BCFs and BAFs for PFAS:

Reviewing and Coding of Literature Values



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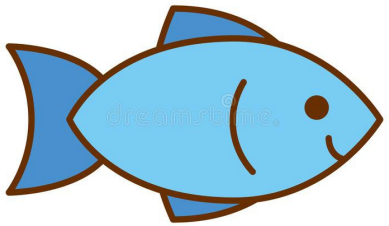
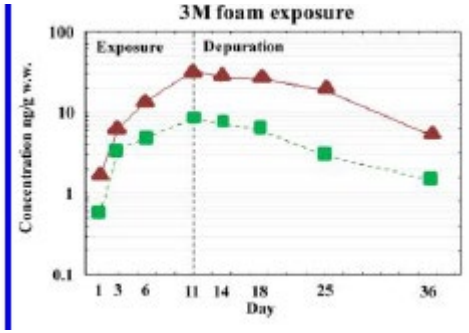
Definitions

- BCF - Bioconcentration Factor
  - $BCF = \frac{C_{biota}}{C_{water}}$ L/kg-ww = (µg/kg-ww)/(µg/L)
  - Laboratory exposure
  - Dosing via water only (uptake across gills)
  - Standard protocols.
    - Steady-state endpoints (or 28-d measurement)
    - Uptake and elimination kinetics





- BAF - Bioaccumulation Factor
  - $BAF = \frac{C_{biota}}{C_{water}}$ L/kg-ww
  - Field exposure
  - All exposure routes
    - Food, water, sediments via skin contact and ingestion

Bioaccumulation: Background

- Why is chemical bioaccumulation important?
  - EPA's Ambient Water Quality Criteria (AWQC) for Protection of Human Health

Noncancer Effects[2]

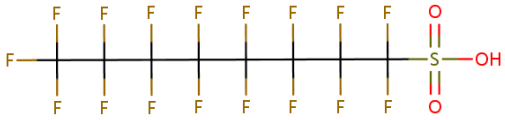
$$AWQC = RfD \cdot RSC \cdot \left(\frac{BW}{DI + \sum_{i=2}^{4} (FI_i \cdot BAF_i)} \right) \qquad \text{(Equation 1-1)}$$

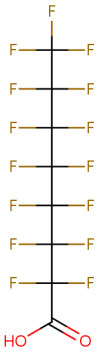
2000 Methodology

DI = drinking water intake
FI = fish intake at trophic levels 2, 3 & 4
BAF = bioaccumulation factor at TLs 2, 3 & 4
BW = human body weight
RfD = reference dose for noncancer effects
RSC = Relative source contribution factor

Equal exposures between DI and FI routes: BAF ≈ 3000
BAF > 3000, dietary exposure primary uptake route
BAF < 3000, water exposure primary uptake route

