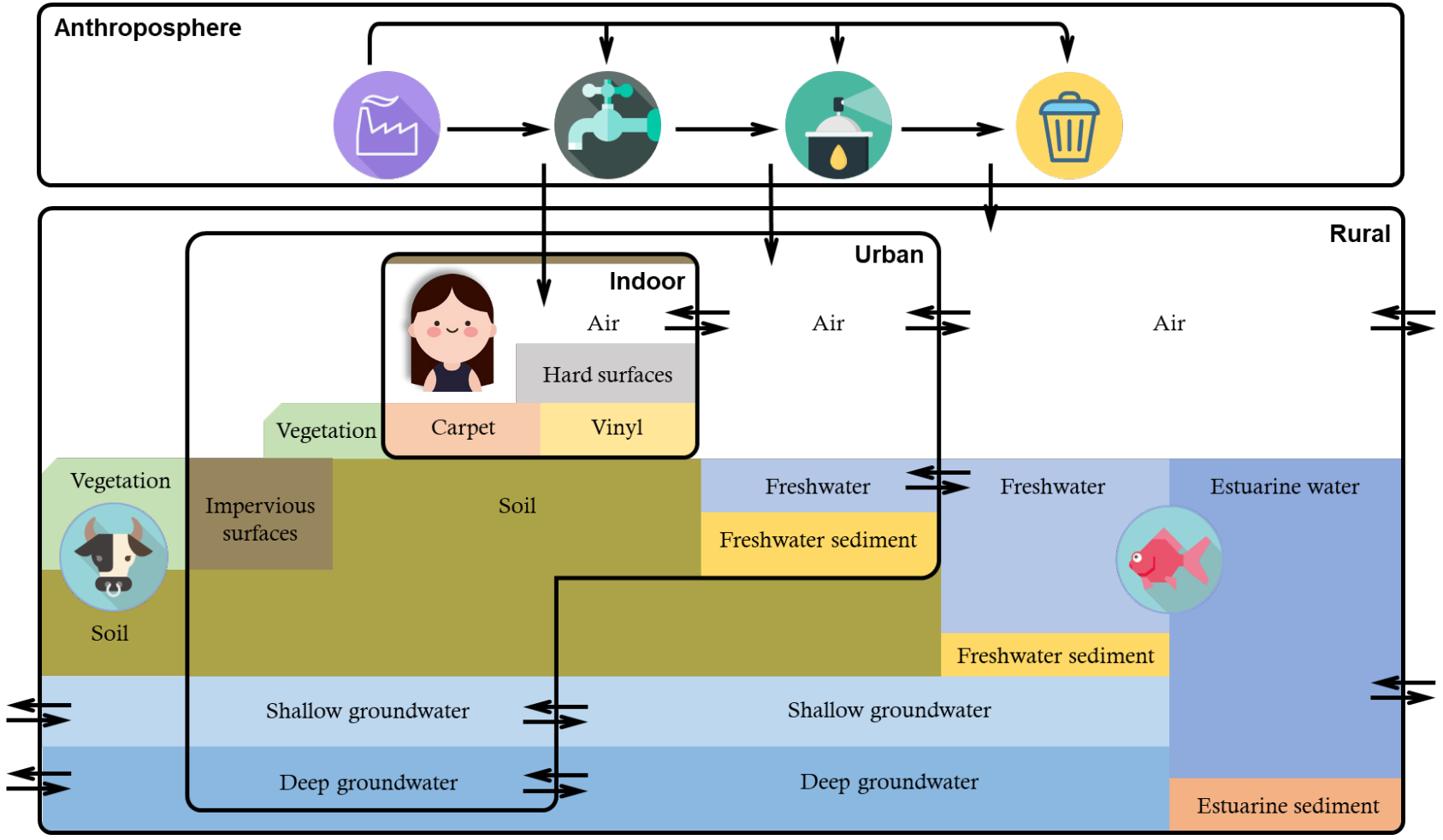
Environ. Contamin.

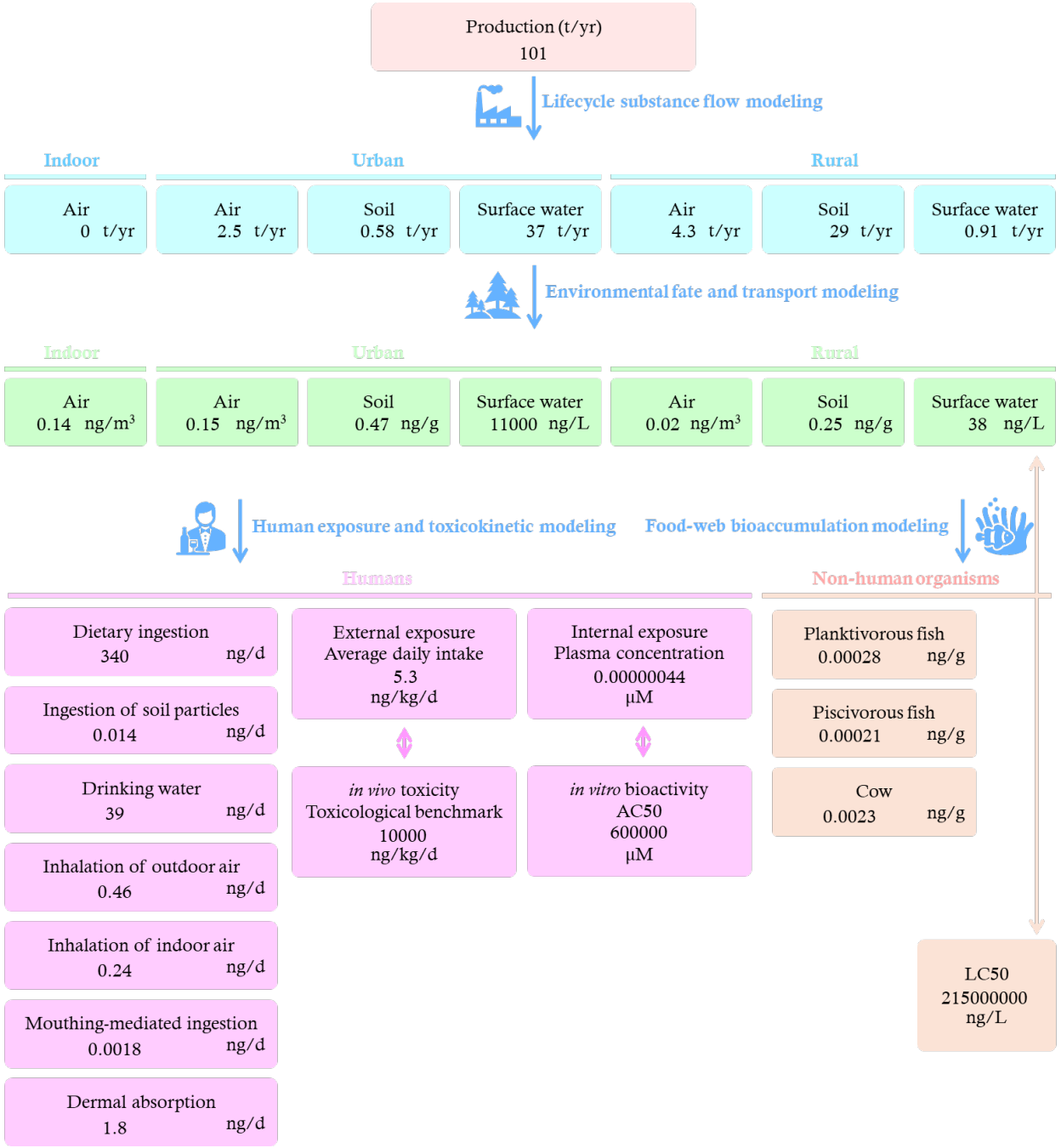
Food-web bioaccumulation modeling

Food Contamin.

