Context and Rationale for Non-Targeted Analysis (NTA) and Other Total PFAS Methods

12:30 p.m. – 1:30 p.m.

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Timothy J. Buckley, Ph.D., Senior Science Advisor, Center for Computational Toxicology and Exposure, EPA

The Public Health Stakes of Total PFAS Methods

Timothy J. Buckley, PhD

Senior Advisor

Center for Computational Toxicology & Exposure

Total PFAS Methods Workshop
Virtual Meeting
October 27, 2021

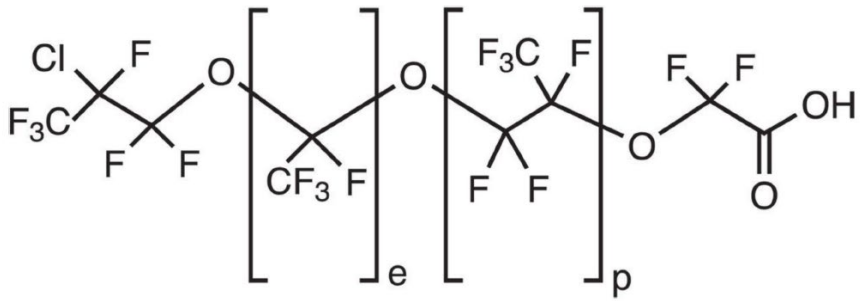
The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency

Adage

If it can't be measured, it is as though it does not exist.

What are the implications for:

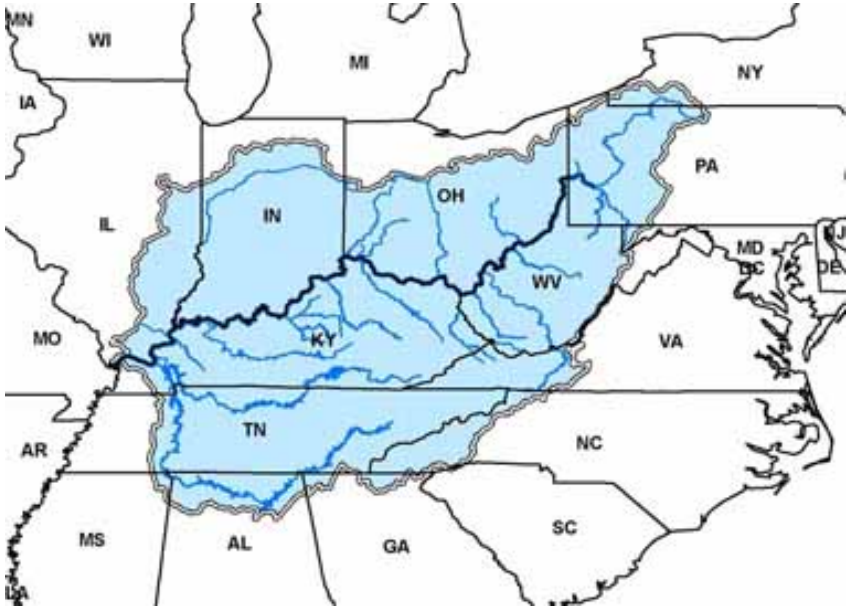
- PFAS manufacturing
- Human exposure
- Public health
- Regulation



For example, the Washington et al. 2020 discovery of PFAS congeners chloro perfluoro polyether carboxylate

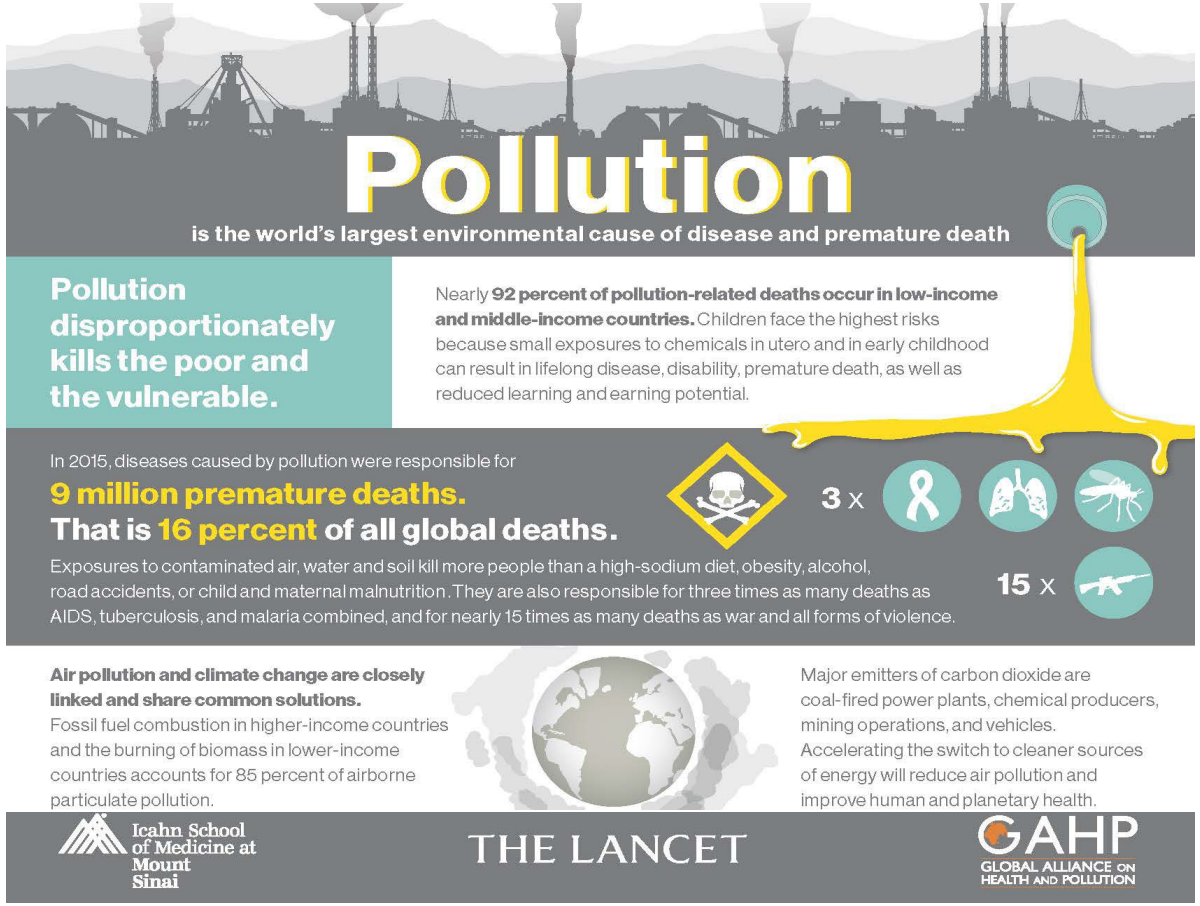
Presentation Flow

- Public health and the larger chemical pollutant context
- The parallel PFAS universe
- The gap: PFAS measured vs likely environmental occurrence?
- The NC Cape Fear River case-in-point
- Summary



