The Case for Managing PFAS as a Chemical Class to Protect Health

David Andrews, Ph.D., Senior Scientist

Environmental Working Group

April 5, 2022

Part 2.

Continued from NEWMOA webinar 3-24-2021

Outline

Finding PFAS

Initial EPA actions

PFAS exposure

Public health perspective on PFAS as a class

Case study (PFAS ethers)

Environmental Working Group

is a non-profit, non-partisan organization dedicated to protecting human health and the environment.

Our Mission

Our mission is simple: To empower you with breakthrough research to make informed choices and live a healthy life in a healthy environment.

Reports

PFCs
GLOBAL CONTAMINANTS
They're Everywhere

THURSDAY, APRIL 3, 2003

PFCS: GLOBAL CONTAMINANTS

Consumers instantly recognize them as household miracles of modern chemistry — Teflon, Scotchgard, Stainmaster, Gore-Tex.

Consumers instantly recognize them as household miracles of modern chemistry, a family of substances that keeps food from sticking to pots and pans, repels stains on furniture and rugs, and makes the rain roll off raincoats. Industry makes use of the slippery, heat-stable properties of these same chemicals to manufacture everything from airplanes and computers to cosmetics and household cleaners.

But in the past five years, the multi-billion dollar "perfluorochemical" (PFC) industry, which underpins such world-famous brands as Teflon, Stainmaster, Scotchgard and Gore-Tex, has emerged as a regulatory priority for scientists and officials at the U.S. Environmental Protection Agency (EPA). The PFC family is characterized by chains of carbon atoms of varying lengths, to which fluorine atoms are strongly bonded, yielding essentially indestructible chemicals that until recently were thought to be biologically inert. No one thinks so now.

JUNE 9, 2008

CREDIBILITY GAP: TOXIC CHEMICALS IN FOOD PACKAGING: DUPONT CLAIMS AT ODDS WITH SCIENCE

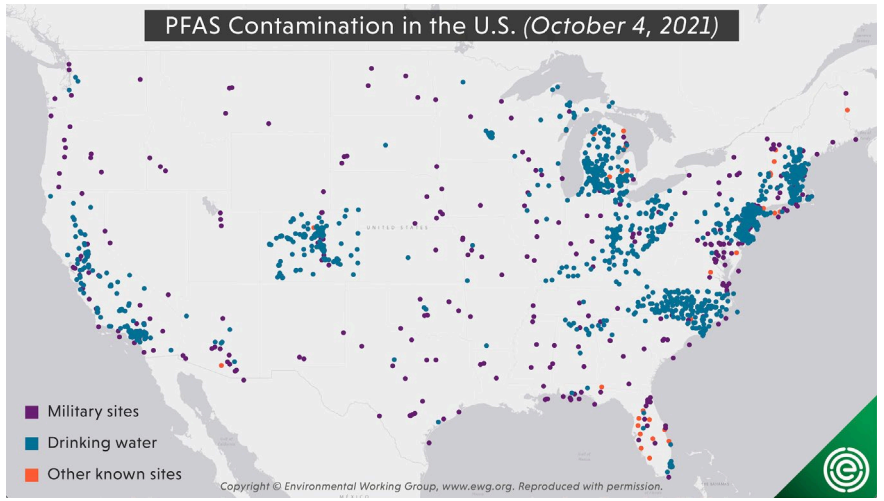
No matter how strong the evidence that PFOA may be harming human health, DuPont spokespeople refute it, year after year: "…PFOA does not harm human health or the environment." (**See DuPont press quotes**) Normally, this might be dismissed as a typical corporate interpretation of study results or just another example of a company over-zealously defending a profitable chemical. But in this case DuPont has gone beyond spin, to a much higher level of deception.

Documents obtained from litigation against DuPont for PFOA contamination of water supplies in West Virginia and Ohio show that DuPont's own ethicists and medical experts found the company's spin on PFOA science to be "misleading", "disingenuous", "unacceptable", and "not supported by the available facts" (DuPont's Epidemiology Review Board 2005-2006).

DuPont's mischaracterizations of the science have long raised concerns from environmental advocates and communities affected directly by their pollution and neglect. But in 2005 and 2006, this misinformation campaign ran into a serious buzzsaw in the form of **DuPont's own Epidemiology Review Board (ERB)**, a group of independent scientists, medical doctors, and ethicists from Harvard, Yale, Georgetown, Johns Hopkins and other prestigious universities, chosen by DuPont to review PFOA epidemiology studies, including several studies of workers at their Parkersburg, West Virginia fluorochemical plant.

Fast Food Companies Asked To Disclose Use Of Toxic Chemicals In Food Packaging

FOR IMMEDIATE RELEASE: THURSDAY, JULY 10, 2003
WASHINGTON — In the growing controversy over the toxicity and pervasiveness of a group of chemicals, the Environmental Working Group (EWG) today asked the CEOs of nine major fast food corporations to disclose the use of the chemicals in their packaging. The chemicals — fluorinated telomers — can break down into perfluorooctanoic acid (PFOA), which is used to make Teflon. PFOA is toxic at low levels and is found in more than 90% of Americans.



Testing for PFAS as a class started in the 60's

These findings suggest that there is widespread contamination of human tissues with trace amounts of organic fluorocompounds derived from commercial products.

Organic Fluorocompounds in Human Plasma: Prevalence and Characterization

W. S. GUY
Department of Basic Dental Sciences, University of Florida, Box J424, Gainsville, Fla. 32610

D. R. TAVES
Department of Pharmacology and Toxicology, University of Rochester, Rochester, N.Y. 14642

W. S. BREY, JR.
Department of Chemistry, University of Florida, Gainsville, Fla. 32611

Taves discovered that samples of his own blood serum contained two distinct forms of fluoride (1-4). Only one of these was exchangeable with radioactive fluoride. The other, non-exchangeable form was detectable as fluoride only when sample preparation included ashing. This paper is concerned with three aspects of this newly discovered, non-exchangeable form: 1) its prevalence in human plasma, 2) how its presence in human plasma affects the validity of certain earlier conclusions about the metabolic handling of the exchangeable form of fluoride, and 3) its chemical nature.

Preliminary work in this laboratory suggested that the non-exchangeable form was widespread in human plasma but did not exist in the plasma of other animals. Ashing increased the amount of fluoride an average of 1.6 ± 0.25 SD μM (range 0.4 - 3.0) in samples of plasma from 35 blood donors in Rochester, N.Y. (5). No such fluoride was detectable (above 0.3 μM) in blood serum from eleven different species of animal including horse, cow, guinea pig, chicken, rabbit, sheep, pig, turkey, mule and two types of monkey (6).

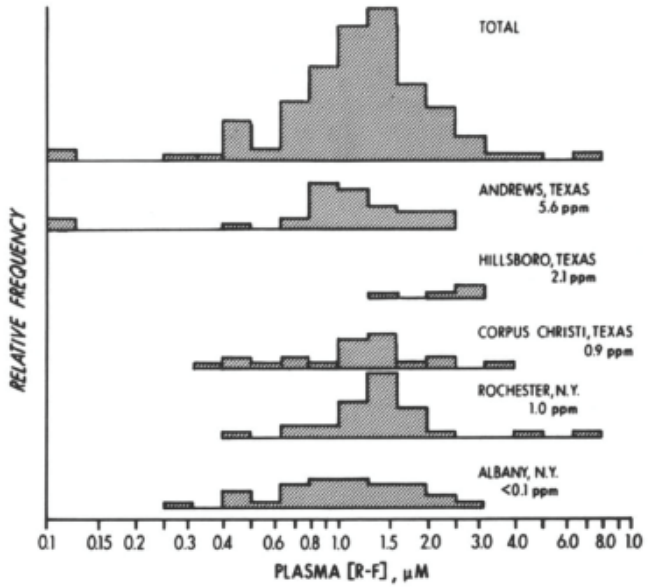


Figure 2. Relationship between the concentration of organic fluorine in human plasma and the concentration of fluoride in the drinking water

2010/2015 PFOA Stewardship Program backstop

- Significant New Use Rule for Long-Chain Perfluoroalkyl Carboxylate and Perfluoroalkyl Sulfonate Chemical Substances
- Proposed rule. 2015