Human exposure & toxicokinetic modeling

Human Contamin.



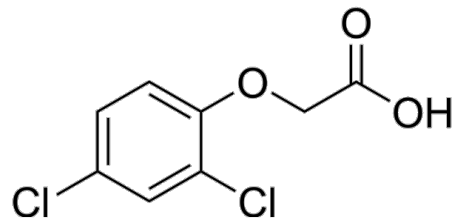


95 Case Study Chemicals

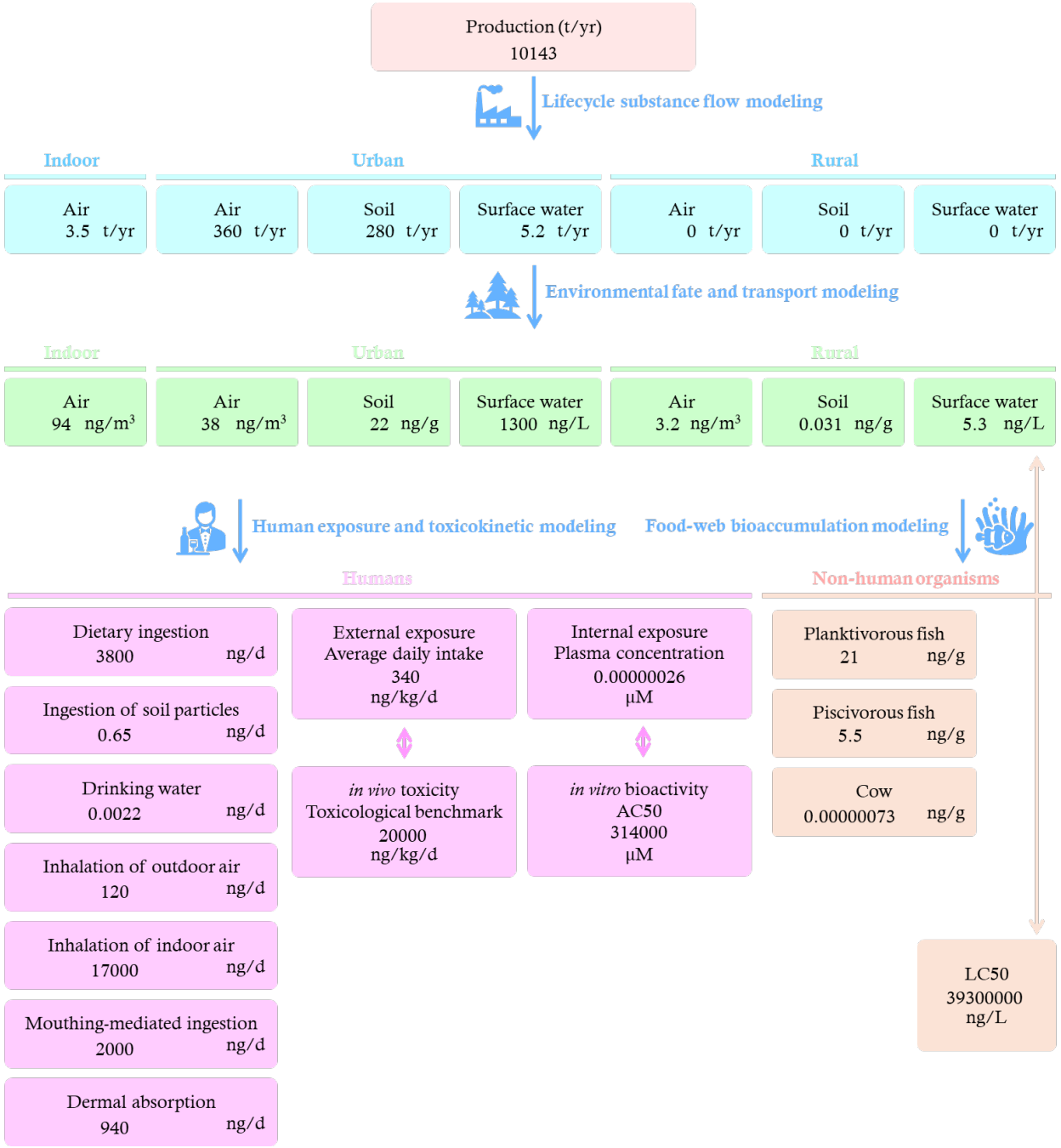
- 6 intermediate and raw chemicals
- 4 solvents
- 66 pesticides, fungicides, herbicides
- 4 construction material additives
- 8 plasticizers
- 7 personal care product ingredients

Subtropical arid American region

Average American general population



2,4-D
Herbicide active ingredient



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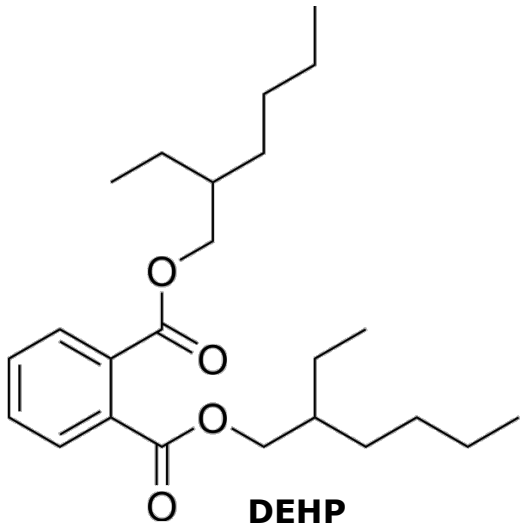
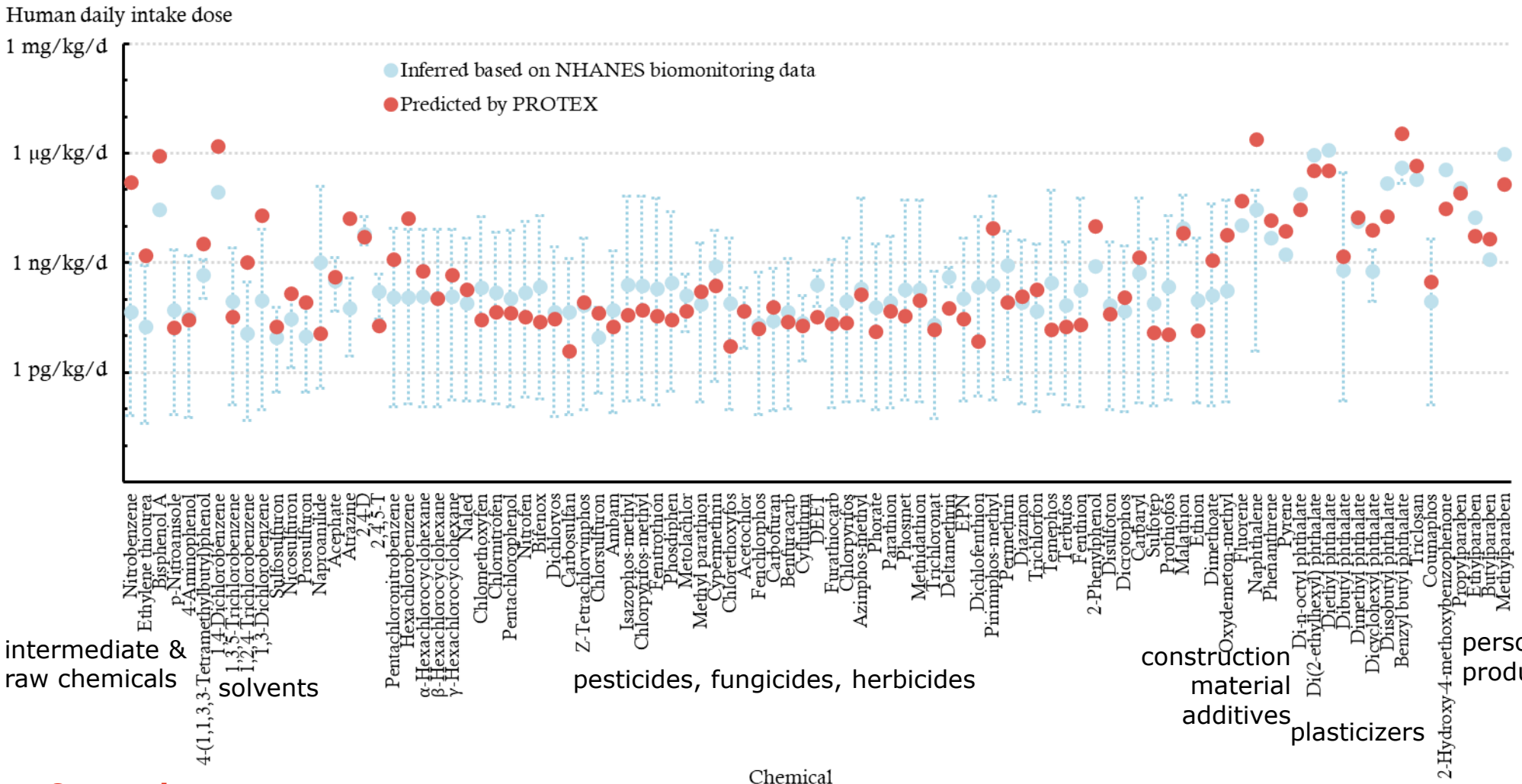


