Tools and Techniques for Chemical Prioritization: Harnessing Publicly Accessible Ecotoxicological Data

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Background

- Over the last decade, there have been substantial increases in the amount of publicly accessible ecotoxicological data and risk assessment tools.
- Practically, this is highly valuable to risk assessors and regulators who are often tasked with assessing the potential ecotoxicological risks of high numbers of chemicals detected in the aquatic environment.
- However, it can be difficult to determine how to effectively harness all this publicly accessible data and/or utilize these open-source tools for data-intensive risk assessments.
- Here, we demonstrate how aquatic benchmarks can be collated and/or developed using data from publicly accessible databases, and then used to prioritize chemicals detected in aquatic environments.
- Utilizing data generated from a 10-year monitoring effort across the Great Lakes Estuaries (2008 – 2018), we apply these benchmarks to prioritize legacy contaminants and chemicals of emerging concern.

Objectives:
- Collate and/or derive aquatic benchmarks for chemicals detected in the Great Lakes Estuaries, utilizing publicly accessible data and open-source databases.
- Compare and contrast benchmark analyses, identifying priority chemicals for management, monitoring, or assessment and general target areas for further ecotoxicological research.

Aquatic Monitoring Data

- Grab and/or composite samples were collected across the Great Lakes Estuaries from 2008 – 2018 (**Figure 1**).
- 67 – 552 chemicals were monitoring for at each site, including pharmaceuticals and personal care products, pesticides (active ingredients + degradates), PAHs/Fuels, industrial/mixed-use chemicals, and wastewater indicators (metabolites, sterols, hormones).
- Overall, **463 unique chemicals** were detected across the Great Lakes Estuaries over the 10-year sampling period.

Lake
- Erie
- Huron
- Michigan
- Ontario
- Superior
- NA
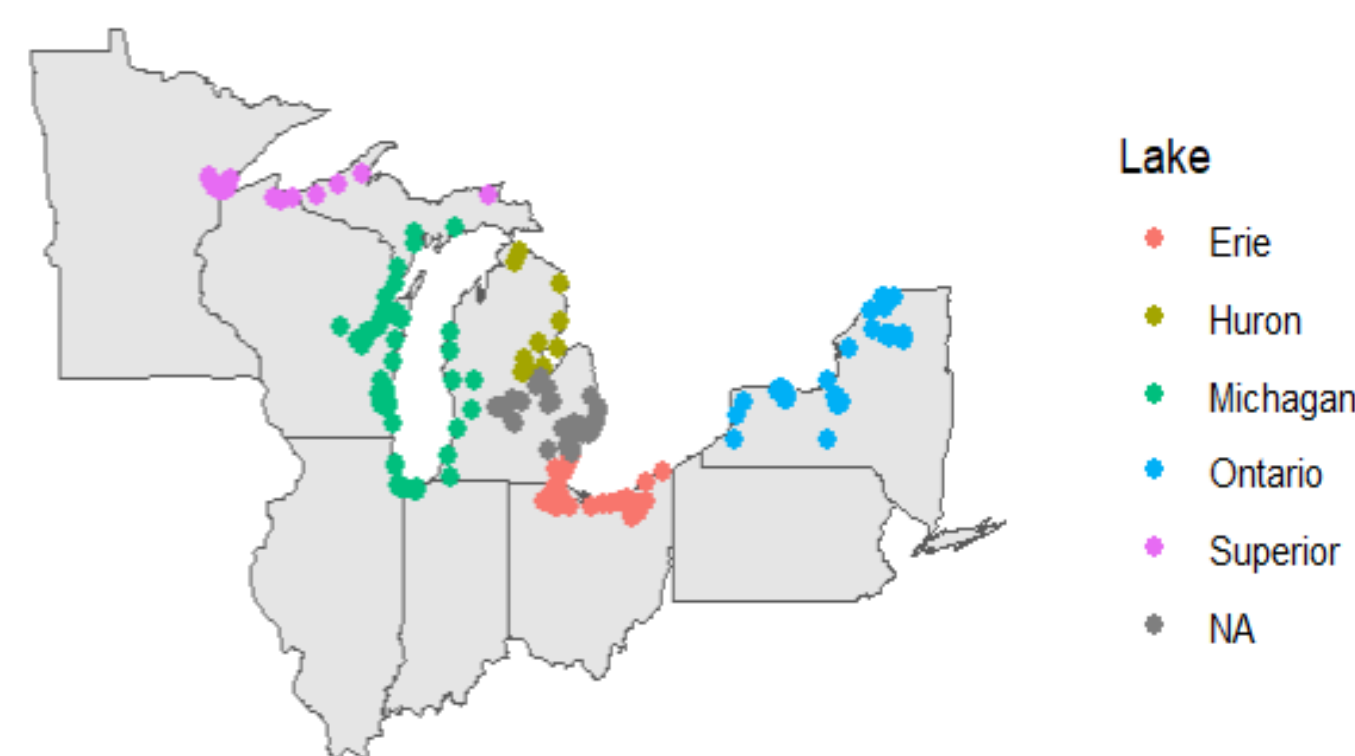
Figure 1 Sample sites across the Great Lakes Estuaries (2008 – 2018) used to collate data used for benchmark-based chemical prioritization.