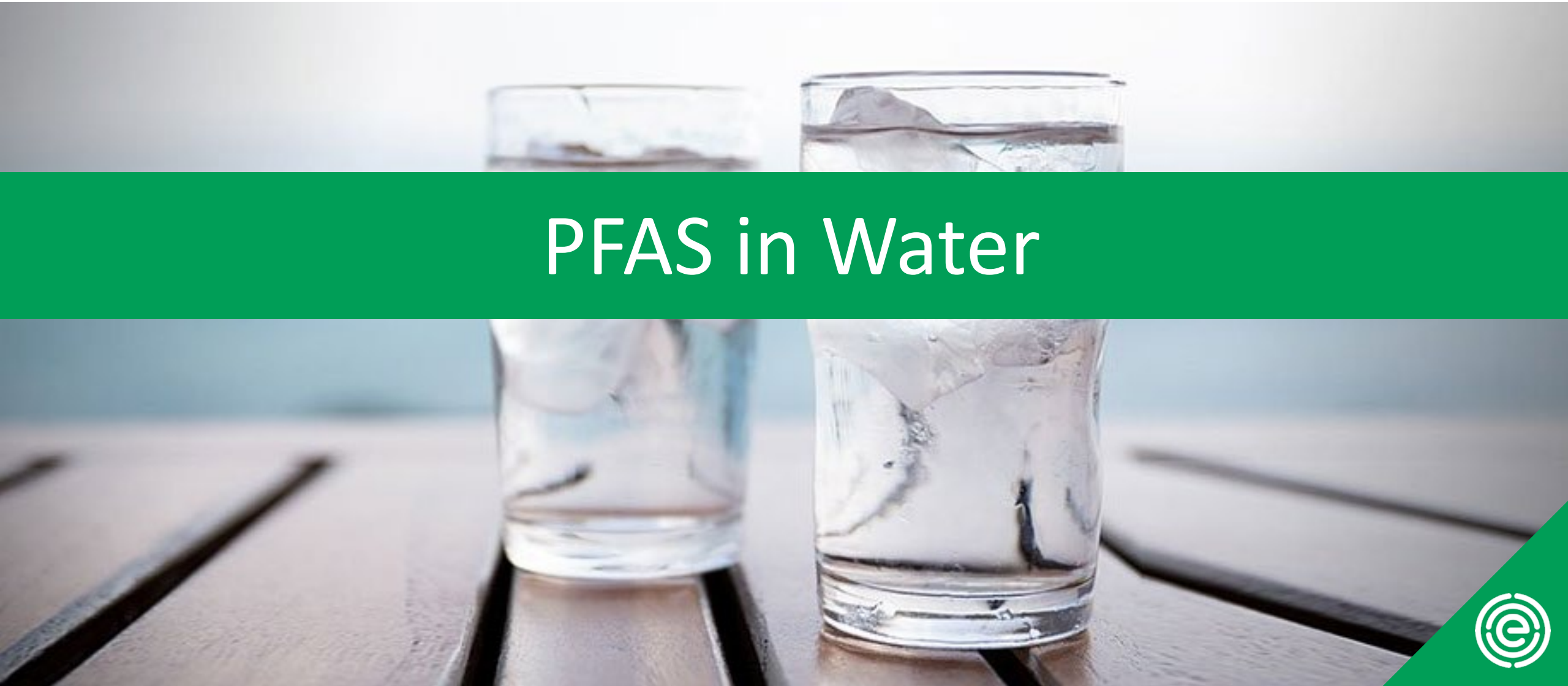
II. Chemical Substances Subject to This Proposed Rule

A. What LCPFAC chemical substances are subject to this proposed SNUR?

LCPFAC chemical substances are synthetic chemicals that do not occur naturally in the environment. The LCPFAC chemical substances identified in this unit, where $5 < n < 21$ or $6 < m < 21$:

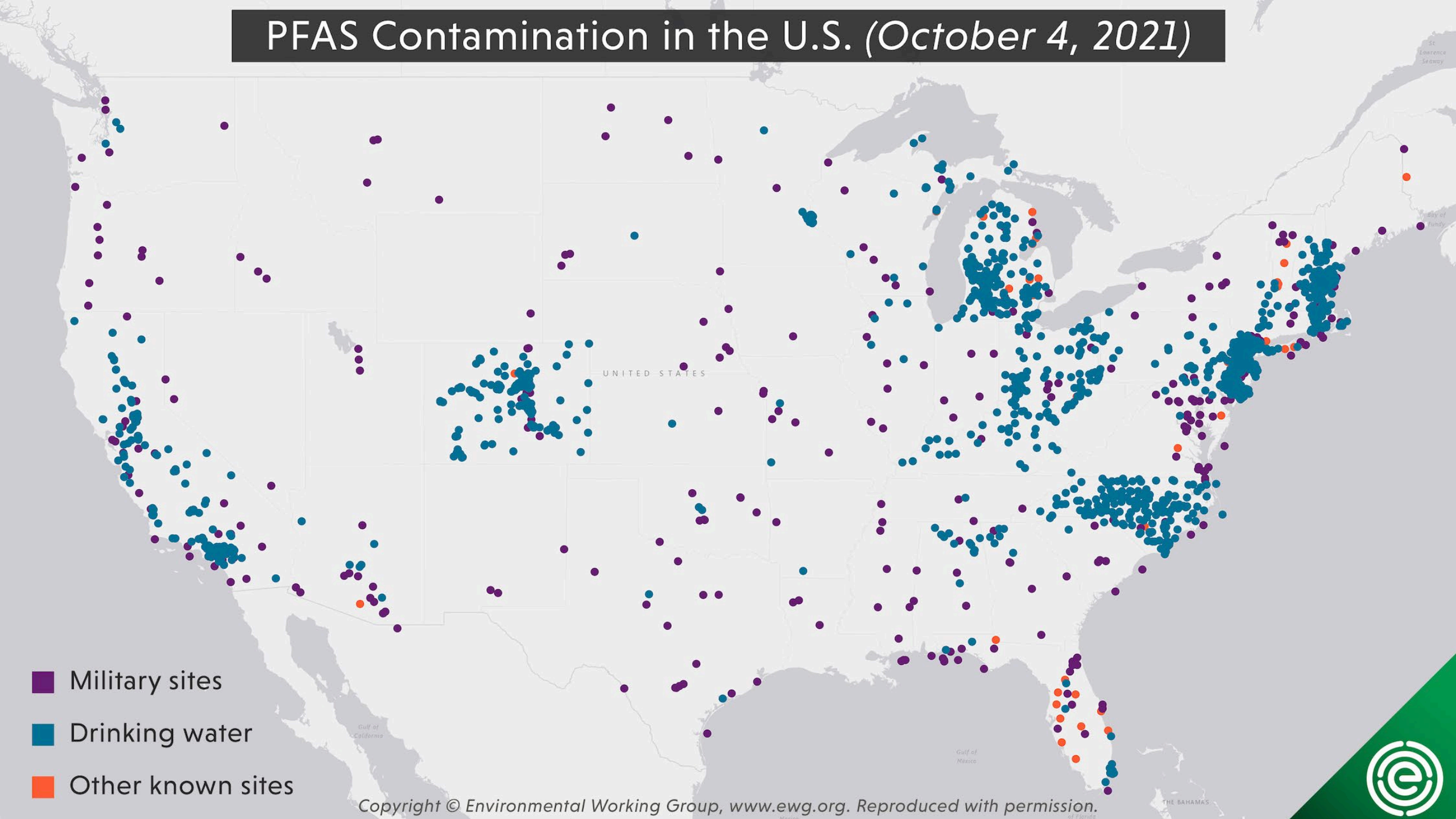
1. $CF_3(CF_2)_n$-COO^-M where M = H^+ or any other group where a formal dissociation can be made.;
2. $CF_3(CF_2)_n$-$CH{=}CH_2$.
3. $CF_3(CF_2)_n$-C(=O)-X where X is any chemical moiety.
4. $CF_3(CF_2)_m$-CH_2-X where X is any chemical moiety.
5. $CF_3(CF_2)_m$-Y–X where Y = non-S, non-N heteroatom and where X is any chemical moiety.