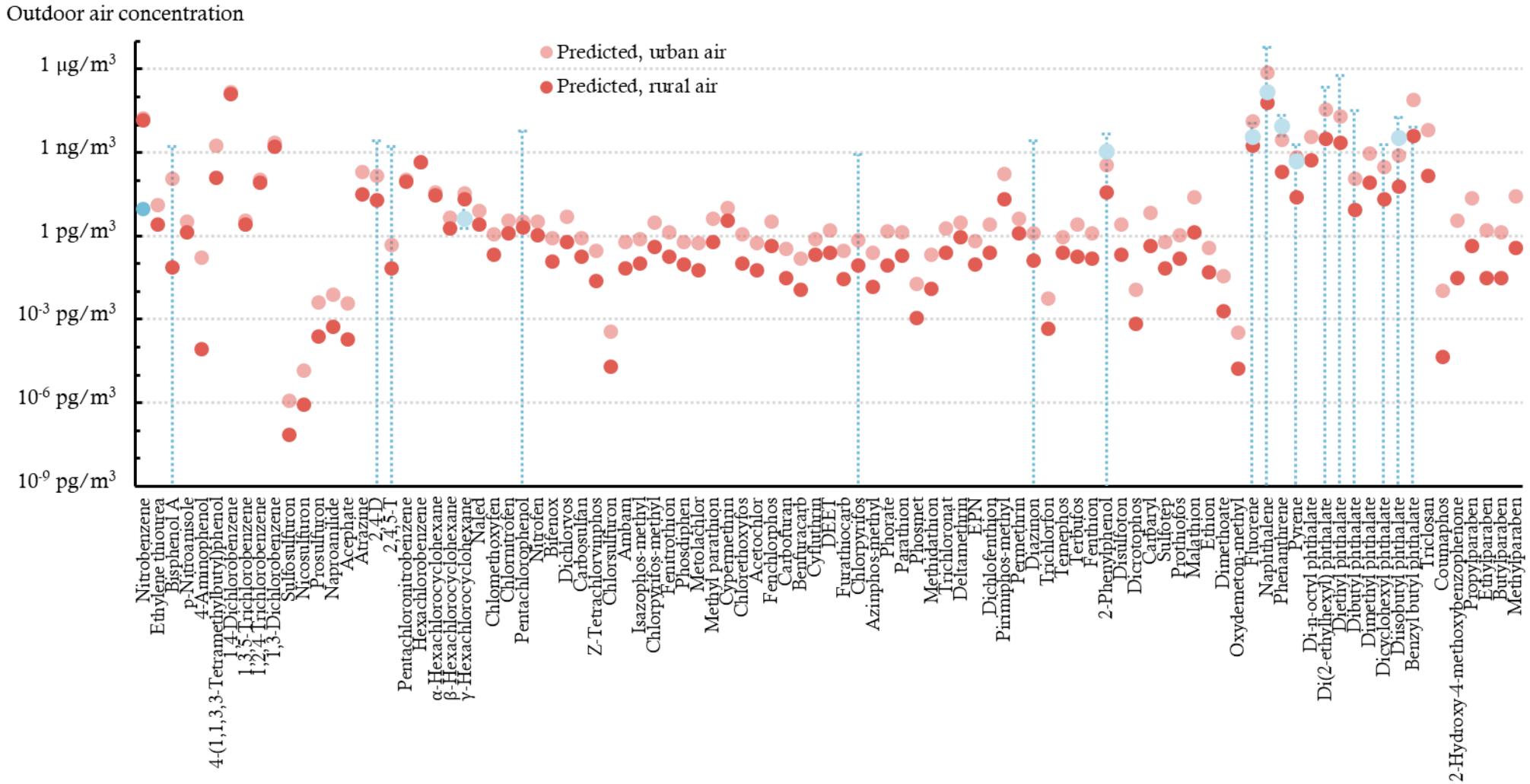
DEHP

Plasticizer in plastic materials

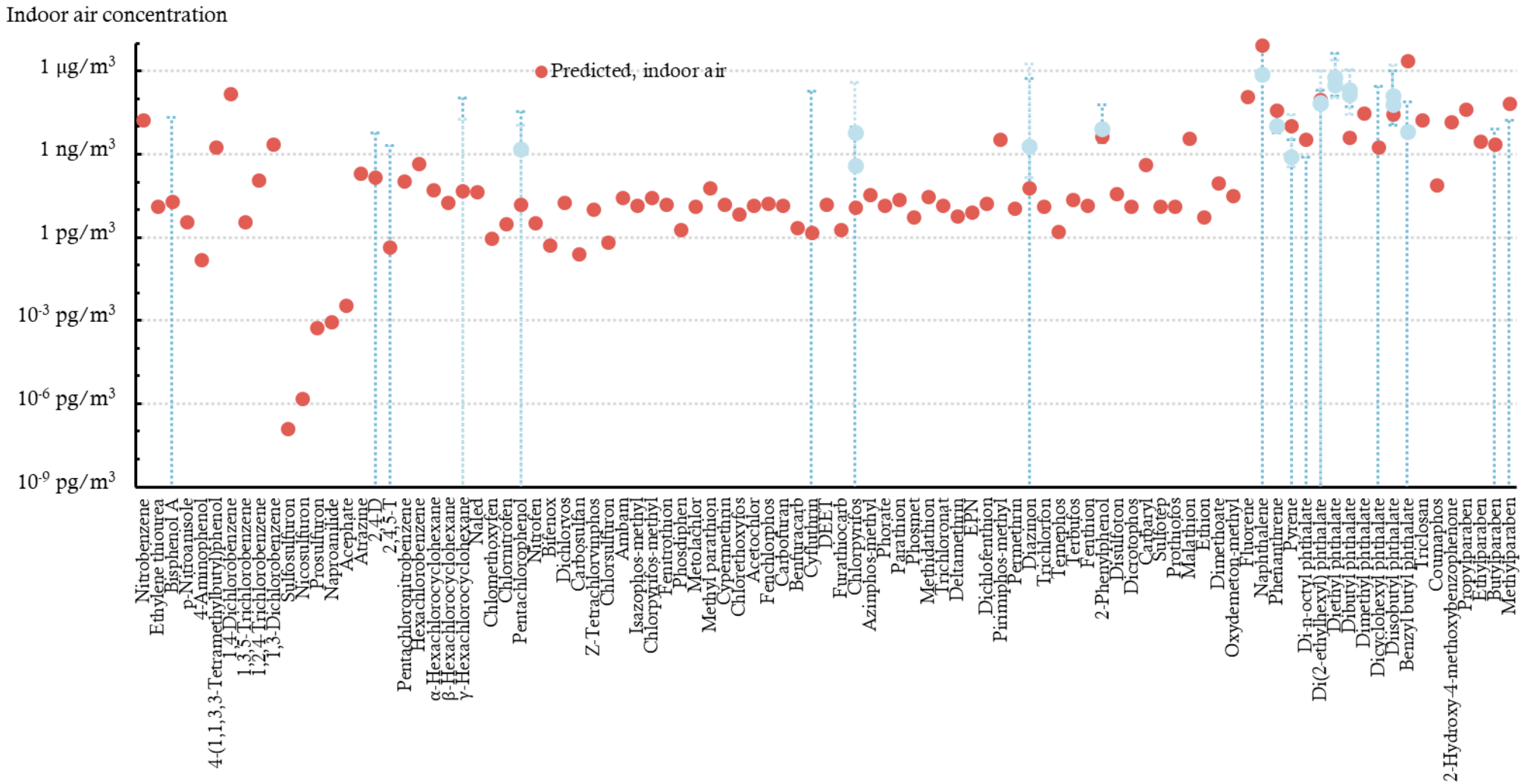
Stepwise Evaluation of Model Performance



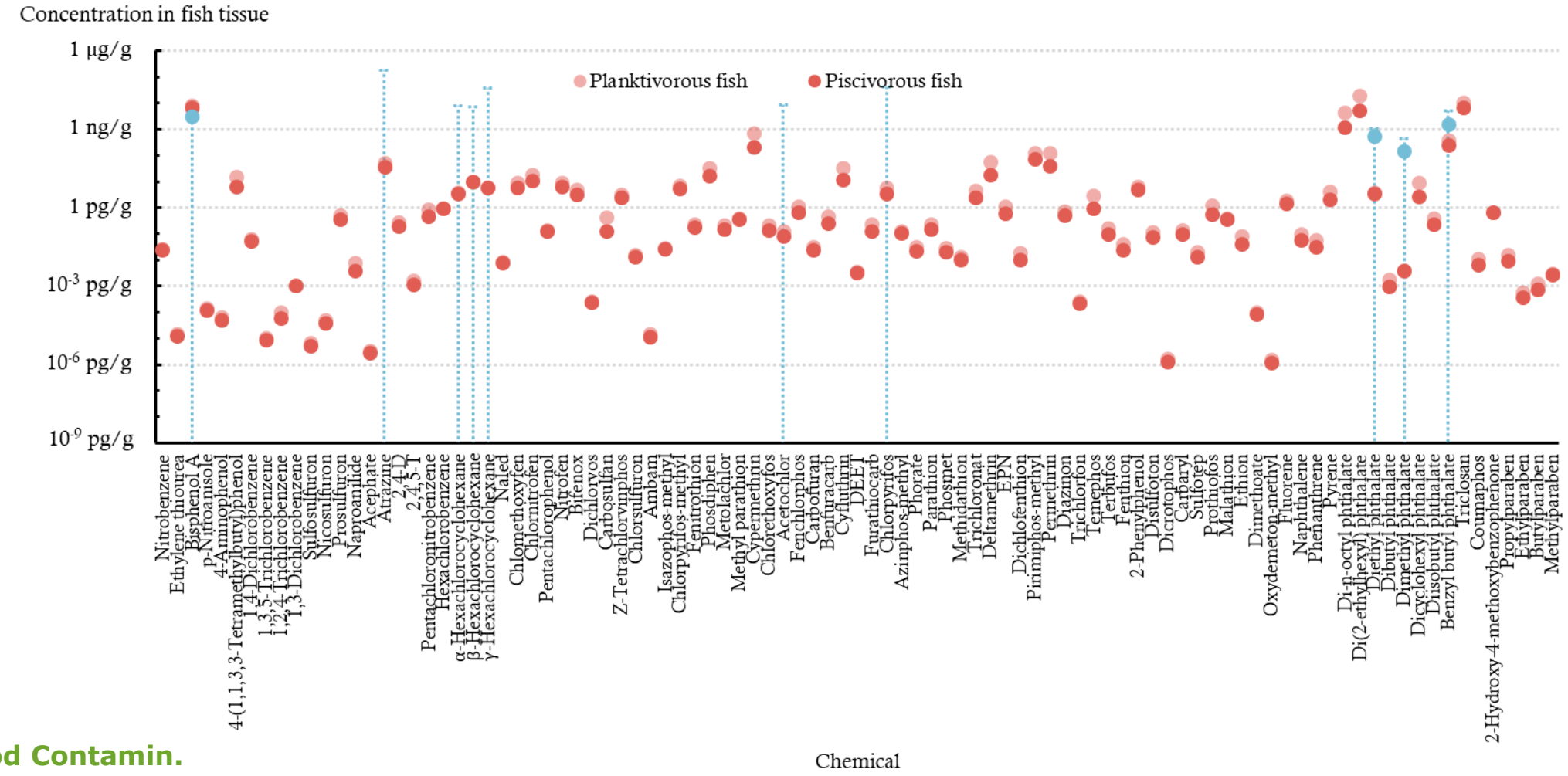
Stepwise Evaluation of Model Performance



