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PFAS: Beyond the Basics Training

Human Health Effects

Ecological Toxicology & Risk Assessment

Regulations

Based on the Sept 2023 published PFAS-1 document. These topics are rapidly changing.

Today’s PFAS Trainers

Brie Sterling	Anju Toolaram	Lisa McIntosh
• PA Department of Environmental Protection	• NYS Department of Health	• Terraphase

ITRC PFAS Resources

ITRC PFAS: https://pfas-1.itrcweb.org/

Guidance Document

13 Fact Sheets

External Tables

PFAS Introductory Training

- Clu-In Archive: https://www.clu-in.org/conf/itrc/PFAS-Introductory/

Other video resources

- Available through links on: https://pfas-1.itrcweb.org
- Quick Explainer Videos
- Longer PFAS Training Modules
- Archived Roundtable Sessions

ITRC PFAS Team: “Beyond the Basics” Training

Training Roadmap

- Guidance Document
  - Section 7.1 Human Health Effects
  - Section 17.2 Additional Information for Human Health Effects
- Our Audience
  - Technical familiarity with PFAS; interested in learning more

Overview of Topics

Health Effects of PFAS other than PFAAs, GenX, & ADONA:

- Ether and Polyether Carboxylates
- Ether and Polyether Sulfonates
- Fluorotelomer Alcohols and Sulfonates

PFAS Epidemiology Studies: recent use in development of toxicity factors and guidelines

Mixtures Assessment

PFAS as a Class

PFAS Inhalation exposure and toxicity

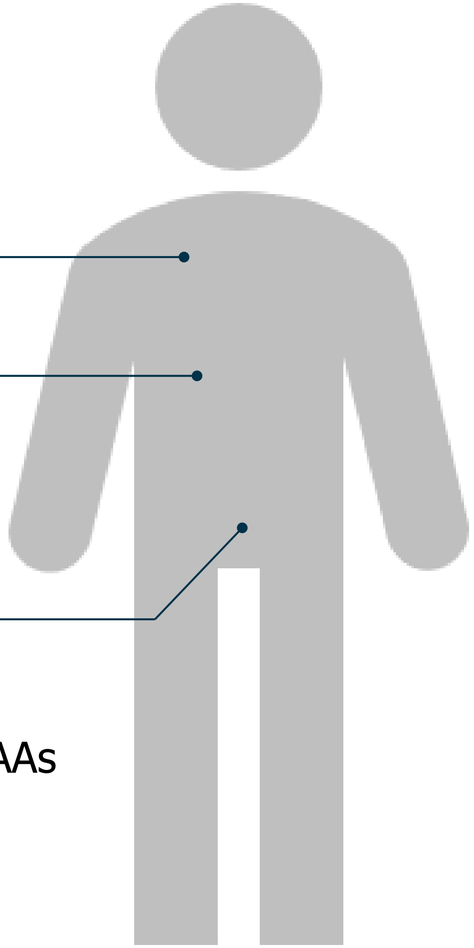
Dermal absorption of PFAS

Biological Fate of Perfluoroalkyl Acids (PFAAs) in Humans[1]

Readily absorbed
Not metabolized*

Distributed predominantly to the liver and blood (serum). Does not accumulate in fat.

Excreted slowly through urine and feces



* Precursors can be metabolized to persistent PFAAs

Long-chain PFAAs are bioaccumulative with elimination half-life of several years.

Cross the placenta and are present in breast milk

[1] see ITRC Technical Regulatory Document, Section 2.2.3.1 for a discussion of PFAAs

PFAS-1, Section 9.1 Figure 9-4 Biological fate of long-chain PFAAs.

Toxicity of PFAS

Similarities and Differences in Toxicity of PFAS in Mammalian Laboratory Animal Studies

Extent of mammalian toxicity data varies widely

- **Extensive** mammalian data for a few PFAS
- **Some** mammalian data for ~20 PFAS
- **No** mammalian data for most PFAS
- *Note*: Carcinogenicity studies for only a few PFAS:
  - *Positive – PFOA, PFOS, GenX*
  - *Negative – PFHxA*

Toxicological effects are generally similar

- All PFAS tested caused **liver toxicity**
- Many PFAS have certain **other effects in common**:
  - Developmental
  - Reproductive
  - Immune
  - Hematological
  - Thyroid

Toxicological potency differs widely

- Generally, long-chain more potent than short-chain
- Longer half-life of long-chain vs. short-chain yields higher levels in body from same dose

ITRC PFAS-1 Section 7.1.4

Comparison of PFAS Toxicity in Mammalian Studies

PFAS-1, Table 9-2 Summary. Adapted from ATSDR 2019.

Compound	# of Carbons	Liver	Develop-mental	Repro-ductive	Immune	Hema-tologic	Thyroid	Neuro-behavioral	Tumors
Perfluoroalkyl Carboxylates									
PFBA	4	■	■	■	□	■	■	□	□
PFPeA	5	□	□	□	□	□	□	□	□
PFHxA	6	■	■	■	□	■	■	□	□ (Negative)
PFHpA	7	■	□	□	□	□	□	□	□
PFOA	8	■	■	■	■	■	■	■	■
PFNA	9	■	■	■	■	■	■	□	□
PFDA	10	■	■	■	■	■	■	■	□
PFUnA	11	■	■	□	■	□	□	□	□
PFDoA	12	■	■	■	■	■	□	■	□
Perfluoroalkyl Sulfonates									
PFBS	4	■	■	■	■	■	■	□	□
PFHxS	6	■	■	□	□	■	■	■	□
PFOS	8	■	■	■	■	■	■	■	■
Per- & Polyfluoroalkyl Ethers and Polyether Carboxylates & Sulfonates; Fluorotelomer Alcohols (Examples)									
ADONA	6	■	■	□	□	■	□	□	□
GenX (HPFO-DA)	6	■	■	■	■	■	■	□	■
ClPFPECAs	8-14	■	□	□	■	■	■	■	□
6:2 FTOH	8 (6 fluorinated)	■	■	■	■	□	□	□	□
8:2 FTOH	10 (8 fluorinated)	■	□	■	■ (uncertain)	□	□	□	□
6:2 FTSA	8 (6 fluorinated)	■	□	□	□	□	□	□	□
6:2 ClPFESA	8	■							
Nafion Byproduct	6	■							

Short-chain PFAS shown in green..
Long-chain PFAS shown in blue.

■ Effect reported in one or more laboratory animal study
□ Effect was evaluated but not found, or effect has not been evaluated

Toxicity of PFAS in Mammalian Species

Short-chain PFAS = green
Long-chain PFAS = blue

Compound	# of Carbons	Liver	Develop-mental	Repro-ductive	Immune	Hema-tologic	Thyroid	Neuro-behavioral	Tumors
Perfluoroalkyl Carboxylates									
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PFPeA	5	□	□	□	□	□	□	□	□
PFHxA	6	■	■	■	□	■	■	□	□ (Negative)
PFHpA	7	■	□	□	□	□	□	□	□
PFOA	8	■	■	■	■	■	■	■	■
PFNA	9	■	■	■	■	■	■	□	□
PFDA	10	■	■	■	■	■	■	■	□
PFUnA	11	■	■	□	■	□	□	□	□
PFDoA	12	■	■	■	■	■	□	■	□
Perfluoroalkyl Sulfonates									
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PFOS	8	■	■	■	■	■	■	■	■
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GenX (HPFO-DA)	6	■	■	■	■	■	■	□	■
ClPFPECAs	8-14	■	□	□	■	■	■	■	□
6:2 FTOH	8 (6 fluorinated)	■	■	■	■	□	□	□	□
8:2 FTOH	10 (8 fluorinated)	■	□	■	■ (uncertain)	□	□	□	□
6:2 FTSA	8 (6 fluorinated)	■	□	□	□	□	□	□	□
6:2 ClPFESA	8	■	□	□	□	□	□	□	□
Nafion Byproduct	6	■	□	□	□	□	□	□	□

Ether & Polyether Carboxylates (ADONA, GenX (HPFO-DA), ClPFPECAs)

Fluorotelomer Alcohols & Sulfonates (6:2 FTOH, 8:2 FTOH, 6:2 FTSA)

Ether & Polyether Sulfonates (6:2 ClPFESA, Nafion Byproduct)

■ Effect reported in one or more laboratory animal study

□ Effect was evaluated but not found, or effect has not been evaluated

Toxicity of PFAS in Mammalian Species

Short-chain PFAS = green
Long-chain PFAS = blue

All PFAS listed that have been tested in mammalian species cause liver toxicity.

Compound	# of Carbons	Liver	Develop-mental	Repro-ductive	Immune	Hema-tologic	Thyroid	Neuro-behavioral	Tumors
Perfluoroalkyl Carboxylates									
PFBA	4	■	■	■	□	■	■	□	□
PFPeA	5	□	□	□	□	□	□	□	□
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PFHpA	7	■	□	□	□	□	□	□	□
PFOA	8	■	■	■	■	■	■	■	■
PFNA	9	■	■	■	■	■	■	□	□
PFDA	10	■	■	■	■	■	■	■	□
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PFDoA	12	■	■	■	■	■	□	■	□
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PFHxS	6	■	■	□	□	■	■	■	□
PFOS	8	■	■	■	■	■	■	■	■
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8:2 FTOH	10 (8 fluorinated)	■	□	■	■ (uncertain)	□	□	□	□
6:2 FTSA	8 (6 fluorinated)	■	□	□	□	□	□	□	□
6:2 ClPFESA	8	■	□	□	□	□	□	□	□
Nafion Byproduct	6	■	□	□	□	□	□	□	□

Ether & Polyether Carboxylates (ADONA, GenX (HPFO-DA), ClPFPECAs)

Fluorotelomer Alcohols & Sulfonates (6:2 FTOH, 8:2 FTOH, 6:2 FTSA)

Ether & Polyether Sulfonates (6:2 ClPFESA, Nafion Byproduct)

■ Effect reported in one or more laboratory animal study

□ Effect was evaluated but not found, or effect has not been evaluated

Toxicity of PFAS in Mammalian Species

- All perfluoroalkyl carboxylates and sulfonates listed that have been tested, as well as certain ether & polyether carboxylates and fluorotelomer alcohols caused developmental and/or reproductive toxicity.