PFAS exposure



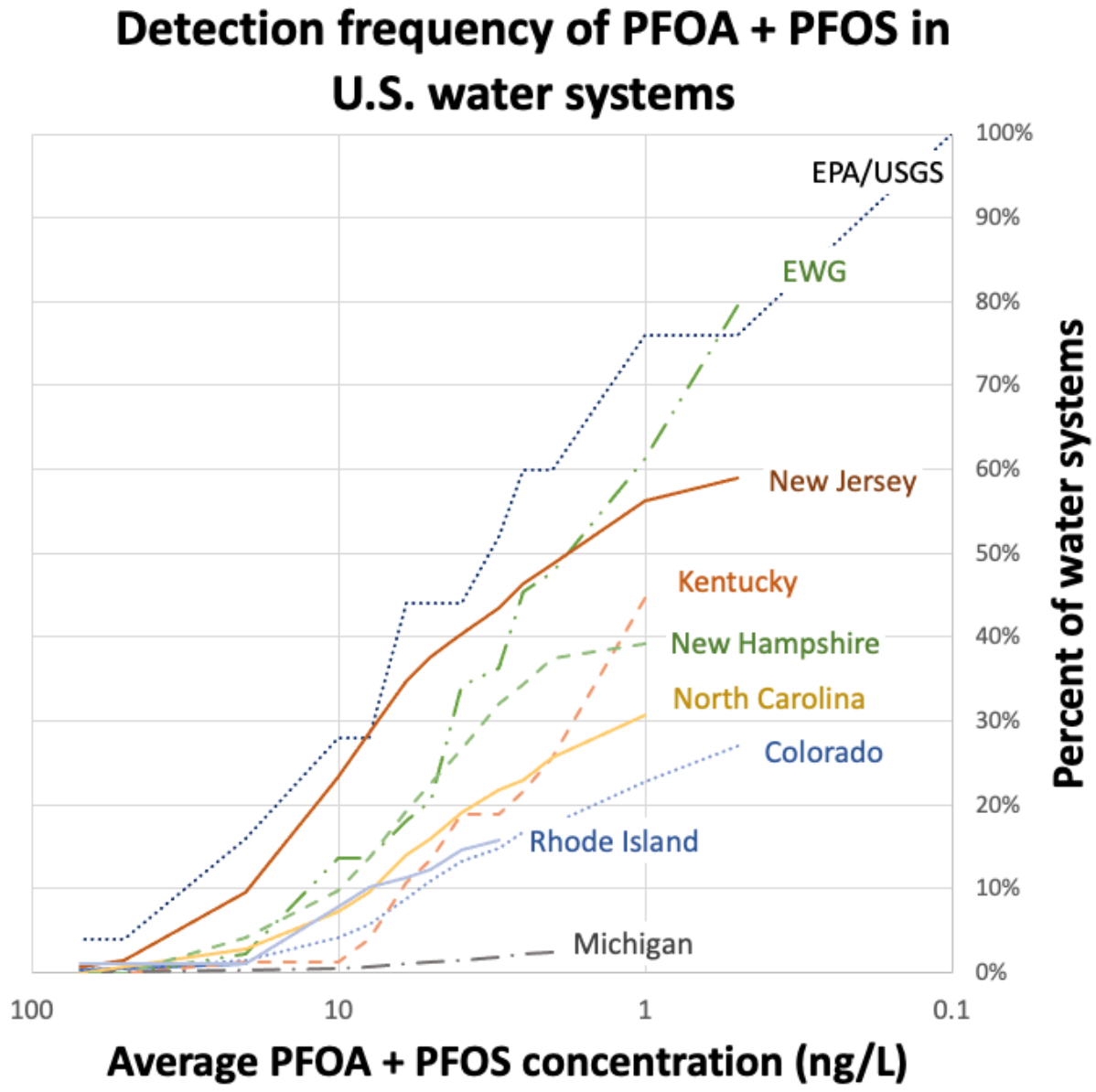
PFAS in Water

PFAS Contamination in the U.S. *(October 4, 2021)*

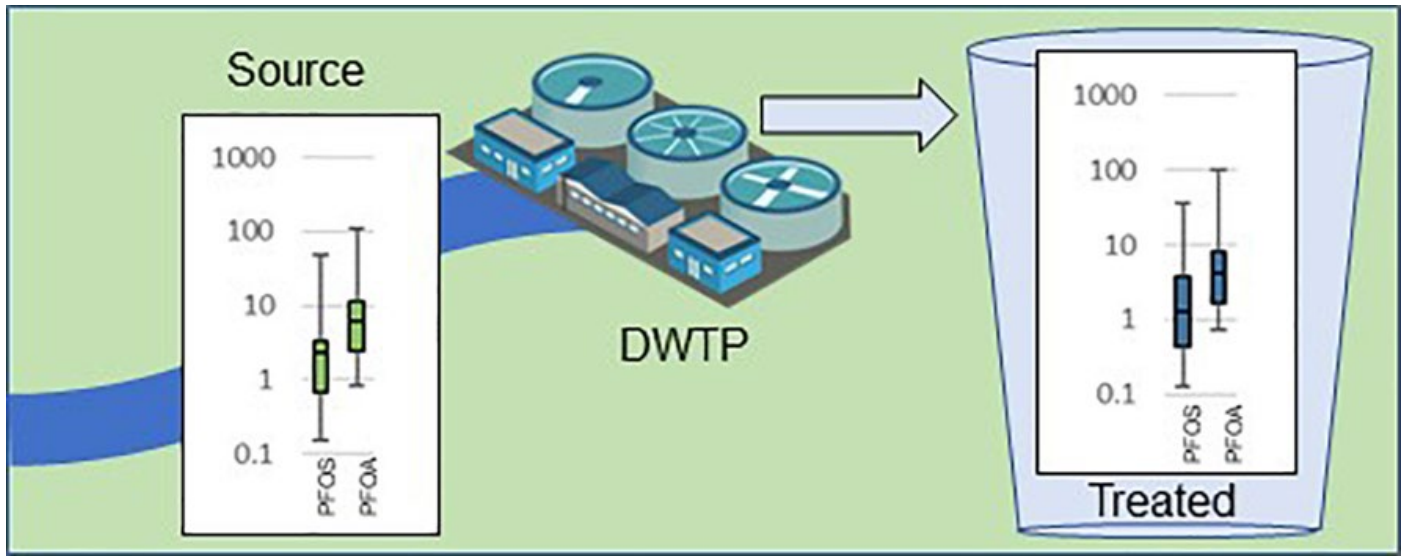


PFOA + PFOS

- Population-Wide Exposure to Per- and Polyfluoroalkyl Substances from Drinking Water in the United States
- ES&T 2020, https://doi.org/10.1021/acs.estlett.0c00713



What is missed when you look at just PFOA + PFOS



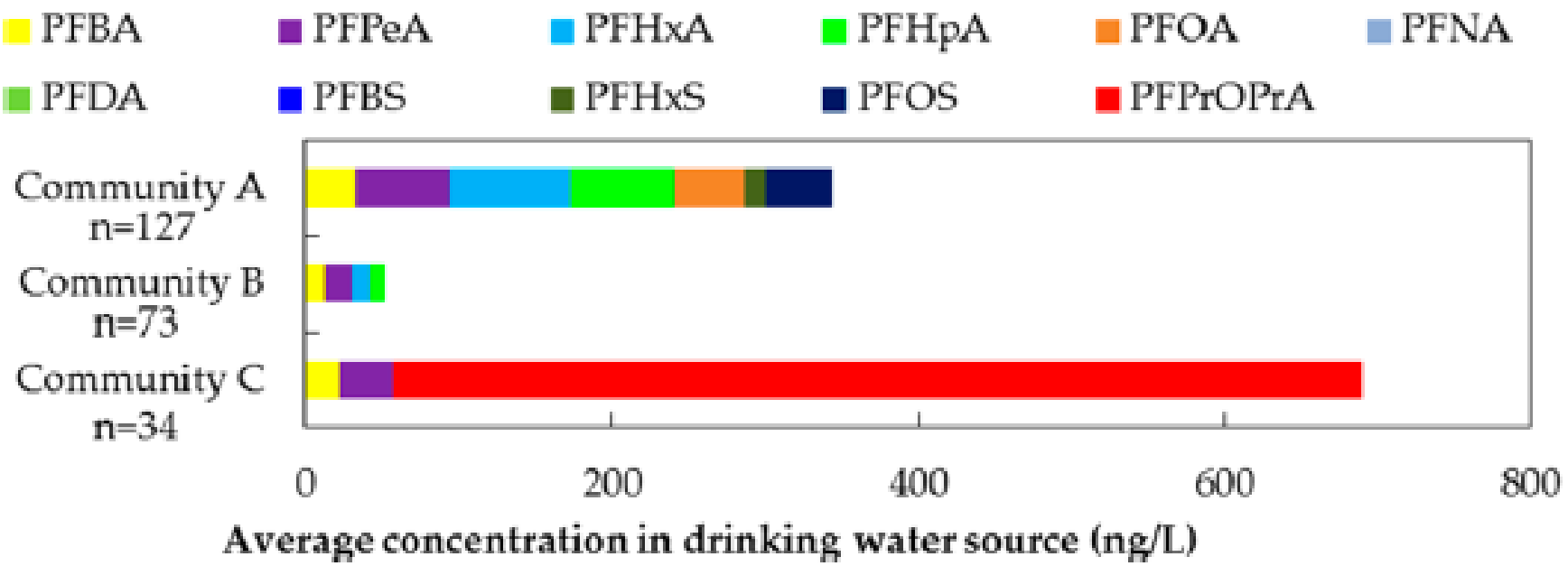
The median total ΣPFOS + PFOA concentration was 5.7 ng/L in the source water and 3.9 ng/L in the treated drinking water.

The median total PFAS (sum of 16) concentration was 21.4 ng/L in the source water and 19.5 ng/L in the treated drinking water.

Per- and polyfluoroalkyl substances in source and treated drinking waters of the United States

Boone JS, Vigo C, Boone T, Byrne C, Ferrario J, Benson R, Donohue J, Simmons JE, Kolpin DW, Furlong ET, Glassmeyer ST. Sci Total Environ. 2019 Feb 25;653:359-369. doi: 10.1016/j.scitotenv.2018.10.245.