Stepwise Evaluation of Model Performance

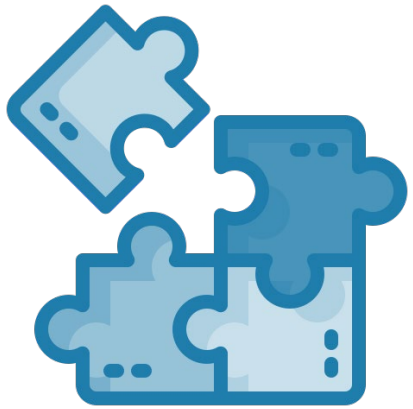


Stepwise Evaluation of Model Performance



Evaluation of Individual Steps in the “PROTEX” Continuum

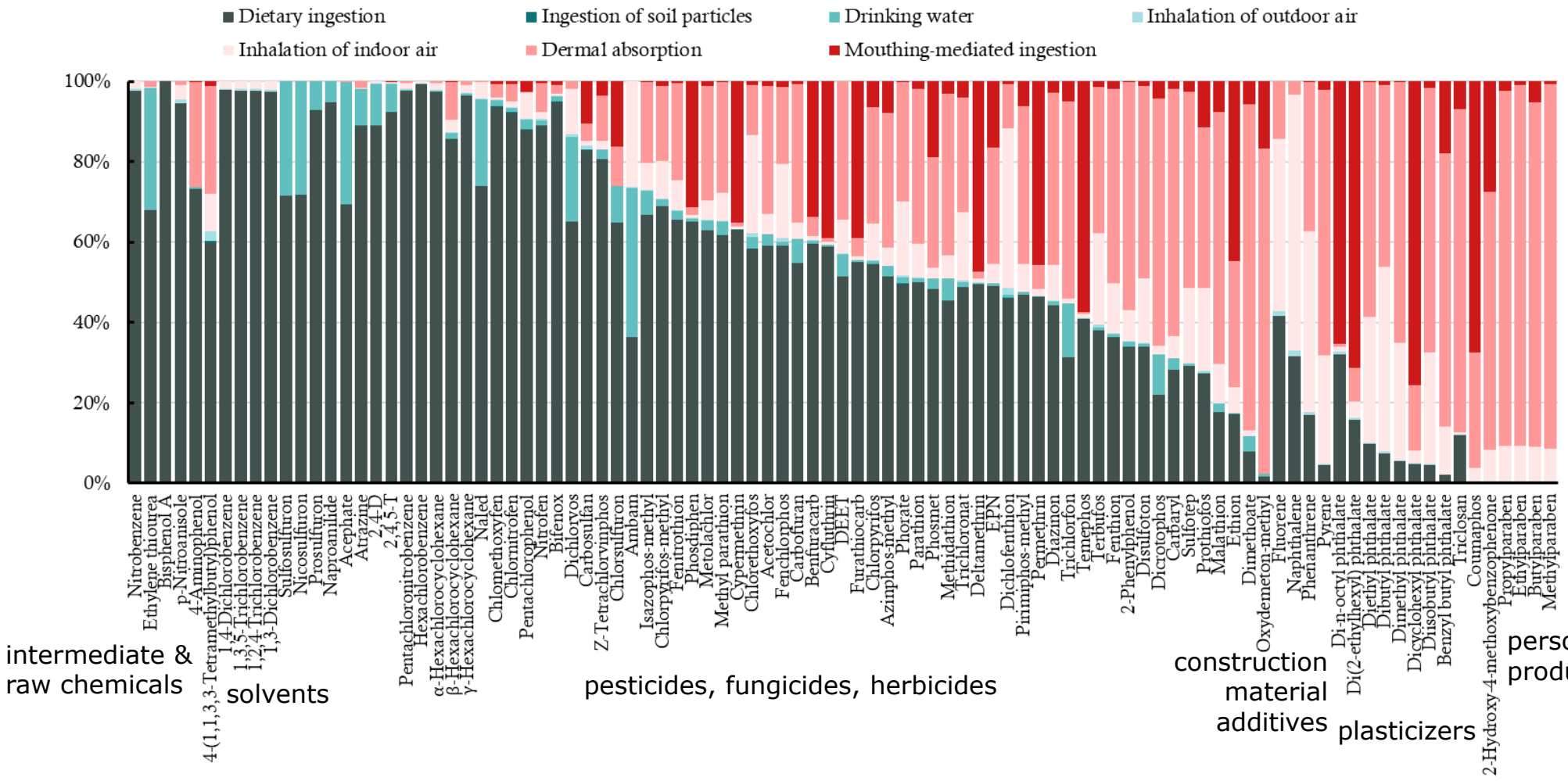
- Stepwise evaluation ensures every stage of the prediction process can be examined and checked, hence enhancing the model’s transparency and accountability.



Pieces together various environmental and biomonitoring data in a coherent framework and maximizes the use of all relevant empirical data in model “ground-truthing”.

Ensures not only that the model performs successfully overall but also that its success is not driven by the cancellation of errors in intermediate predictions by chance.

