Norman A. Richardson, Daniel J. Chappie,
Pamela J. Rodgers, and Stephanie A. Hines
Environment Business Line
May 23, 2017

Bridging Data Gaps for Ecological Assessment of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS)

Battelle Fourth International Symposium on Bioremediation and Sustainable Environmental Technologies

May 23, 2017

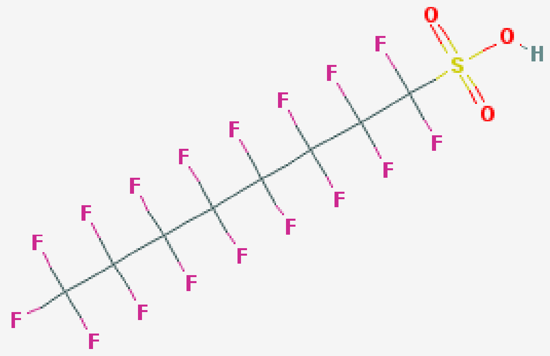
BATTELLE

Overview

- Background on PFAS chemistry and environmental fate
- Why an extrapolation process is needed for ecotoxicity data
- Extrapolation framework to identify PFAS surrogates
- Suggestions to refine framework

Chemical Background

- PFAS Nomenclature
  (Buck et al., 2011)
- Focus on <u>per</u>fluoroalkyl acids (PFAA)
  - Most published data
  - Functional groups – sulfonides and carboxylic acid
  - Long v. short carbon chain length
- Fate and transport characteristics
  - C-F bond allows for extreme stability in environment, greater for 6^+C
  - Groups exhibit hydrophobic and lipophobic traits, micelle formation
- Federal interest in PFAS sites



PFOS, C8

BATTELLE

Groundwater Occurrence at US Military Sites

PFAS	U.S. EPA Unregulated Contaminant Monitoring Rule?	EPA Human Health Risk-based Standard (Type of Standard)	Reported in Groundwater at US Military Sites (√ to √ √ √ – Lower to Higher Frequency)
PFHxA	No	--	√√√
PFHpA	Yes	--	√
PFOA	Yes	(HAL = 70 ppt)	√√√
PFNA	Yes	--	√
PFBS	Yes	(PPRTV RfD)	√
PFOS	Yes	(HAL = 70 ppt)	√√√
6:2 FTSA	No	--	√√√

-- Not Available

HAL – Health Advisory Level (70 ppt as combined conc.)

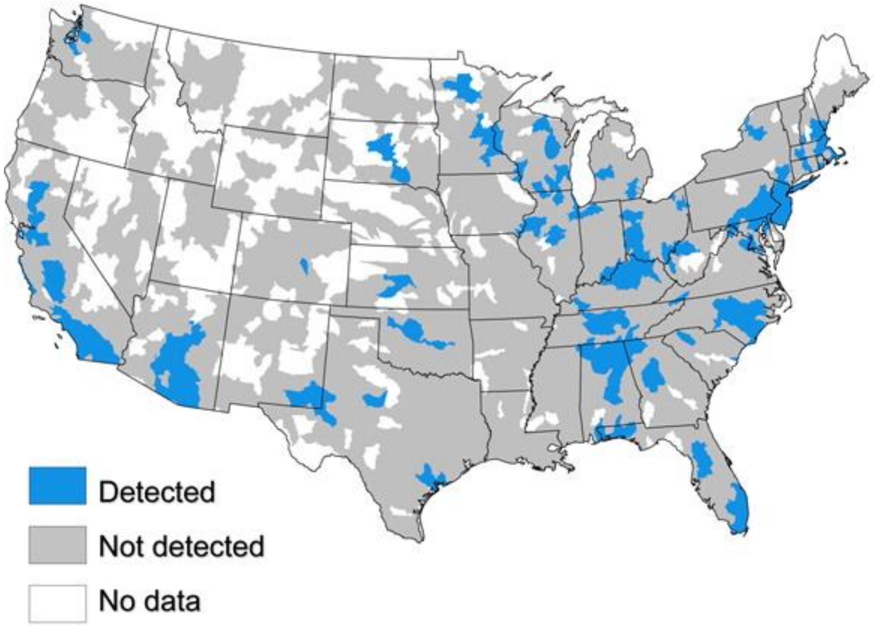
PPRTV – Provisional Peer Reviewed Toxicity Value