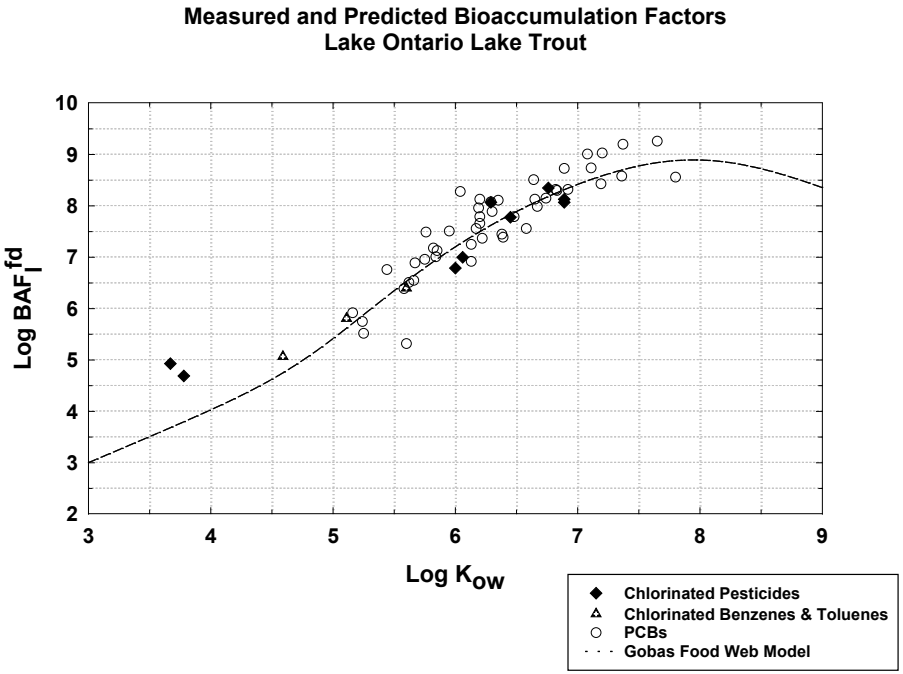
PFAS

- Per- and polyFluorinated Alky Substances (PFAS)
  - 4730 PFAS-related CAS (OECD 2018)
  - PFOS 

PFOA 

  - Numerous uses
    - Fire fighting foams (AFFF)
    - Stain resistance and flammability
      - Carpets, furniture
    - Water-repellent clothing
    - Surface coatings (non-stick cookware)
    - Electroplating
    - …

Bioaccumulation of Legacy Chemicals



- Models for legacy chemicals
  - PCBs, DDTs, PCDD/Fs …
  - Uptake and excretion processes controlled by diffusional mass transport processes
  - Lipids major storage tissue
- **NOT applicable to PFAS**
  - Different processes
    - Renal transporters
    - Binding to cytosolic fatty acid binding proteins & to albumin
  - Model development in its infancy
    - Decade or two to develop???

Needs & Path Forwards

- OW
  - Actively developing ambient water quality criteria
    - Human health & aquatic life and aquatic dependent wildlife
    - PFOS and PFOA
- OPPTS (TSCA)
  - Screening of new PFASs
- OLEM (Superfund)
  - Needs data for setting cleanup levels
- States & DOD actively developing their own criteria
  - Fish consumption advisories by states
- **Path Forwards:**
  - Use Empirical BAF data in criteria development

PFAS

- Persistent
  - Do not degrade
- Toxic
  - Some PFAS are toxic to fish, wildlife and/or humans
- Bioaccumulative
  - Some PFAS accumulate in tissues

- QuestionS:
  - What do we know about PFAS bioaccumulation?
  - What are the gaps in knowledge for PFAS?

Literature Searching

- Two steps
  - Ecotoxicology Knowledgebase (ECOTOX)
  - SWIFT review

ECOTOX Searching

- Developed a series of chemical-based search terms (2018 search)
  - Chemical Abstracts Service registry numbers (CASRN or CAS): 207
  - Chemical names: 174
    - synonyms, tradenames, and other relevant forms, i.e., metabolites, degradants, parent compounds and related chemicals
- Libraries searched:
  - Current Contents, ProQuest CSA, Dissertation Abstracts, Science Direct, Agricola, TOXNET, and UNIFY
- Yielded: >29,000 citations
- Removal non-relevant papers yields: 8181 citations
  - Non-relevant papers: Duplicates, analytical methods, human health, bacteria, terrestrial studies with inhalation route of exposure, PFAS was not the chemical of study
- Creation of RIS files
  - Bibliographic citation file saved in a format developed by Research Information Systems
- Searches 2019, 2020 & 2021

# of Citations	FY18	FY19	FY20	FY21
Citations	29,775	98,789	487,497	693,215
Reviewed	8,181	7,158	140,966	47,816

SWIFT Review

- SWIFT
  - “Sciome Workbench for Interactive computer-Facilitated Text-mining”
  - Freely available software
- Import RIS files
  - Automatically tag documents in various categories
  - One can develop their own tags
  - Search terms/tags
    - BCF (bioconcentration factor), BAF (bioaccumulation factor), BSAF (biota-sediment accumulation factors), bioaccumulation, bioconcentration, uptake, depuration, and accumulation

SWIFT Review

- Identified citations
  - Obtained and reviewed
- Coded papers with applicable data
  - Is endpoint reported?
  - Are data provided to derived the endpoint?
    - Concentrations in aquatic organism and water
- 280 papers coded to date
  - 13 in review
  - Not codable:
    - Reviews (code original source)
    - Reports have only data for tissue or water only