Human Exposure Patterns



intermediate & raw chemicals

solvents

pesticides, fungicides, herbicides

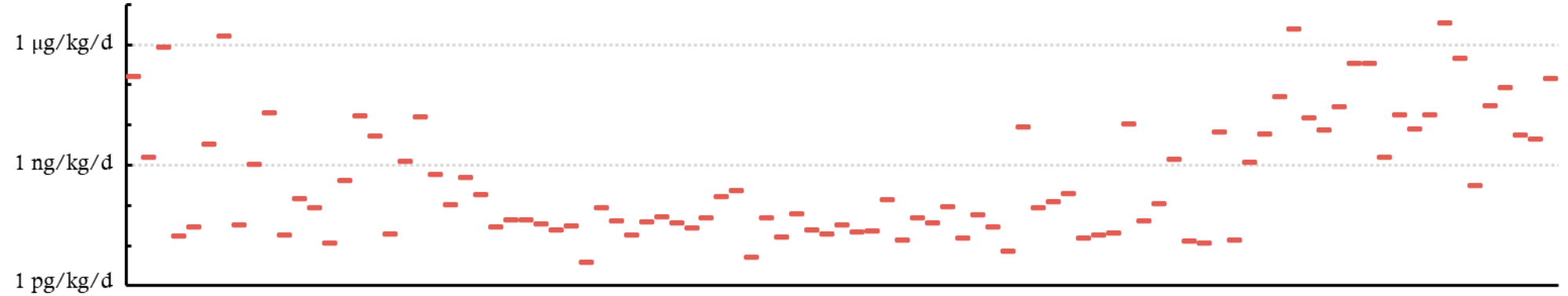
construction material additives

plasticizers

personal care product ingredients

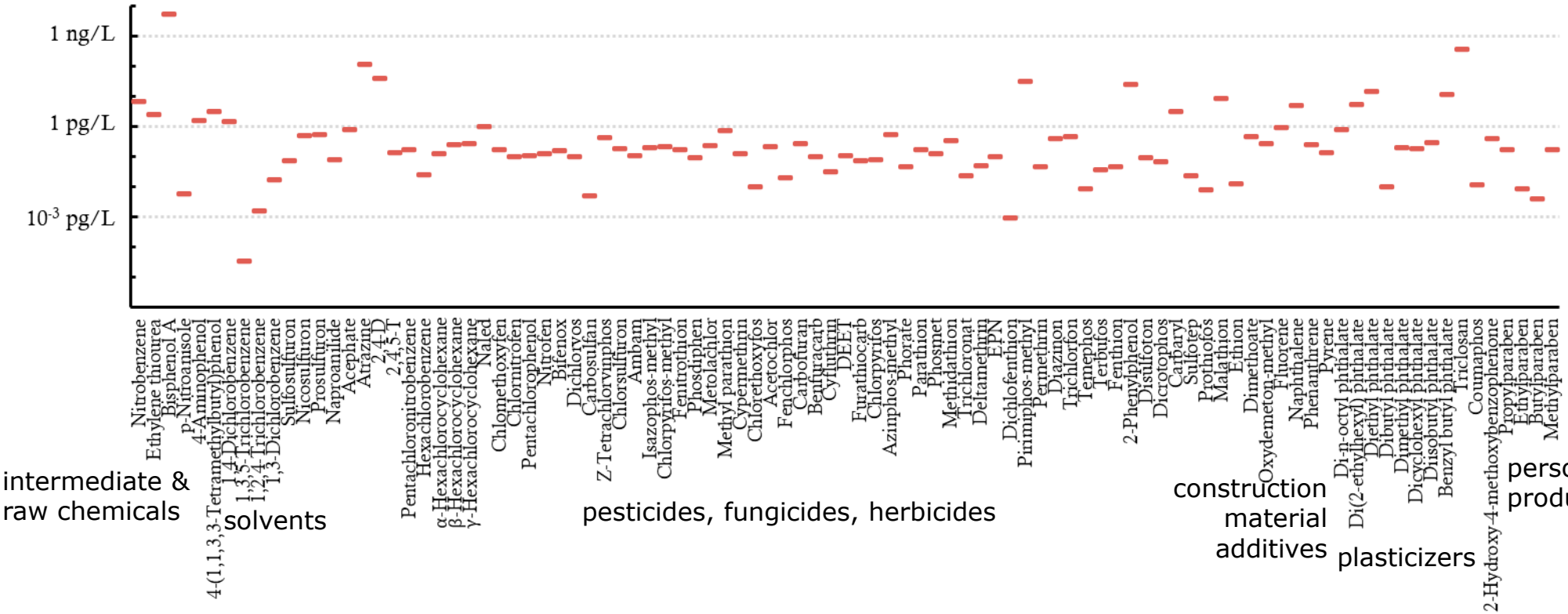
Human external exposure

Human daily intake dose



