Per- and Poly-Fluorinated Alkyl Substances Chemical Action Plan (PFAS CAP) – 2019 Updates

New Analytical Methods Chapter

In 2017, the Washington State departments of Ecology and Health shared draft PFAS CAP chapters with external parties for review and comment. Comments received are available online. This document a new 'chapter.' Ecology and Health are sharing chapters with interested parties prior to the May 15, 2019 PFAS CAP webinar (*previously planned for March*). Chapter updates will be discussed during the May webinar. We expect to publish the entire Draft PFAS CAP around July 2019 followed by a 60-day comment period.

On May 15, 2019, Ecology and Health will host a PFAS CAP webinar to:
- Briefly review activities underway: firefighting foam, food packaging, drinking water.
- Review updated/new chapters – comments will be accepted on the updated chapters. Responses will be provided after the 2019 public comment period (summer 2019).
- Discuss preliminary recommendations – requesting comments and suggestions from interested parties – due June 3, 2019.
- Submit comments online.

Quick summary of PFAS CAP efforts:
- PFAS CAP Advisory Committee and interested parties met in 2016, 2017 and 2018.
- September 2017 Draft PFAS CAP chapters posted:

Intro/Scope	Environment
Biosolids	Health
Chemistry	Regulations
Ecological Toxicology	Uses/Sources

- March of 2018, Ecology and Health published the Interim PFAS CAP.
- The 2019 updated PFAS CAP "chapters" to be posted (in the order we expect to post on the PFAS CAP website):

Biosolids	*Fate and Transport (new)*
Ecological Toxicology	*Analytical methods (new)*
Environment	Chemistry
Regulations	*Economic analysis (new)*
Uses/Sources	*Preliminary*
Health	*Recommendations (new)*

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This document is posted on the PFAS CAP Website - https://www.ezview.wa.gov/?alias=1962&pageid=37105

Analytical Methods and Techniques

Summary

There are variety of analytical methods available for the analysis of per- and polyfluoroakyl substances (PFAS) in the environment and consumer products. Analytical methods and techniques for PFAS analysis are still evolving. Currently, few methods are validated and published. A multi-laboratory validated method, USEPA method 537.1 version 1.0 (USEPA 2018) was published in November 2018 for the analysis of 18 PFAS analytes in drinking water.

Method 537.1 is a solid phase extraction (SPE) liquid chromatography/tandem mass spectrometry (LC/MS/MS). Surrogate and internal standards are used to monitor for analyte loss due to sample preparation, instrument drifts, or matrix effects. This method is limited to the analysis of selected PFAS in drinking water sample.

Other published standard methods for PFAS analysis that have not been multi-laboratory validated include the American Society for Testing and Materials International (ASTM) D7979-17 (ASTM 2017). This method is a direct injection method that requires very little sample preparation. The method can be applied for wide range of liquid environmental samples such as surface water, ground water, and wastewater influent and effluents. Another method, ASTM D7968-17a (ASTM 2017a), was developed for analyzing PFAS in soil matrices.

ASTM methods D7979-17 and D7968-17a use external standard quantitation, which does not account for analyte loss during sample preparation, instrument drift, or matrix effects and hence it is most suitable for clean matrices with little to no matrix interferences.

International Organization for Standardization (ISO) Method 25101 (ISO 2009) is another standard method for the determination of the linear isomers of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) in unfiltered samples of drinking water, ground water and surface water (fresh water and sea water).

Most of the available standards are based on liquid chromatography with tandem mass spectrometry (MS) detectors (LC-MS/MS) and analyses for around 12-30 compounds, principally perfluorinated alkyl acids (PFAAs) with a handful of known polyfluorinated precursors for which standards are available.

While the available standard methods are amenable for the analysis of specific targeted PFAS analytes such as PFAAs. The quantitative analysis of other PFAS is often difficult due to lack of appropriate reference standard materials. Therefore, the full extent and distribution of PFAS impacts from precursors, toxicity and their associated risk from the PFAS class are generally limited.

Non-targeted analytical techniques have been developed that measure the total mass of PFAS. Four available non-standard methods can measure the total PFAS concentration in multiple matrices. These includes:

- Total Oxidizable Precursors (TOP) Assay
- Particle Induced Gamma Emission (PIGE)

- Combustion ion chromatography (CIC) methods with
    - Extractable organic fluorine (EOF)
    - Adsorbable organic fluorine (AOF)
- Quadrupole Time of Flight-Mass Spectroscopy (QTOF-MS)

Many of the available standard methods for PFAS analysis do not account for all known PFAS. Human exposures to PFAS are generally not from individual PFAS but from a complex mixture and analytical techniques are limited for determining which PFAS constituents are in a given mixture. Hence, the full extent of PFAS contamination could be underestimated when targeted analytical methods are used to quantify PFAS concentration. The complexity of PFAS, the production of commercial mixtures, and the tendency to generate intermediate transformation products present a performance challenge for current targeted methods.