Short-chain PFAS = green
Long-chain PFAS = blue

Ether & Polyether Carboxylates

Fluorotelomer Alcohols & Sulfonates

Ether & Polyether Sulfonates

Compound	# of Carbons	Liver	Develop-mental	Repro-ductive	Immune	Hema-tologic	Thyroid	Neuro-behavioral	Tumors
			Perfluoroalkyl Carboxylates						
PFBA	4	■	■	■	□	■	■	□	□
PFPeA	5	□	□	□	□	□	□	□	□
PFHxA	6	■	■	■	□	■	■	□	□ (Negative)
PFHpA	7	■	□	□	□	□	□	□	□
PFOA	8	■	■	■	■	■	■	■	■
PFNA	9	■	■	■	■	■	■	□	□
PFDA	10	■	■	■	■	■	■	■	□
PFUnA	11	■	■	□	■	□	□	□	□
PFDoA	12	■	■	■	■	■	□	■	□
			Perfluoroalkyl Sulfonates						
PFBS	4	■	■	■	■	■	■	□	□
PFHxS	6	■	■	□	□	■	■	■	□
PFOS	8	■	■	■	■	■	■	■	■
			Per- & Polyfluoroalkyl Ethers and Polyether Carboxylates & Sulfonates; Fluorotelomer Alcohols (Examples)						
ADONA	6	■	■	□	□	■	□	□	□
GenX (HPFO-DA)	6	■	■	■	■	■	■	□	■
ClPFPECAs	8-14	■	□	□	■	■	■	■	□
6:2 FTOH	8 (6 fluorinated)	■	■	■	■	□	□	□	□
8:2 FTOH	10 (8 fluorinated)	■	□	■	■ (uncertain)	□	□	□	□
6:2 FTSA	8 (6 fluorinated)	■	□	□	□	□	□	□	□
6:2 ClPFESA	8	■	□	□	□	□	□	□	□
Nafion Byproduct	6	■	□	□	□	□	□	□	□

Basis for Toxicity Factors & Drinking Water Guidelines

Non-cancer effects in animal studies – previous basis for all PFAS toxicity factors and drinking water guidelines

Human studies or cancer in animal studies - basis for several recent toxicity factors and proposed drinking water guidelines

In general, toxicity factors & criteria based on human data or cancer are substantially more stringent than earlier values based on non-cancer effects in animals

Final and draft USEPA toxicity factors for PFAS

PFAS	RfD (ng/kg/day)	Status	Basis	CSF $(mg/kg/day)^{-1}$	Status	Basis
PFBA	1000	Final - IRIS	Rat – liver, thyroid	---	---	---
PFHxA	500	Final - IRIS	Rat - developmental	---	---	---
PFOA	0.03	Final – OW	Human – immune, developmental, cardiovascular	29,300	Final – OW	Human – kidney tumors
PFNA	3	Draft – OW	Mouse - developmental	---	---	---
	0.0007	Draft- IRIS	Human - developmental	---	---	---
PFDA	0.002	Final - IRIS	Human – immune, developmental	---	---	---
PFBS	300	Final - CPHEA	Mouse - thyroid	---	---	---
PFHxS	2	Draft - OW	Rat - thyroid	---	---	---
	0.0004	Final - IRIS	Human - immune	---	---	---
PFOS	0.1	Final - OW	Human – developmental, cardiovascular	39.5	Final - OW	Rat – liver tumors
GenX	3	Final - OW	Mouse - liver	---	---	---
Perfluoropropanoic acid	500	Final - CPHEA	Rat -liver	---	---	---
Lithium bis [(trifluoro-methyl)sulfonyl]azanide (HQ-115)	300	Final - CPHEA	Rat - developmental	---	---	---

IRIS – Integrated Risk Information System www.epa.gov/iris OW – Office of Water. CPHEA – Center for Public Health and Environmental Assessment www.epa.gov/aboutepa/about-center-public-health-and-environmental-assessment-cphea

Human Epidemiological Data as Basis for Toxicity Factors

European Food Safety Authority (EFSA) - TWI for total of PFOA/PFOS/PFNA/PFHxS

- Maternal exposure causing ↓ vaccine response in breastfed children @ 1 yr

USEPA Office of Water (2024) - MCLs for PFOA and PFOS

- ***PFOA Cancer Slope Factor:*** ↑ kidney cancer in general population
- ***PFOA RfD:*** ↓ vaccine response in children; ↑ in low birth weight; ↑ total cholesterol (co-critical effects)
- ***PFOS RfD:*** ↑ in low birth weight; ↑ total cholesterol (co-critical effects)

MCL – Maximum Contaminant Level
RfD – Reference dose
TWI – tolerable weekly intake

ITRC PFAS-1 Section 7.1.3

Human Epidemiological Data as Basis for Toxicity Factors

California EPA Drinking Water Public Health Goals (PHGs) for PFOA and PFOS (2024)

- ***PFOA Cancer Slope Factor*** ↑ kidney cancer in general population & communities with drinking water exposure (***primary basis of PHG***).
- ***PFOA RfD*** ↑ serum level of liver enzyme, ALT (indicator of liver damage)
- ***PFOS Cancer Slope Factor*** rat liver tumors (***primary basis of PHG***).
- ***PFOS RfD*** ↑ total cholesterol

USEPA Integrated Risk Information System (IRIS) Reference Doses (2023, 2024)

- ***PFHxS*** ↓ vaccine response in children
- ***PFDA*** ↓ vaccine response in children; ↓ birth weight
- ***PFNA (Draft)*** ↓ birth weight

Health Effects Basis of Updated Minnesota Drinking Water Guidelines

PFOA

Previous: 35 ng/L (mouse developmental)

Updated (2024):

- **Cancer: 0.0079 ng/L**
- **(human kidney cancer)**
- Non-cancer: 2.4 ng/L (human - decreased vaccine response)

PFOS

Previous: 15 ng/L (mouse immune)

Updated (2024):

- Cancer: 7.6 ng/L (rat liver tumors)
- **Non-cancer: 2.3 ng/L (human – decreased birth weight)**

Assessing Toxicity of PFAS Mixtures

Exposure is rarely to a single PFAS

Multiple PFAS present in environmental media and human blood

Interactions may be

Additive

Synergistic (> additive)

Antagonistic (< additive)

General Approaches for Assessing Toxicity of PFAS Mixtures

Laboratory toxicology studies

- Defined mixtures - known concentrations of individual PFAS
- Undefined mixtures - complex mixtures of known & unidentified PFAS (e.g., AFFF)

Risk assessment approaches for predicting mixture toxicity

- Based on assumptions about toxicological interactions among PFAS

Toxicology Studies of PFAS Mixtures

Small # of available studies overall

Types of studies

- ***In vitro* (cultured cells)**
  - Endpoints evaluated: receptor activation, gene expression, cell viability, general toxicity
- **Zebrafish** (model species for mammalian toxicity)
  - Endpoints evaluated: lethality, reproductive, developmental, behavioral effects
- **Mammals (mice and rats)**
  - Very few studies; first study published in 2020
  - Endpoints evaluated: reproductive, developmental, metabolic, hepatic, immune effects

In general, toxicological interactions are complex

- Additive, synergistic, and antagonist interactions
- Differ among PFAS, concentrations, and endpoints

Risk Assessment of PFAS Mixtures - Approaches

Total Concentration (simple additive)

- Assumes toxicity & potency of all included PFAS are identical
  - Basis for some state drinking water guidelines for 5 or 6 long-chain PFAAs such as: MA, ME, VT

Hazard Index (HI)

- Sum of ratios of dose of each PFAS to RfD
- Assumes toxicity is additive, with individual PFAS differing in potency
  - Can be used when RfDs based on either the same or similar toxicity endpoint
  - Basis for final USEPA (2024) drinking water standard for PFBS, PFHxS, PFNA, and GenX

ITRC PFAS-1 Section 9.1.3.1

USEPA drinking water standard based on Hazard Index for total concentration of four PFAS

PFAS	Health-based Water Concentration (HBWC; ng/L, ppt)	Critical Effect (all based on lab animal data)
PFHxS	**10**	**Thyroid**
Gen X (HFPO-DA)	**10**	**Liver**
PFNA	**10**	**Develop-mental**
PFBS	**2000**	**Thyroid**

All 4 PFAS do not need to be present.

Applied when 2 or more of the 4 PFAS are detected.

MCL is exceeded if Hazard Index (HI) is >1.

$$\text{Hazard Index} = \left(\frac{[\text{GenX}_{\text{water}}]}{[10\text{ ppt}]}\right) + \left(\frac{[\text{PFBS}_{\text{water}}]}{[2000\text{ ppt}]}\right) + \left(\frac{[\text{PFNA}_{\text{water}}]}{[10\text{ ppt}]}\right) + \left(\frac{[\text{PFHxS}_{\text{water}}]}{[10\text{ ppt}]}\right)$$

Risk Assessment of PFAS Mixtures – Approaches (Cont.)

