Next Generation Ecological Hazard Assessment

Challenges and Opportunities

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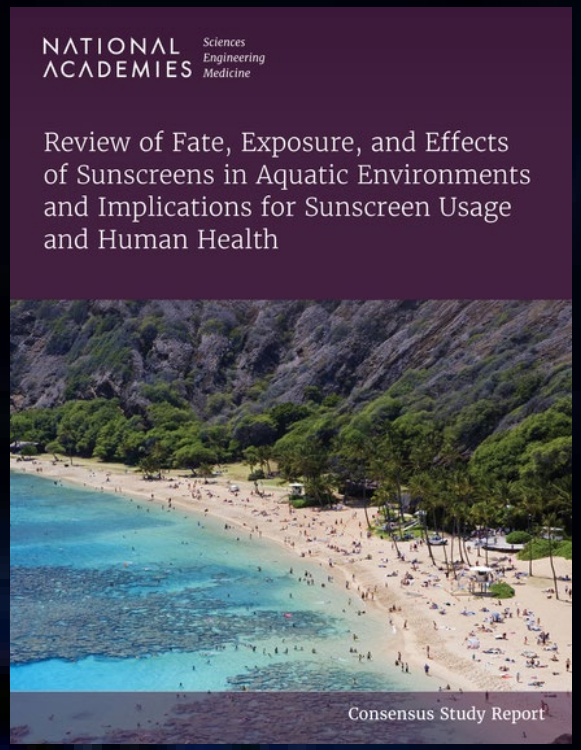
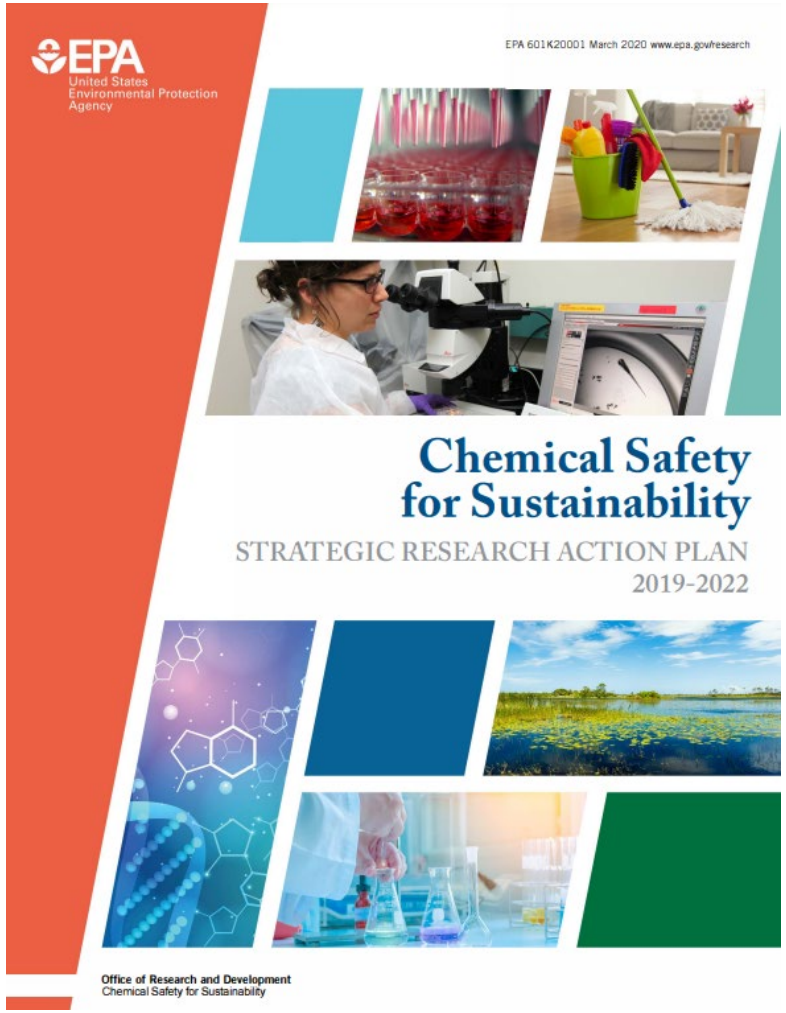