Research on PFAS concluded that short-chain PFAAs (as replacement for long-chain PFAS) are as persistent as long-chain PFAAs. This highlights the concern of short-chain PFAAs as replacement for long-chain PFAAs. There is insufficient information on the toxicity of short-chain PFAAs to exclude sub-lethal long-term effects. The majority of the estimated 4700 PFAS currently on the world market have very limited or no toxicity information indicating a critical data gap on the full extent of PFAS toxicity.

<u>Measuring PFAS as a class (total PFAS) due to their persistent nature and toxicity is a more appropriate way to assess exposure and risk to human health and the environment.</u> Due to the limitation of available standard methods, non-targeted analytical techniques that can measure the total PFAS concentration in multiple matrices is preferred. The selection of any non-targeted method depends on the selectivity and inclusivity for a given application.

An important shortcoming of the non-targeted methods is that they are not standardized or multi-laboratory validated. The use of these methods is limited to research and investigation. Their result cannot be use for estimating toxicological effects, preventing the use of these methods for regulatory purposes.

Introduction

The objective of this chapter is to evaluate the current available analytical techniques/methods for the analysis of PFAS in the environment and consumer products. This review includes an assessment of the standard and non-standard analytical methods for the analysis of PFAS. The performance challenges with current standard methods for PFAS analysis and suggested analytical techniques for measuring PFAS are discussed.

PFAS are synthetic chemicals that have been used in industry and consumer products worldwide since the 1950s. They have been used in non-stick cookware, water-repellent clothing, stain resistant fabrics and carpets, some cosmetics, some firefighting foams, and products that resist grease, water, and oil. More discussion of the chemistry and uses are provided in other chapters.

Buck et al. (2011) provides an expanded overview of PFAS in the environment, terminology, classification, and their contributory sources. The United States Environmental Protection Agency (USEPA 2017h) has an online resource for PFAS. ITRC has developed a series of fact sheets that summarize the latest science and emerging technologies regarding PFAS. The ITRC

fact sheet describes methods for evaluating PFAS in the environment, including on laboratory Analytical Methods for PFAS (ITRC, 2018).

There are several published papers and literature reviews on analytical methods or techniques for the determination of PFAS in various matrices (De Voogt et al. 2006; Jahnke et al. 2009; Berger et al. 2011). The analytical methods used for PFAS determination are dominated by chromatography, mostly in combination with mass spectrometric detection.

High performance liquid chromatography (HPLC) hyphenated with conductivity or fluorimetric detection, and gas chromatography combined with flame ionization or electron capture detection have been used for PFAS analysis (Trojanowicz et al. 2013; Mahmoud et al. 2009; Moody et al. 2001; Schultz et al. 2004). These methods are used for the analysis of specific targeted PFAS analytes. Most PFAS fractions are quantified during targeted liquid chromatography mass spectrometric (LC/MS/MS) analysis, however, only few commercially relevant internal standards are available. Without internal standards, definitive identification and quantitative analysis are difficult or impossible.

Published standard methods for PFAS analysis

The following standard methods have been used for PFAS analysis. For detailed procedure and quality control requirements for each method see the referenced standard methods

USEPA Method 537 version 1.1

The primary methodology for PFAS analysis, USEPA, (2008) Method 537, Version 1 (validated), is a liquid chromatography/tandem mass spectrometry (LCMS/MS) method. It was first published in 2009 to determine 14 PFAS analytes in drinking water. The method was recently updated to include four more PFAS (shown with an asterisk in Table 1). Method 537.1.1 (USEPA, 2018) is used for targeted determination of PFAS, specifically for selected PFAAs such as PFOS, PFOA and other PFAAs in drinking water by Solid Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS).

Table 1: EPA Method 537.1.1 November 2018

Chemical Acronym	Chemical Name
11Cl-PF3OUdS*	11-chloroeicosafluoro-3-oxaundecane-1-sulfonic acid
9Cl-PF3ONS*	9-chlorohexadecafluoro-3-oxanone-1-sulfonic acid
ADONA*	4,8-dioxa-3H-perfluorononanoic acid
HFPO-DA*	Hexafluoropropylene oxide dimer acid
NEtFOSAA	N-ethyl perfluorooctanesulfonamidoacetic acid
NMeFOSAA	N-methyl perfluorooctanesulfonamidoacetic acid
PFBS	Perfluorobutane sulfonic acid
PFDA	Perfluorodecanoic acid
PFDoA	Perfluorododecanoic acid