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## Aquatic Benchmark Collation and Derivation
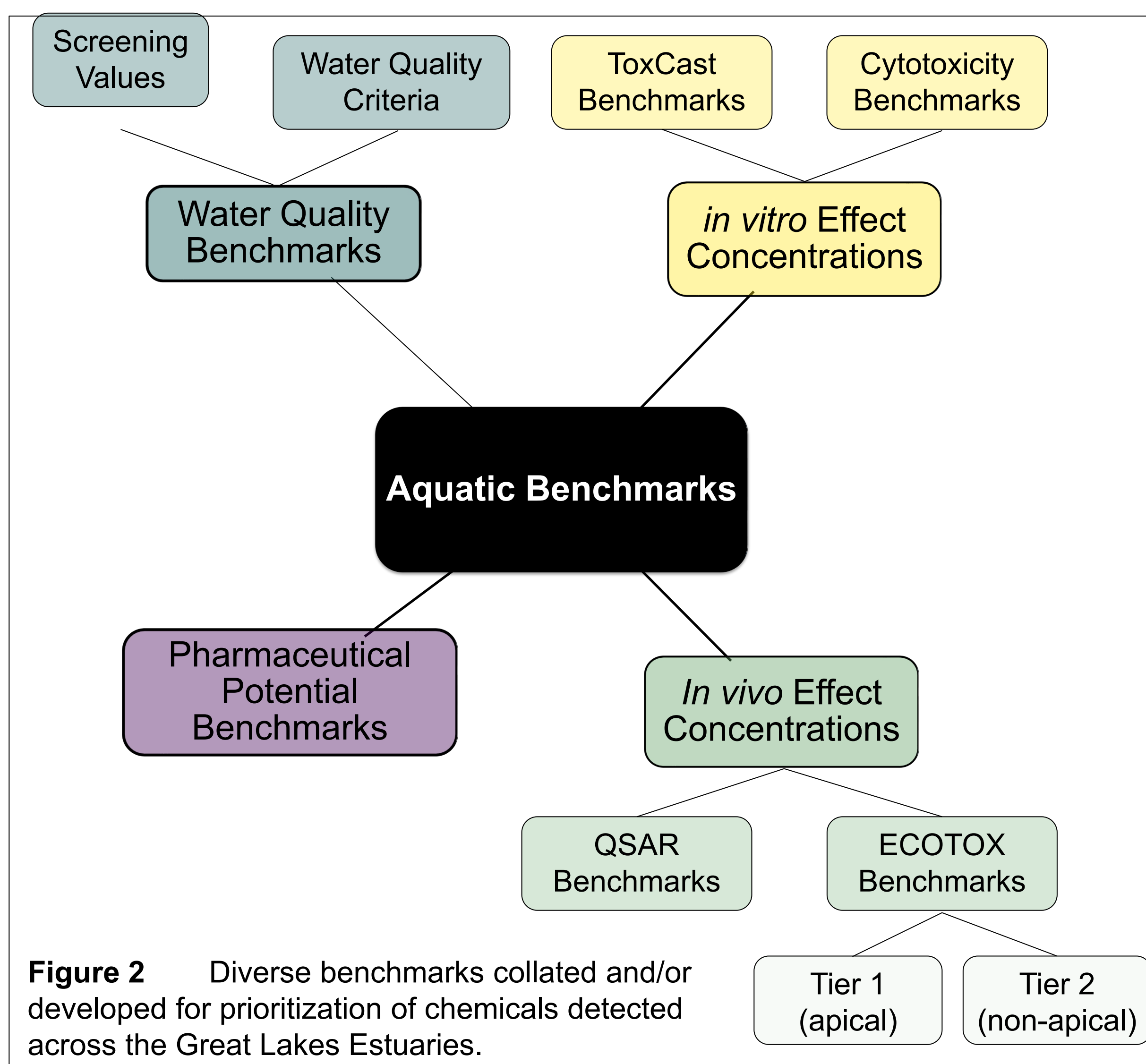
Figure 2 Diverse benchmarks collated and/or developed for prioritization of chemicals detected across the Great Lakes Estuaries.