What is missed when you look at just PFOA + PFOS

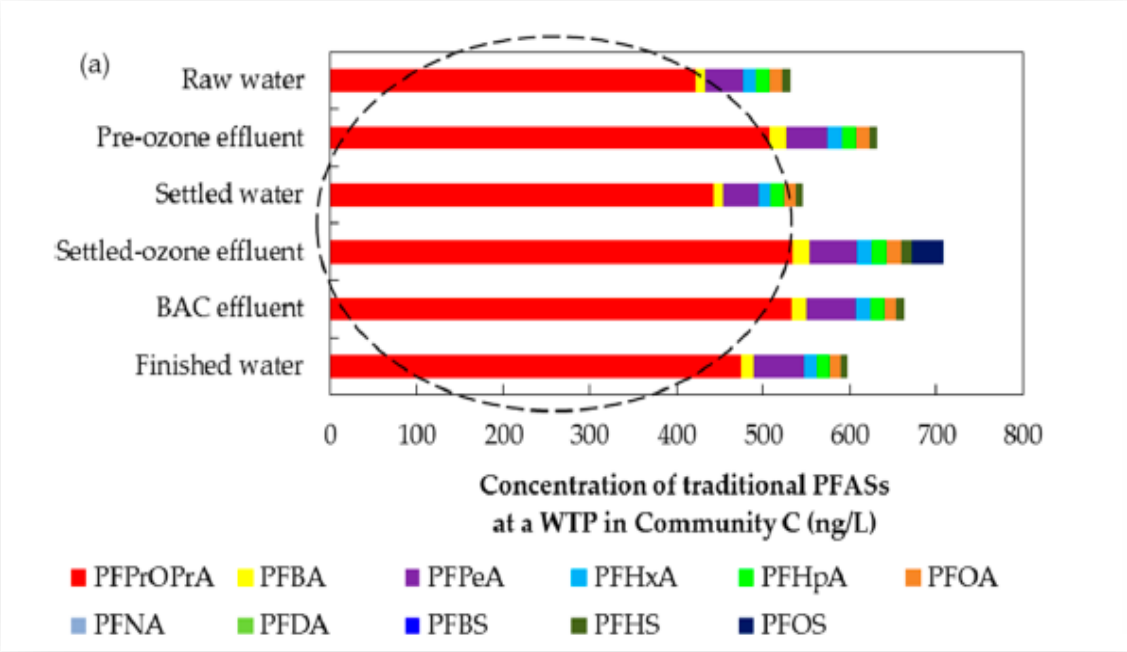


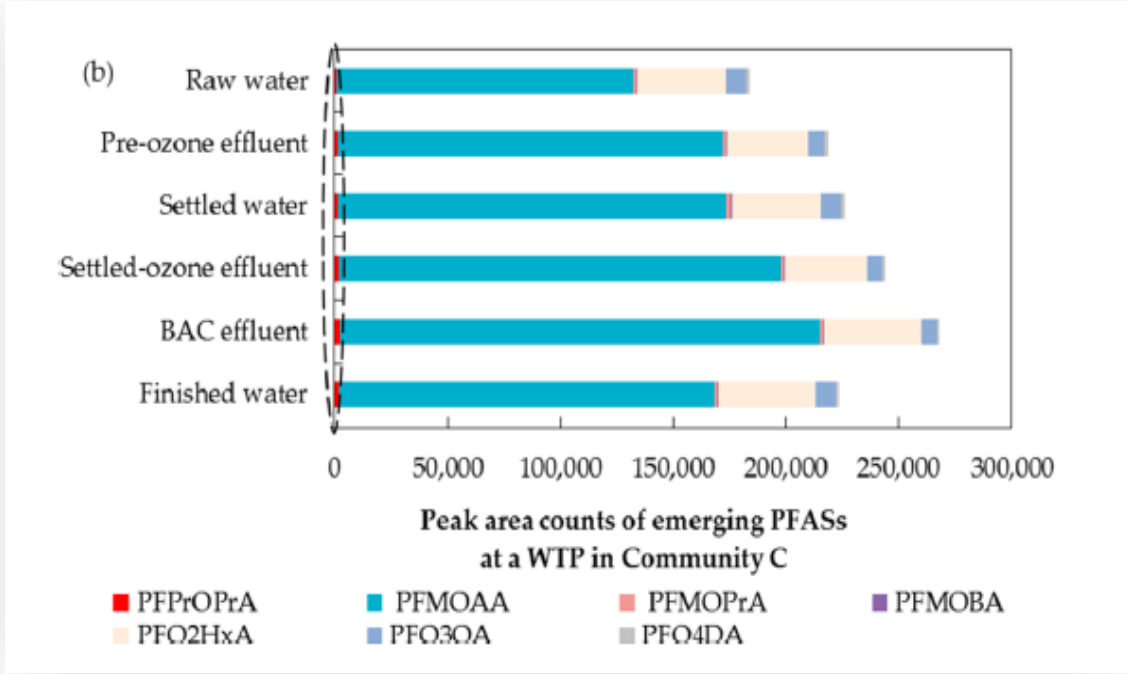
Legacy and Emerging Perfluoroalkyl Substances Are Important Drinking Water Contaminants in the Cape Fear River Watershed of North Carolina

Mei Sun, Elisa Arevalo, Mark Strynar, Andrew Lindstrom, Michael Richardson, Ben Kearns, Adam Pickett, Chris Smith, and Detlef R. U. Knappe

Environ. Sci. Technol. Lett. 2016, 3, 12, 415–419

What is missed when you look at just PFOA & PFOS





Remember these

Tap Water Contributions to Plasma Concentrations of Poly- and Perfluoroalkyl Substances (PFAS) in a Nationwide Prospective Cohort of U.S. Women

Table 5

Extractable organic fluorine levels from tap water samples matched by city at five locations in Massachusetts (MA1 – MA5) in 1989–1990[a] and 2016[b]

Extractable organic fluorine (ng/L)	MA1		MA2		MA3		MA4		MA5	
	1989–1990	2016	1989–1990	2016	1989–1990	2016	1989–1990	2016	1989–1990	2016
PFOA	0.2	6.2	0.5	1.7	0.9	4.8	0.6	0.9	1.3	0.9
PFOS	0.4	1.6	0.4	0.8	1.2	4.2	0.5	0.3	0.6	0.3
Other PFCAs	0.1	7.4	0.8	4.2	1.3	9.6	0.6	1.7	0.0	5.1
Other PFSAs	0.3	4.3	0.3	1.7	1.5	5.6	0.2	0.7	0.4	0.1
PFOS precursors	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Unknown	6.7	135.6	19.8	105.2	2.9	39.4	0.2	58.5	5.4	9.6

[a]1989–1990 tap water samples were collected from five participants' home addresses, one sample at each location.
[b]2016 tap water samples were collected in the cities from the same municipal water supplies as original participant's homes. Two samples were collected at each location.

Hu XC, Tokranov AK, Liddie J, Zhang X, Grandjean P, Hart JE, Laden F, Sun Q, Yeung LWY, Sunderland EM. Environ Health Perspect. 2019 Jun;127(6):67006. doi: 10.1289/EHP4093.