Public Health Context

- Pollution is known to be a leading public health threat
- A large proportion of the environment-attributed disease is of unknown etiology
- Effects likely underestimated
- Exposure and effects are poorly understood
- Chemical production and release to the environment vastly outpace ability to test and measure



Source: Landrigan et al. 2017

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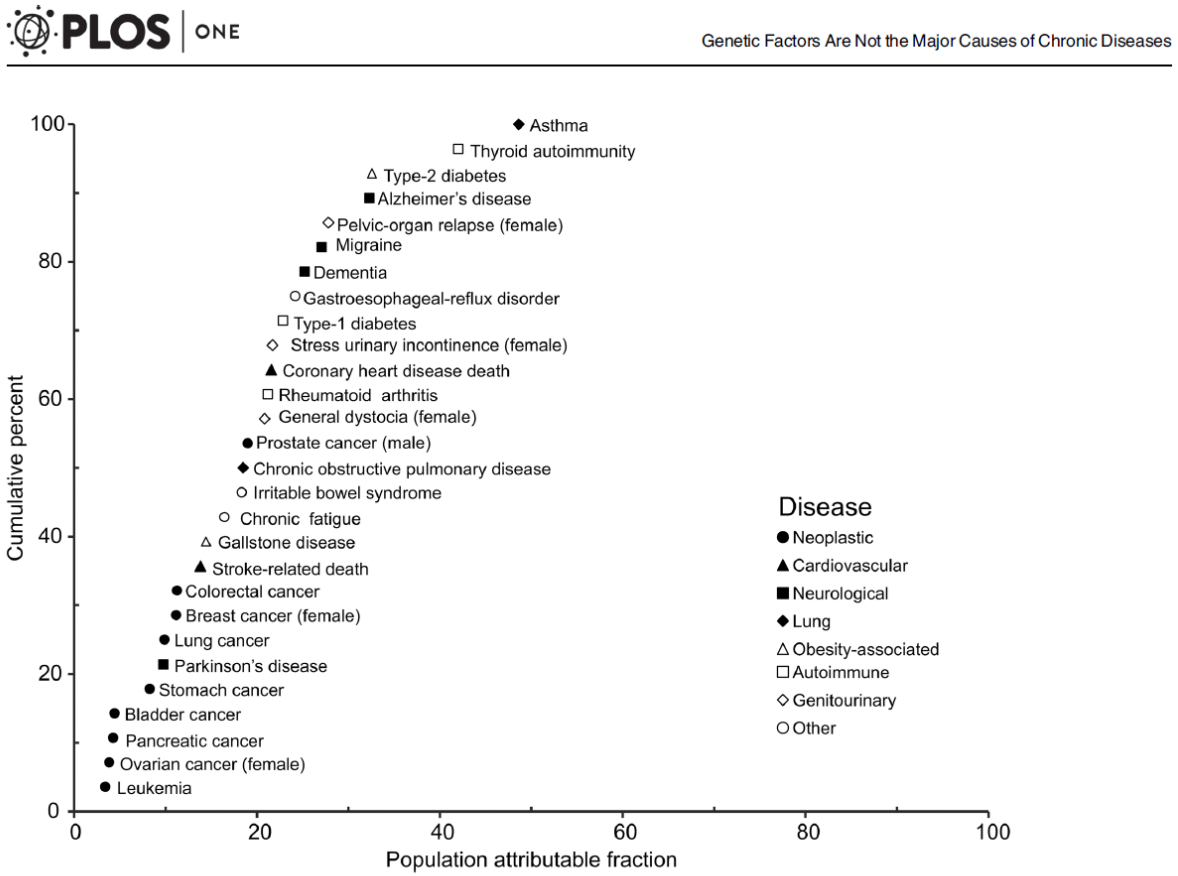

Fig 1. Population attributable fractions (PAFs) for 28 disease phenotypes estimated from studies of monozygotic twins. Sources of data and statistics are summarized in Table 2.

Source: Rappaport, 2016

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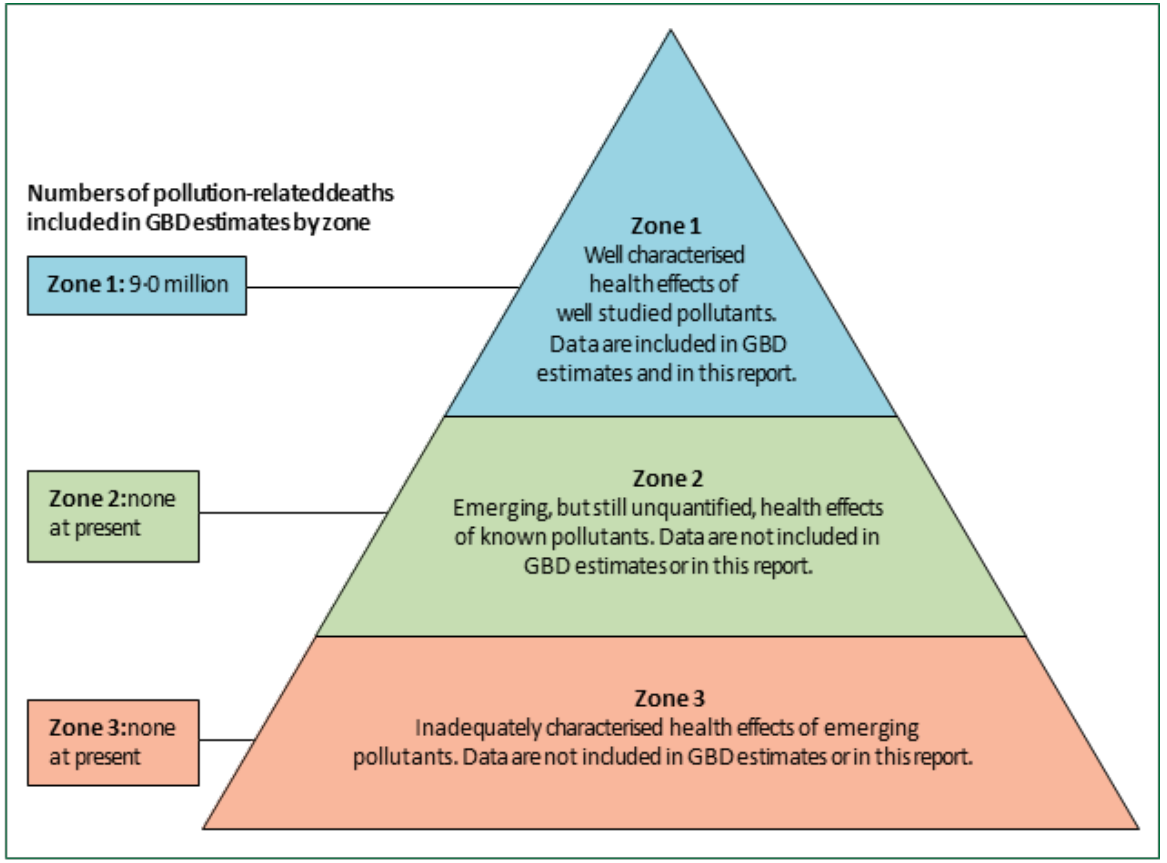