Table 1 Diverse benchmarks collated and/or developed for prioritization of chemicals detected across the Great Lakes Estuaries.
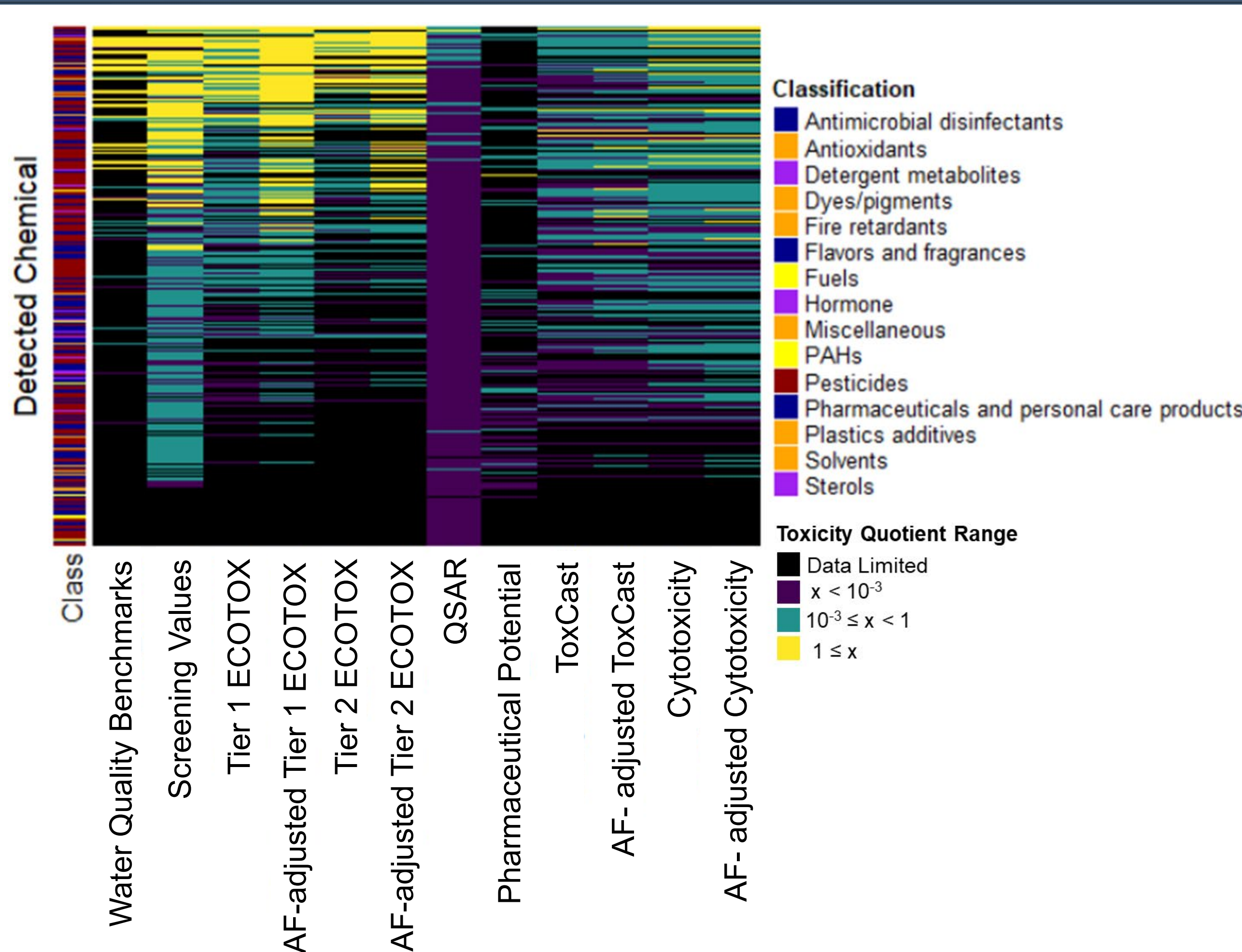
Benchmark	Description	Derivation	Source(s)
Water Quality Benchmarks	Current (provisional or approved) water quality guidelines recommended by international, federal, state, tribal, or provincial regulatory agencies.	Minimum water quality benchmark available	[1 – 10]
Screening Values	Historical water quality guidelines and screening values recommended by regulatory and/or government groups.	Minimum screening value available.	[11 – 18]
Tier 1 ECOTOX	Apical in vivo effect concentrations for aquatic vertebrates, aquatic invertebrates, and/or aquatic plants, both unadjusted (minimum effect value) and application-factor adjusted (accounting for study duration, data richness, and available endpoints).	Minimum in vivo effect concentration (unadjusted + adjusted with application factor)	[19]
Tier 2 ECOTOX	Non-apical in vivo effect concentrations for aquatic vertebrates, aquatic invertebrates, and/or aquatic plants, both unadjusted (minimum effect value) and application-factor adjusted (accounting for study duration, data richness, and available endpoints).		
QSAR	Acute toxicity estimates for aquatic vertebrates, invertebrates, and plants derived using quantitative structure-activity relationships and baseline toxicity equations.	Minimum value of all consensus estimates of acute toxicity.	[20 – 24]
Pharmaceutical Potential	Maximum (or peak) serum concentration that a drug achieves following dosing (C_{max}) for each pharmaceutical, indicating pharmaceutical potency.	Maximum available C_{max}.	[25]
Cytotoxicity	Lower limit of cytotoxic burst concentration for each chemical, determined using results from in vitro bioassays carried out through the ToxCast testing efforts, both unadjusted and application-factor adjusted (accounting for data richness).	Lower limit of cytotoxic burst (unadjusted + application factor adjusted).	[26 – 28]
ToxCast	Activity concentration at cut-off (ACC) derived from in vitro assays carried out through the ToxCast testing effort, both unadjusted and application-factor adjusted (accounting for data richness and number of potentially perturbed pathways).	Minimum activity concentration at cut-off (ACC) (unadjusted + application factor adjusted).	[26 – 27]