Identified Knowledge Gaps for UV Filter Toxicity/Hazard

- Limited chronic data
- Limited species coverage
- Limited data on degradates
- Few studies span levels of org
- Limited sediment toxicity data
- Lack of community level studies
- Need to address mixtures

- These same knowledge gaps apply to most chemicals in commerce
- Chemical safety decisions are made daily – despite these knowledge gaps

US EPA Office of Research and Development



Problem Statement:

Tens of thousands of chemicals are currently in use and hundreds more are introduced to the market every year. Environmental exposures most typically occur as complex chemical mixtures

Traditional approaches to evaluate chemical toxicity and exposure are expensive and do not fully reflect all biological responses and exposure pathways

EPA CSS Program Vision:

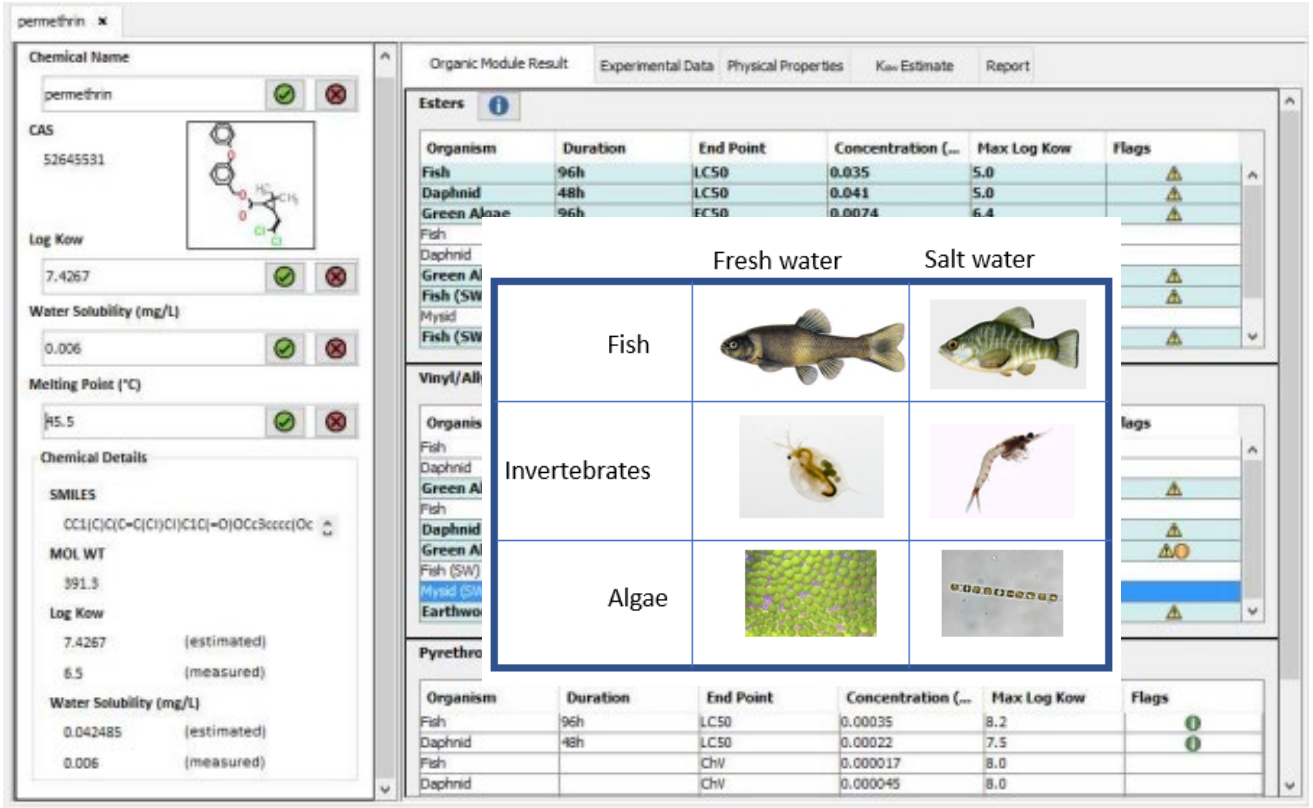
Accelerating the pace of chemical assessment to enable our partners and stakeholders to make informed and timely decisions concerning the potential impacts of environmental chemicals