Figure 3: The pollutome

Source: Landrigan et al., 2017

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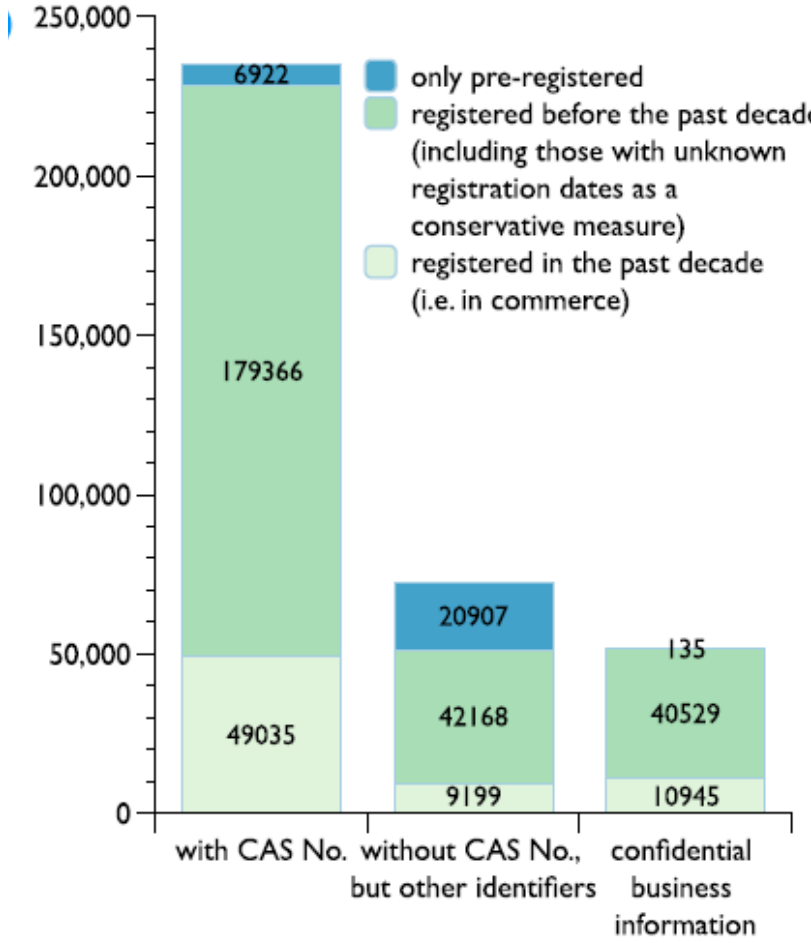
Chemicals Registered for Production and Use Across 19 Countries



Source: Wang et al. 2020

Habitable Planet

- Chemical pollution identified as “not yet quantified” as one of ten planetary boundaries
- Earth has limited capacity to assimilate chemical pollution
- Impacts on human health and ecosystems
- Quantifying chemical environmental burden is essential

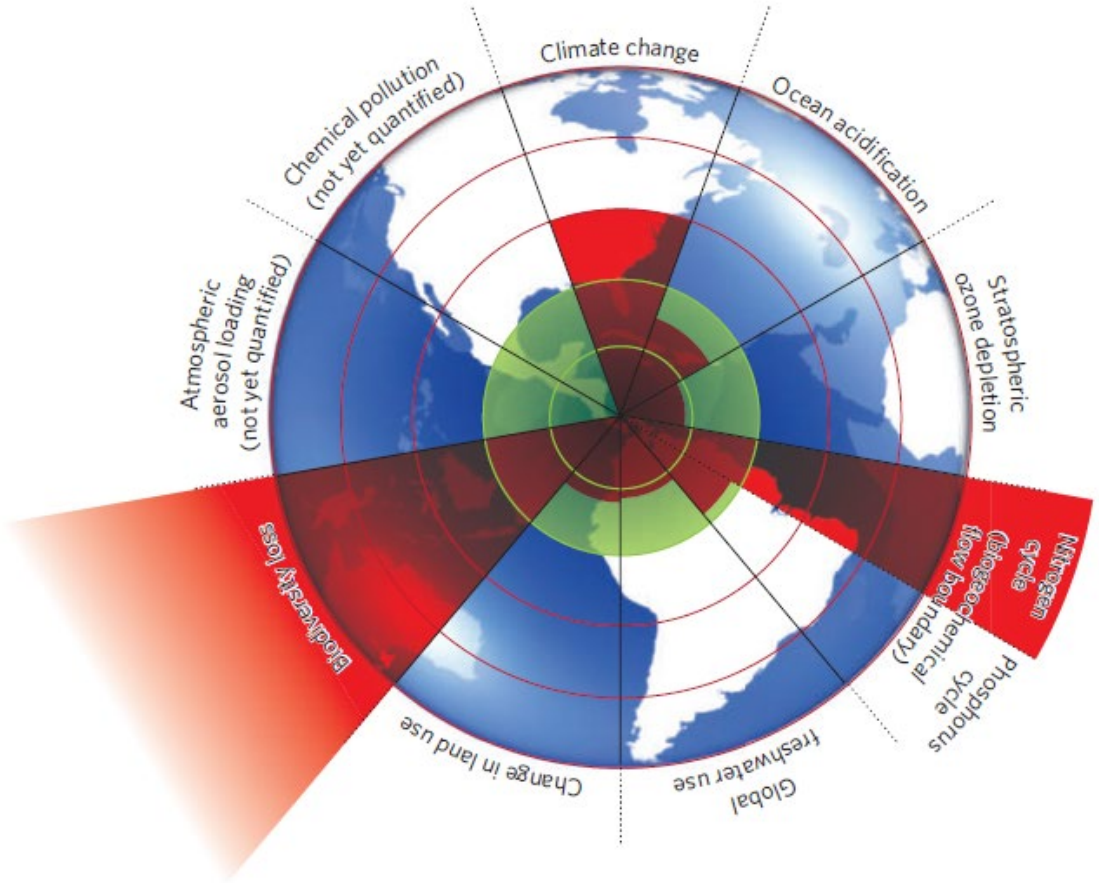
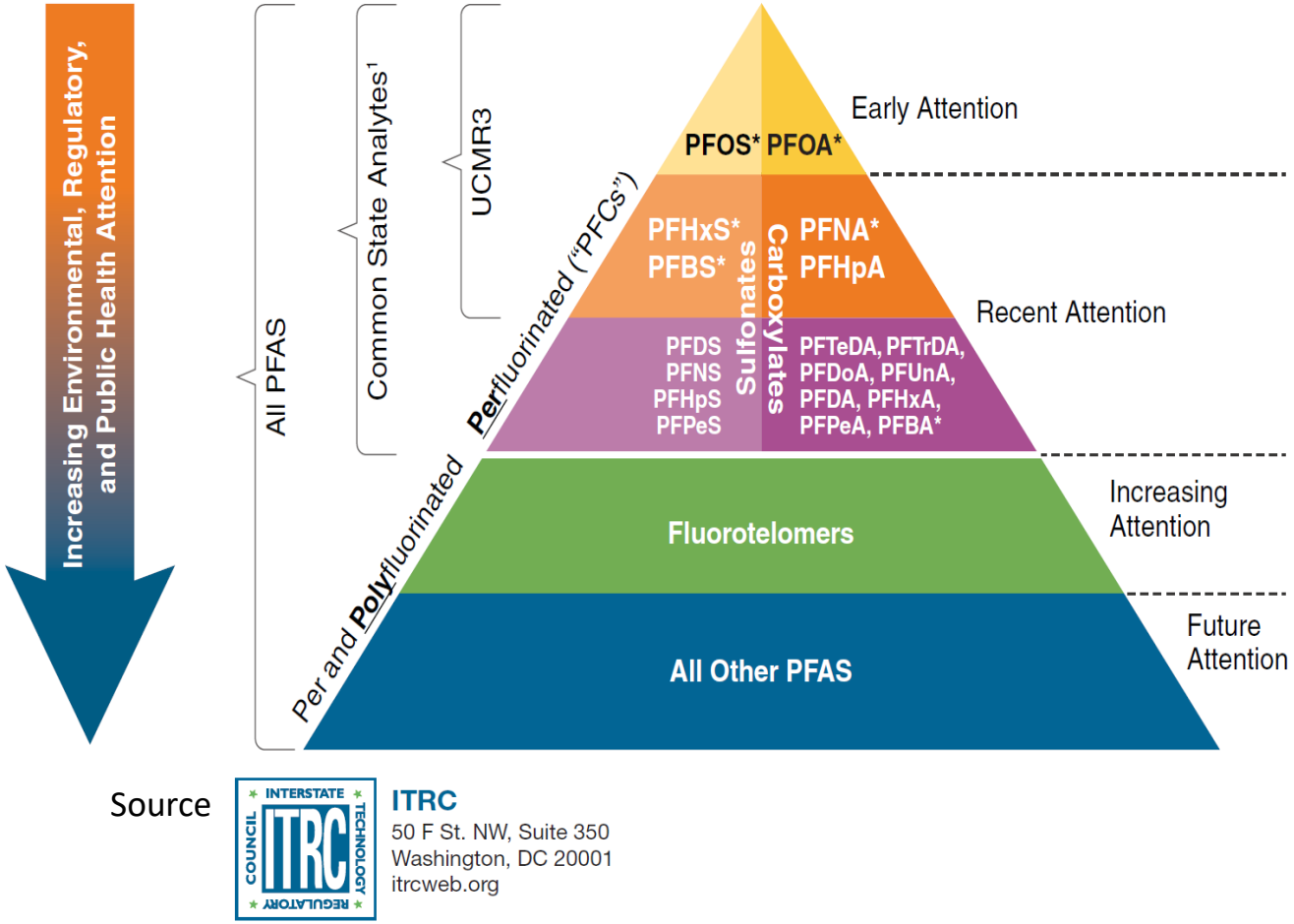