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Comparison of Benchmarks to Aquatic Monitoring Data
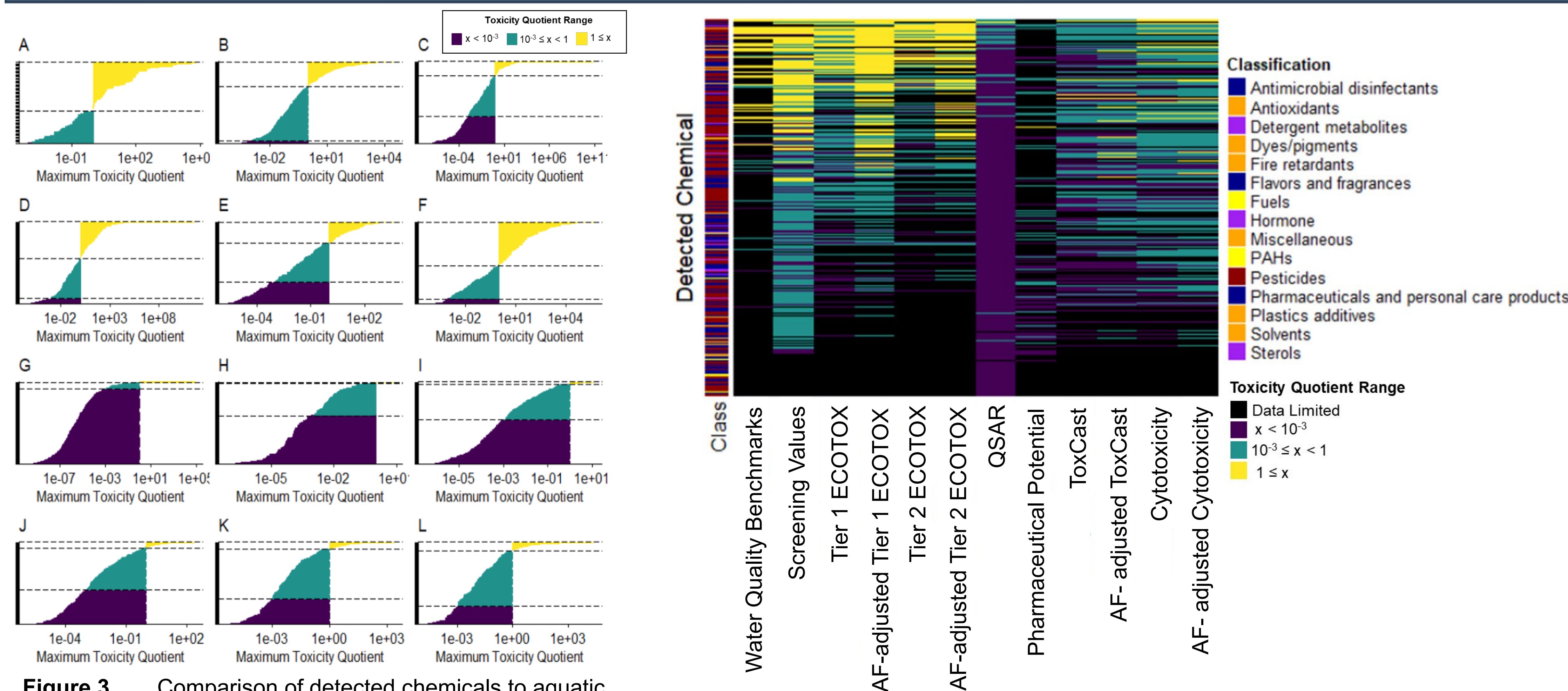
Figure 3 Comparison of detected chemicals to aquatic benchmarks, demonstrating exceedence distributions across different benchmark types:
(A) Water Quality Benchmarks; (B) Screening Values; (C – D) Tier 1 ECOTOX (unadjusted + AF-adjusted); (E – F) Tier 2 ECOTOX (unadjusted + AF-adjusted); (G) QSAR; (H) Pharmacological Potential; (I – J) ToxCast (unadjusted + AF-adjusted); (K-L) Cytotox (unadjusted + AF-adjusted).