Chemical Acronym	Chemical Name
PFHpA	Perfluoroheptanoic acid
PFHxA	Perfluorohexanoic acid
PFHxS	Perfluorohexane sulfonic acid
PFNA	Perfluorononanoic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonic acid
PFTA	Perfluorotetradecanoic acid
PFTrDA	Perfluorotridecanoic acid
PFUnA	Perfluoroundecanoic acid

* Chemicals added to method 537.1.1

New analytes in the updated method include the GenX chemical, hexafluoropropylene oxide dimer acid (Kato et al. 2008; Strynar et al. 2015). However, non–targeted liquid chromatography with high-resolution mass spectrometer (LC-HRMS) can be applied to identify additional suspected or uncharacterized PFAS if analytical standards are available for PFAS identification and quantification (McDonough et al. 2018).

Method 537 is specified for PFAS in drinking water by solid phase extraction (SPE). As a result, it is not amenable to an expanded list of PFAS compounds or to analysis of other sample matrices without modification of the method. For example, it would not work well for the determination of PFAS in consumer products or non-water matrices. Proprietary non-standard methods based on modifications of method 537 are used by various commercial laboratories for the determination of PFAS in non-drinking water samples.

As part of the laboratory selection process for non-drinking water analysis (e.g. consumer product).The laboratory analytical procedure should be evaluated to ensure all parameters meet acceptance criteria for all analytical QC elements. The QC elements should be evaluated to ensure that they are set at levels that meet the project's measurement quality objectives (MQOs). The laboratory should also provide an initial demonstration of capability (IDC).

The QC criteria should not be less stringent than the criteria found in the U.S. Department of Defense (DoD) Quality Systems Manual (QSM), Version 5.1, Appendix B, Table B-15 (USDOD 2017a) or later version

Currently, DoD's QSM for Environmental Laboratories, Version 5.1.1, Table B-15 (DoD 2017) provides the most current and comprehensive set of quality standards for PFAS analysis. These performance-based standards outline specific quality processes for sample preparation, instrument calibration and analysis when working with PFAS. The DoD QSM, Version 5.1, Table B-15, criteria currently require isotope dilution quantitation of PFAS. The isotope dilution method accounts for interferences caused by complex sample matrices and bias introduced by sample preparation and instrumental issues.

Quantitation of linear and branch isomers of PFAS

Many PFAS may be present as mixtures of linear and branched isomers (chemicals with the same chemical formula, but different molecular structures) depending on the manufacturing process that was used. These structural differences are important because they may affect how the compounds behave in the environment and may provide an indicator of their source. Accurate quantification of PFAS that are mixtures of linear isomers and branched isomers in environmental matrices can be difficult (Riddell et al. 2009).

However, they may be useful in understanding sources of PFAS and the age of the source, since the production of isomers varies by manufacturing processes. The different molecular structure of the isomers may also have implications for partitioning, fate and transport of PFAS in the environment.

With EPA method 537, laboratories had difficulty in quantifying both linear and branch isomers of PFOA. To account for linear and branched isomers of PFOA, EPA recommends that integration and quantitation of drinking water samples include peaks that represent both linear and branched isomers. EPA notes that the correct application of the method is to calibrate using a certified quantitative standard that includes both the linear and branched isomers of each analyte, if available. As of the release of EPA technical advisory (EPA 815-B-16-021, 2016), there is no certified quantitative mixed standard for PFOA, the available PFOA standards can be used to account for mixed isomers.

Since there is currently no certified quantitative PFOA standard that contains both linear and branched isomers that can be used to quantitate in the traditional manner, EPA recommends that until such standard is available, labs use the following approach:

- Calibrate instrumentation using a certified quantitative standard containing only the linear isomer.
- Identify the branched isomers by analyzing a "*qualitative/semi-quantitative*" PFOA mixed standard that includes both linear and branched isomers (Wellington Laboratories, cat#: T-PFOA or equivalent) and compare retention times and tandem mass spectrometry transitions.
- Quantitate PFOA by integrating the total response (i.e., accounting for peaks that are identified as linear and branched isomers) and relying on the initial calibration with the linear-isomer quantitative standard.

ISO Method 25101: SPE – water

ISO 25101:2009 specifies a method for the determination of the linear isomers of PFOS and PFOA in unfiltered samples of drinking water, ground water and surface water (fresh water and sea water) using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) (ISO 2009, reviewed 2014). Analytes are extracted from water sample by solid phase extraction (SPE) followed by solvent elution and determined by liquid chromatography tandem mass spectrometric detection. Other isomers may be reported separately as non-linear isomers and qualified as such. The method is applicable to a concentration range of 2.0 ng/l to 10,000 ng/l for PFOS and 10 ng/l to 10,000 ng/l for PFOA. Depending on the matrix, the method

may also be applicable to higher concentrations ranging from 100 ng/l to 200,000 ng/l after suitable dilution of the sample or reduction in sample size.