Figure 1 | Beyond the boundary. The inner green shading represents the proposed safe operating space for nine planetary systems. The red wedges represent an estimate of the current position for each variable. The boundaries in three systems (rate of biodiversity loss, climate change and human interference with the nitrogen cycle), have already been exceeded.

Rockstrom et al. 2009

Diamond et al. 2015

Parallels of the PFAS and Chemical Landscape



Source

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Washington, DC 20001
itrcweb.org

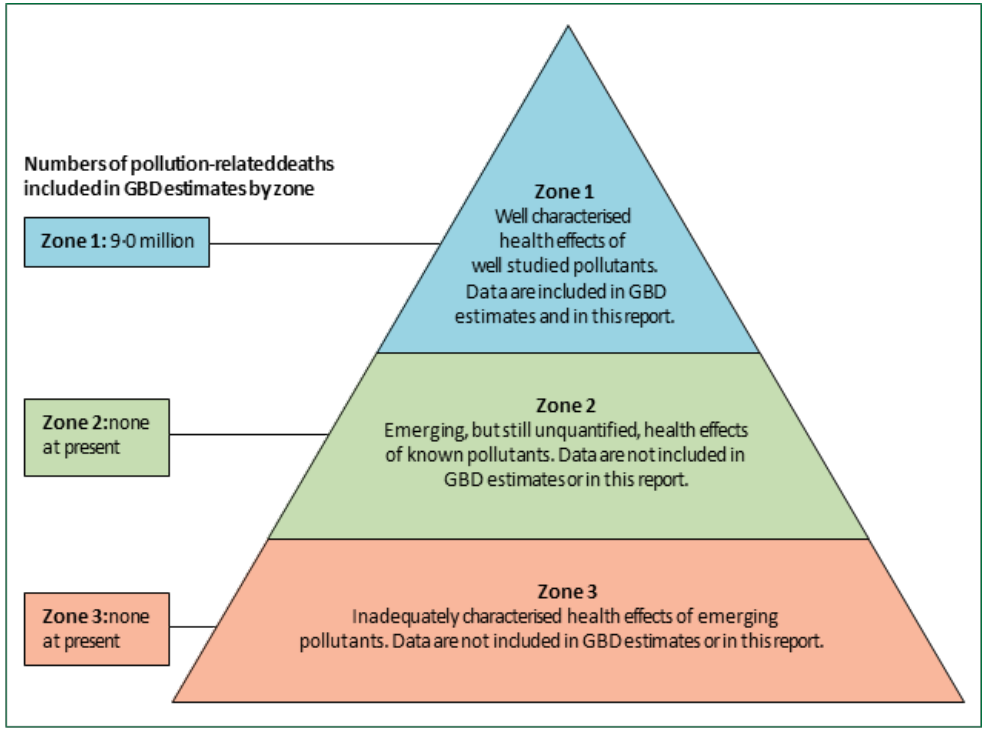


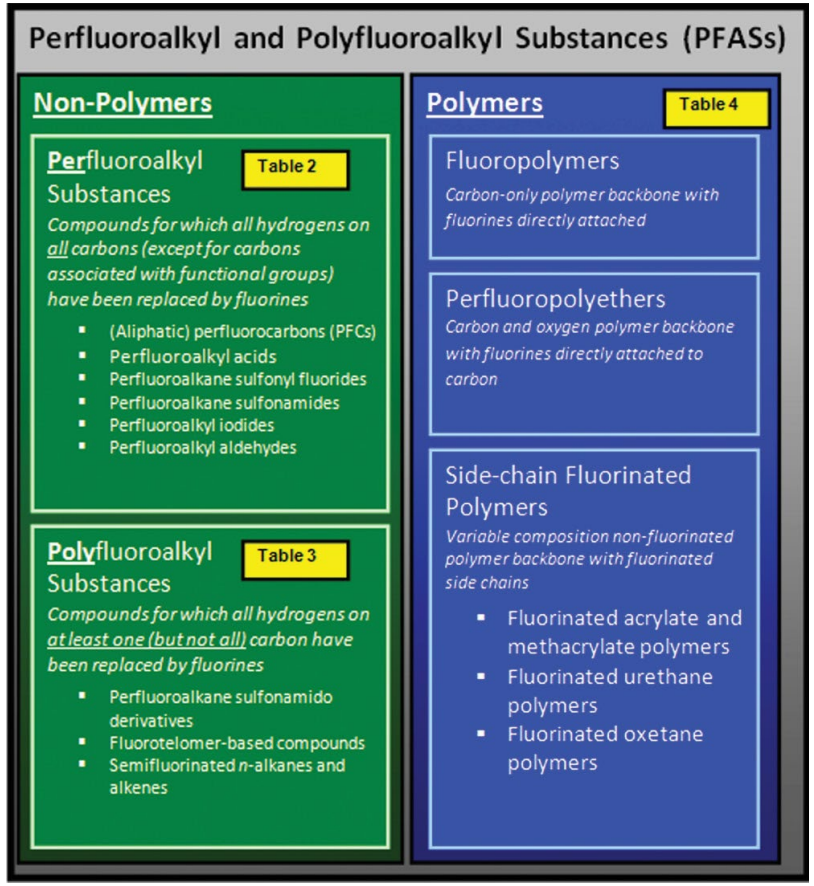
Figure 3: The pollutome

Source: Landrigan et al., 2017

What is the PFAS Universe?