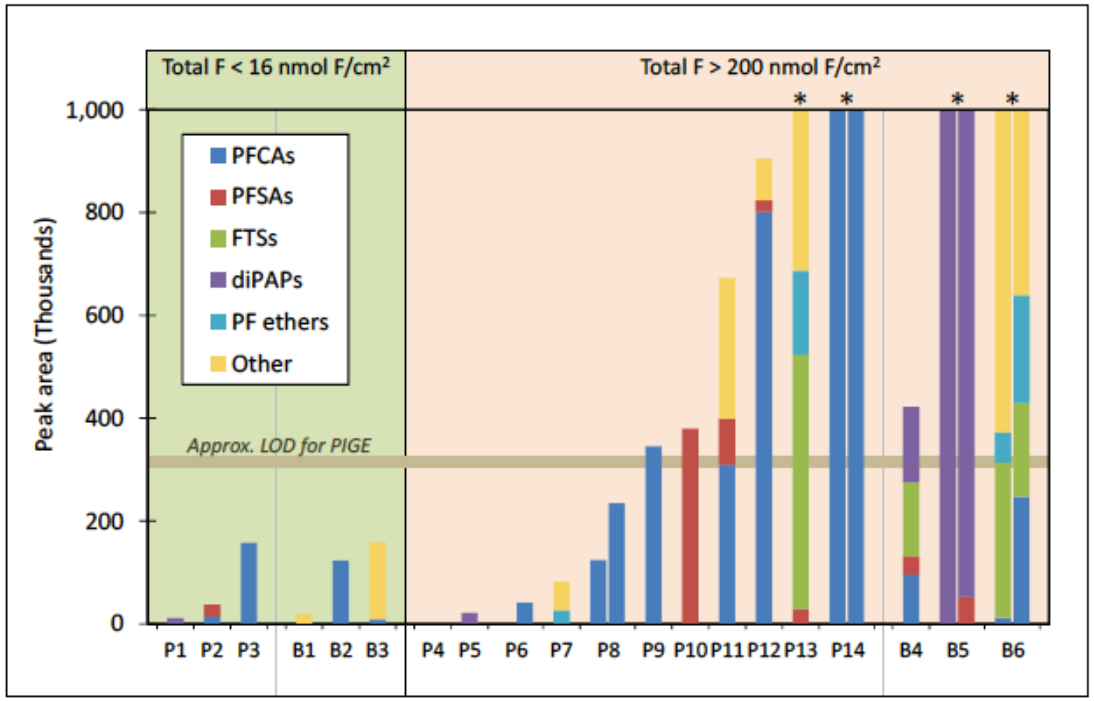
PFAS in food packaging

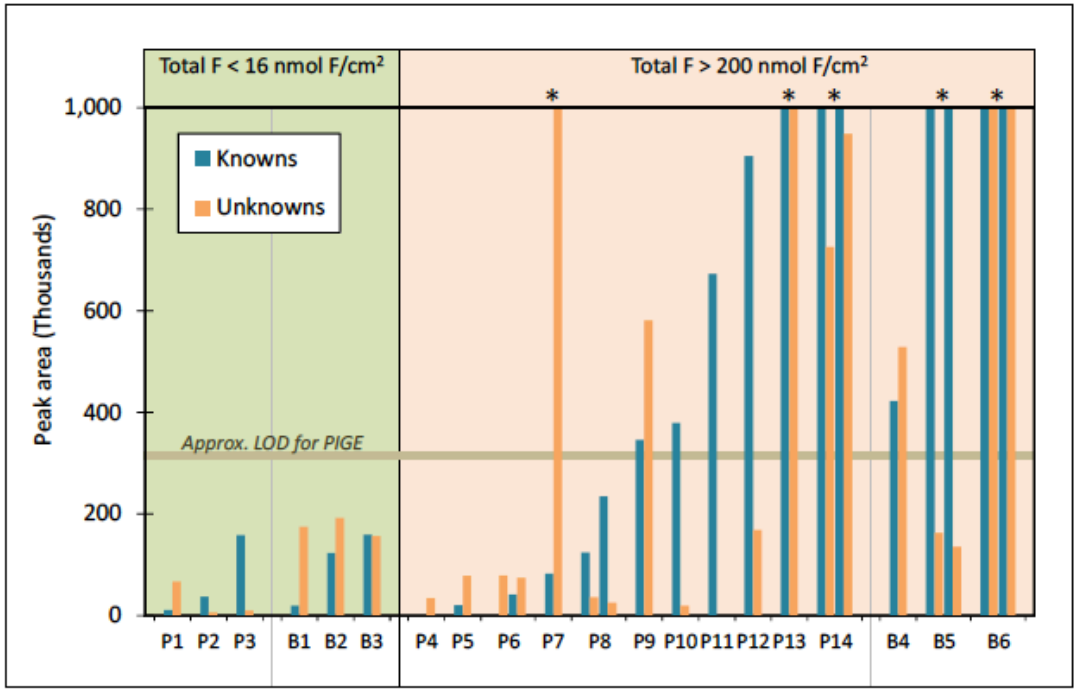
Fluorinated Compounds in U.S. Fast Food Packaging

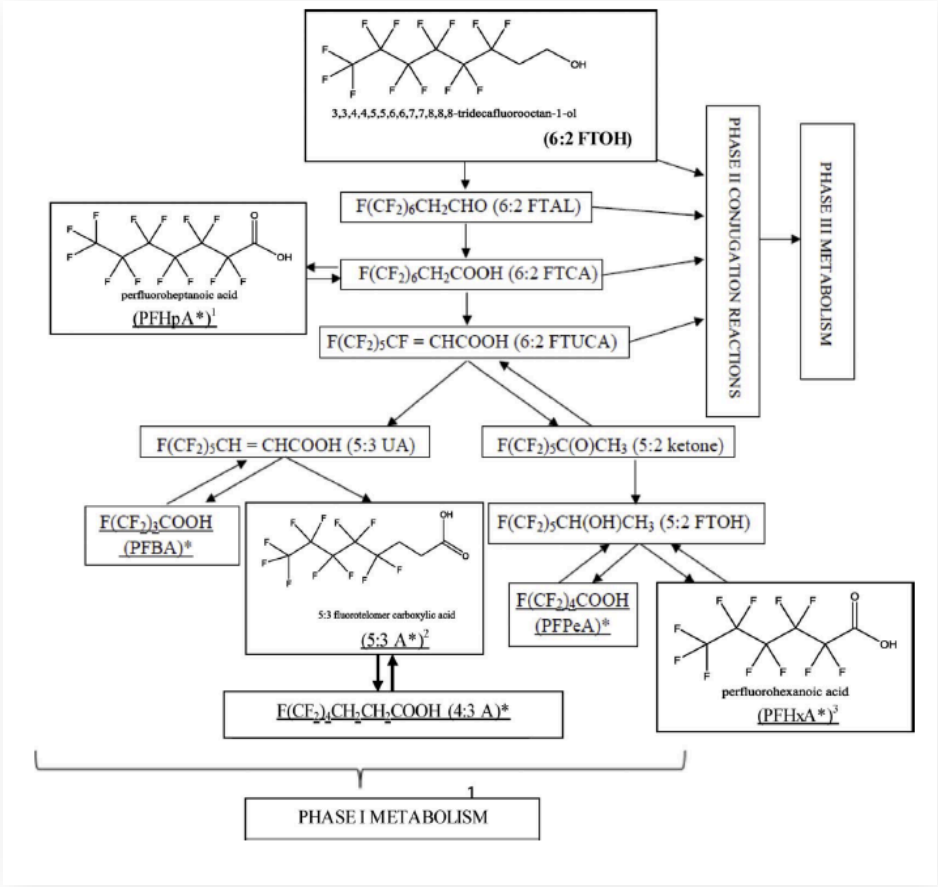
Laurel A. Schaider[*†], Simona A. Balan[‡], Arlene Blum[§ı], David Q. Andrews[⊥], Mark J. Strynar[#], Margaret E. Dickinson[▽], David M. Lunderberg[▽], Johnsie R. Lang[○], and Graham F. Peaslee[@]

View Author Information

Cite this: *Environ. Sci. Technol. Lett.* 2017, 4, 3, 105−111
Publication Date: February 1, 2017
https://doi.org/10.1021/acs.estlett.6b00435







Kabadi et al, Food and Chemical Toxicology 112 (2018) 375–382

FDA Announces the Voluntary Phase-Out by Industry of Certain PFAS Used in Food Packaging

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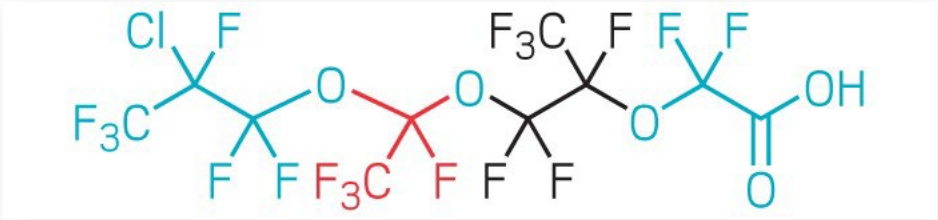
Constituent Update

July 31, 2020

The U.S. Food and Drug Administration (FDA) is announcing the voluntary phase-out of a certain type of short-chain per- and poly-fluoroalkyl substances (PFAS), that contain 6:2 fluorotelomer alcohol (6:2 FTOH), which may be found in certain food contact substances used as grease-proofing agents on paper and paperboard food packaging.

Today's announcement follows an FDA post-market scientific review and analysis of data from rodent studies finding biopersistence of 6:2 FTOH. While the findings were in rodents, the data point to the potential that 6:2 FTOH may also persist in humans following dietary exposure. Further scientific studies are needed to better understand the potential human health risks from dietary exposure resulting from authorized food contact substances for short-chain PFAS that contain 6:2 FTOH. This phased market removal balances uncertainty about the potential for public health risks with minimizing potential market disruptions during the COVID-19 public health emergency.



Positive statistical associations between the LVE Substances' level in the blood and triglycerides albumin, albumin/globulin ratio, and FT3, and negative statistical associations for alpha-2-globulins, IgG, IgM, and estradiol.

Structure from https://cen.acs.org/environment/persistent-pollutants/Solvay-withheld-PFAS-toxicity-data/99/web/2021/01

Bloomberg Law, May 2019

Environment & Energy

The Environmental Protection Agency building in Washington, D.C.

Photographer: Mark Wilson/Getty Images

INSIGHT: The Case for Regulating All PFAS Chemicals as a Class

May 20, 2019, 6:00 AM

Listen

The Environmental Working Group's David Andrews outlines why he believes chemicals called per- and polyfluoroalkyl compounds should be regulated as a class. This is part of a point-counterpoint series paired with one from the American Chemistry Council's Jessica Bowman.