Reduce and eliminate vertebrate animal testing to the extent that the replacement approaches are, at least, as informative as in vivo tests

Develop new approach methodologies for both hazard and exposure and demonstrate ways to effectively utilize them in decision-making

Transform chemical testing, screening, prioritization, and risk assessment practices

NAMs have been very effective in ecological hazard assessment



- Quantitative structure-activity relationships (QSARs) have been used by the U.S. Environmental Protection Agency since 1981 (>40 years) to predict the aquatic toxicity of new industrial chemicals in the absence of test data.
- As of 2015 709 QSARs had been developed for 111 organic chemical classes and integrated into ECOSAR.
- Acute and chronic
- Fresh water and marine
- Fish, inverts, and algae

- Adequate for most chemicals exhibiting “baseline” toxicity via non-polar narcosis (≈85% of industrial chemicals)

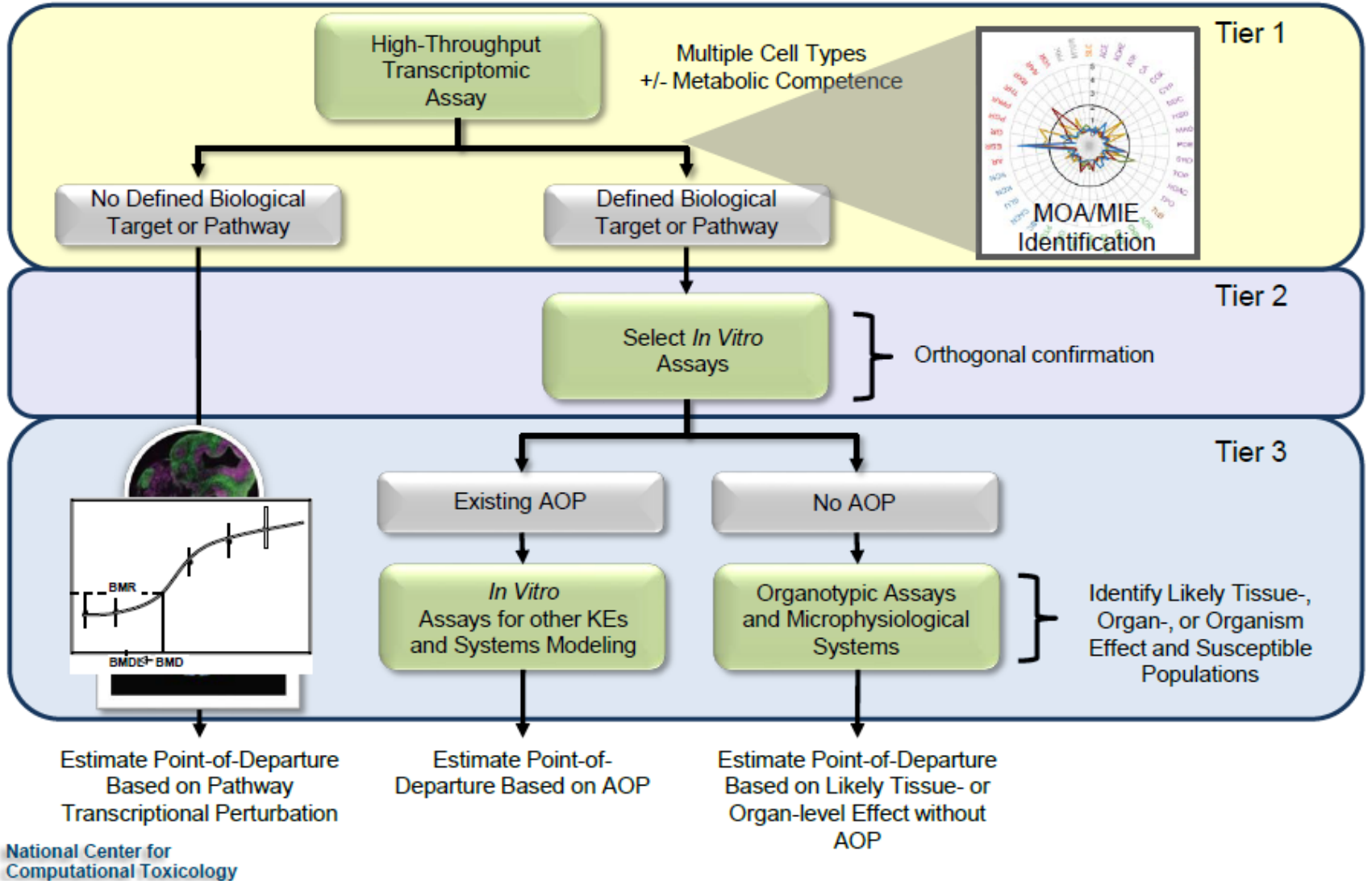
Operation Manual for the ECOlogical Structure-activity Relationship Model (ECOSAR) Class Program v. 2.2 (Feb. 2022).
https://www.epa.gov/system/files/documents/2022-03/operation-manual-v.2.2_1.pdf