It depends on who you ask / how you define

- **Potential for environmental release/exposure?**
  - Defining classification and nomenclature (Buck et al. 2011)
  - Number of chemicals estimated as >3000 (Wang et al. 2017)
  - OECD lists 4730 PFAS (OECD, 2018)
  - TSCA lists 1346 with 669 active (FRN 2021-13180)
  - EPA's Chem Dashboard: 33 lists of PFAS with the number on list ranging from 8 to 9252 (https://comptox.epa.gov/dashboard/chemical_lists)



What is the PFAS Universe?

- **What we observe**
  - Multimedia Monitoring Database (MMDB) n=43 (Isaacs et al. in preparation)
  - NHANES 2011-2018 n=16 (https://www.cdc.gov/exposurereport/pfas_early_release.html)
  - UCMR3 n=6; UCMR5 n=29 (https://www.epa.gov/dwucmr)
  - EPA Drinking Water Methods 533 & 537.1 n=29 (https://www.epa.gov/sites/default/files/2019-12/documents/table_of_pfas_methods_533_and_537.1.pdf)
  - PFAS Analytical Standards <100 (McDonough et al. 2018)

What is the Gap: Targeted vs Total?

- **Firehouse dust (Massachusetts):** $\sum_{24}$ PFAS quantified in 39 samples from 15 stations represented **1.2%** of total PFAS measured by particle-induced gamma ray emission (PIGE) (Young et al. 2021)
- **Swedish cosmetics**. $\sum_{39}$ PFAS quantified in 28 cosmetics represented **<1.3%** of extractable organofluorine (EOF) and 11–28% in three other cosmetics with the highest concentrations. The EOF only accounted for an average 9% of total fluorine, which, unlike EOF, would include inorganic fluoride and any PFAS or other organofluorine compounds that were not extractable (Schultes et al. 2018)
- **Papers & textiles.** $\sum_{73}$ ionic PFAS accounted for up to **0.41%** of total fluorine; volatile PFASs accounted for 0.021-14 of the total nmol F/cm^2 determined by PIGE (Robel et al. 2017)
- **Food packaging**. $\sum_{44}$ PFAS explained up to **0.28%** of EOF and **0.011%** of total fluorine in a small Swedish study of disposable food packaging (Schultes et al. 2019)
- **Japan coastal sea water.** 60–90% of organic fluorine unknown (Miyak et al. 2007)
- **Human serum (Swedish population n=130)**. $\sum_{63}$ PFAS explained 40% and 51% of EOF in women and men, respectively (Aro et al. 2021)

How Big is Our PFAS Blind Spot

- The ratio of “likely occurring” (1000s) to “observable” (10s) on the order of 100

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Analogy to navigating public health with PFAS exposure blind spots

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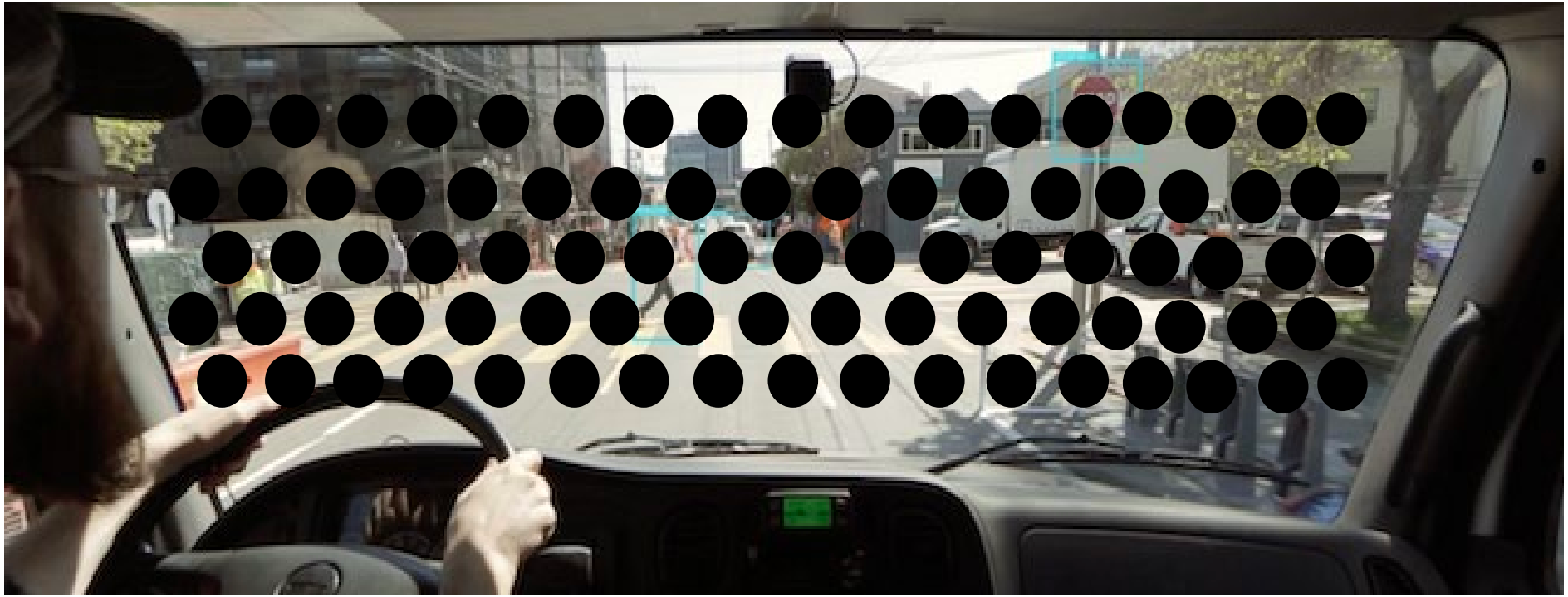