Relative Potency Factor (RPF)(or Toxicity Equivalency Factor)

- Each PFAS is assigned an RPF (e.g., 0.1, 10)
  - Based on potency compared to index compound (e.g., PFOA) with RPF of 1
- Assumes dose additivity
- Similar approach used for other chemical classes (e.g., dioxins) that have common mode of action (MOA)
- RPFs based on liver effects in rats proposed for 22 PFAS (Bil et al., 2021)
  - More uncertain than use for dioxins and organophosphates because PFAS have multiple MOAs that may differ among PFAS and toxicological effects

Addressing PFAS as a Class

- Chemical-by-chemical regulation not feasible for every PFAS of interest
  - Estimated 12,000+ total PFAS, > 4,700 in global commerce,
  - Significant time, resources to develop chemical, physical, toxicological data for each PFAS
  - To date, < 20 PFAS are well-studied toxicologically

- Some researchers propose to group (and regulate) subsets of PFAS
  - **Based on Intrinsic properties** (persistence, toxicity, structure, bioaccumulative potential, environmental mobility)
  - **To inform risk assessment** (total organofluorine, additive toxicity, relative potency factors, similarity of adverse effects, mode of action, toxicokinetics)

ITRC PFAS-1 Section 7.1.7

Regulation of PFAS as a Class – Implementation

Limit ongoing uses of PFAS to those with Essential Use	Prohibit sale of certain product categories if they contain *any* PFAS
▪ European Commission (2020) and others proposed this approach ▪ Determination of **Essential Use** challenging; many points of view	▪ California DTSC applied this to carpets or rugs, treatments for converted textiles, leathers, plant fiber-based food packaging ▪ California banned use of ***any*** PFAS “intentionally added” to cosmetics

Inhalation Exposure and Toxicity of Negatively Charged PFAS

Negatively charged PFAS

Examples: PFAAs such as PFOA and PFOS; perfluoroalkyl ether carboxylates such as HFPO-DA [GenX]

Low volatility

Indoor air inhalation exposure primarily via house dust (major source is carpets, furniture)

Worker inhalation exposure primarily via aerosols bound to airborne dust

Very limited inhalation toxicity data:

Toxic effects similar to oral studies.

Inhalation RfCs developed by states: based on route-to-route extrapolation from oral studies

ITRC PFAS-1 Section 7.1.8

Inhalation Exposures and Toxicity of Neutral PFAS

Neutral PFAS

Examples: fluorotelomer alcohols [FTOHs]; perfluorinated sulfonamides [FOSA]; sulfonamide ethanols [FOSE]

Volatile

Indoor air inhalation exposure

Residences, offices, schools, outdoor apparel and carpet stores, ski waxing facilities

No inhalation toxicity studies located in literature review

Available data: absorption and metabolism are similar via inhalation and oral exposure.

Suggests oral and inhalation toxicity are similar

ITRC PFAS-1 Section 7.1.8

Dermal absorption of PFAS

- Limited information on absorption, toxicity of PFAS after dermal exposure.
- **Recent rodent data**: dermal absorption of perfluoroalkyl carboxylates and sulfonates and polyfluoroalkyl phosphoric acid diesters (diPAPs).
- **Recent human data**: PFOA mixed with sunscreen was absorbed through the skin
- **Current evidence**: dermal absorption from soils or water not expected to be an important exposure route for the general public
- **Dermal absorption of PFAS**: a topic of high interest, with additional studies likely

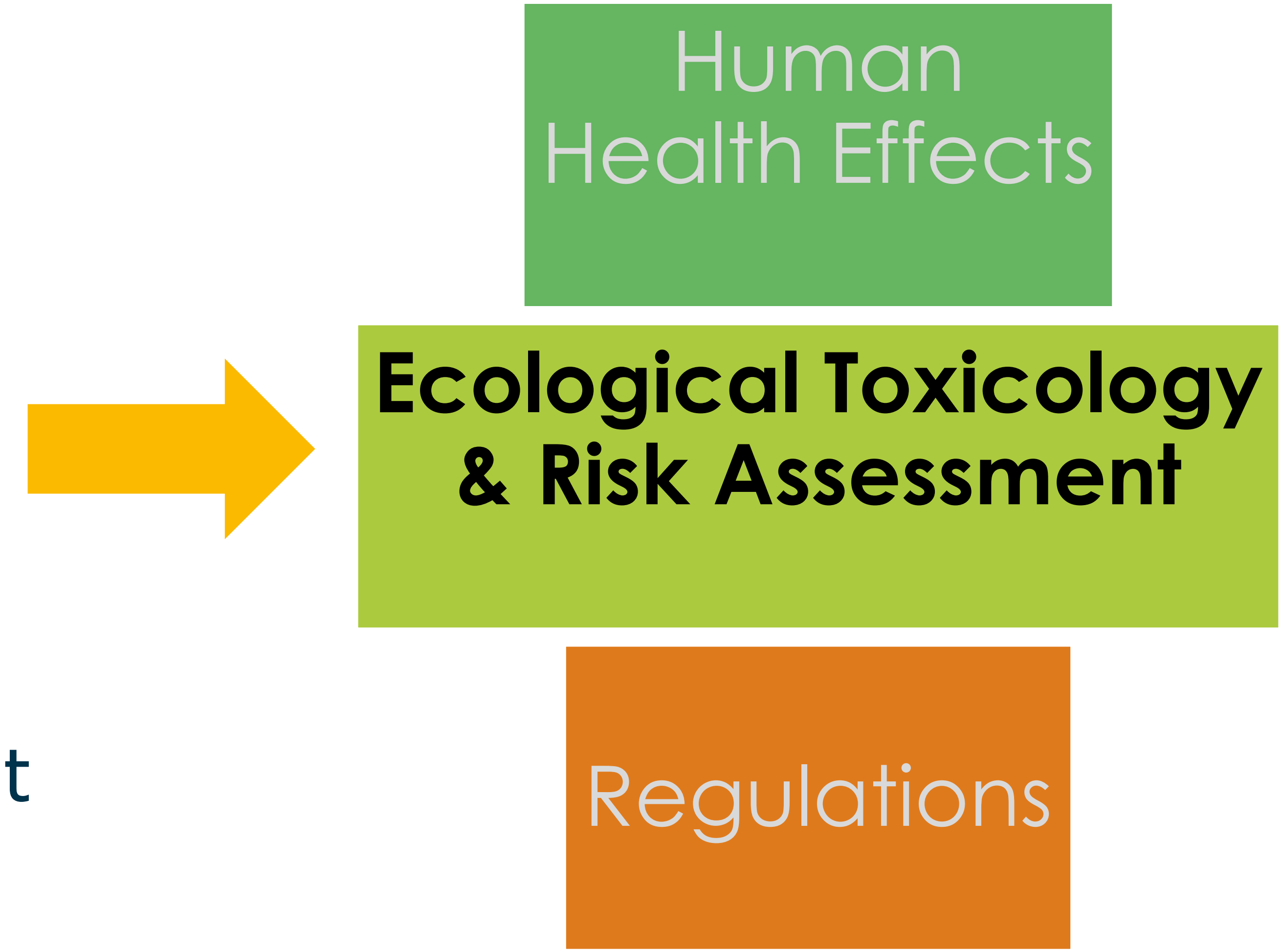
Emerging/Changing Information

- Information is changing quickly – snapshot in time
- IARC conclusions for carcinogenicity of PFOA, PFOS (Dec 2023)
- USEPA National Primary Drinking Water Regulations (MCLs) for PFAS (2024)
- New "Priority Topics" to be addressed in 2024/2025

Questions

Training Roadmap

- Overview of ecological exposures
- Ecotox 101 – key concepts/terminology
- Ecological toxicity studies
- Ecological risk assessment
- Advancing the science: uncertainties/data gaps



ITRC PFAS Guidance Document: Section 7.2 – Ecological Toxicity

- Section 7.2 – Ecological Toxicity
  - High-level summary of ecotoxicological data
  - Discussion of uncertainties and data needs
- Section 9.2 – Ecological Risk Assessment
  - Summary of information for and challenges with PFAS
- Sections 5.5, 5.6, and 17.3.3 – PFAS biological uptake

References with links to complete citations can be found in the PFAS-1 document.