In 1968, a scientist named Donald Taves discovered that samples of his own blood contained a distinct form of fluoride, which he later surmised was widespread in people because of the extensive use of organic fluoride-based compounds in consumer products. He was right: Today these fluorinated chemicals, or PFAS, are detected in nearly every person on Earth.

David Andrews
Environmental Working Group

Related Articles

INSIGHT: With PFAS One-Size-Fits-All Isn't the Answer
May 20, 2019, 6:00 AM

Companies

Environment & Energy

An employee inspects machinery on the production line inside acoatings manufacturing facility in Buk, Poland, on July 5, 2016.

Photographer: Bartek Sadowski/Bloomberg via Getty Images

INSIGHT: With PFAS One-Size-Fits-All Isn't the Answer

May 20, 2019, 6:00 AM

Listen

The American Chemistry Council's Jessica Bowman explains why she believes chemicals called per- and polyfluoroalkyl compounds should not be regulated as a group. This is part of a point-counterpoint series paired with one from the Environmental Working Group's David Andrews, who argues for regulating the chemicals as a class.

The modern world is a marvel of innovation, ideas, and inventions that have transformed our daily lives and the course of history. When Thomas Edison said, "there's a way to do it better—find it," the world took note. Today, whether we are talking about technology, transportation, medicine, or science, our lives are better because of innovation. This is certainly true when it comes to chemistry, an essential building block for a healthier, safer, more sustainable, and more productive world.

Unfortunately, innovation in chemistry and the critical role it plays in our way of life are too often overshadowed by hyperbole in today's public discourse, most notably when it comes to the safety and use of chemicals. While scary sound bites might

Jessica Bowman
FluoroCouncil

Related Articles

INSIGHT: The Case for Regulating All PFAS Chemicals as a Class
May 20, 2019, 6:00 AM

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https://news.bloomberglaw.com/environment-and-energy/insight-the-case-for-regulating-all-pfas-chemicals-as-a-class
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GLOBAL PERSPECTIVE

Scientific Basis for Managing PFAS as a Chemical Class

Per- and Polyfluoroalkyl Substances (PFAS)

Perfluoroalkyl acids and perfluoroalkylether acids (PFAA), e.g.

- **perfluoroalkyl carboxylic acids (PFCA)**, C_nF_{2n+1}-COOH, e.g. PFOA
- **perfluoroalkane sulfonic acids (PFSA)**, C_nF_{2n+1}-SO_3H, e.g. PFOS
- **perfluoroalkyl phosphonic acids (PFPA)**, C_nF_{2n+1}-PO_3H_2
- **perfluoroalkyl phosphinic acids (PFPiA)**, $(C_nF_{2n+1})(C_mF_{2m+1})$-$PO_2H$
- **perfluoroalkylether carboxylic acids (PFECA)**, e.g. $C_2F_5OC_2F_4OCF_2COOH$
- **perfluoroalkylether sulfonic acids (PFESA)**, e.g. $C_6F_{13}OCF_2CF_2SO_3H$

Precursors to PFAA, e.g.

- **perfluoroalkane sulfonyl fluoridess (PASF)**
- **perfluoroalkanoyl fluorides (PACF) and their derivatives**, $C_nF_{2n+1}SO_2$-R / $C_nF_{2n+1}CO_2$-R
- **n:2 fluorotelomer-based substances** $C_nF_{2n+1}CH_2CH_2$-R
- **per- and polyfluoroalkylether-based substances** e.g. $C_nF_{2n+1}OC_mF_{2m+1}$-R

→ **side-chain fluorinated polymers** e.g. (meth)acrylate, urethane, or oxetane polymers with non-fluorinated backbones and fluorinated side-chains

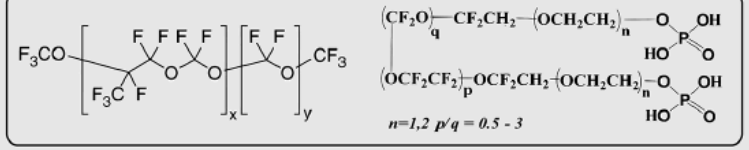
→ **non-polymers** R = NH, $NHCH_2CH_2OH$, etc.

- **some hydrofluorocarbons (HFCs**, e.g. C_nF_{2n+1}-C_mH_{2m+1}), **hydrofluoroethers (HFEs**, e.g. $C_nF_{2n+1}OC_mH_{2m+1}$) and **hydrofluoroolefins (HFOs**, e.g. C_nF_{2n+1}-$CH{=}CH_2$);
- **perfluoroalkyl** ($C_nF_{2n+1}C(O)C_mF_{2m+1}$) and **semi-fluorinated** ($C_nF_{2n+1}C(O)C_mH_{2m+1}$) **ketones;**
- **perfluoroalkyl alcohols** ($C_nF_{2n+1}OH$)

Fluoropolymers, e.g.

- polytetrafluoroethylene (**PTFE**), -$(CF_2CF_2)_n$-
- polychlorotrifluoroethylene (**PCTFE**), -$(CF_2CFCl)_n$-
- polyvinylidene fluoride (**PVDF**), -$(CF_2CH_2)_n$-
- fluorinated ethylene propylene (**FEP**), -$(CF_2CF_2)_n$-$(CF_2C(CF_3)F)_m$-

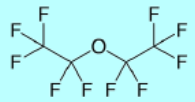
Perfluoropolyethers, e.g.



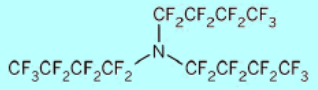
Other PFAS*, e.g.

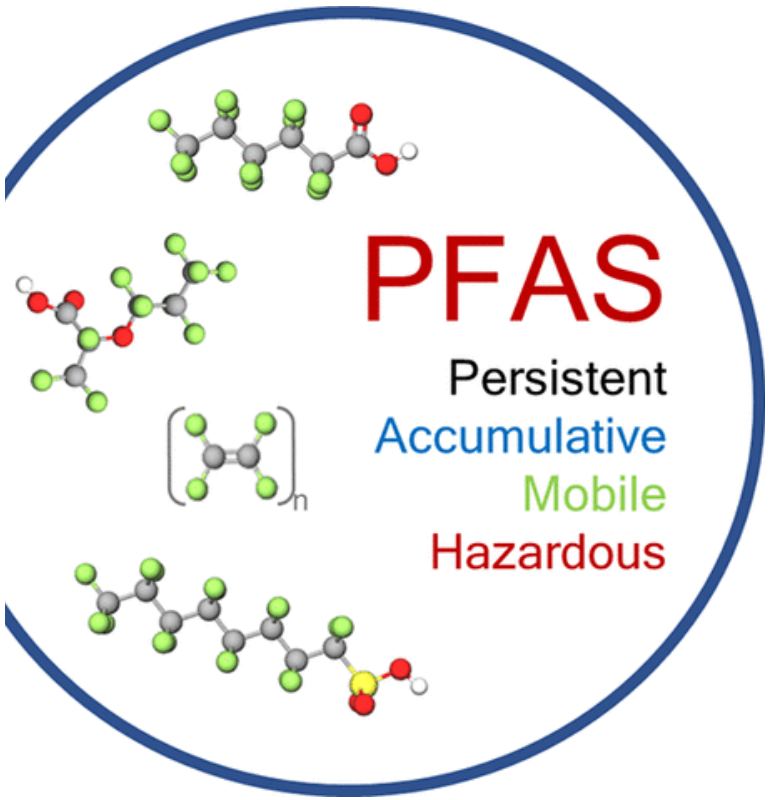
perfluoroalkanes, e.g.

perfluoroalkylethers, e.g.



perfluoroalkylamines, e.g.