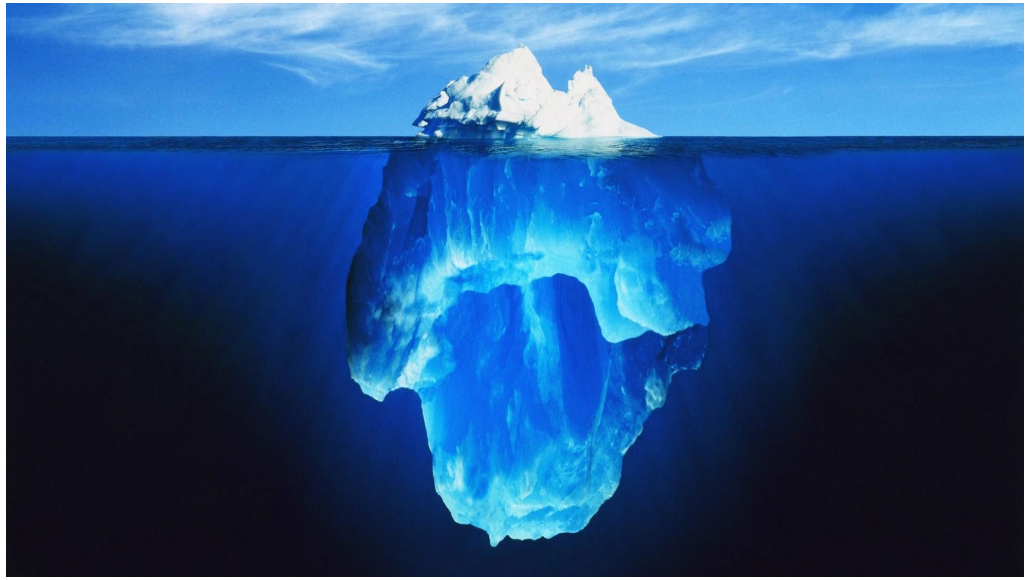
PFAS Health Concerns

- Evidence available for limited number of PFAS
  - perfluorooctane sulfonic acid (PFOS)
  - perfluorooctanoic acid (PFOA)
  - perfluorohexane sulfonic acid (PFHxS), and
  - perfluorononanoic acid (PFNA)
- Laboratory animal evidence shows changes in liver, thyroid, immune and pancreatic function
- Epidemiologic evidence (associative)
  - Pregnancy-induced hypertension/pre-eclampsia (PFOA, PFOS)
  - Increases in serum hepatic enzymes, particularly alanine aminotransferase (ALT), and decreases in serum bilirubin levels (PFOA, PFOS, PFHxS)
  - Increases in serum lipids, particularly total cholesterol and low-density lipoprotein (LDL) cholesterol (PFOA, PFOS, PFNA, PFDA)
  - Decreased antibody response to vaccines (PFOA, PFOS, PFHxS, PFDA)
  - Cancers of the testis and kidney (PFOA)

Source: ATSDR (2021) Toxicological Profile for Perfluoroalkyls

Motivation for Total PFAS Methods

- Greatly expanded PFAS chemical space measurement window
- Timeliness of measurement capability relative to release, occurrence, exposure, and risk
  - We can not assess the health concern of a contaminant that we can not measure
  - This lag can be decades long
  - During this lag, public health is vulnerable
  - Total PFAS methods can eliminate or greatly reduce this lag



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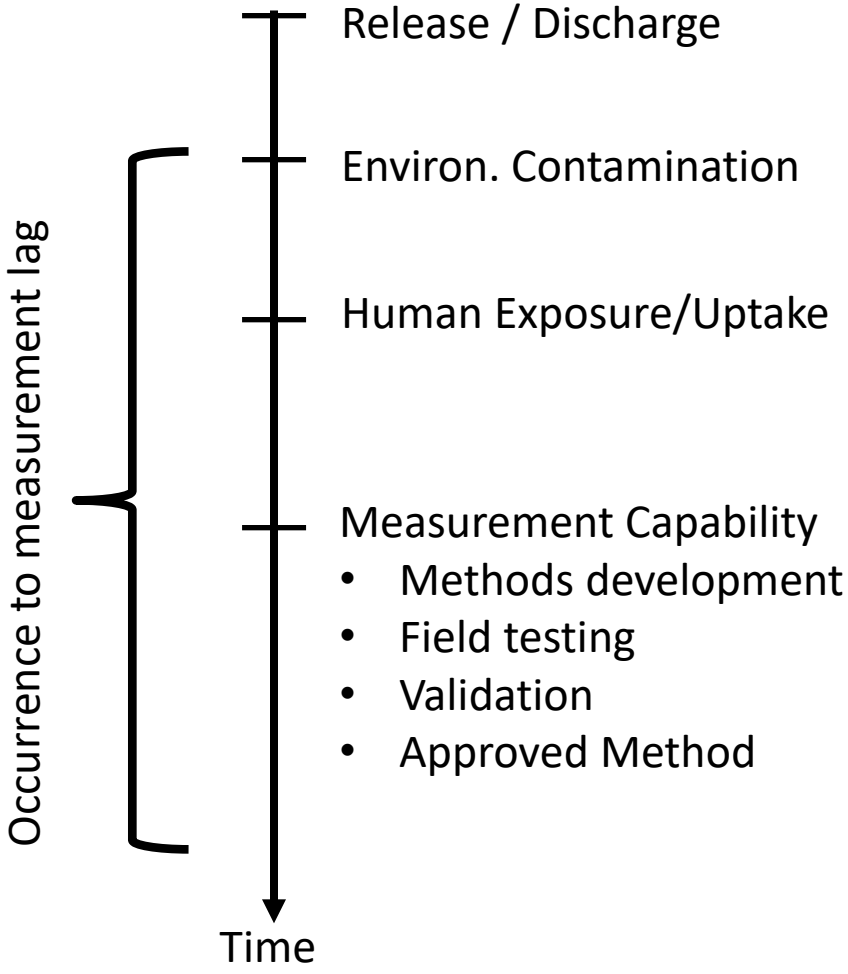

Cape Fear River Case-in-Point

Environmental Science & Technology

Article

November 2015

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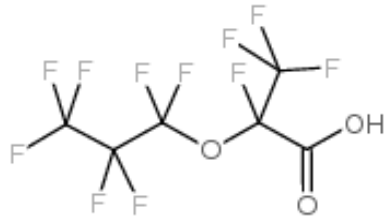
Identification of Novel Perfluoroalkyl Ether Carboxylic Acids (PFECAs) and Sulfonic Acids (PFESAs) in Natural Waters Using Accurate Mass Time-of-Flight Mass Spectrometry (TOFMS)

Mark Strynar,[*,†] Sonia Dagnino,[†,‡] Rebecca McMahen,[†,‡] Shuang Liang,[†,‡] Andrew Lindstrom,[†] Erik Andersen,[†] Larry McMillan,[§] Michael Thurman,[∥] Imma Ferrer,[∥] and Carol Ball[⊥]