Criteria: Sampling performed in EPA's UCMR3, presence of EPA risk-based standard, and reported presence at military sites

PFAS in Surface and Ground Water Drinking Supplies

- Hu et al. (2016) assessed EPA UCMR3 data from ground and surface water
- Surface water detections for all PFAS tested
  - PFBS, PFHxS, PFHpA, PFOA, PFOS, PFNA
  - ng/L levels
- Similar suite of compounds present as in previous study

Hydrological Units with Detectable PFAS



Source: Hu et al. 2016

ES&T Letters

BATTELLE

Sources and Release Pathways to Water Sources

Source Examples:

AFFF use, manufacture of consumer products

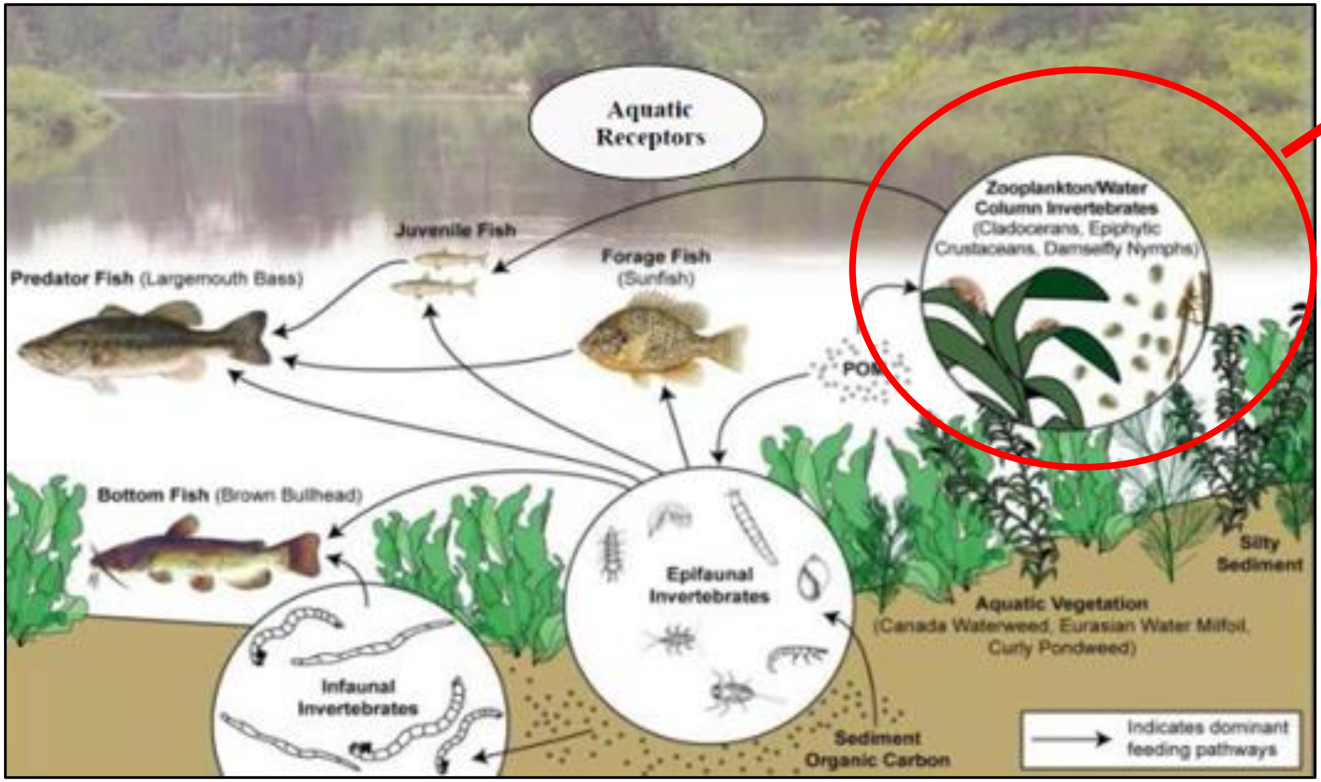
Release Pathways:

- Soil contamination release to ground and/or surface water
- Direct discharge or through WWTP to surface water
- Release to air and then regional or global movement

Exposure of Ecological Receptors

Daphnia

Source: Wikipedia (2017)



Source: Fisheries and Oceans Canada (2014)

Exposure via direct contact with water and particulate organic matter

Food source for juvenile fish

Summary of Available Ecotoxicity Data for *Daphnia*

PFAS	*Daphnia magna* 48-hour EC_5/NOEC	*Daphnia magna* 21-day EC_5/NOEC
PFBA	>4281	--
PFHxA	596	724
PFOA	125 - 297*	6.3 - 21*
PFNA	93	0.008
PFDA	77	--
PFBS	2183*	707*
6:2 FTSA	>112	--
PFOS	0.8 - 71*	<0.008 - 5.3

Carbon Length

Literature Review Date: October 2016

Key Data Gap:

Fluoroalkyl sulfonic acids have limited toxicity data

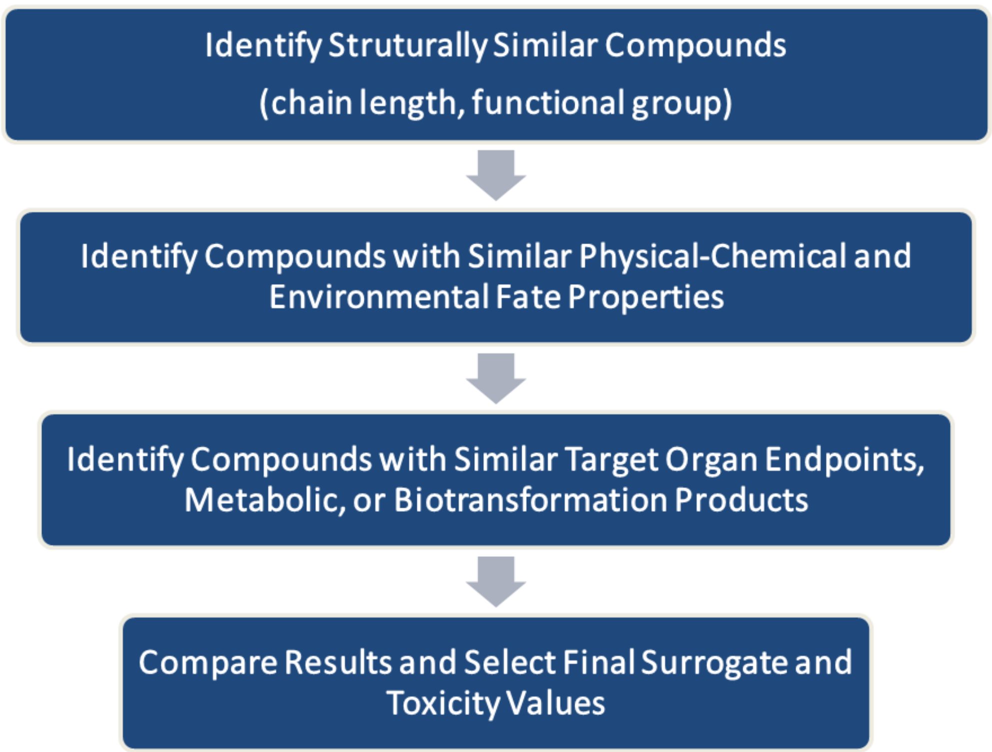
** Genus mean acute values*
Citations available upon request