Coding Process

- Excel template
  - Completed template for each citation individually

- Fields
  - Chemical name, chemical abbreviation, CAS, and citation
  - Endpoint & concentration data (units)
  - Organism, taxonomy, tissue (whole body, fillet, blood …)
  - When available, weight, length, age, sex …
  - BCF – kinetic information
  - BAF – sampling design information
    - Numbers of samples, samples' spatial and temporal coordination

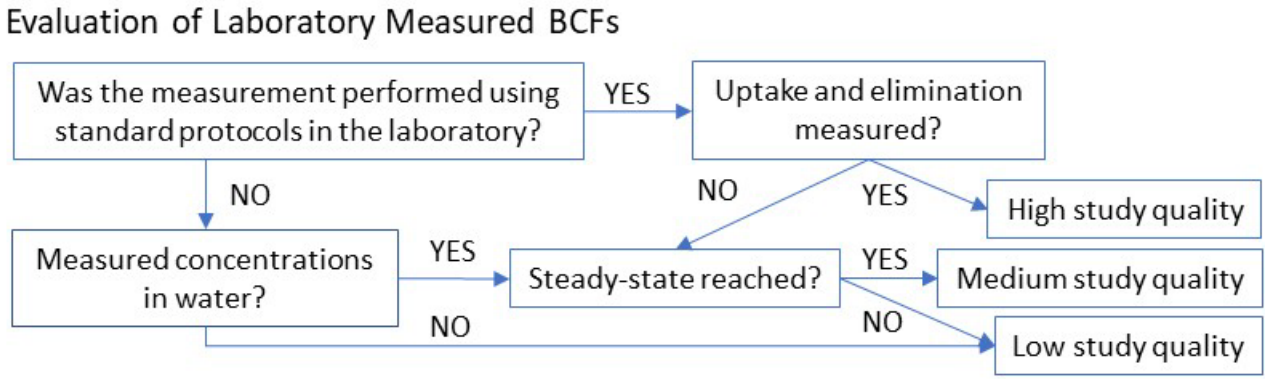
Coding Process

- Field studies
  - Concentrations are often reported being below the detection limit (<MDL).
    - Left censoring
  - There are techniques for addressing this issue in risk assessment.
    - Superfund ½ MDL
    - Statistical techniques, e.g., Kaplan–Meier
- Endpoint coded:
  - Only when **all** tissue and water samples above detection limit (MDL)
    - No coding if < 100% quantification