Next Generation Blueprint of Computational Toxicology at the U.S. Environmental Protection Agency

Broad Screen
- HTTr - transcriptomics
- HTPP – cell painting
- HTM - metabolomics

Targeted Screen
- MoA-relevant QSAR
- MoA-relevant bioactivity screening

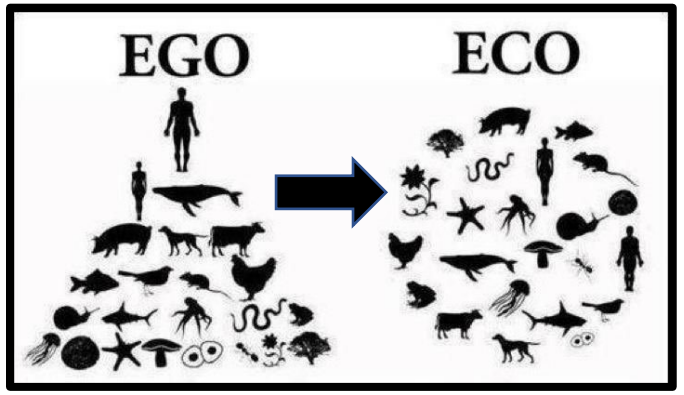
Complex Systems
- AOPs
- Tiered testing / IATA
- Organotypic models
- Physiological / ecological models



National Center for Computational Toxicology

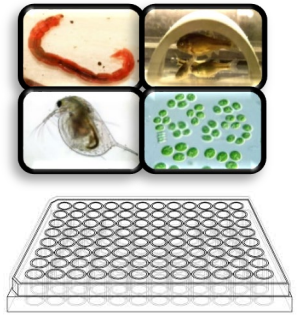
Ecological High Throughput Testing

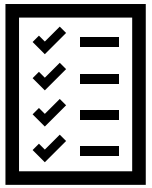
Broad pathway coverage in humans/mammals alone is not enough



Expanding HTP approaches to wider range of organisms (e.g., Eco-HTTr) – fish, invert, algae.