Conceptual Model for Ecological Receptors

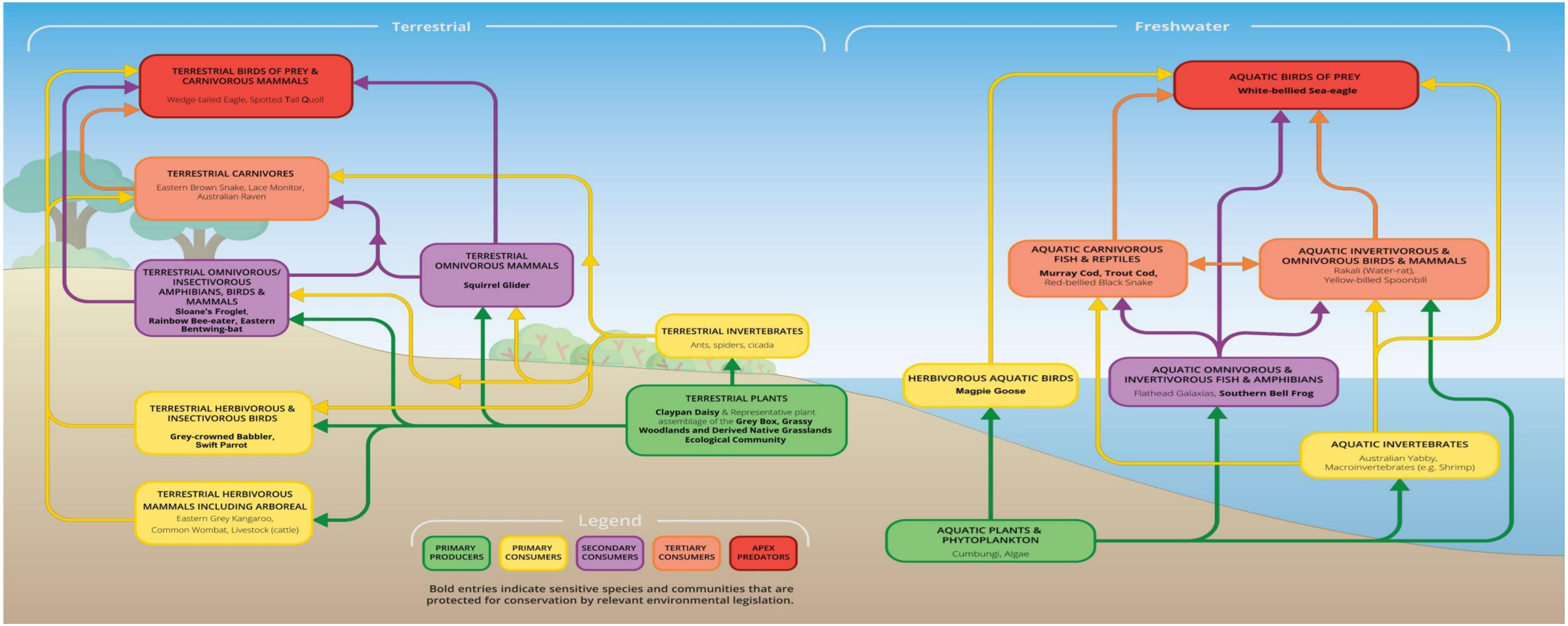


Figure Source: Jacobs Group (Australia). Used with permission.

Biological Uptake of PFAS

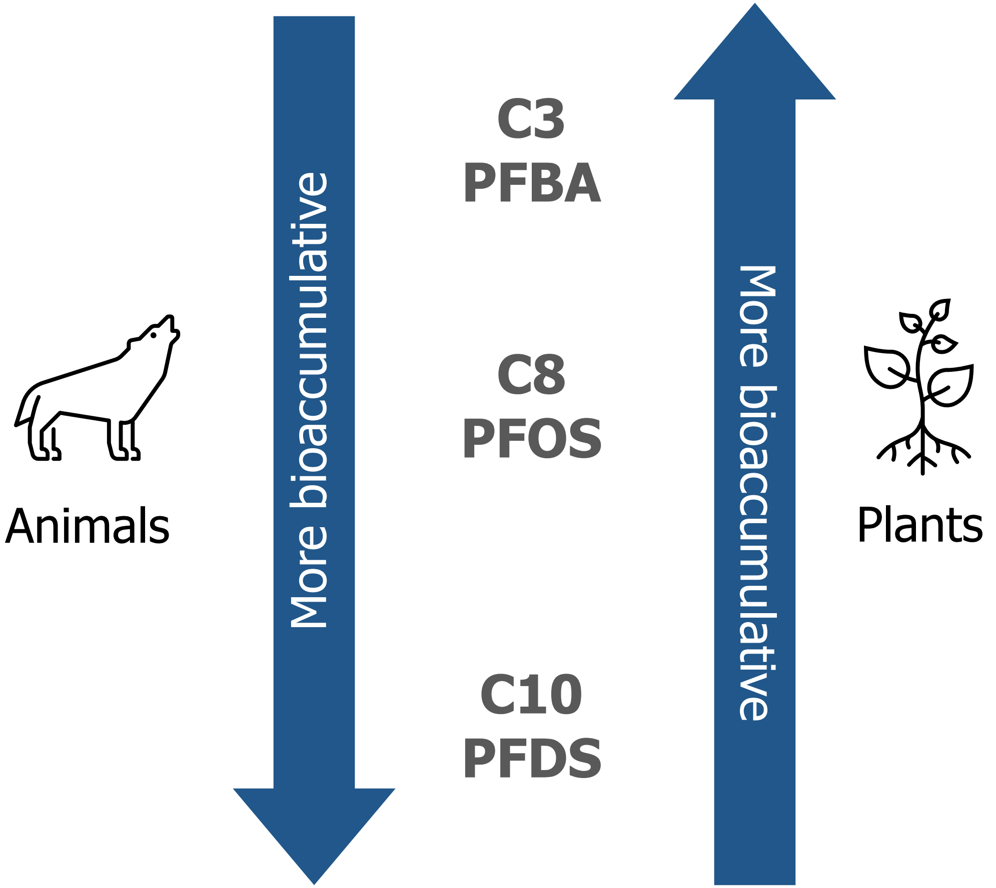
Bioconcentration:
Uptake from water

Bioaccumulation:
Uptake from all surrounding sources

Biomagnification:
Increasing concentrations with increasing trophic levels

Depends on:

- PFAS structure
- Media geochemistry
  e.g., TOC, CEC, pH
- Organism



Bioaccumulation is highly variable

ITRC PFAS-1 Sections 5.5, 5.6, and 17.3.3

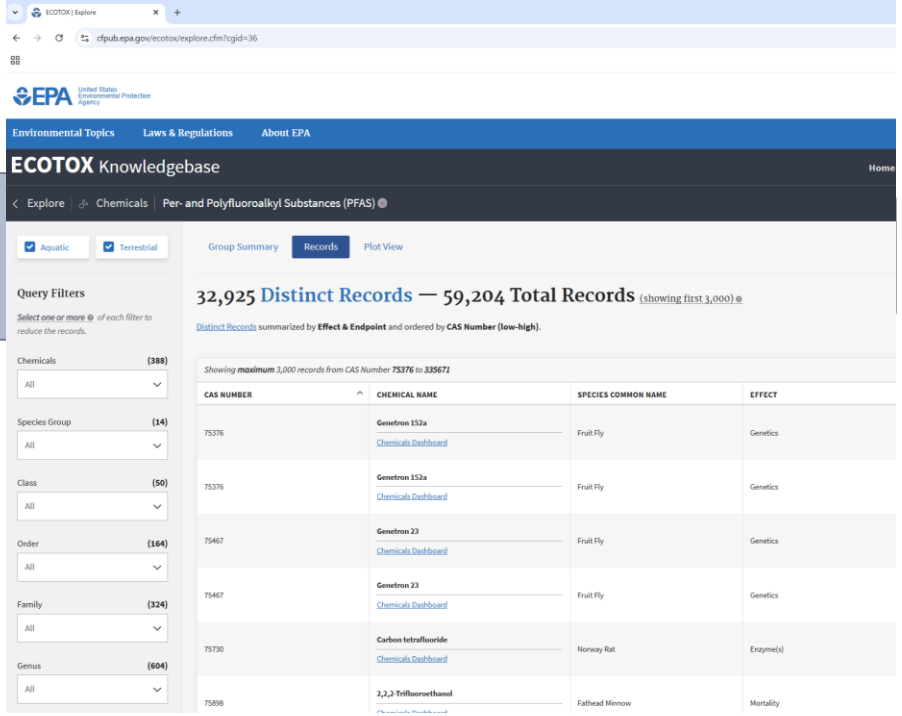
Ecological Toxicity 101

Typical Toxicological Endpoints – "Apical Endpoints"

- Survival
- Growth
- Reproduction

Key sources of data

- Scientific literature
  - USEPA ECOTOX Knowledgebase: https://cfpub.epa.gov/ecotox/
- Federal/State regulations/advisories
- Professional organizations



Invertebrates – Terrestrial

Terrestrial invertebrates appear to be less sensitive to PFAS than their aquatic counterparts.

- Toxicity on **ppm** level
- Most studies on earthworms
- Potential trans-generational effects

Field/soil conditions (soil type, pH etc.) modify toxicity

- PFOS toxicity for 2 different species of soil invertebrates was ~2-4x ↑ when organisms were tested on sandy loam versus clay loam

Data lacking

- Many PFAS, species not tested
- Better understanding of relationship between toxicity and field conditions

Invertebrates – Aquatic and Benthic

Aquatic Studies

- Most data for PFOS, PFOA and acute studies
- Highly variable across species
  - Low to moderate (>10 parts per million, ppm) for acute exposures
  - High to very high (parts per billion [ppb] to ppm) for chronic exposures
    - Chironomids, damselflies particularly sensitive, 1-10 ppb
  - Comparable between freshwater and marine species

Benthic (Sediment) Studies

- Fewer studies compared to aquatic tests
  - Even fewer for marine species
  - Sublethal effects observed in 10-100 ppm range
- Simpson et al. 2021 –one of more comprehensive studies (amphipod, copepod, crab, bivalves)
  - Toxicity influenced by organic carbon (OC), dissolved PFOS fraction in water

ITRC PFAS-1 Section 7.2.2.1

Fish

- Most studies on PFOS
  - Acute effects typically between 1-100 mg/L
  - Chronic effects observed in some species <1 mg/L

USEPA National Recommended Water Quality Criteria

Constituent	NRWQC-Freshwater (mg/L)	
	CMC	CCC
PFOS	0.071	0.00025
PFOA	3.1	0.1

Constituent	Acute Freshwater Benchmark (mg/L)
PFBA	5.3
PFHxA	4.8
PFNA	0.65
PFDA	0.5
PFBS	5
PFHxS	0.21
8:2 FTUCA	0.037
7:3 FTCA	0.012

https://www.epa.gov/wqc/national-recommended-water-quality-criteria-aquatic-life-criteria-table