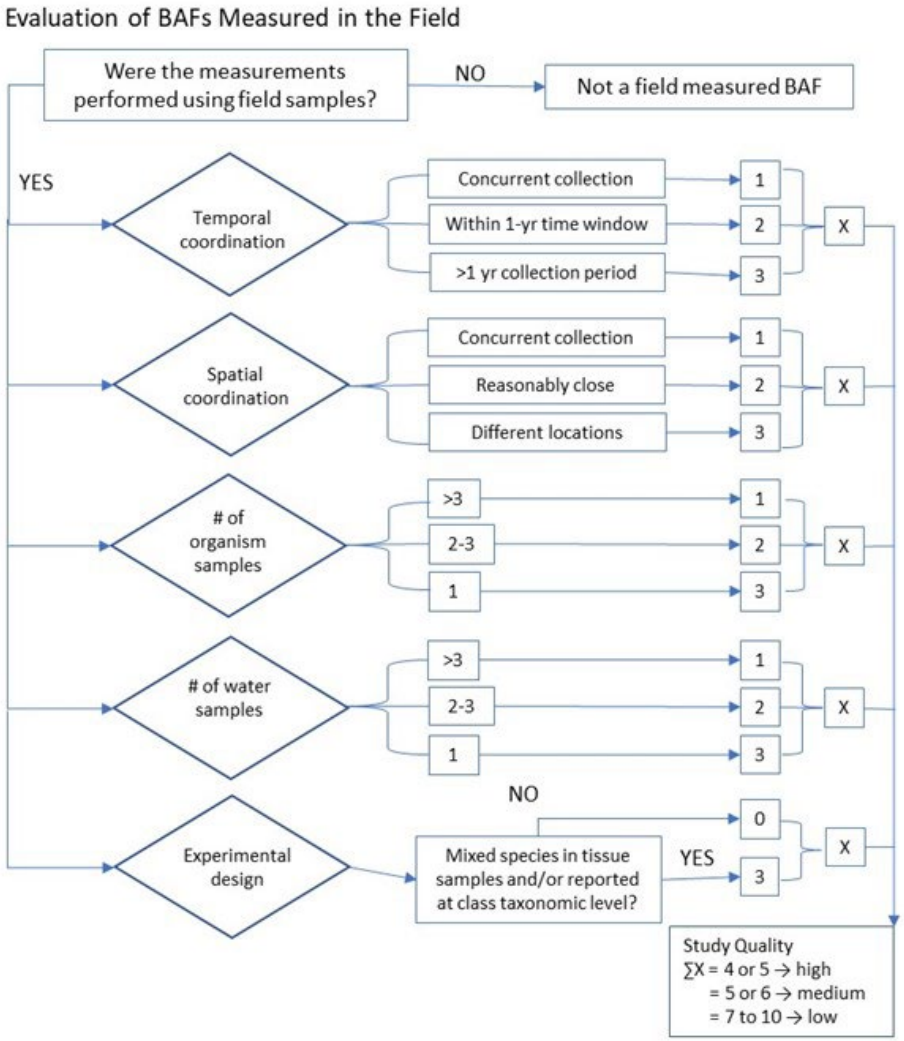
Coding process: Study quality

- How good are the measurements?
  - Field studies: Wide variety of study designs
  - Ranking system of high, medium and low study quality
    - Klimisch et al 1997
      - 1 ("Reliable"), 2 ("Reliable with Restrictions"), 3 ("Not Reliable")
  - Importance of the ranking cannot be understated!

Study quality evaluation for BCF measurements



Study quality evaluation for BAF measurements



Study Quality

- BCFs & BAFs 8,479
  - High 35%
  - Medium 23%
  - Low 42%

Issues in Coding

- Unclear
  - Laboratory procedures
  - Sampling locations and collection times
  - Numbers of samples collected and analyzed
  - Data calculations, <MDL
  - Units
- Raw data (concentrations in tissue and water) don't align with reported BCF/BAFs.
  - QA/QC check: Template computes BCF/BAFs from concentration data
- Unusual reporting units
  - Concentrations in tissue on dry weight
    - wet weight is standard
  - Concentrations in sediment on wet weight
    - dry weight is standard
- Endpoints reported
  - Range of values (min-max)
  - Confidence limits

Data Set Synthesis

- Created master Excel file from templates
- Flat file:
  - Endpoints recorded as reported
  - Endpoints converted to units of L/kg-ww
  - BCFs
    - Standard protocols: BCF_{SS} & BCF_K are reported
      - Preference given to BCF_K

- Easily uploaded to data base programs by others

	CAS	Abbreviation	Log BCF Steady-State (mean)	Log BCF Steady-State (stdev)	Log BCF Steady-State (min)	Log BCF Steady-State (max)	Log BCF Steady-State (lower CI)	Log BCF Steady-State (upper CI)	Log BCF Steady-State (arithmetic or logarithmic)	Log BCF Steady-State (units)

Log BCF Steady-State (units)		Log BCF Kinetic (mean)	Log BCF Kinetic (stdev)	Log BCF Kinetic (min)	Log BCF Kinetic (max)	Log BCF Kinetic (lower CI)	Log BCF Kinetic (upper CI)	Log BCF Kinetic (arithmetic or logarithmic)	Log BCF Kinetic (units)		BCF Adjustment (DW to WW)	Finalized log10 BCF (L/kg-ww)

Log BAF (mean)	Log BAF (stdev)	Log BAF (min)	Log BAF (max)	Log BAF (lower CI)	Log BAF (upper CI)	Log BAF (arithmetic or logarithmic)	Log BAF (units)		BAF Adjustment (DW to WW)	Finalized log10 BAF (L/kg-ww)

Data Set Synthesis

- Flat file has sheet with list of coded papers
  - Short name used in the templates
  - Complete citation

BCF data	OECD 305	ku	ku - sd	units	days of uptake	ke	ke - sd	units	days of elimination	half-life (days)	half-life sd (days)	SS	Kinetic	Exposure Concentrations	Study Quality: BCF

BAF	BAF: # of water samples	BAF: start date for water sampling	BAF: end date for water sampling		BAF: # of biota samples	BAF: start date for biota sampling	BAF: end date for biota sampling	Average weight (g)	Average Length (cm)	Sex (F/M)	Average Age	Age (sd)	General experimental design	Water & Biota spatial coordination	Water & Biota temporal coordination	Number Biota Samples	Number of Water Samples	Study Quality: BAF

