Developing Protective Aquatic Life Values for Data-Limited PFAS Chemicals

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Note - Opinions are those of the authors, and content does not necessarily reflect EPA position or policy.

Criteria Development and Minimum Data Requirements (MDRs)

- The "1985 Guidelines" (*Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses)* establishes the approach for developing aquatic life criteria in the United States
  - Toxicity data generally must be available for 8 representative taxa to meet the MDRs in order to develop criteria for freshwater aquatic life; similar requirements have been established for estuarine/marine criteria
  - MDR objective: Protect ecosystems and most genera (the aquatic community) from adverse effects resulting from exposure to toxicants, without *requiring* detailed knowledge of a chemicals' mode of action

MDRs for the Development of Freshwater Criteria

SALMONID

SECOND FISH FAMILY

CHORDATA

PLANKTONIC CRUSTACEAN

BENTHIC CRUSTACEAN

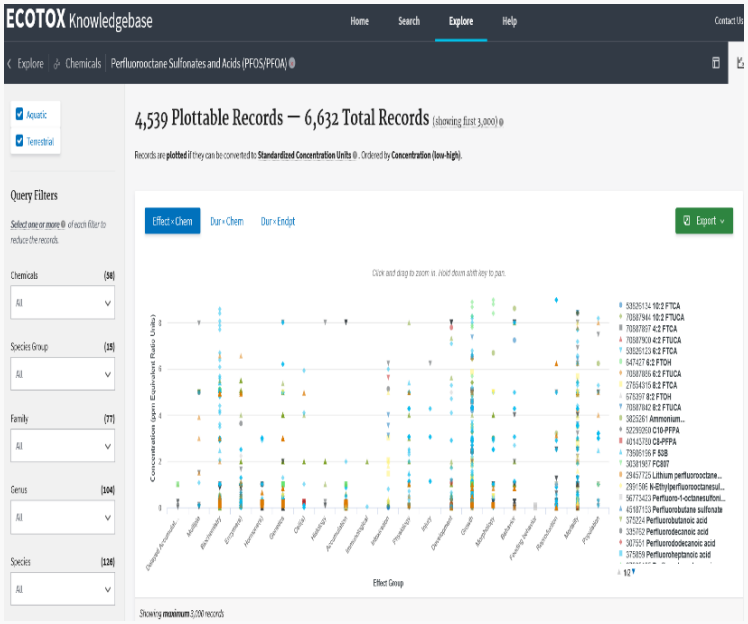
INSECT

ROTIFERA, ANNELIDA, MOLLUSCA

OTHER INSECT OR MOLLUSC

Evaluating Existing PFAS Data: ECOTOX Knowledgebase

- Publicly available database of chemical-specific toxicity data for aquatic life, terrestrial plants and wildlife
  - Curated, reviewed data from >48,000 publications from open and grey literature
  - Data forms basis for development of most aquatic life criteria



Overview of Available PFAS Data

- There are currently 96 individual CAS numbers for PFAS compounds identified by the ECOTOX Knowledgebase
- PFOS and PFOA represent the most frequently tested; several other PFAS compounds have limited data
- Common taxa tested: fish, aquatic and (some) terrestrial invertebrates
- Some apical studies, but few “standardized” tests; gene expression/biomarkers commonly reported effects

Available PFAS Toxicity Data and MDRs

- MDRs appear to be met for PFOA and PFOS
- US EPA is currently reviewing data for these chemicals
  - Toxicity data are now being evaluated to *confirm* available data are acceptable for quantitative use (and MDRs are met) in criteria development
  - See Poster TP292
    - ***Reviewing Current Toxicity Literature to Evaluate Available Data to Support the Development of Draft PFOA and PFOS Aquatic Life and Aquatic-Dependent Wildlife Ambient Water Quality Criteria***

Available PFAS Toxicity Data and MDRs

- Toxicity data are rapidly increasing, but remain limited for most PFAS chemicals
- PFAS chemicals represent a large, structurally-complex universe of chemicals
  - More than 3,000 PFAS chemicals have been estimated to occur on the global market (Wang et al. 2017)
- MDRs are not currently met for other PFAS compounds