Reptiles/Amphibians

- No reptile information in PFAS-1
  - Department of Defense Strategic Environmental Research and Development Program (SERDP)
  - https://apps.dtic.mil/sti/trecms/pdf/AD1154448.pdf
- Mainly PFOS, frogs, early life stages
  - Acute effects ~ >10 mg/L
  - Chronic ~1-2 mg/L or lower
    - Developmental/thyroid effects observed
  - Mesocosm study indicates potential underestimation of toxicity (Flynn et al. 2021)
- Pandelides et al., 2023 – critical review, amphibians


Photo by L. McIntosh, used with permission

Birds

- Studies for only a small handful of PFAS, avian species – quails, duck
  - Diet, egg injection studies
    - Reproductive, developmental effects; mortality
  - Few mixtures studies
- Field validation focused mostly on terrestrial species – swallows
- No strong relationship between PFAS exposure and potential effects
- Potential indirect effects, such as food supply impacts

Mammals

- Published lab toxicity data for more PFAS than other taxa
- Significantly more effects measured
  - Focus on answering human health questions
  - Relevance to populations?
- A few field studies, but many confounders
- Use of non-apical endpoints may yield unrealistic results when conducting ERAs

ITRC PFAS-1 Section 7.2.3.4

Plants

- Endpoints: emergence, survival, shoot height/weight
- Preferential uptake of short-chain PFAS
- Aquatic- mainly PFOS, very small # of species
  - Acute toxicity ~ 10-100 mg/L
  - Chronic toxicity range overlaps acute
- Terrestrial –focus on crop plants
  - Chronic toxicity ~ 50 to >1,000 mg/kg
  - Highly variable among and even within species
  - Organic content, PFAS chain length influences toxicity

PFAS Mixtures and Foam: It's Complicated!

Few mixtures studies available

Few foam studies available

Conflicting results

- Variable even within same study, depending on endpoint
- Limited understanding of mechanism of action

Natural versus laboratory environment

- Many confounding factors
- Need for more lab and field data

Advancing the Science: Data Gaps and Uncertainties

Representation

- Species
- PFAS other than PFOS, PFOA
- Mixtures
- PFAS-containing foam

Bioaccumulation

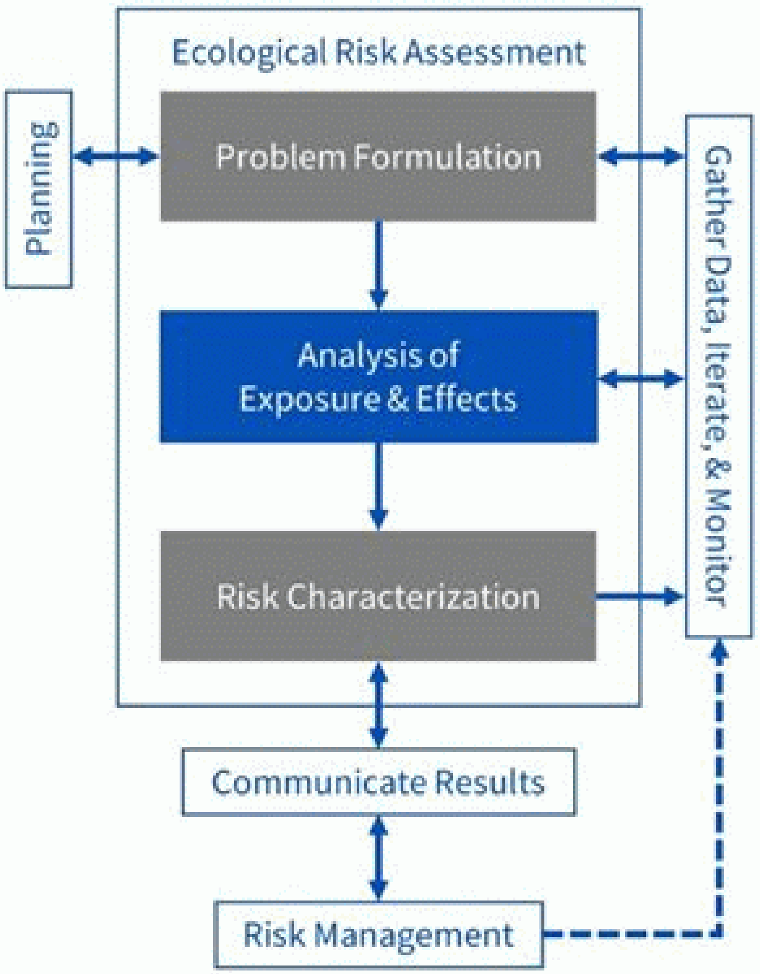
- Factors modulating bioaccumulation
- Bioaccumulation models appropriate for PFAS

Ecological relevance

- Individual vs. population
- Relating environmental exposure and toxicity
- Secondary effects on populations

Ecological Risk Assessment of PFAS

- Overall framework
- Screening-level ERA (SLERA)
  - Comparison of media concentrations to benchmarks
    - Conservative, not very site-specific
- Baseline ERA (BERA)
  - Multiple lines of evidence
  - Site-specific



ITRC PFAS-1 Section 9.2

Graphic from USEPA, Conducting an Ecological Risk Assessment: https://www.epa.gov/risk/conducting-ecological-risk-assessment

ERA Guidance for PFAS

- Several SLERA documents available:
  - Department of Defense Strategic Environmental Research and Development Program (SERDP) (Conder et al., 2020; Divine et al., 2020; Grippo et al., 2024 [Argonne Nat'l Labs])
  - McCarthy et al., 2017
  - Zodrow et al., 2021

- Values are NOT to be used as default clean-up levels

Science is always evolving!

SLERA: Standards and Benchmarks

- Surface Water Quality Standards/Criteria
  - Aquatic life vs. food chain
- Benchmarks –concentrations by medium
- Toxicity reference values – dose by organism
  - Extrapolation to other species? Variability in PFAS sensitivity
- PFAS lacking benchmarks/criteria – how to handle

Summary of published PFAS ecological benchmarks

Soil	Surface Water	Sediment	Tissue/Other
Argonne 2024 Conder et al. 2020 Divine et al. 2020	USEPA NRWQC AWQC – individual states/boards Conder et al. 2020 Divine et al. 2020 Argonne 2024 ECCC 2018 (Canada) ANZECC/ARMCANZ (CRC CARE 2018) European Union 2011, 2013	NPCA Simpson et al. 2021 Divine et al. 2020	USEPA NRWQC ECCC 2018 (Canada-draft) European Union 2011, 2013

Estimating exposure/risk via diet

- Food chain model inputs:
  - media concentrations, intake and life history assumptions, physiological differences

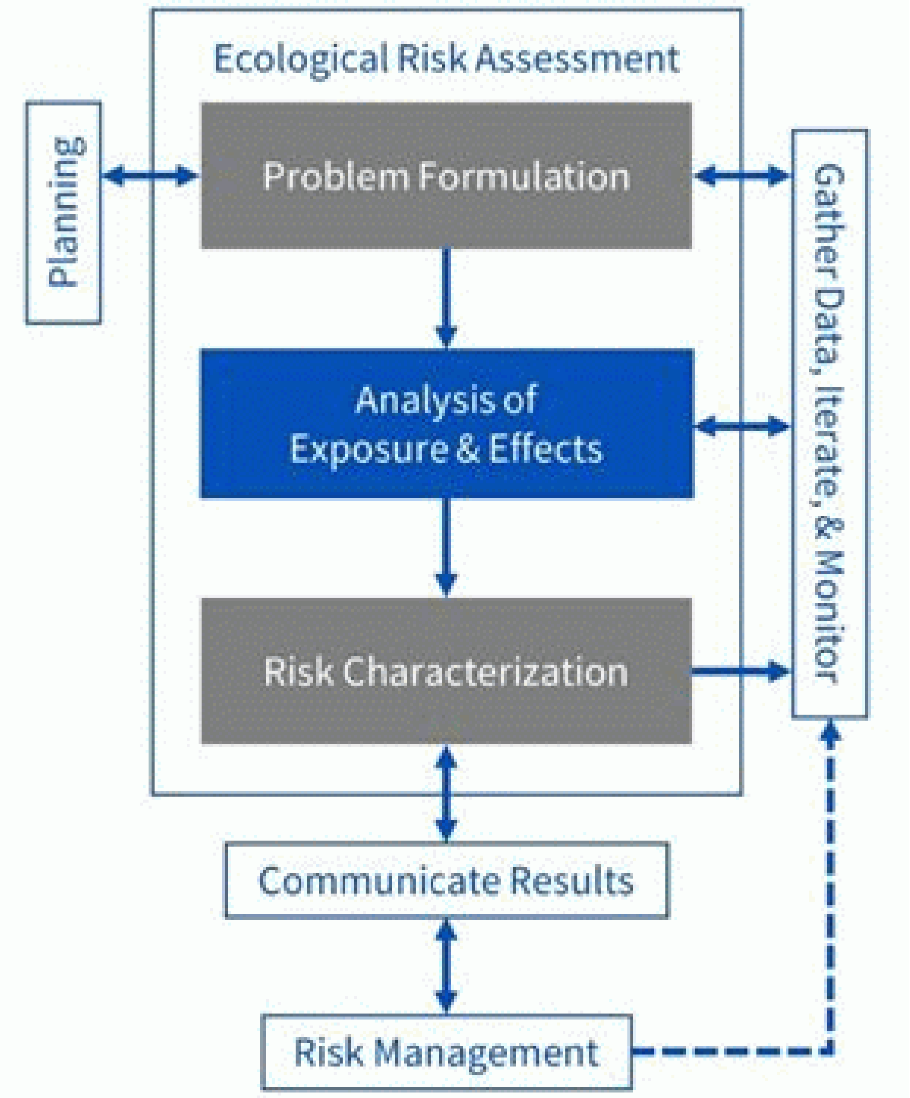
- Analytical challenges

- Bioaccumulation models
  - Uptake factors (BCF, BAF, BSAF)
  - Environmental modifiers like OC