Mixture Exposure	Concentration in Biota (mean)	Concentration in Biota (stdev)	Concentration in Biota (units)	Concentration in Biota (MDL)	Comments - Biota Samples	Concentration in Water (mean)	Concentration in Water (stdev)	Concentration in Water (units)	Concentration in Water (MDL)	Comments - Environmental Media

Marine, Brackish, Freshwater	Comments - Marine, Brackish, Freshwater		Taxonomy Name Level	kingdom	phylum	class	order	family	genus	*species*	ITIS TaxID	NCBI TaxID	GBIF TaxID

Data Availability:

Bioconcentration Factors (BCF = $C_{biota}/C_{water,}$ laboratory)
Bioaccumulation Factors (BAF = $C_{biota}/C_{water,}$ field)

- Data rich
  - Carboxylic & Sulfonic acids
    - PFOS & PFOA
- Data poor
  - Ethers, Fluorotelomers & Phosphates
    - GenX, 8:2 FTOH, 6:2 FTSA
- Quality varies widely
    - Field measurements
    - OECD 305 BCF methodology: high quality
- Number of measurements
  - 22 taxonomic classes
  - Fish > Bivalves, Malacostraca (shrimp, crabs …) & Plants (Magnoliopsida)
  - Field (BAFs) > Laboratory (BCFs) measurements

Burkhard, L.P., 2021. Environ Toxicol Chem. 40(6) 1530-1543
Corrigendum 2021 Environ Toxicol Chem. 40(10) 2935-2940

Carboxylic Acids

BCFs and BAFs for PFCA (median ± standard deviation [n])

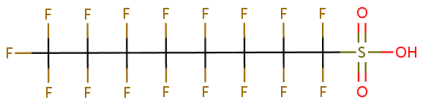
Chemical	Tissue Bioaccumulation Metric CAS Number	whole body Log BCF Steady-State Log BCF Kinetic	muscle/fillet Log BCF Steady-State Log BCF Kinetic	liver Log BCF Steady-State Log BCF Kinetic	whole body Log BAF	muscle/fillet Log BAF	liver Log BAF
Carbonyl Compounds - OECD Structure Category 100							
Carboxylic acids - OECD Structure Category 102							
PFBA	45048-62-2	1.18 ± 0.08(2)	-0.22 ± 1.15(5)	1.8 ± 1.23(5)	2.16 ± 1.68(6)	0.47 ± 0.96(40)	0.37 ± 1.11(3)
PFPeA	45167-47-3	-0.05 ± ---(1)	-0.64 ± 1.21(3)	1.15 ± 1.53(3)	1.74 ± 2.45(5)	0.15 ± 1.46(18)	1.48 ± 1.43(4)
PFHxA	92612-52-7	0.98 ± 0.3(3)	0.4 ± 1.01(5)	1.73 ± 0.99(5)	1.4 ± 1.51(11)	0.09 ± 1.34(19)	2.79 ± 1.62(6)
PFHpA	120885-29-2	1.26 ± ---(1)	0.51 ± 1.24(3)	1.78 ± 1.2(3)	1.8 ± 1.24(10)	-0.16 ± 1.27(32)	0.92 ± 0.99(6)
PFOA	45285-51-6	1.38 ± 0.61(14)	0.82 ± 1.18(7)	1.93 ± 1(13)	2.16 ± 0.87(48)	0.9 ± 1.14(105)	1.97 ± 1.05(48)
PFNA	72007-68-2	2.78 ± 0.51(6)	2.8 ± 0.4(4)	3.79 ± 0.24(3)	2.8 ± 1.15(41)	2.07 ± 0.76(88)	2.84 ± 0.73(20)
PFDA	73829-36-4	3.79 ± 0.48(3)	3.81 ± 0.54(4)	2.98 ± 0.93(8)	3.45 ± 0.62(43)	3.06 ± 0.49(72)	3.72 ± 0.65(30)
PFUnDA	196859-54-8	3.57 ± 0.31(5)	3.97 ± 0.88(4)	3.41 ± 0.74(8)	3.47 ± 1.01(21)	3.89 ± 0.77(54)	4.34 ± 0.72(27)
PFDoDA	171978-95-3	3.64 ± 0.6(8)	4.12 ± 0.83(4)	4.46 ± 1.16(4)	2.18 ± ---(1)	4.5 ± 1.57(28)	4.32 ± 1.52(17)
PFTrDA	862374-87-6	4.34 ± 0.46(2)	4.51 ± 0.85(2)	5.22 ± 1.08(2)	--	4.66 ± 0.16(3)	5.43 ± ---(1)
PFTeDA	365971-87-5	4.4 ± 0.56(4)	4.96 ± 0.62(2)	4.74 ± 1.09(3)	--	4.38 ± ---(1)	5.08 ± ---(1)
PFHxDA	67905-19-5	3.68 ± 0.01(2)	--	--	--	--	--
PFOcDA	16517-11-6	2.57 ± 0.09(2)	--	--	--	--	--