Computational assessment of pathway conservation – can also be used to maximize pathway coverage with minimum species representation



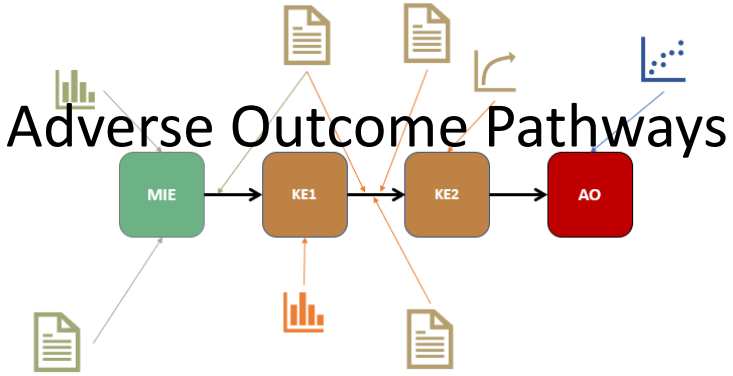


Standard protocols, acceptance criteria, reporting frameworks

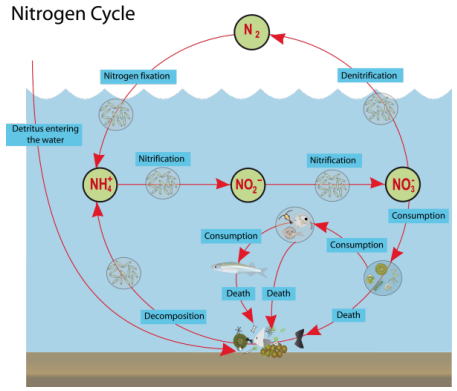
Can help address:

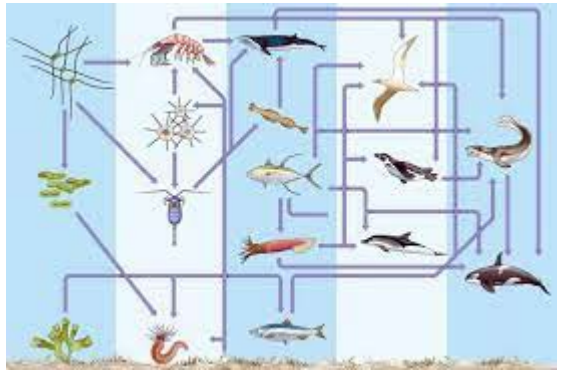
- *Limited chronic data*
- *Limited species coverage*
- *Limited data on degradates*
- *Mixtures*

Knowledge assembly/synthesis -> Models



Link observed bioactivity (molecular/cellular) to apical hazard(s)





Do not have the resources to examine the impacts of every chemical:

- Across multiple levels of biological organization
- Across a wide range of species
- In a field-relevant context

Need to leverage existing knowledge

- About physiological and ecological processes
- Available data on response of systems to different types of perturbations

Use measurements we can make as inputs to models based on our best current understanding of systems.