- Availability of toxicity reference values (TRVs)

Beyond benchmarks: evaluating PFAS in a BERA

- Treat like any other constituent in BERA
  - Problem formulation
  - Analysis of exposure
  - Analysis of effects
  - Risk characterization



Graphic from USEPA, Conducting an Ecological Risk Assessment: https://www.epa.gov/risk/conducting-ecological-risk-assessment

Conclusions

Wealth of data available, but only for select PFAS

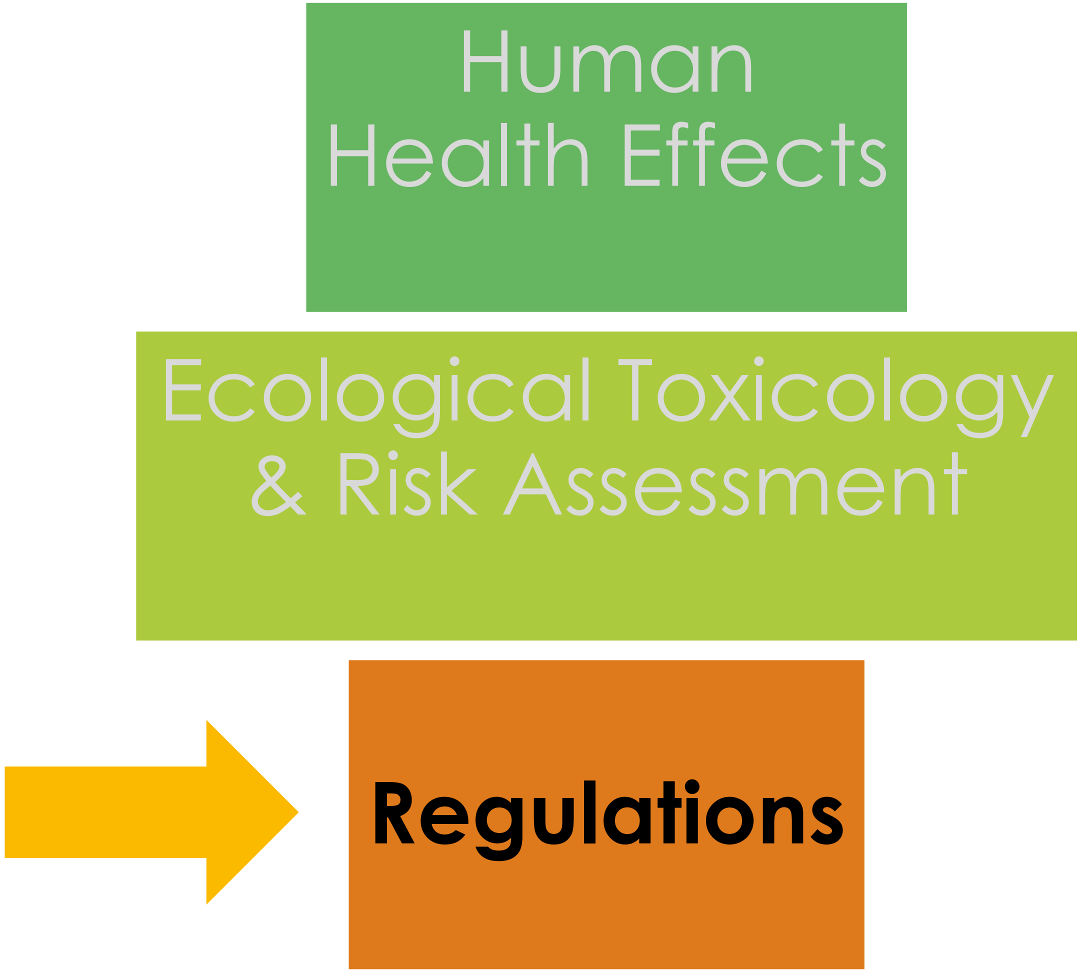
- PFAS exposure can result in adverse effects
- Effects highly variable across media and organisms
- Environmental conditions affect uptake, toxicity

Treat PFAS like other chemicals for SLERA or BERA

- Follow EPA guidance
- Use benchmarks/criteria
- Understand uncertainties

Training Roadmap

- Regulatory Programs Table
- Groundwater, Soil, and Air Quality Values Tables
- Status of Federal Regulations, impacts on State Regulations
- AFFF Alternatives/ Replacement



Regulatory Programs Table

- Statutes and regulations as well as some policy and guidance – https://pfas-1.itrcweb.org
    - All States and US Territories listed including those with no regulations
    - Federal
    - International
  - Focus on finalized PFAS specific statutes and regulations
  - Included policy and guidance that adopts PFAS values by reference
  - Independent compilation and updates from regulatory agency websites, and ITRC PFAS Team discussion
- To provide updates email itrc@itrcweb.org

States and Territories – Example

State	Agency	Program Area	Topic	Description	Legislation or Executive order	Web Link	Date accessed
Alaska (AK)	Alaska Department of Environmental Conservation (ADEC)	Spill Prevention and Response	AFFF	ADEC has formally designated several PFAS found in AFFF as hazardous substances. Any release of PFAS from AFFF or other sources must be reported to the State as required under 18 AAC 75.300	18 AAC 75.300	https://dec.alaska.gov/spar/csp/pfas/firefighting-foam	4/6/2024
Arizona (AZ)	Arizona Department of Environmental Quality (AZ DEQ)	Use of AFFF Containing PFAS	AFFF	Prohibits the use of Class B firefighting foam for training purposes	Arizona SB 1526	https://www.azleg.gov/legtext/54leg/1r/laws/	4/6/2024
Arkansas (AR)	Arkansas Division of Environmental Quality (DEQ)	None found	Other	Arkansas DEQ and Department of Health (DOH) - No indication of PFAS activities found	None found	https://www.adeq.state.ar.us/	4/6/2024

Federal Regulations

Agency	Program Area	Topic	Description	Legislation	Web Link	Date Accessed
USEPA	The Toxic Substances Control Act (TSCA)	Hazardous substances	On September 28, 2023, the EPA announced new PFAS reporting and recordkeeping requirements transpiring from the TSCA Section 8(a)(7) amendment by the FY 2020 NDAA. Rule is retroactive to 2011. Nearly 1,500 fluorinated compounds subject to reporting. EPA is requiring any person that manufactures (including import) or has manufactured (including imported) PFAS or PFAS-containing articles in any year since January 1, 2011, to electronically report information regarding PFAS uses, production volumes, disposal, exposures, and hazards.	TSCA Section 8(a)(7) amendment by the FY 2020 NDAA	www.epa.gov/assessing-and-managing-chemicals-under-tsca/tsca-section-8a7-reporting-and-recordkeeping	12/2/2024
USEPA	Resource Conservation and Recovery Act (RCRA)	Hazardous substances	In February 2024, EPA released two proposed regulations RCRA to protect communities from PFAS and other emerging chemicals of concern. These rules would add nine PFAS, their salts and structural isomers, to the list of RCRA hazardous constituents and would assure that EPA's regulations clearly reflect EPA's and authorized states' authority to require cleanup of the full range of substances that RCRA intended.	RCRA	https://www.epa.gov/superfund/designation	12/2/2024

International Regulations

Location	Agency	Program Area	Topic or Focus Area	Description	Web Link	Date Accessed
European Union	European Food Safety Authority (EFSA)		Cleanup levels or criteria	In September 2020, the European Food Safety Authority (EFSA) set a new safety threshold (a group tolerable daily intake) for the primary PFAS that accumulate in the body.	www.efsa.europa.eu/en/news/pfas-food-efsa-assesses-risks-and-sets-tolerable-intake	4/17/2024
Germany	Federal Ministry of Health	None	General	In addition to regulation under the EU, Germany has also submitted a further restriction proposal for specific PFAS. There is an ongoing restriction proposal by Germany and Sweden for a number of perfluorinated carboxylic acids including their salts and precursors.	https://echa.europa.eu/hot-topics/perfluoroalkyl-chemicals-pfas	4/17/2024
Italy	National Health Service	Italian National Health Institute	Drinking water	The Italian National Health Institute set maximum values for some PFAS in drinking water as a result of the detection of PFAS in surface water and groundwater in the Veneto Region.	https://academic.oup.com/eurpub/article/28/1/180/3852033	4/17/2024

Environmental Media Values Tables

Focus on waters (groundwater, drinking water, and surface water), soils, and air

- All States and US Territories with values
- Federal
- International

https://pfas-1.itrcweb.org

Soil and Water Values Tables – Development

Independent compilation & updates from regulatory agency websites, & ITRC PFAS Team forum