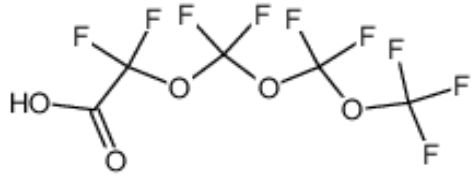
Table 1. Accurate Mass of Polyfluorinated Compounds and In-Source Artifacts Found in Extracted Water Samples

number	formula	CAS no.	name	[M][a]	[M − H]⁻ m/z	[2M − 2H + Na]⁻ m/z	[2M − H]⁻ m/z
Monoether PFECAs							
1	$C_3HF_5O_3$			179.9846	178.9773	380.9438	358.9619
2	$C_4HF_7O_3$			229.9813	228.9740	480.9372	458.9553
3	$C_5HF_9O_3$	863090-89-5		279.9782	278.9709	580.9310	558.9491
4	$C_6HF_{11}O_3$	13252-13-6	undecafluoro-2-methyl-3-oxahexanoic acid	329.9750	328.9677	680.9247	658.9427
5	$C_7HF_{13}O_3$			379.9718	378.9645	780.9182	758.9363
6	$C_8HF_{15}O_3$			429.9686	428.9613	880.9118	858.9299
Polyether PFECAs							
7	$C_7HF_{13}O_7$	39492-91-6	perfluoro-3,5,7,9,11-pentaoxadodecanoic acid	443.9515	442.9442	908.8776	886.8957
8	$C_6HF_{11}O_6$	39492-90-5	perfluoro-3,5,7,9-butaoxadecanoic acid	377.9598	376.9525	776.8942	754.9123
9	$C_5HF_9O_5$	39492-89-2	perfluoro-3,5,7-propaoxaoctanoic acid	311.9681	310.9608	644.9108	622.9289
10	$C_4HF_7O_4$	39492-88-1	perfluoro-3,5-dioxahexanoic acid	245.9764	244.9691	512.9274	490.9455
PFESAs							
11	$C_7HF_{13}O_5S$	66796-30-3[b]		443.9337	442.9264		
12	$C_7H_2F_{14}O_5S$			463.9399	462.9326		

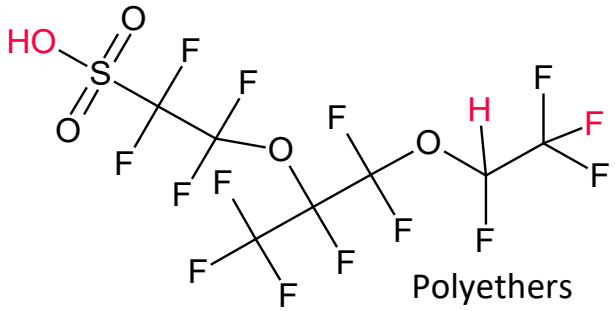
Example Structures



Monoether (6): GenX (HFPO-DA)



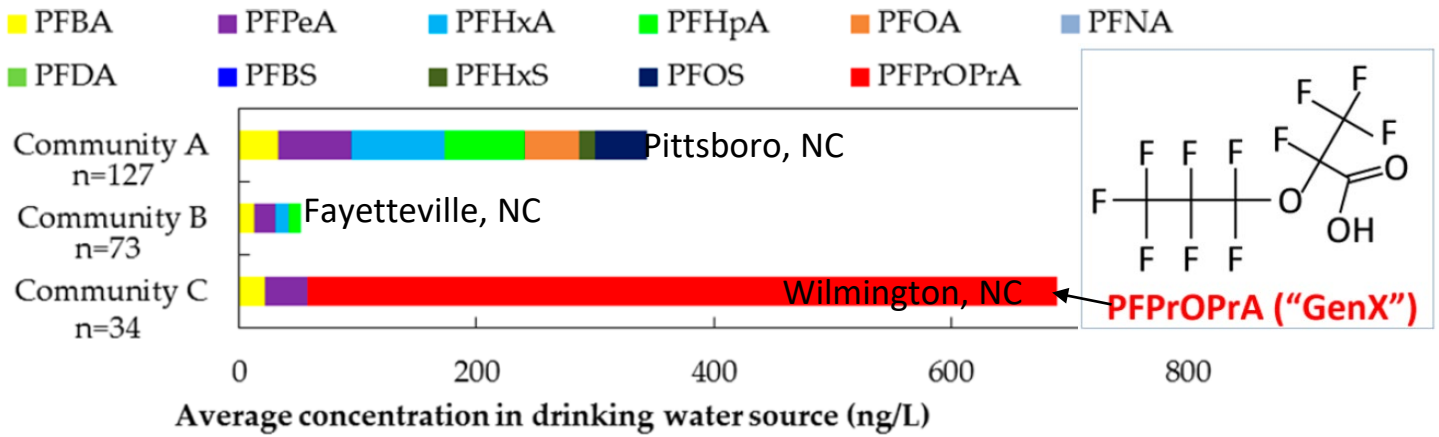
Polyethers (4):



Polyethers sulfonates (2):

GenX Quantified

- **GenX found in drinking water downstream of Chemours**



Environmental Science & Technology Letters

November 2016

Letter

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

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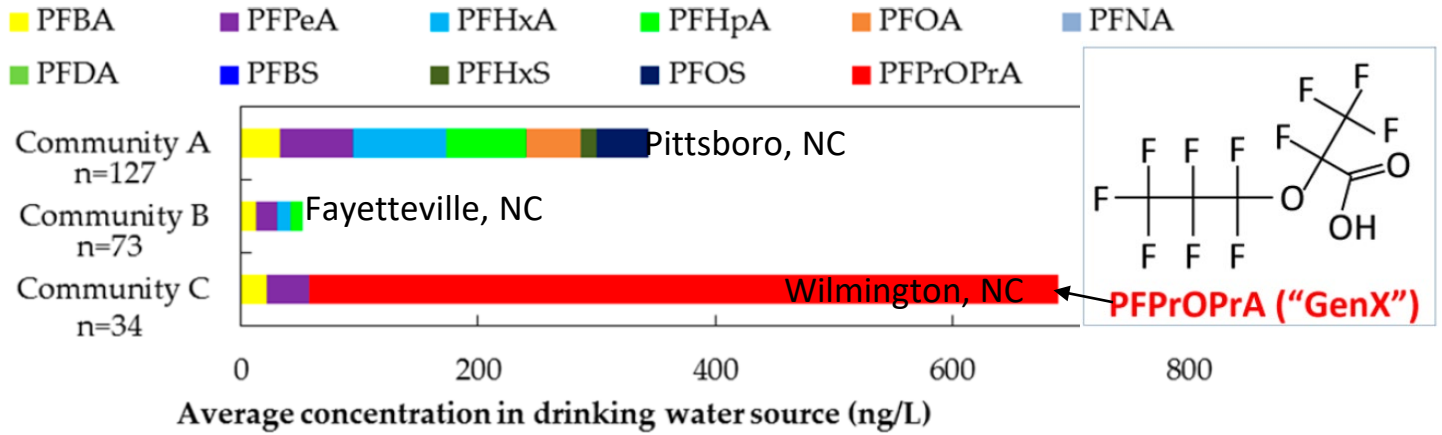