Aquatic species external exposure

Water concentration for aquatic species



intermediate & raw chemicals

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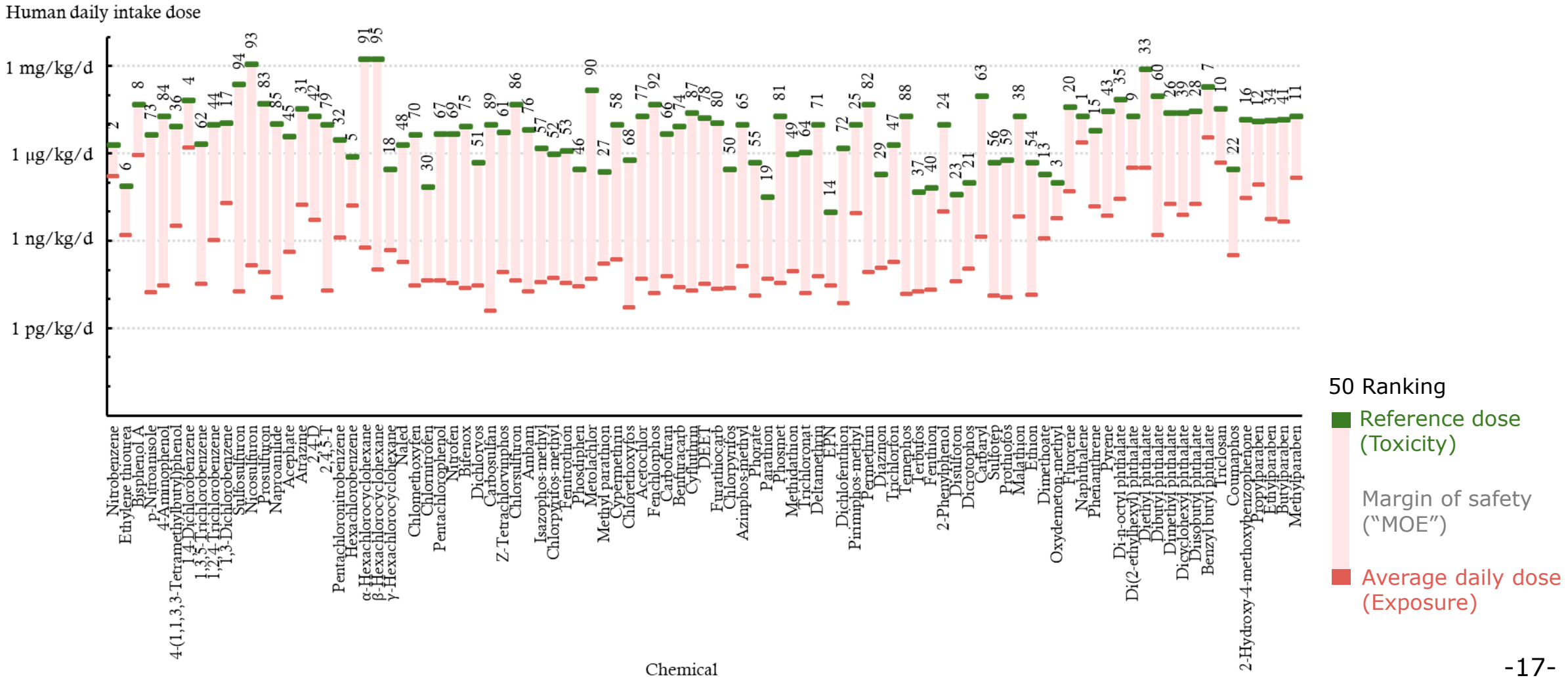
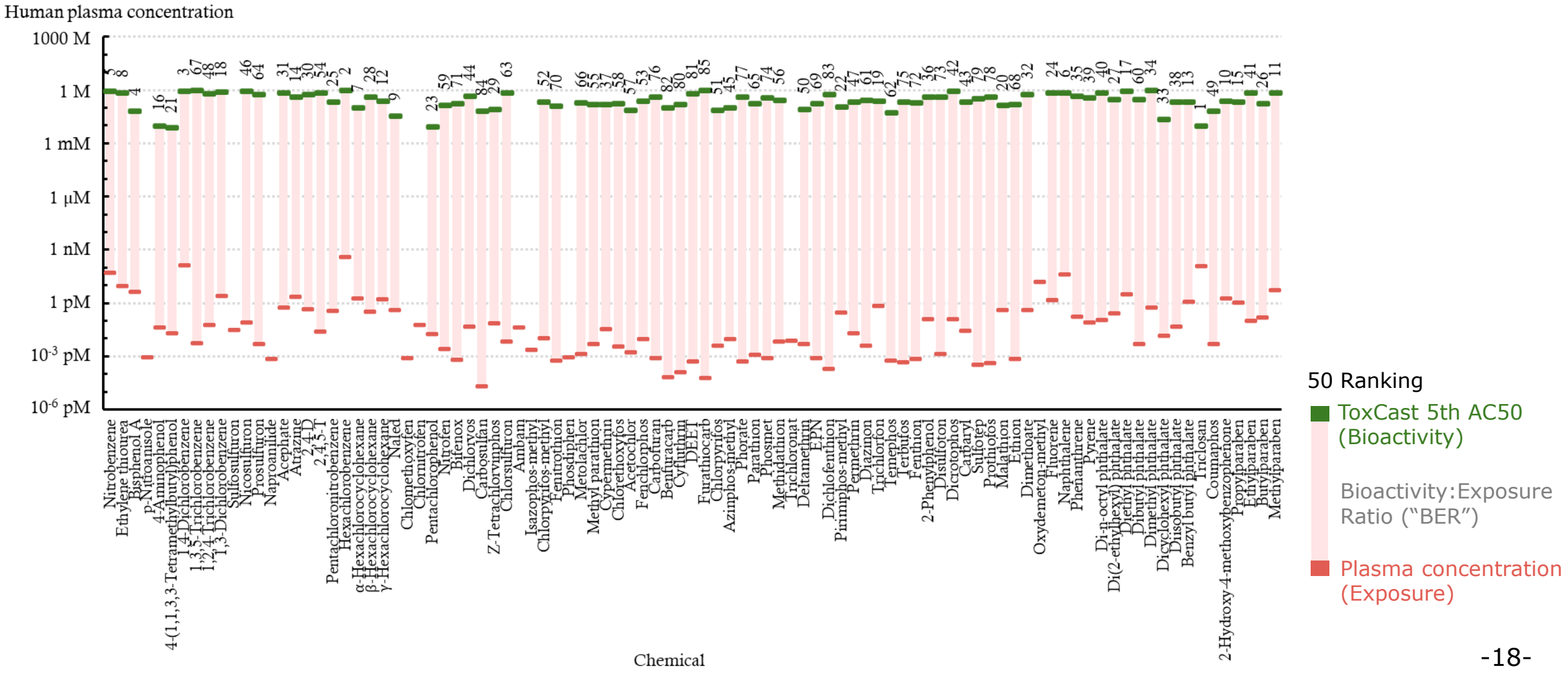
Risks to Human Health: Traditional "Dose-based" Approach