Available PFAS Toxicity Data and MDRs

- PFSA and PFCA examples – Number of studies and MDRs met

PFAS Compound	Number of Studies in ECOTOX*	Number of Freshwater MDRs Met*
Perfluoroalkyl Sulfonic Acids (PFSAs)		
Sulfluramid	18	3
Potassium perfluorobutanesulfonate	7	1
Perfluorobutane sulfonate	5	1
Perfluorobutane sulfonic acid	3	1
Perfluorooctane sulfonyl fluoride	1	0
Perfluoroalkyl Carboxylic Acids (PFCAs)		
Perfluorodecanoic acid	17	4
Perfluorododecanoic acid	10	3
Perfluorononanoic acid	27	3
Perfluorobutanoic acid	12	3
Perfluoroundecanoic acid	3	3
Perfluorohexanoic acid	8	2
Trifluoroacetic acid	3	2
Perfluoropropionic acid	2	2
Perfluoropentanoic acid	5	2
Perfluorooctadecanoic acid	1	1
Perfluorohexadecanoic acid	2	1
Perfluoroheptanoic acid	7	1
Perfluorotetradecanoic acid	5	1
Perfluorotridecanoic acid	4	1

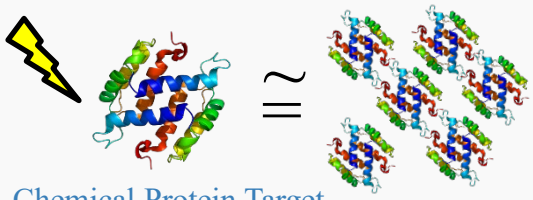
* = As of March, 2019

How Might We Address Data- Limited PFAS Chemicals?
Areas for Exploration

- US EPA will be evaluating possible approaches for developing protective aquatic life values for other PFAS chemicals
  - Following the evaluation of available data to support the development of draft PFOA/PFOS criteria
  - Approaches will be first explored with PFOA/PFOS database, followed by the evaluation of possible approaches with databases for selected PFAS chemicals not meeting MDRs
- ***Examples*** of approaches under consideration
  - Extrapolating effects data
  - Grouping chemicals having specific modes of action
  - Tailoring data needs to the PFAS group being evaluated
  - Incorporating a broader range of available data

Extrapolating Effects: A Bioinformatics-Based Approach

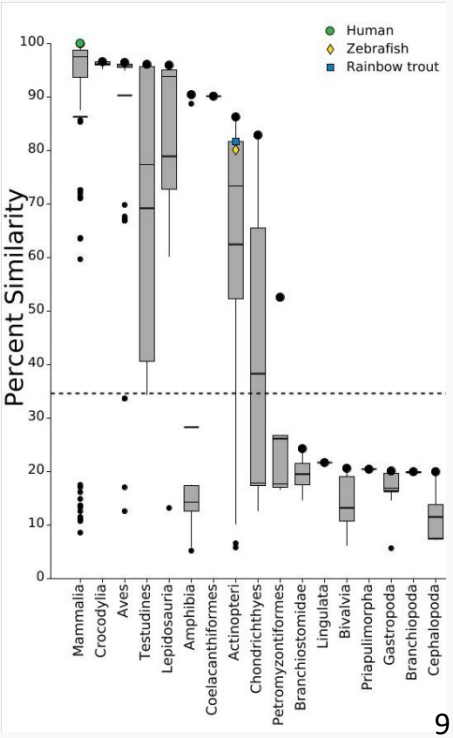
- Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS)*
  - Uses similarity in protein structure for a known sensitive species to predict toxicity to other species with a well-defined molecular target
  - Analyzes protein sequences from thousands of species to identify all species potentially sensitive to a chemical or class of chemicals



Chemical Protein Target in Target Species

Compare to millions of proteins from thousands of species to predict potential cross-taxa susceptibility

Cross-Species Homology of PPARα



*LaLone et al. 2016. Sequence alignment to predict across species susceptibility (SeqAPASS): A web-based tool for addressing the challenges of species extrapolation of chemical toxicity. Tox. Sci. 153, 228-245.