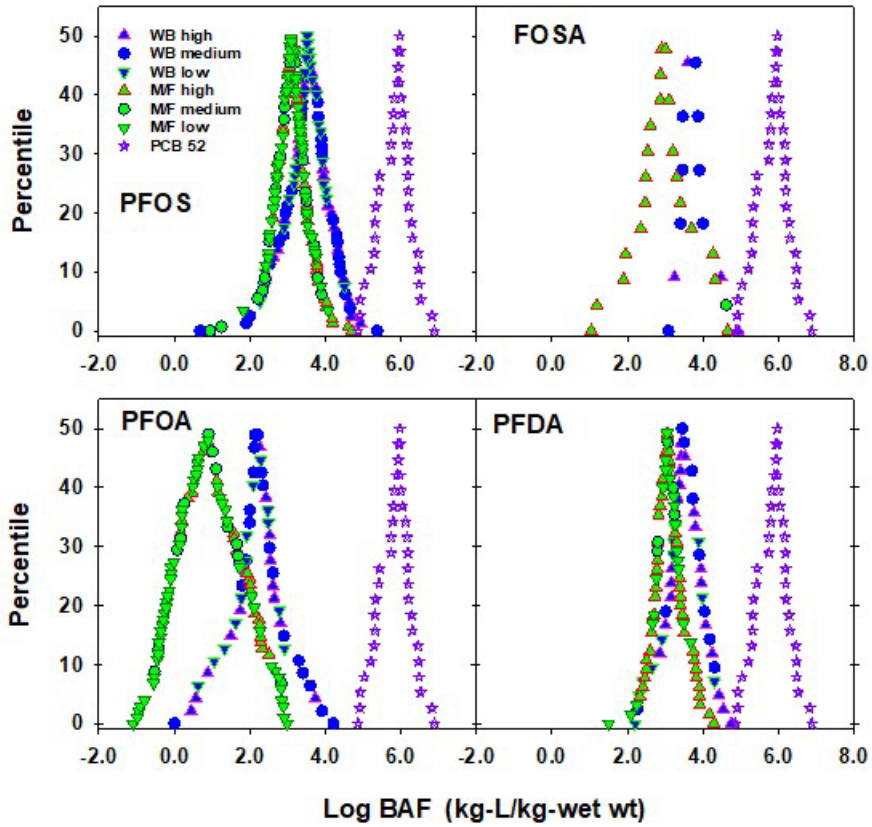
Sulfonic Acids

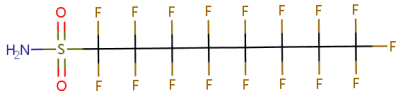
BCFs and BAFs for PFSA (median ± standard deviation [n])