EC_5 - Effect Concentration for 5% (mg/L)
NOEC – No Observed Effect Conc.(mg/L)

Extrapolation Process Needed

- Suite of PFAS usually present in environment
- Scarce ecological toxicity data, esp. for sulfonate forms
- Insufficient toxicity data to develop RPF, TEF, or QSAR
- Selected tiered weight of evidence approach for extrapolation
  - Leverage available knowledge
    - Increasing chain length associated with increasing ecotoxicity
    - Sulfonic acids more toxic than carboxylic acids
  - Transparent process for qualitative decisions in surrogate selection

Tiered Weight of Evidence (WOE) Framework



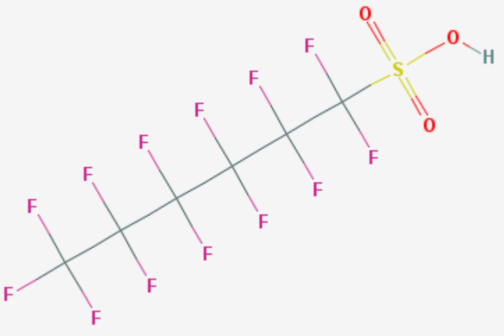
Modified from Wang et al. 2012
Regul Tox and Pharm

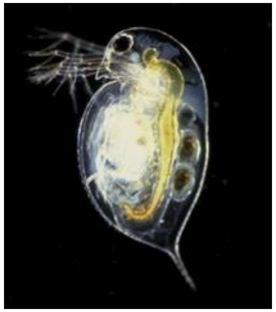
- Modified from Wang et al. 2012 approach for human health toxicity
- Can evaluate structure, fate, biotransformation or metabolism, and toxic action
- Tiering implies that all steps may not be completed
- Gaps provide research direction

Development of Test Case: Chemical, Receptor, Endpoint

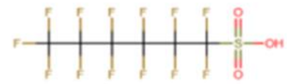
- PFAS: Perfluorohexanesulfonic acid (PFHxS)
- Why?
  - Ecotoxicity data gaps
  - Reported in groundwater and surface water
  - Preference to identify “shorter” carbon length (6C)
- Ecological receptor: *Daphnia magna*
  - Most common aquatic organism in PFAS testing
- Endpoints for acute toxicity
  - Immobilization
  - Survival or reproductive effects

CAS: 355-46-4





Tier 1: Identify Structurally Similar Compounds

Compound		Carbon Length	Functional Group	Structure	Percent Similarity
Target	PFHxS	6	sulfonate		100
Potential Surrogates	PFBS	4	sulfonate		98.5
	PFHxA	6	carboxyl		62.9
	PFOS	8	sulfonate		99.6
	PFDS	10	sulfonate		99.6

Source: ChemIDplus, A TOXNET DATABASE, National Institutes of Health

Comparison of carbon length and functional group

Tier 2: Identify Compounds with Similar P-C and Fate Properties

Caution – Data Gaps Ahead

Measure of Solubility → Limited experimental data, PFAS or specialized models needed (e.g., Xiao et al. 2013), general tools lack training data with C-F, consider micelle formation

pKa → Low pKa result in anionic form for some PFSAs (sulfonamides), debate on environmentally relevant value for PFCAs (Buck et al. 2011)

Kow → Partition into protein due to hydrophobicity and lipophobicity, traditional tests must be modified

Ding and Peijnenburg, 2013 Crit Rev Sci Technol

Tier 2: Identify Compounds with Similar P-C and Fate Properties

Compound		Carbon Length	Structural Percent Similarity	Water Solubility (mg/L)	pKa	Log Kow
Target	PFHxS	6	100	7.59 QSPR	0.14*	NA
Potential Surrogate	PFBS	4	98.5	Range of 4.6E+4 to 5.6E+4 (K salt, Exp.)	0.14*	NA
	PFHxA	6	62.9	29.5 QSPR	0.840	0.70
	PFOS	8	99.6	0.21 QSPR 20 - 498 Exp.	0.14*	3.36 and 2.45
	PFDS	10	99.6	NA	NA	NA

Data gaps in physical chemical data

Variability in reported data with difference between prediction and exp.