Carol F. Kwiatkowski, David Q. Andrews, Linda S. Birnbaum, Thomas A. Bruton, Jamie C. DeWitt, Detlef R. U. Knappe, Maricel V. Maffini, Mark F. Miller, Katherine E. Pelch, Anna Reade, Anna Soehl, Xenia Trier, Marta Venier, Charlotte C. Wagner, Zhanyun Wang, and Arlene Blum. **Environ. Sci. Technol. Lett. 2020, 7, 8, 532–543**

GLOBAL PERSPECTIVE

Scientific Basis for Managing PFAS as a Chemical Class

- Extreme persistence & potential for harm
  - A more efficient approach is needed to address thousands of PFAS (per- and polyfluoroalkyl substances)

- Most consistent feature (persistence)
  - leads to – accumulation in the environment, including water, air, sediment, soil, plants, and living organisms including people
- High mobility

- PFAS chemical features lead to a broad range of adverse health outcomes associated with exposure

Carol F. Kwiatkowski, David Q. Andrews, Linda S. Birnbaum, Thomas A. Bruton, Jamie C. DeWitt, Detlef R. U. Knappe, Maricel V. Maffini, Mark F. Miller, Katherine E. Pelch, Anna Reade, Anna Soehl, Xenia Trier, Marta Venier, Charlotte C. Wagner, Zhanyun Wang, and Arlene Blum. **Environ. Sci. Technol. Lett. 2020, 7, 8, 532–543**

PFAS are a moving target

- Lots of change since this talk was proposed
- Regulations at the state and federal levels
- Analytical methods development
- New PFAS definitions (OECD, EPA …)
- EPA testing strategy – PFAS groups

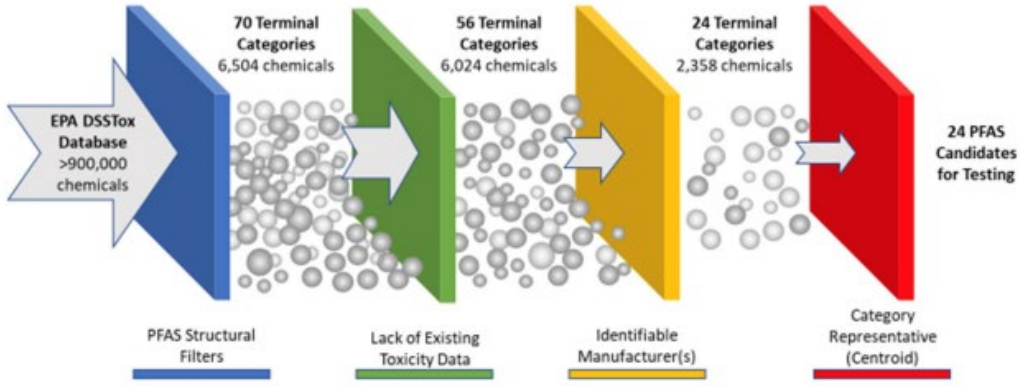


Figure 6: Overview of the Process for Identifying Initial Testing Candidates

fluorinated pharmaceuticals

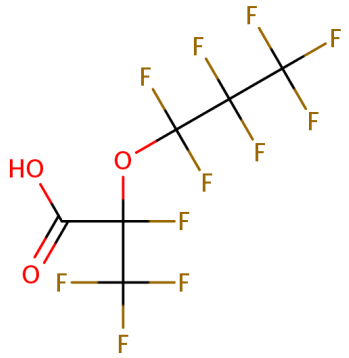
Table 3. Number of pharmaceuticals included under different definitions of PFAS (% of 360)

Definition	Number (%) organofluorine pharmaceuticals
Buck et al. (2011)	8 (2.2)
OECD (2018)	5 (1.4)
OECD (2021)	107 (30)
Glüge et al. (2020)	22 (6.1)
TURA (2021a)	6 (1.7)
TURA (2021b)	4 (1.1)
U.S. EPA OPPT (2021)	5 (1.4)
≥1 Fully Fluorinated Carbon[a]	337 (94)
All Organofluorine[b]	360 (100)

[a]Authorities whose legislation defines PFAS as a class of fluorinated organic chemicals containing at least one fully fluorinated carbon atom (NDAA, WA, ME, VT, CA).
[b]NGOs that advocate for broader definitions of PFAS to include all organofluorines.

Hammel et al, Implication of PFAS definitions using fluorinated pharmaceuticals. iScience 2021.

Case study - per- and polyfluoroalkyl ether acids



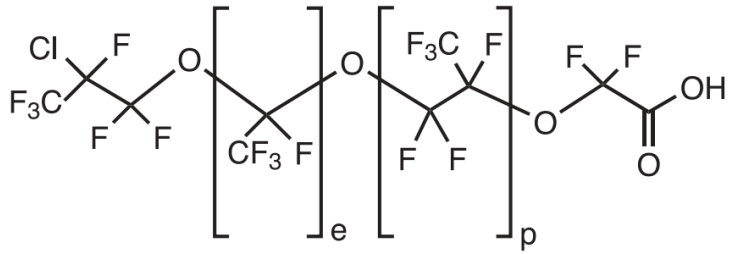


Fig. 1. A chloroperfluoropolyether carboxylate (ClPFPECA) identified by nontargeted MS analyses in soil samples from New Jersey. In the New Jersey

Table 2. Comparison of Reference Doses (RfDs) for Four PFAS

PFAS Chemical	Chronic RfD (mg/kg-day)
GenX chemicals (EPA 2021)	0.000003
PFBS (EPA 2021)	0.0003
PFOA (EPA 2016)	0.00002*
PFOS (EPA 2016)	0.00002*

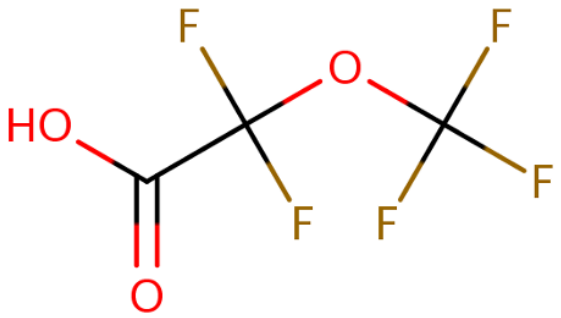
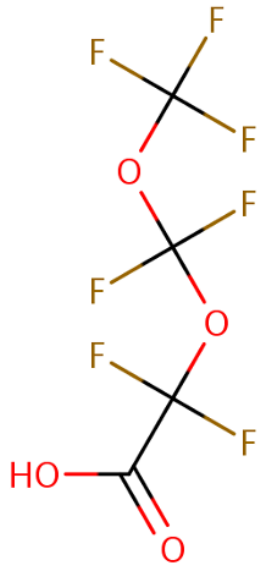
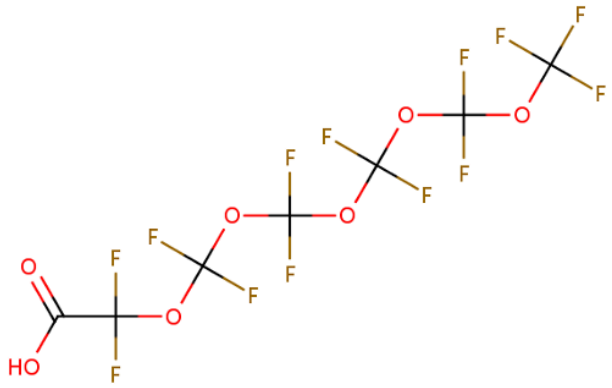
*Note: EPA is currently reevaluating toxicity information for PFOA and PFOS and therefore this value is subject to change.

- Solvay has described the ClPFPECAs as "replacements"
- half-life 2.5-3 years
- “an order of magnitude more bioaccumulative than PFOS in white perch liver”
- New Jersey Interim Specific Ground Water Quality Standard of 2 ppt

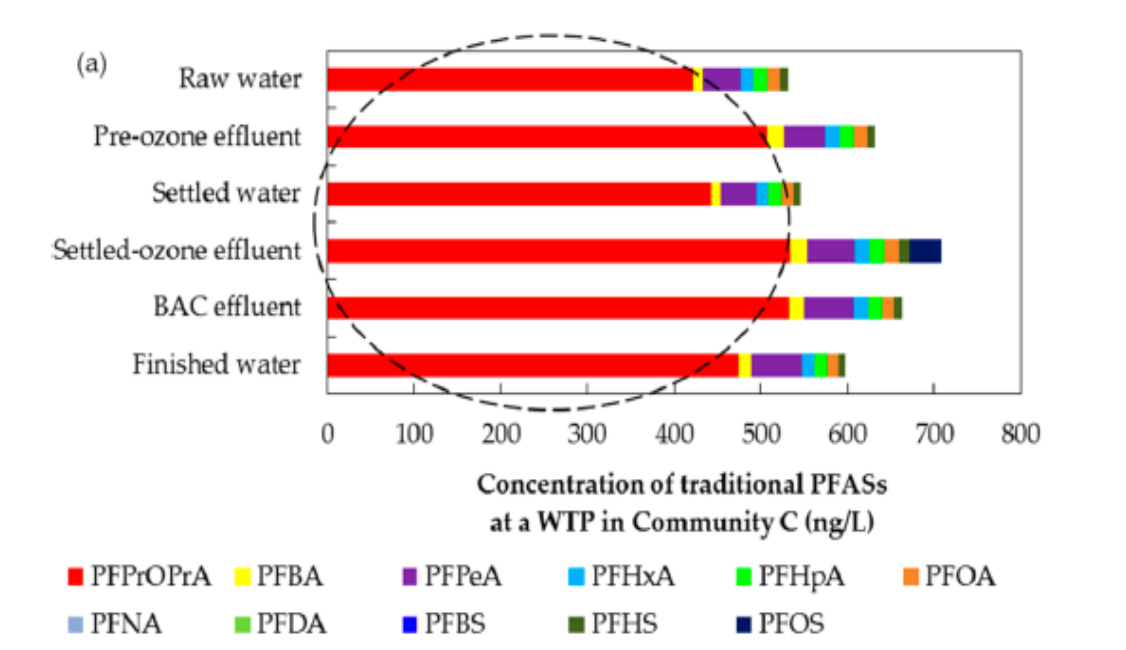
- Washington et al, Nontargeted mass-spectral detection of chloroperfluoropolyether carboxylates in New Jersey soils, Science 2020.
- https://www.nj.gov/dep/dsr/supportdocs/NewSupportDocuments.html
- https://www.epa.gov/system/files/documents/2021-10/genx-final-tox-assessment-general_factsheet-2021.pdf