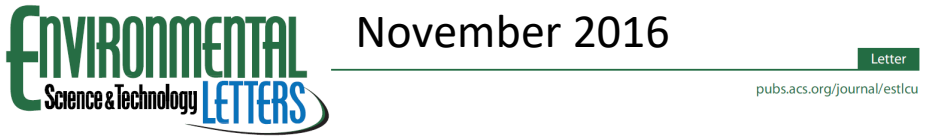

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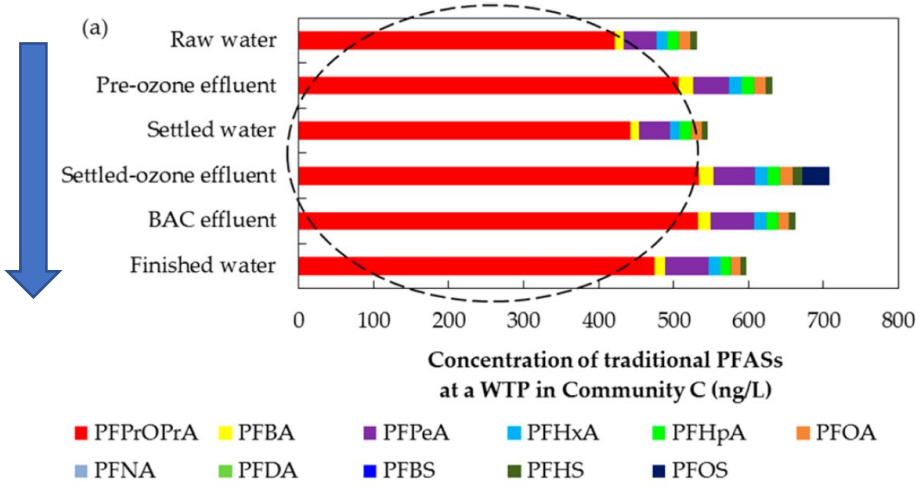
- **Effectiveness of treatment at a conventional WTP**



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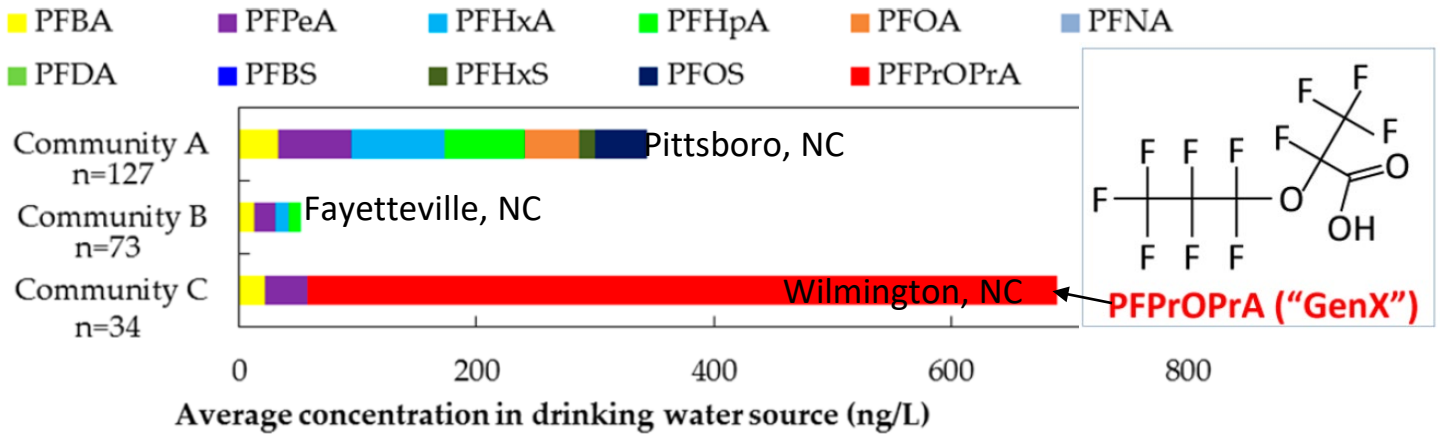

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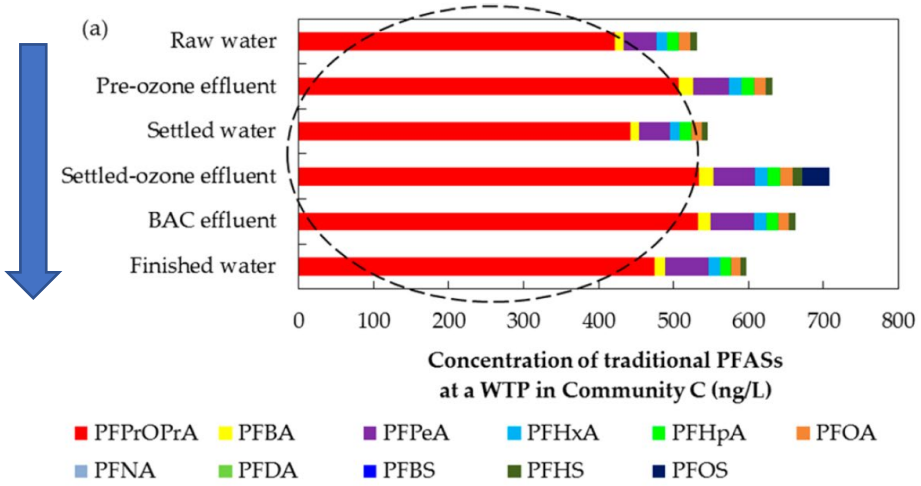

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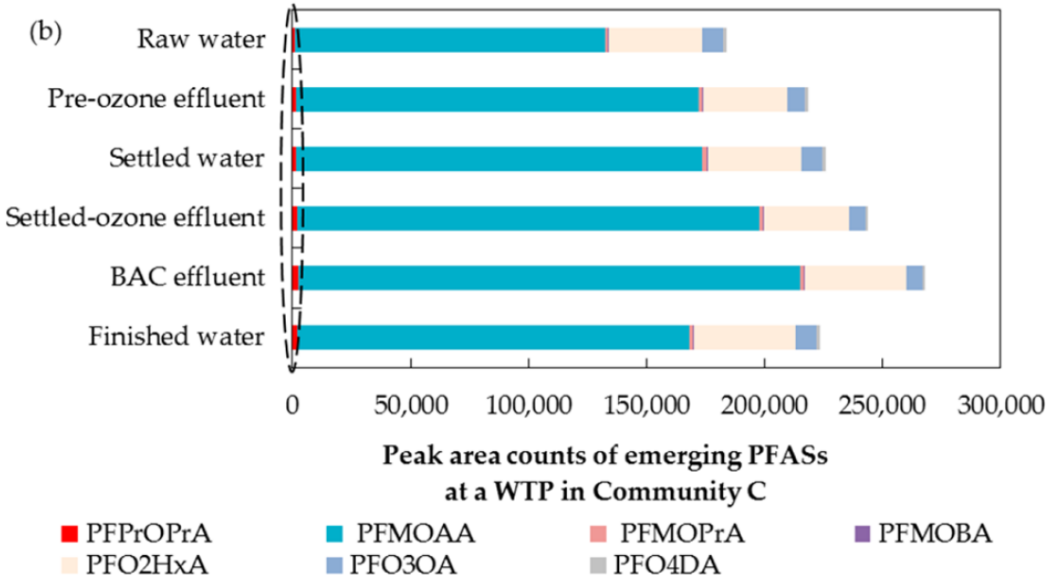
- **And "tip of the iceberg" of total PFAS present**



Summary

- PFAS archetypal of chemical threat to public health and habitable planet
  - Chemical landscape is vast and unknown
- Targeted/traditional measurement methods capture small percentage of PFAS likely present
- Total PFAS methods complement targeted methods and will advance public health interest
  - Greatly expanded exposure / occurrence window
  - Shortens time from release to detection

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Thank you!

Questions?