Classification
- Antimicrobial disinfectants
- Antioxidants
- Detergent metabolites
- Dyes/pigments
- Fire retardants
- Flavors and fragrances
- Fuels
- Hormone
- Miscellaneous
- PAHs
- Pesticides
- Pharmaceuticals and personal care products
- Plastics additives
- Solvents
- Sterols

Toxicity Quotient Range
- Data Limited
- $x < 10^{-3}$
- $10^{-3} \leq x < 1$
- $1 \leq x$

Figure 4 Comparison of exceedences (toxicity quotient range = x ≥ 1, highlighted in yellow on heat map) and data availability (data limitations highlighted in black on heat map) across different benchmark types* collated to evaluate the ecotoxicological potential of chemicals detected in grab and/or composite samples collected from watersheds across the Great Lakes Estuaries (2008 – 2018).

Key Findings

- Data availability significantly varied across benchmark types:
  - QSAR, Screening, and ToxCast/Cytotox benchmarks had the highest amounts of available data (**96, 82, & 57% data coverage**)
  - Water Quality, Pharmaceutical, and Tier 2 ECOTOX benchmarks had the lowest amounts available data (**14, 29, 32 % data coverage**).
- Benchmark exceedence also significantly varied across benchmark types:
  - Water Quality, AF-adjusted Tier 1 + 2 ECOTOX, and Screening benchmarks had the highest amount of chemicals with TQ > 1 (**60, 44, 53, 30 % exceedence** across data-available chemicals).
  - QSAR, Pharmaceutical, ToxCast, and Cytotoxicity benchmarks had the lowest amounts of chemicals with TQ > 1 (**0.2, 0.01, 2, 8 % exceedence** across data-available chemicals).
- Benchmark analysis highlighted **13 high priority chemicals:**
  - **12 chemicals** exceeded water quality and in vivo benchmarks:
    - 9 pesticides (atrazine, chlorpyrifos, dichlorvos, diazinon, imidacloprid, pentachlorophenol, diuron, metribuzin, carbaryl), 1 personal care product (triclosan), and 2 industrial chemicals (bis(2-ethylhexyl) phthalate, pyrene).
  - **1 compound** exceeded all water quality, in vivo, and in vitro benchmarks:
    - Bisphenol A

This analysis demonstrated that publicly accessible data and open-source programs can be efficiently integrated and used for large-scale ecotoxicological risk assessment and chemical prioritization.

Acknowledgements