Followed by verification of sources

Environmental Council of States

Various updates including 2024 update on state PFAS standards

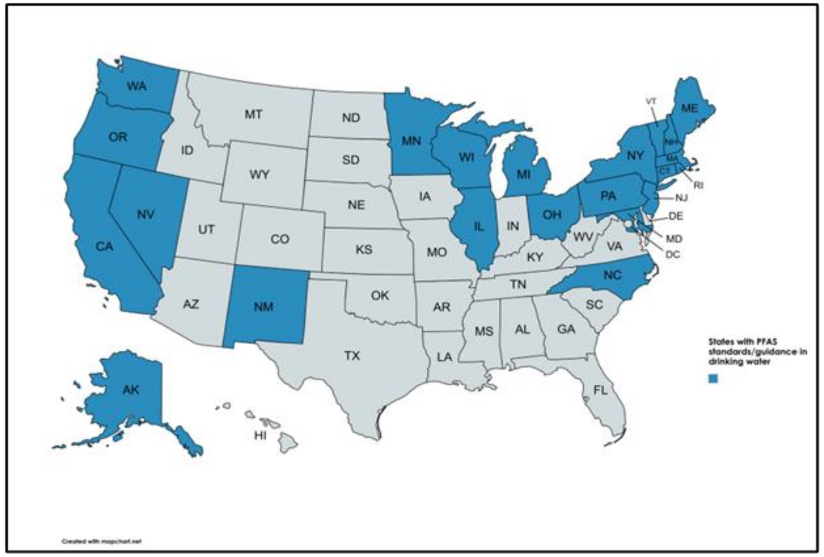
Water Values Tables

Location	Agency / Dept	Year Last Updated	Standard / Guidance	Type	Promulgated Rule (Y/N/O)	Footnote	PFOA 335-67-1	PFNA 375-95-1	PFBS 375-73-5	PFOS 1763-23-1
Alaska (AK)	DEC	2016	CL	GW	Y		0.400			0.400
	DEC	2018	Action Level	DW/GW/SW (HH DW)	N	a	0.070			0.070
California (CA)	SWRCB	2022	NL	DW	N		0.005		0.500	0.007
	SWRCB	2022	RL (CA)	DW	Y		0.010		5	0.040
	OEHHA	2024	PHG	DW	N		0.000007			0.001
Colorado (CO)	DPHE	2018	GQS	GW	Y	d	0.070			0.070
	WQCC	2020	Translation Levels	GW/SW (HH DW)	Y	q	0.070	0.070	400	0.070

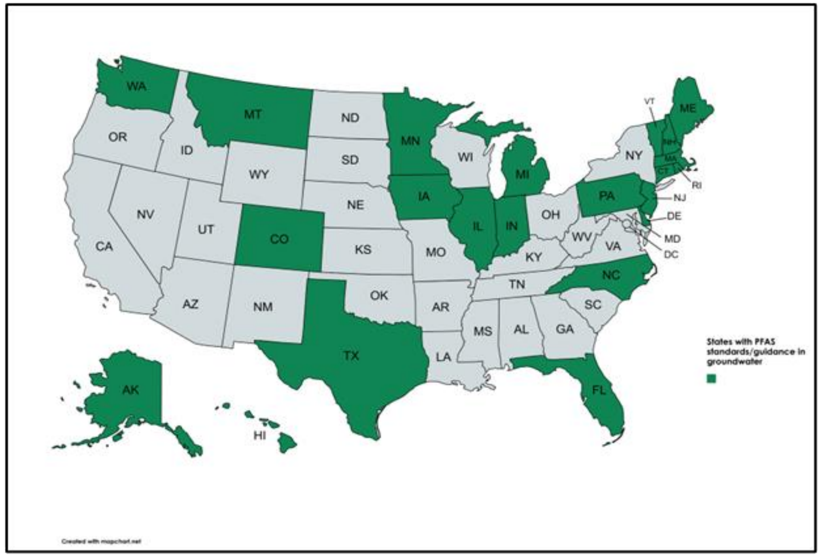
Soil Values Tables

Location	Department	Year Last Updated	Type	Sub-type	Standard	PFOA 335-67-1	PFNA 375-95-1	PFBS 375-73-5	PFOS 1763-23-1
Alaska	DEC	2017	GW/SW Protection		CL	0.0017			0.003
	DEC	2017	Direct Contact		CL[d]	1.3			1.3
Connecticut	DEEP	2018	GW/SW Protection	Protection of GA/GB GW	APS GA PMC	0.0014	0.0014		0.0014
	DEEP	2018	Direct Contact	Residential	APS RDEC	1.35	1.35		1.35
Delaware	DNREC	2024	Direct Contact		Screening Level	0.000019	0.019	1.9	0.00063

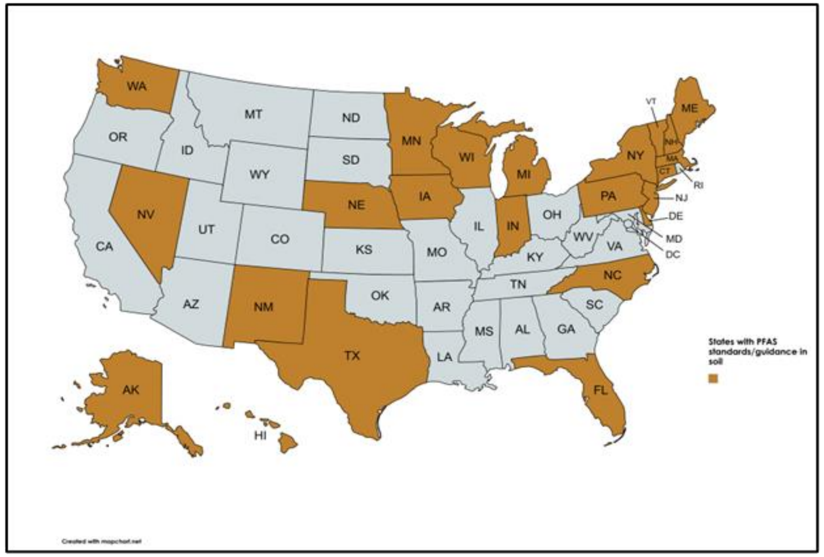
States with PFAS Water and Soil Values



States with Drinking Water Values



States with Groundwater Values



States with Soil Values

Includes promulgated, proposed and screening values, check primary sources for basis of values and enforcement status as of the November/December 2024 ITRC Environmental Media Values tables.

Figure Source: WSP. Used with permission

Soil and Water Values Tables - Findings

USEPA now has promulgated criteria for waters and soils (as of April 2024)

9 states with MCLs for drinking water

- MA, MI, NH, NJ, NY, PA, RI, VT, WI

20 states with promulgated criteria for screening, action, reporting, or other non-drinking water values

Criteria from 10 additional countries included in the table

Soil values from USEPA and 23 states

Additional countries: Australia, Canada, EU, Denmark, Germany, Italy, Netherlands, Norway, Sweden, UK

Air Quality Tables

Air criteria only

- All types of air criteria currently available
- Within the US

Development

- Environmental Council of States
  - 2024 update on state PFAS standards
  - Appendix E – State air criteria
- Independent verification and updates from state websites
- Information from state regulators on ITRC PFAS team

https://pfas-1.itrcweb.org

Air Quality Tables

Location	Agency / Dept	Year Last Updated	Standard / Guidance	Type	Promulgated Rule (Y/N/O)	PFOA 335-67-1	PFNA 375-95-1	PFBS 375-73-5	PFOS 1763-23-1
New Jersey (NJ)	NJDEP	2022	Reference Concentration	--	N	0.007			0.006
	NJDEP	2022	Screening Reference Concentration	--	N				
New York (NY)	NYSDEC	2021	AGC	Annual Average	N	0.0053			
Texas (TX)	TCEQ	2022	ESL	1 hr	N	0.05			0.1
	TCEQ	2022	ESL	Annual Average	N	0.005			0.01
	TCEQ	2023	Reference Concentration	--	N	0.0041	0.028	4.9	0.081

Air Quality Values Tables – Findings

- No federal criteria
- Six states with criteria (MI, MN, NH, NJ, NY, TX)
- Three types
  - Ambient air limits – similar to national ambient air quality standards
  - Screening model limits – for model outputs used in air permitting
  - Reference concentrations – toxicity based; to be used to develop regulatory criteria
- Various timeframes 1-hr, 8-hr, 24-hr, annual

Federal Actions – National Defense Authorization Act (NDAA)

2018 NDAA contained first PFAS related requirement

Subsequent NDAAs number of PFAS related requirements increased

NDAA required actions from multiple federal agencies

- Department of Defense (DoD)
- Center for Disease Control and Protection/Agency for Toxic Substances and Disease Registry (CDC/ATSDR)
- United States Environmental Protection Agency (USEPA)

Federal Actions – Department of Defense (DoD)

Identify facilities with potential PFAS impacts

- Coordination with local and state regulators for assessment of local drinking water and remedial alternatives

Assess health implications to service members, veterans, DoD firefighters, etc.