Risks to Human Health: NAM "Concentration-based" Approach



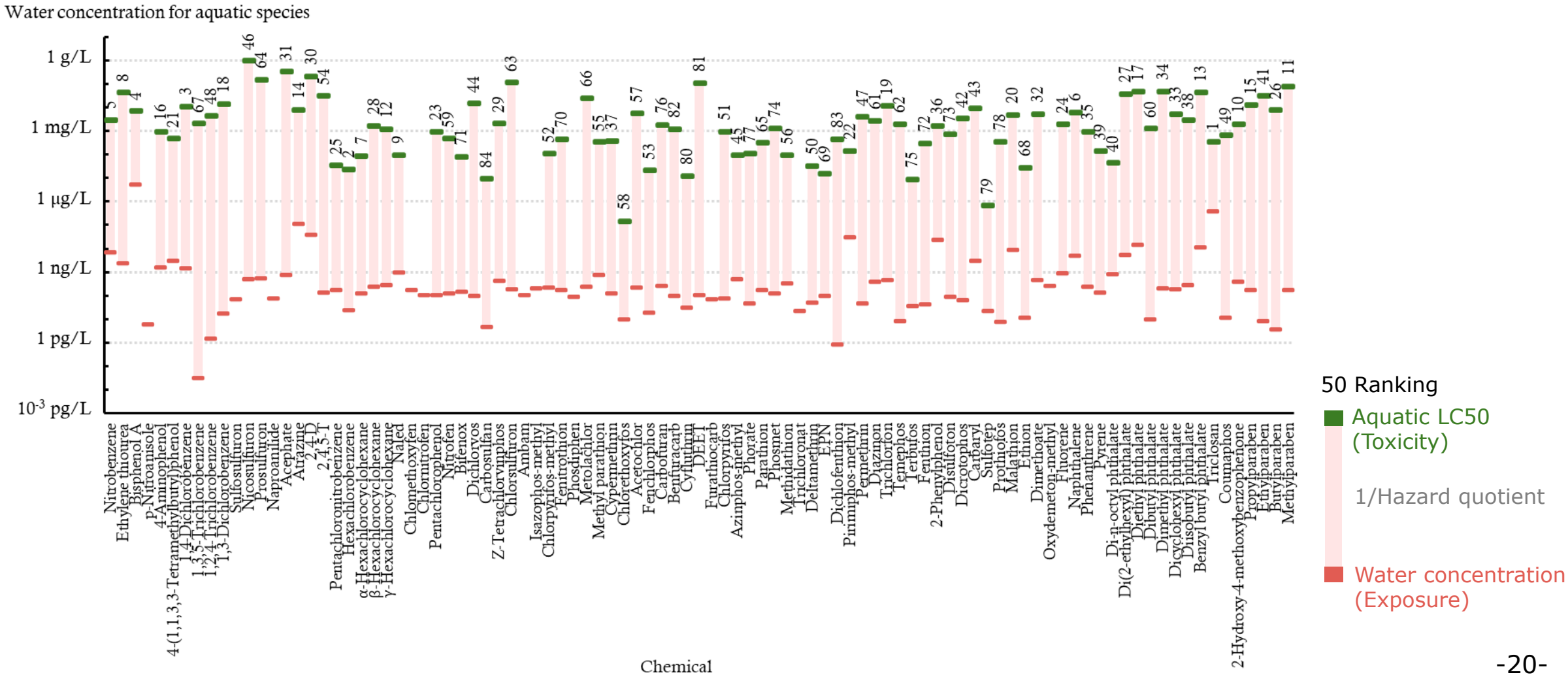
Consistency between Dose- & Concentration-based Approaches

Top	MOE-based ranking	BER-based ranking
1	Naphthalene	Triclosan
2	Nitrobenzene	Hexachlorobenzene
3	Oxydemeton-methyl	1,4-Dichlorobenzene
4	1,4-Dichlorobenzene	Bisphenol A
5	Hexachlorobenzene	Nitrobenzene
6	Ethylene thiourea	Naphthalene
7	Benzyl butyl phthalate	α-Hexachlorocyclohexane
8	Bisphenol A	Ethylene thiourea
9	Di(2-ethylhexyl) phthalate	Naled
10	Triclosan	2-Hydroxy-4-methoxybenzophenone

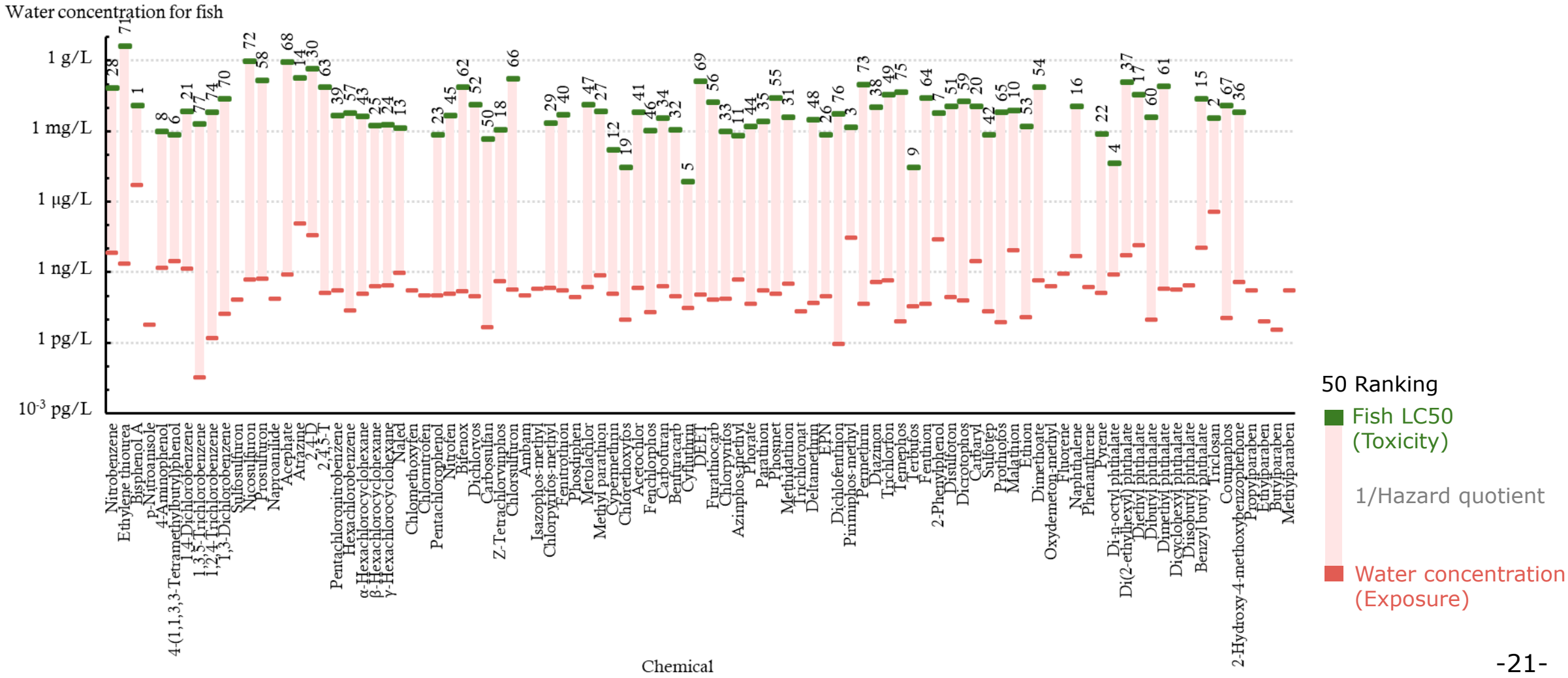
- The Spearman's rank correlation coefficient is 0.6 between the dose-based and concentration-based rankings
- This consistency highlights the potential of using both *in vivo* toxicity data and *in vitro* bioactivity as protective estimates of human health effects, supporting their feasibility in chemical screening and prioritization