- Accept that those predictions will not be perfect

Making our data more accessible and impactful

Data hub

- Data repository
- Interoperable
- Known provenance

Data mart

- Compilation of decision-relevant data
- Regular updates

Decision support tool

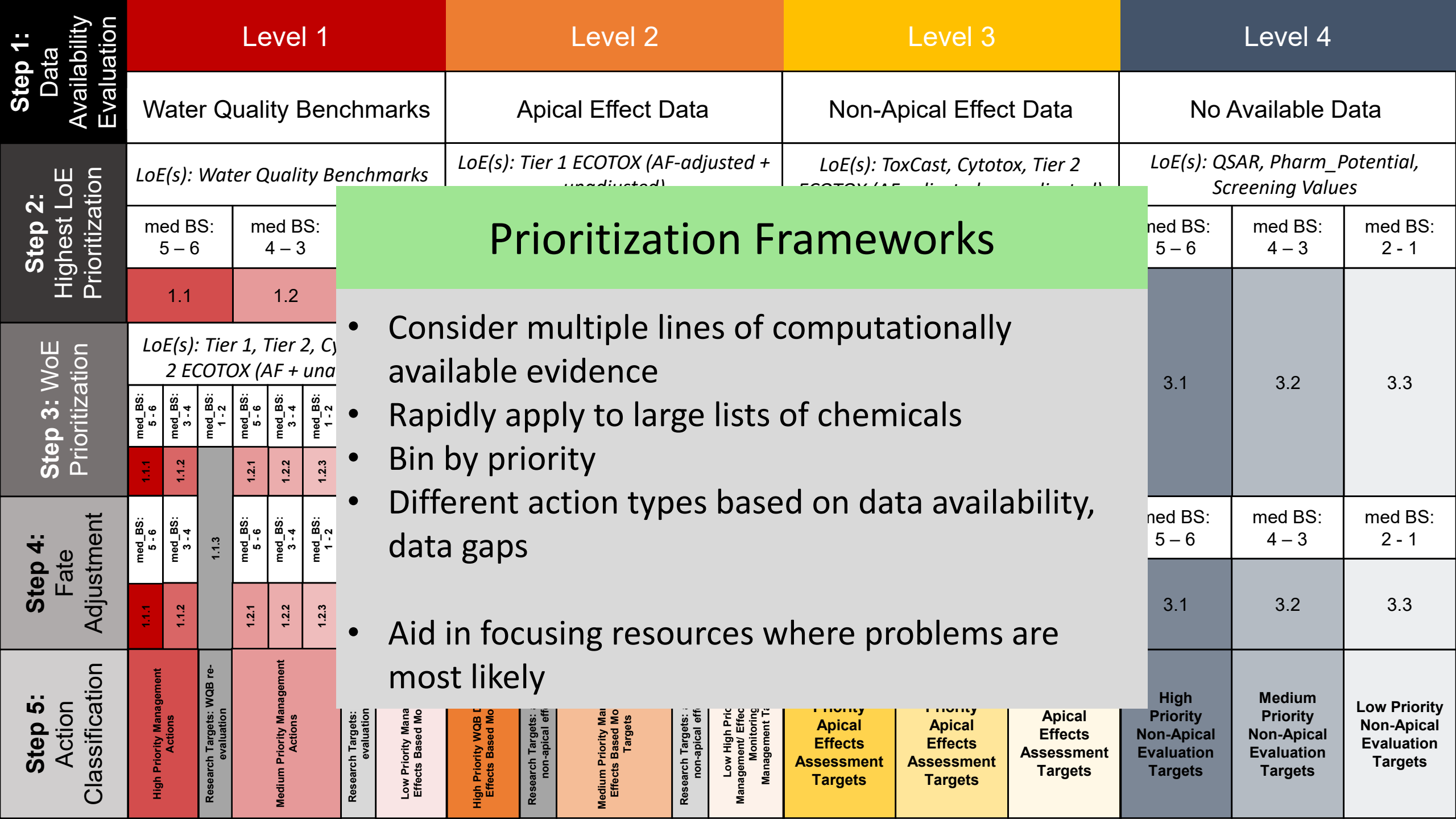
- Customized interface
- Filter, process, visualize

Data quality can be challenging to assess computationally

Prioritization Frameworks

- Consider multiple lines of computationally available evidence
- Rapidly apply to large lists of chemicals
- Bin by priority
- Different action types based on data availability, data gaps

- Aid in focusing resources where problems are most likely



Knowledge gaps are the reality we live with

What can we do?

New Approach Methodologies	Generate hazard information more rapidly and cost effectively
Predictive models (generalized)	Leverage existing knowledge to build models to predict what we can't measure easily
Data / knowledge infrastructure	Make the data we do have easier to access and use
Triage / prioritize	Focus resources where we're most likely to have problems and on the most critical data gaps
Iterate	Utilize what we learn and where we make mistakes to improve