Sources: Ding and Peijnenburg 2013, *Steinle-Darling 2008

BATTELLE

Tier 3: Identify Compounds with Similar Toxicity Profiles

- Scarce data on ecotoxicity mode of action or mechanisms for *Daphnia*
- Body surface sorption dominates bioaccumulation (Dai et al. 2013)
- Inference of potential for non-specific mechanisms for some PFAS
  - Barmentlo et al. (2015) described consistent exposure concentrations for mortality and sublethal endpoints across 48-hour and 21-day exposures of PFHxA
- New approaches - e.g., transcriptomics described in Houde et al. (2016) to assess potential for endocrine disruption
- Tier 3 Decision: Insufficient data to currently distinguish among PFAS surrogate compounds

Compare Outputs Across Tiers

Identify Struturally Similar Compounds
(chain length, functional group)

Identify Compounds with Similar Physical-Chemical and Environmental Fate Properties

Identify Compounds with Similar Target Organ Endpoints, Metabolic, or Biotransformation Products

Compare Results and Select Final Surrogate and Toxicity Values

PFAS	*Daphnia magna* 48-hour EC_5/NOEC	Source	*Daphnia magna* 21-day EC_5/NOEC	Source
PFOS	0.8 - 71*	(b, d, f, g)	<0.008 - 5.3	(b, f, h, i)

Tier 1- Structurally similar: PFBS, PFOS, and PFDS

Tier 2 - Similar P-C and fate: Insufficient data to distinguish

Tier 3: Target organ, metabolic, biotransformation: Insufficient data to distinguish

Compare results –
Select PFOS as surrogate

1) Structurally similar
2) Conservative choice because 8C sulfonamide relative to 6C target compound PFHxS

BATTELLE

Assessment of the Proposed Extrapolation Process

- May complete more tiers of process for carboxylic acid versus sulfonic acid functional groups due to data availability
- Targets key research gaps for sulfonic acid functional group compounds
- Process can be agnostic with regard to toxicity data type
  - "New" computational approaches to ecotoxicity can be readily incorporated with traditional data for robust assessment
- Ready for prime time?
  - Maybe, tiered process facilitates use for low data PFAS compounds
  - Targeted data generation could improve process

Refining the Assessment of Ecotoxicity for PFAS Compounds I

- Use the extrapolation process to identify and then direct research to address known data gaps
- Consider innovative practices to fill basic chemical properties data gaps (e.g., Xiao et al. 2013)
- Evaluation of potential confounding of chemical properties and toxicity data by unaccounted presence of micelles
- Laboratory toxicity testing with *Daphnia* for 6 to 8 target PFAS representing gradient of different size/functional groups

Refining the Assessment of Ecotoxicity for PFAS Compounds II

- Consider toxicity testing using well characterized environmental mixtures of PFAS compounds from defined sources for additional data to evaluate surrogate approach
  - e.g., similar approach used for environmental PCB mixtures

Summary

- Tiered weight of evidence extrapolation framework has utility for ecological toxicity assessment of PFAS
  - More available data to implement for carboxyl vs. sulfonates
- Data gaps limit progress through all tiers, but process was developed for data rich and data poor surrogate selection
- Framework provides transparent and systematic approach to identify surrogates
- Framework can be used to direct research to address important data gaps necessary for predictions

BATTELLE

Thank you!

Questions:

hiness@battelle.org

BATTELLE

It can be done