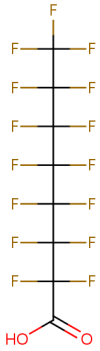
Chemical	Tissue Bioaccumulation Metric CAS Number	whole body Log BCF Steady-State Log BCF Kinetic	muscle/fillet Log BCF Steady-State Log BCF Kinetic	liver Log BCF Steady-State Log BCF Kinetic	whole body Log BAF	muscle/fillet Log BAF	liver Log BAF
Sulfonyl Compounds - OECD Structure Category 200							
Sulfonic Acids - OECD Structure Category 202							
PFBS	375-73-5	1.06 ± 0.49(7)	0.09 ± 1.15(4)	1.74 ± 1.06(5)	2 ± 1.13(5)	1.35 ± 0.84(16)	1.18 ± 0.34(5)
PFHxS	355-46-4	2.07 ± 0.25(6)	1.34 ± 0.19(2)	2.41 ± 0.4(4)	2.3 ± 0.74(25)	1.28 ± 0.86(56)	2.18 ± 0.58(17)
PFHpS	375-92-8	--	--	--	--	2.2 ± ---(1)	3.2 ± 0.1(3)
PFOS	1763-23-1	3.01 ± 0.66(21)	3.27 ± 0.96(7)	3.17 ± 0.88(17)	3.52 ± 0.78(81)	3.09 ± 0.6(155)	3.74 ± 0.84(61)
PFDS	335-77-3	--	--	3.21 ± ---(1)	1.3 ± ---(1)	--	4.2 ± 0.15(3)
PFECHS	PFECHS	--	--	--	--	--	--
Sulfonamides - OECD Structure Category: 203.01							
FOSA	754-91-6	--	--	--	3.7 ± 0.53(12)	2.95 ± 0.94(24)	4 ± 0.2(11)
Sulfonamidoacetic acids - OECD Structure Category: 203.05							
MeFOSAA	2355-31-9	--	--	--	4.1 ± 0.16(2)	--	--
EtFOSAA	2991-50-6	--	--	--	3.5 ± 0.06(2)	--	3.45 ± 0.21(2)
Perfluoroalkane sulfonyl amido ethanols, phosphate esters (SAmPAPs) - OECD Structure Category: 203.02							
SAmPAP	2965-52-8	1.42 ± ---(1)	--	--	--	--	--

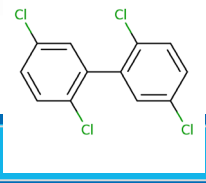
Fish Bioaccumulation Factors (BAFs)





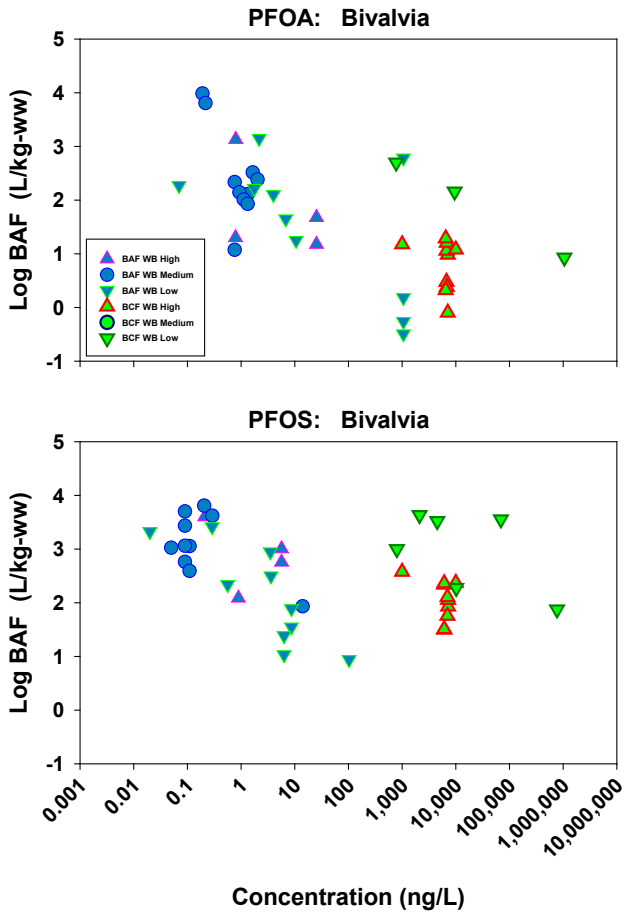






Gaps & Limitations

- Effects of concentration
- Freshwater = Marine???
- Species consumed by humans
  - Carboxylic & Sulfonic acids
    - Enough BCF/BAF data
  - Ethers, Fluorotelomers & Phosphates
    - Need measurements
- Effects of mixtures
- Expected values for BAFs
- Uptake & elimination rate
  - Limited information/data
- Biotransformation rates
  - Ethers and Fluorotelomers
- Mechanistic models
  - Initial stages of development



Questions
Acknowledgements & Contact Information

Thank you!

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