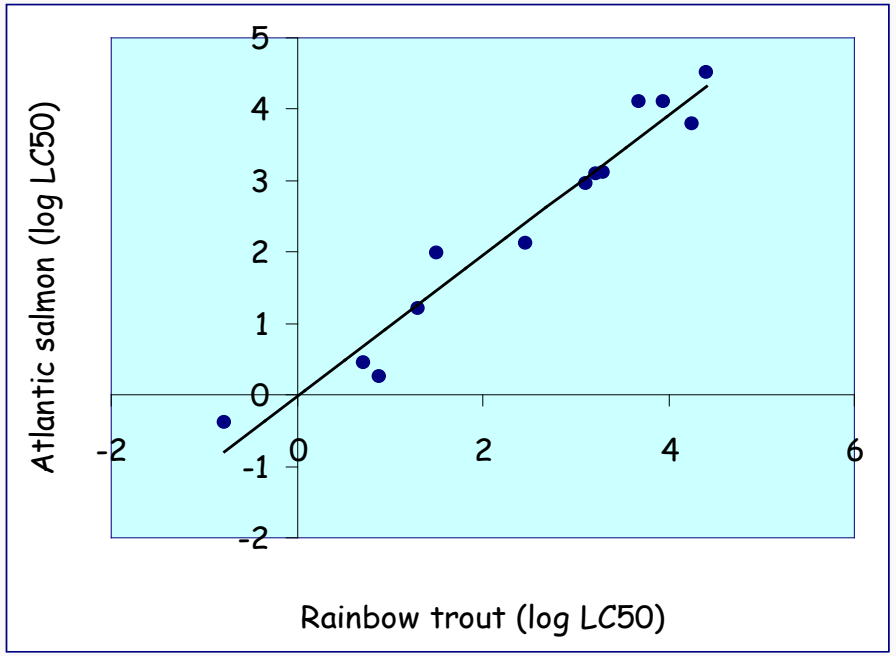
Extrapolating Effects: A Bioinformatics-Based Approach

- Approach could be applied to acute or chronic toxicity
- For protective aquatic life value development, approach could be used to identify groups of species that are likely or unlikely to be sensitive to a chemical
  - Analysis could then focus on potentially sensitive species
  - Insensitive species or groups (based on MOA) may not be considered necessary for criteria derivation

Extrapolating Effects: An Approach Based on Phylogenic Relationship

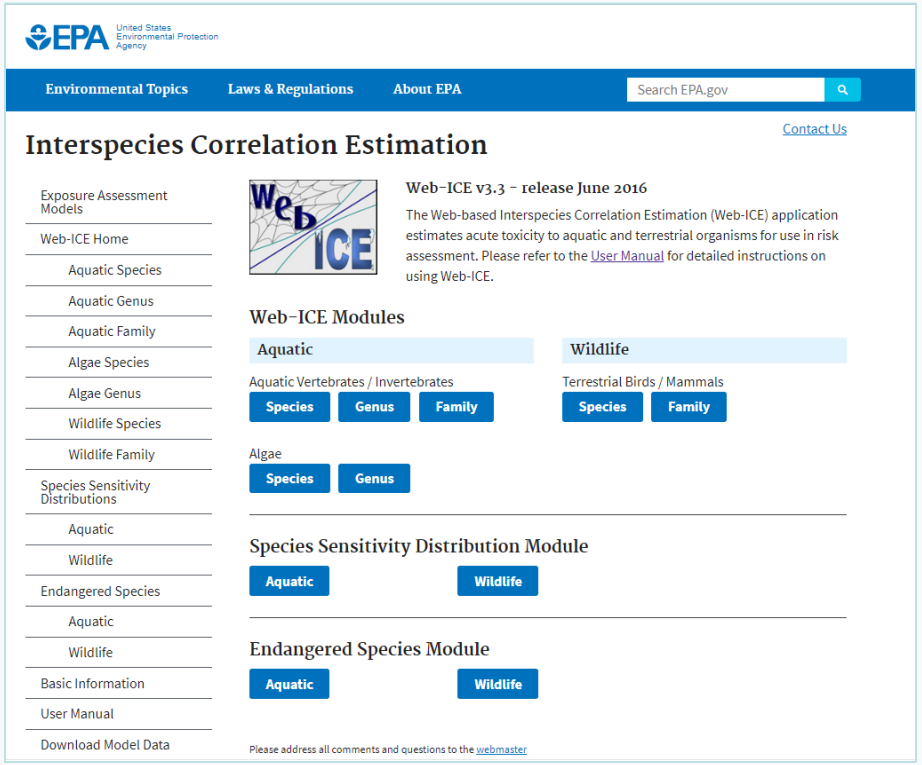
- Web Interspecies Correlation Estimation (WebICE)
  - Acute toxicity to a species (genus or family) could be predicted based on the relationship of the target and surrogate species (genus or family) across multiple chemicals
  - Based on log transformed inter-taxa regression models; most appropriate surrogate selected by user based on taxonomic relatedness, model slope, model goodness of fit, etc.