Support research into Aqueous Film Forming Foam (AFFF) and alternatives and replacement

https://www.acq.osd.mil/eie/eer/ecc/pfas/

Federal Actions – CDC/ATSDR & USFDA

CDC/ATSDR

- https://www.atsdr.cdc.gov/pfas/index.html
- Evaluate PFAS exposure in communities near military bases that are known to have had PFAS in their drinking water, groundwater, or other sources of water

U.S. Food and Drug Administration (USFDA)

- https://www.fda.gov/food/environmental-contaminants-food/and-polyfluoroalkyl-substances-pfas
- Banned long-chain PFAS from use in food contact applications in US

Federal Actions – USEPA Programs

- Toxics Release Inventory (TRI)/ Emergency Planning and Community Right-to-Know (EPCRA)
- Toxic Substances Control Act (TSCA)
- Comprehensive Environmental Response, Compensation and Liability Act (CERCLA)
- Resource Conservation and Recovery Act (RCRA)
- Clean Water Act/National Pollutant Discharge Elimination System (NPDES)
- National Primary Drinking Water Regulation (NPDWR)/Unregulated Contaminant Monitoring Rule (UCMR)

USEPA has majority of fed regs

USEPA Program Regulations – TRI & TSCA

- Toxics Release Inventory (TRI)
  - NDAA for 2020 added numerous PFAS
    - 2025 added nine PFAS
  - Updated multiple times including reducing the reporting amount guidelines
  - Requires reporting with no de minimus exemptions for all uses
  - EPCRA – provides framework for adding PFAS annually
- Toxic Substances Control Act (TSCA)
  - Manufacturers and importers report uses, production volumes, disposal, exposures, and hazards

USEPA Program Regulations – CERCLA & RCRA

- CERCLA Final Rule (2024)
  - Designating PFOS and PFOA as hazardous substances

- RCRA proposed rule (2/2024)
  - Revise definition of hazardous waste
  - List nine PFAS as hazardous constituents

Proposed Hazardous Constituents (2024):
PFOA
PFOS
PFBS
HFPO-DA (Gen-X)
PFNA
PFHxS
PFDA
PFHxA
PFBA

USEPA Program Regulations – Clean Water Act (CWA)

- National Pollutant Discharge Elimination System (NPDES)
  - Wastewater
  - Recommendations for permit writers and pre-treatment authorities
  - Restrict levels of PFAS discharge from facilities
- Effluent Limitation Guidelines (ELG) Plan 15
  - Pre-treatment standards required to reduce PFAS in leach discharges at landfills and expand ongoing studies
- Water Quality Criteria
  - Surface water
  - Protect Aquatic life

USEPA Program Regulations – Safe Drinking Water Act (SDWA)

- UCMR3
  - 2013 to 2015
  - Included six PFAS
- UCMR5
  - 2023 to 2025
  - 29 PFAS
  - Lower reporting limits
  - 66% of total expected data released as of Jan 16, 2025

Public water system definition:	Provides water for human consumption to at least 15 service connections or serves an average of at least 25 people for at least 60 days a year.

ITRC PFAS-1 Section 8.2.2.4

USEPA Program Regulations – SDWA

- Drinking water regulation (4/2024)
  - Establish maximum contaminant levels (MCLs)
  - Health-based levels

PFAS Compound	MCLG (ppt)	MCL (ppt)
PFOA	Zero	4.0
PFOS	Zero	4.0
PFHxS	10	10
PFNA	10	10
HFPO-DA (GenX)	10	10
Mixture of 2 or more of PFHxS, PFNA, PFBS, GenX	HI of 1 (unitless)	HI of 1 (unitless)

$$\text{Hazard Index} = \left(\frac{[GenX_{water}]}{[10\text{ ppt}]}\right) + \left(\frac{[PFBS_{water}]}{[2000\text{ ppt}]}\right) + \left(\frac{[PFNA_{water}]}{[10\text{ ppt}]}\right) + \left(\frac{[PFHxS_{water}]}{[10\text{ ppt}]}\right)$$

State Impacts – Federal Drinking Water Regulations

- States with promulgated state drinking water MCL equivalent values
  - Adopt federal values
  - Which are lower/more restrictive
- States with values proposed but not promulgated
  - Adopt federal values
- States with no values
  - Adopt federal values

Federal Actions – Department of Defense (DoD)

Identify facilities with potential PFAS impacts,

- Coordination with local and state regulators for assessment of local drinking water and remedial alternatives

Assess health implications to service members, veterans, DoD firefighters, etc.

Support research into Aqueous Film Forming Foam (AFFF) and alternatives and replacement

https://www.acq.osd.mil/eie/eer/ecc/pfas/

Firefighting Foam System Replacement

Fluorine-free Foam (F3) Status

DoD/Airports	Industrial Users	Municipal Users
• Certified Milspec F3 is available • Certified F3 is available	• Transitions occurring where State regulatory drivers exist • Transitions expected to ramp up in 2024	• Certified F3 is available • Transitions occurring where support of State take-back programs

ITRC PFAS-1 Section 3.11.1.3

Alternatives Assessment

Evaluate F3 alternatives in terms of regrettable substitution. Tickner (2022) offers six guiding considerations, including:

1. Determine the chemical's function
2. Define the application-specific use scenario(s)
3. Establish and/or use performance standards
4. Use a range of performance standard benchmarks
5. Consider technical performance separately from technical feasibility.
6. Determine acceptable tradeoffs

Tickner, J. 2022. Advancing Safer Alternatives to AFFF: Lessons Learned From a SERDP Funded-Initiative. SERDP Project WP19-1424: SERDP-ESTCP. www.serdp-estcp.org/projects/details/da4a70e8-393f-493b-98b9-93ac1f3ad2af

Certifications for F3 Alternatives- Examples

For US DoD and FAA Part 139 Airports

- In January 2023, a new performance specification was published (MIL-PRF-32725) for F3 land-based applications.
- Mil-spec concentrate has no intentionally-added PFAS and maximum of 1 ppb of PFAS
- For approved products, go to https://qpldocs.dla.mil/

For other foam users

- Consider other product certification organizations
- CPA GreenScreen requires no intentionally-added PFAS and no more than 1 ppm total organic fluorine in product
- For approved products, go to https://www.greenscreenchemicals.org/certified/fff-standard

Note Variability by Requirement/ Certification:
Permitted concentration of unintentionally-added PFAS

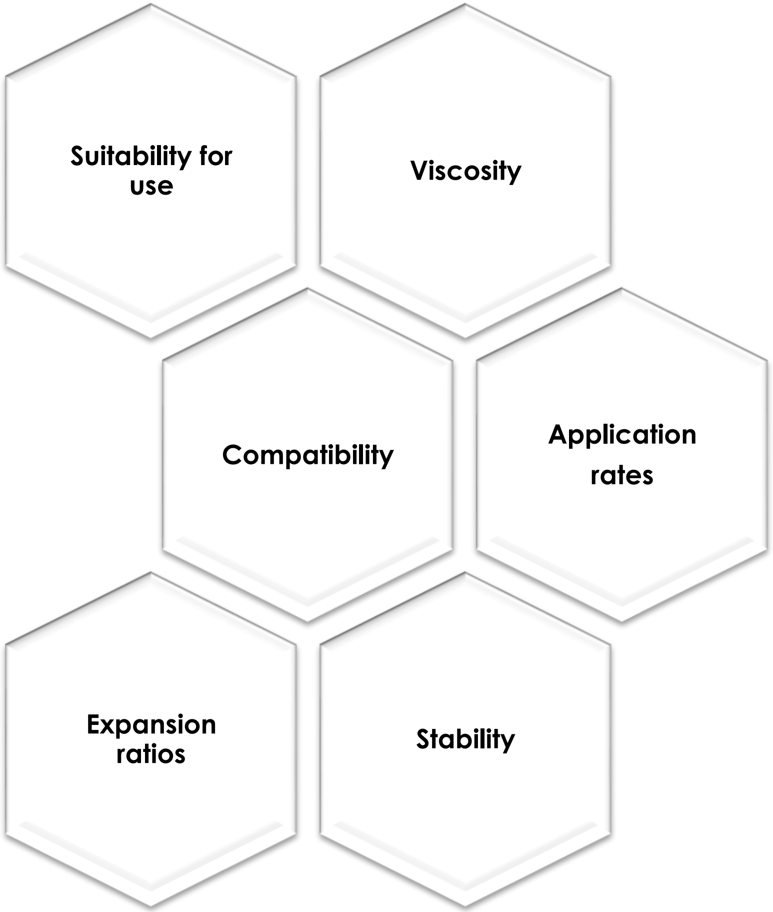
Analytical methodology used to analyze and measure unintentionally-added PFAS

Responsibility for verification and validation

Firefighting Foam and Foam System Replacement

Consider:

- performance specifications, system modifications, decontamination and disposal
- clean-out vs replacement options
- alternatives to using fire foam for specific hazards such as: Water Mist; Dry Chemical; Containment flooring systems; separation and exposure protection
- Other factors:
  - What are the current system performance requirements for the foam?
  - What application techniques are anticipated?
  - How Clean does the System need to be for replacement foam application?



ITRC PFAS-1, Section 3.11.3 AFFF Transition Planning, Table 3-5 Example Case Studies.

System Decontamination During Replacement

- ✓ A thorough clean-out is recommended although rebound effects have been proven consistently to occur and continue to be studied

- ✓ The degree of cleanliness required and the cost balance between cleaning and replacing system components should be considered

- ✓ Currently there are no regulatory guidelines or requirements pertaining to degree of cleanliness

- ✓ Studies are on-going to evaluate best practices for clean-out. A study by CTDEEP (2022) suggests
  - Proprietary cleaning agents were more effective than plain water rinses (>99% vs. ~95% removal)
  - Residual PFAS levels remain that can still cross-contaminate F3
  - Logistics and cost are significant
  - No "one-size-fits-all" approach

Treatment Technologies Training

Stabilization and Landfill Disposal

Non-destructive

AFFF mixed with stabilizer

Immobilized and encapsulated

Deep Well Injection

Non-destructive

Injected into tectonically stable strata

Incineration

Destructive

AFFF destroyed or mineralized via heat

Efficacy under study

Potential Future Disposal Technologies

New destructive technologies are under development

Interim Guidance on the Destruction and Disposal of Perfluoroalkyl and Polyfluoroalkyl Substances and Materials Containing Perfluoroalkyl and Polyfluoroalkyl Substances (USEPA, 2024)

ITRC PFAS-1, Table 3-4 and Section 3.10 AFFF Disposal.

Questions

Feedback Form & Certificate: https://www.clu-in.org/conf/itrc/PFAS-BTB-HH