Scan this QR code for more info about comparison between dose- & conc-based approaches

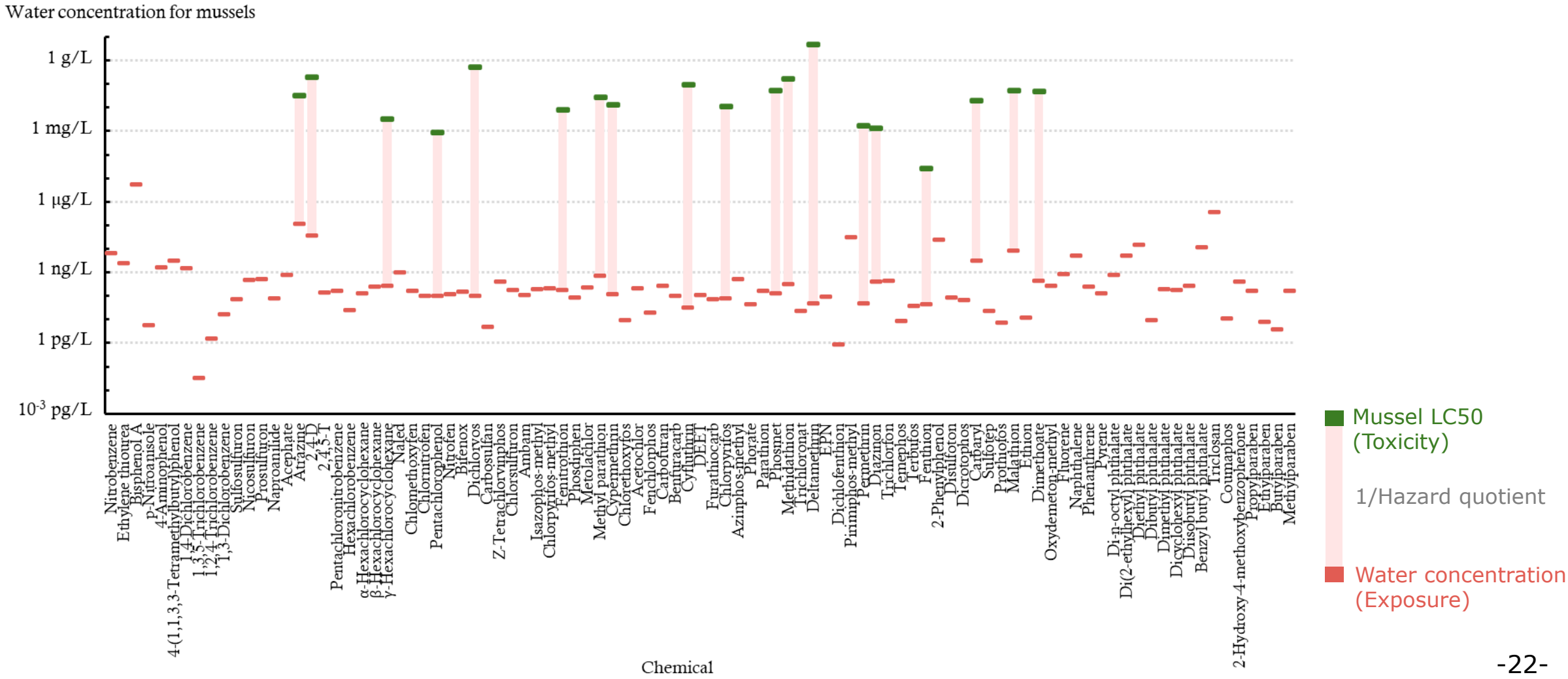
Risks to Ecological Health: All Aquatic Species Available in ECOTOX



Risks to Ecological Health: Fish



Risks to Ecological Health: Mussels



Consistency between Aquatic Species & Fish

- The Spearman's rank correlation coefficient is 0.84 between rankings based on all available aquatic species and fish
- This consistency indicates the abundance of fish data in ECOTOX and underscores the need for more comprehensive data on other aquatic species

Top	Aquatic species-based ranking	Fish-based ranking
1	Triclosan	Bisphenol A
2	Bisphenol A	Triclosan
3	Pirimiphos-methyl	Pirimiphos-methyl
4	Chlorethoxyfos	Di-n-octyl phthalate
5	Sulfotep	Cyfluthrin
6	Di-n-octyl phthalate	4-(1,1,3,3-Tetramethylbutyl)phenol
7	2-Phenylphenol	2-Phenylphenol
8	Atrazine	4-Aminophenol
9	Naled	Terbufos
10	4-(1,1,3,3-Tetramethylbutyl)phenol	Malathion

Prioritization for Further Scrutiny

Top	MOE-based ranking	BER-based ranking	Aquatic species-based ranking	Fish-based ranking
1	Naphthalene	Triclosan	Triclosan	Bisphenol A
2	Nitrobenzene	Hexachlorobenzene	Bisphenol A	Triclosan
3	Oxydemeton-methyl	1,4-Dichlorobenzene	Pirimiphos-methyl	Pirimiphos-methyl
4	1,4-Dichlorobenzene	Bisphenol A	Chlorethoxyfos	Di-n-octyl phthalate
5	Hexachlorobenzene	Nitrobenzene	Sulfotep	Cyfluthrin
6	Ethylene thiourea	Naphthalene	Di-n-octyl phthalate	4-(1,1,3,3-Tetramethylbutyl)phenol
7	Benzyl butyl phthalate	α-Hexachlorocyclohexane	2-Phenylphenol	2-Phenylphenol
8	Bisphenol A	Ethylene thiourea	Atrazine	4-Aminophenol
9	Di(2-ethylhexyl) phthalate	Naled	Naled	Terbufos
10	Triclosan	2-Hydroxy-4-methoxybenzophenone	4-(1,1,3,3-Tetramethylbutyl)phenol	Malathion

Take-home Messages

- Incorporating both humans and non-human organisms into chemical risk assessments is essential for achieving a more comprehensive, multifaceted, and balanced approach to support informed decision-making in the "One Health" context.
- The PROduction-To-EXposure (PROTEX) framework offers significant potential for advancing this goal.

Acknowledgments
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