Log-linear models of the relationship between the acute toxicity (LC50/EC50) of chemicals tested in two species



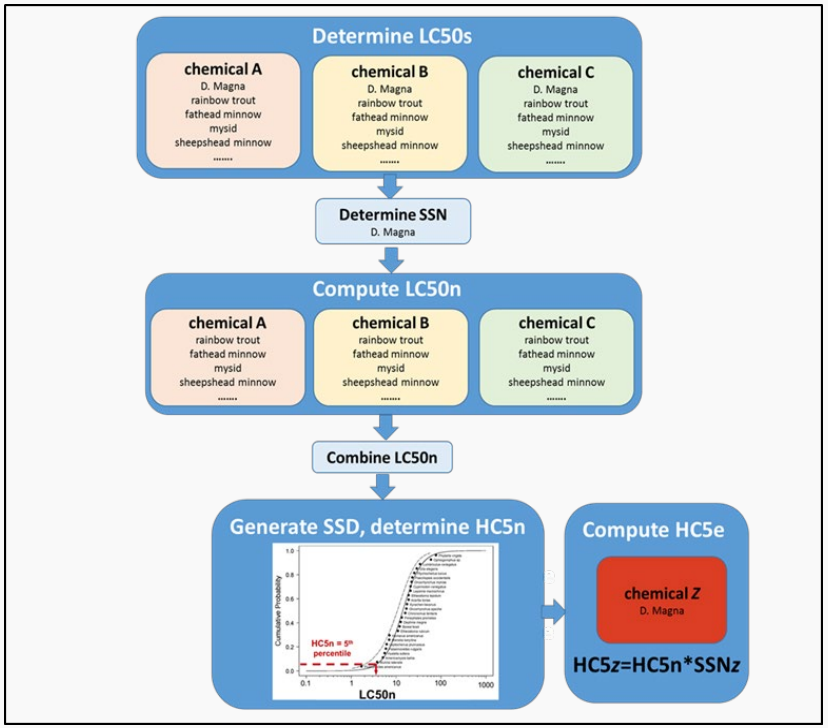
Extrapolating Effects: An Approach Based on Phylogenic Relationship

- For protective aquatic life value development, approach could be used to fill missing MDR groups or to complete SDs