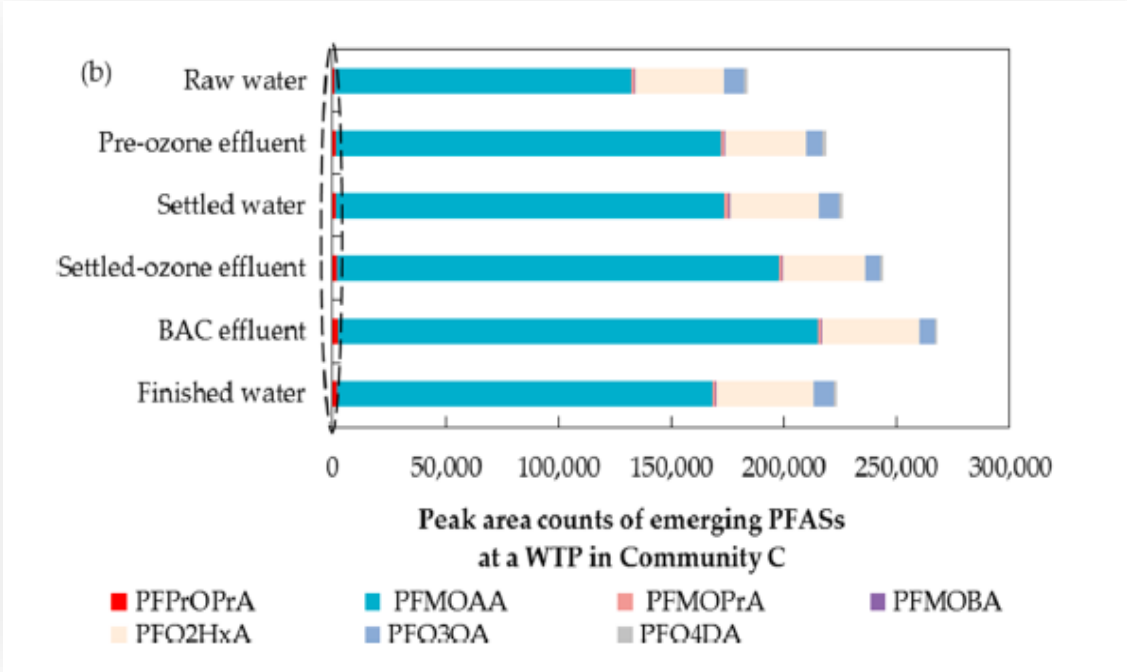
A few compounds that straddle the line between definitions of PFAS

PFMOAA, PFO2HxA, PFO3OA, PFO4DA, PFO5DoA

PFMOAA	PFO2HxA	PFO5DoA or PFO5DoDA
		

File images from https://comptox.epa.gov/dashboard/chemical/details/DTXSID00408562





Sun et al . , **Environ. Sci. Technol. Lett. 2016, 3, 12, 415–419**

In serum testing in 2017-2018

PFO4DA was detected in 99% of samples

PFO5DoA was detected in 88% of samples

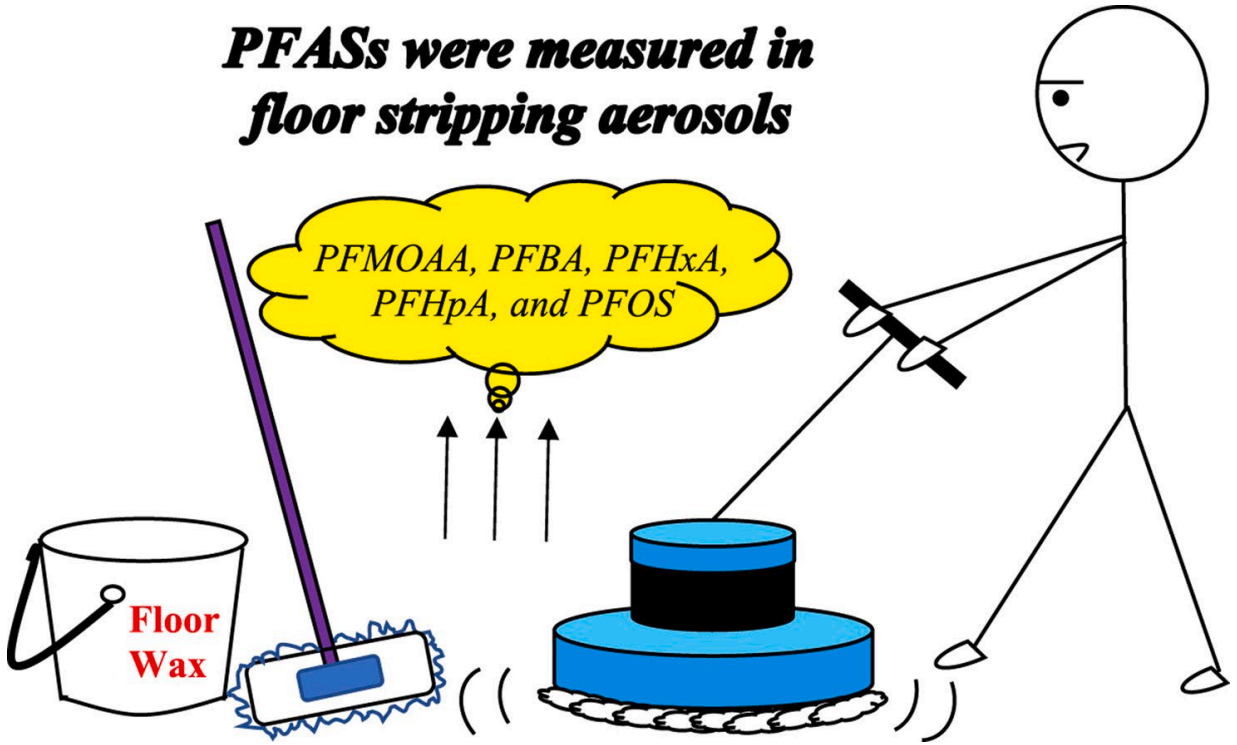
PFO3OA was detected in 28% of samples

PFMOAA not tested for

6 months after ending exposure, levels of PFO5DoA decreased 28% and levels of PFO4DA decreased 65%.

Kotlarz N et al. Measurement of Novel, Drinking Water-Associated PFAS in Blood from Adults and Children in Wilmington, North Carolina. Environ Health Perspect. 2020 Jul;128(7):77005. doi: 10.1289/EHP6837.

Per- and Polyfluoroalkyl Substances (PFASs) in Airborne Particulate Matter ($PM_{2.0}$) Emitted During Floor Waxing: A Pilot Study.



Zhou J, Baumann K, Chang N, Morrison G, Bodnar W, Zhang Z, Atkin JM, Surratt JD, Turpin BJ. Atmos Environ (1994). 2022 Jan 1;268:118845. doi: 10.1016/j.atmosenv.2021.118845.

More PFMOAA

- 100% of people in a study of nearly one thousand residents living near a fluorochemical plant in China had detectable perfluoroalkyl ether carboxylic acids such as PFMOAA in their serum samples.
  - these compounds comprised 7% of the residents total PFAS body burden
  - if PFOA was excluded these chemicals made up nearly 30% of the PFAS body burden. In

- a study of aquatic organisms in the Xiaoqing River estuary in China, PFMOAA accounted for 32.5% of the total PFAS measured in organisms. For rural residents estimated daily intake values were 6.7 times higher for PFMOAA than for any other PFAS compounds.

PFAS?

YES	NO
• OECD 2021 • Fully fluorinated • Glüge et al.	• OECD 2018 • Buck et al. 2011 • U.S. EPA working definition

- The current U.S. EPA definition for a PFAS used by the Office of Research and Development and defined within the TSCA section 8(a)(7) proposed rule and the EPA testing strategy, is

  “a structure that contains the unit R-CF2-CF(R')(R''), where R, R', and R'' do not equal "H" and the carbon-carbon bond is saturated (note: branching, heteroatoms, and cyclic structures are included)... For example, chemicals with (-CF2-) that are not (-CF3) are expected to degrade in the environment and most substances with only one terminal carbon (-CF3) are expected to degrade to trifluoroacetic acid, which is a well-studied non-PFAS.”

How is the definition used?

- These compounds are not on the TSCA inventory and would not be subject to test orders

- Proposed TSCA Section 8(a)(7) reporting rule requires - “including both byproducts that are separated from that other substance or mixture and impurities that remain in that substance or mixture.”