Populating a Sensitivity Distribution by Grouping Chemical Data

- Normalized Hazard Concentrations: HC5n*

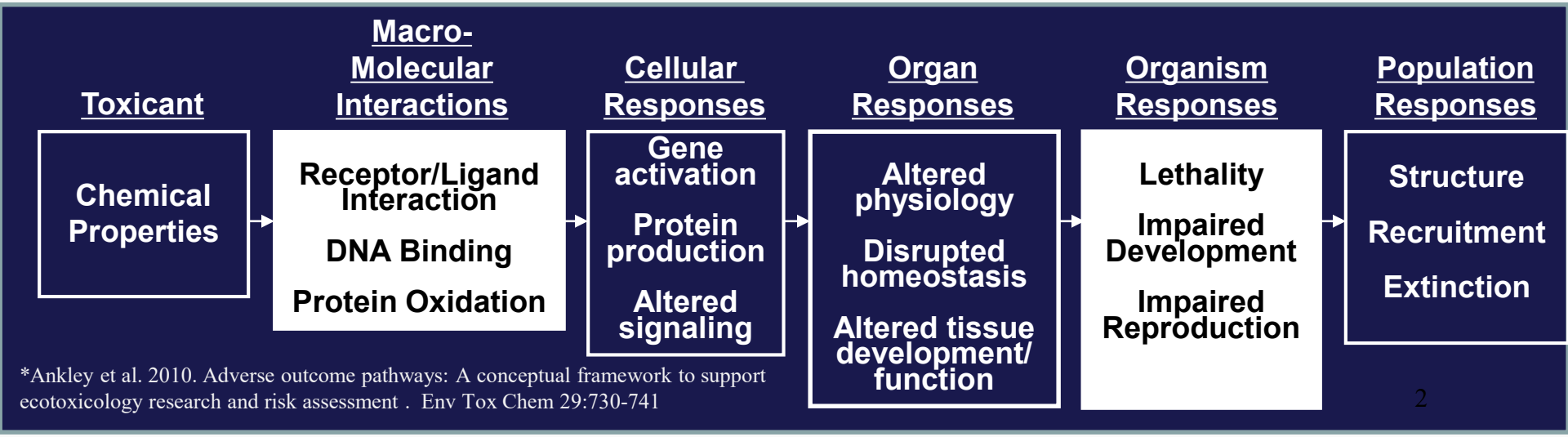


- Toxicity data for multiple chemicals *with same Adverse Outcome Pathway (AOP)* could be combined to generate a single HC_{05} for that chemical group
- Complete dataset not required for individual chemicals
- Resulting value is an estimate of the chemical-specific HC5
- Represents possible approach for developing protective aquatic life values for groupings of related chemicals

*Giddings et al. 2019. Derivation of combined species sensitivity distributions for acute toxicity of pyrethroids to aquatic animals. Ecotoxicology 28:242-250

Adverse Outcome Pathways and the Development of Protective Aquatic Life Values

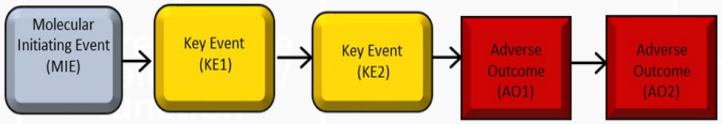
- An AOP* is a conceptual framework that portrays existing knowledge concerning the linkage between a direct molecular initiating event and an adverse outcome, at a level of biological organization relevant to risk assessment
- For the development of protective aquatic life values, information about a chemical provided by an AOP could support a derivation process more tailored to the toxicological properties of a chemical



*Ankley et al. 2010. Adverse outcome pathways: A conceptual framework to support ecotoxicology research and risk assessment . Env Tox Chem 29:730-741

Adverse Outcome Pathways and the Development of Protective Aquatic Life Values

- Specifically, for the development of protective aquatic life values, the AOP framework could
  - Organize and integrate complex datasets
  - Support a hypothesis-driven approach to value derivation and aid the identification of relevant assessment and measurement endpoints, as part of problem formulation
  - Provide critical information about what apical hazards can be credibly linked with a chemical mode of action
  - Improve cross-species and cross-chemical extrapolation of effects, including identification of potentially sensitive and insensitive species/endpoints mediated through a particular mode of action
  - Identify critical data gaps, and taxa for which additional data may not be needed



Considerations for Incorporating Data Into Criteria Derivation

- Considerations for the collection of additional toxicity data
  - Data Evaluation Records outline and document data evaluation steps and use decisions
- Incorporating a broader range of test data
  - Microcosm, mesocosm, and field study data are being considered for use in criteria development

Summary and Conclusions

- MDRs appear to be met for PFOA and PFOS, and US EPA is in the process of reviewing the quality of the available data for these chemicals
- PFAS chemicals represent a large, structurally-complex universe of chemicals, and MDRs are not currently met for other PFAS compounds
- US EPA is exploring approaches to support the development of protective aquatic life values for additional data-limited PFAS chemicals

Thank you!

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