ASTM D7979: Direct injection – surface/wastewater

ASTM D7979 have been successfully used in the determination of selected PFAS in water matrices (e.g. sludge and wastewater influent and effluent) using liquid chromatography (LC) and detection with tandem mass spectrometry (MS/MS) (ASTM 2017). This method adheres to a technique known as selected reaction monitoring (SRM) or sometimes referred to as multiple reaction monitoring (MRM). This is not a drinking water method; performance of this test method has not been evaluated on drinking water matrices. ASTM D7979 is a performance based method, and alternative operating conditions can be used to perform this method provided data quality objectives are attained. It is a direct injection method that does not require sample preparation.

ASTM D7979 (2017) currently covers the analysis of 21 PFAS compounds, with 10 additional compounds listed for consideration in the appendix of the method. Eight additional PFAS compounds including three emerging PFAS compound of interest (11Cl-PF3OUdS, 9Cl-PF3ONS and ADONA) have been determined by the method to a total of 39 PFAS analytes (Waters, 2018).

ASTM D7968: solids (soil)

This method was developed by USEPA Region 5 Chicago Regional Laboratory, and has been successfully used for the determination of selected PFAS in a soil matrix (ASTM, 2017a). It is similar in scope to ASTM D7979-17 and uses solvent extraction, filtration, followed by liquid chromatography (LC) and detection with tandem mass spectrometry (MS/MS) to qualitatively and quantitatively determined PFAS in soil. Analytes detected with this method include: eleven perfluoroalkyl carboxylic acids, three perfluoroalkyl sulfonates, decafluoro-4- (pentafluoroethyl) cyclohexanesulfonate, and six fluorotelomers. Table X1.1 of the method lists ten additional PFAS analytes that may be determined by this standard.

This is also a performance-based method and alternative operating conditions can be used to perform this method provided that all data quality objectives defined in the method are attained. It is recommended that quality control and quality assurance requirements, if not well defined in the standard methods, must not be less stringent than the PFAS requirement found in DoD QSM (2017), Version 5.1 or later, Appendix B, and Table B-15, for media types.

PFAS Analysis Standard methods summary:

- USEPA Method 537 Version 1
  - Multi-laboratory validated standard method
  - Prescriptive, performed as specifically written.
  - Is not amenable to expanded list of PFAS compounds or other sample matrices.
  - Targeted method for selected PFAS analysis in drinking water.

- ISO Method 25101 (ISO 2009): SPE – water
  - Valid standard method

- o Targeted method for the determination of the linear isomers of PFOS and PFOA in unfiltered samples of drinking water, ground water and surface water (fresh water and sea water)
  - o Involves extensive sample preparation.

- ASTM D7979 (ASTM 2017): Direct injection – surface/wastewater
  - o Allows for quick sample turnaround time due to minimal sample preparation.
  - o Performance based, and more PFAS analytes determined including emerging analytes of interest with this method than any other standard method.
  - o Valid method for the determination of selected PFAS in non-drinking water samples.
  - o New "replacement PFAS" can be included in the method.
  - o Could be modified for consumer product analysis following appropriate extraction procedure.

- ASTM D7968 (ASTM 2017a): solids
  - o Allows for quick sample turnaround time due to minimal sample preparation.
  - o Valid method for the determination of selected PFAS in soil samples.
  - o New "replacement PFAS" can be included in the method.
  - o Performance based method

USEPA method 537 version 1.1 (USEPA 2008), a multi-laboratory validated method, uses SPE extraction of the sample. Surrogate and internal standards are used to monitor for analyte loss due to sample preparation, instrument drifts, or matrix effects.

ISO 25101:2009 method is a published method for determination of linear isomers of PFOA and PFOS in unfiltered drinking, surface, and groundwater samples. ISO 21675, an undertaking by the National Institute of Advanced Industrial Science and Technology, Japan is undergoing an interlaboratory trial for validation of up to 32 PFAS analytes in a wide range of aqueous matrices including drinking water, surface water, wastewater and sea water.

Both the ASTM methods (D7979 & D7968) use external standard quantitation, which does not account for analyte loss during sample preparation, instrument drift, or matrix effects and it is most suitable for clean matrices with little to no matrix interferences. ASTM standard methods D7979 and D7968 are not multi-laboratory validated

Non–specific methods for PFAS analysis

Many of the available standard methods for PFAS analysis do not account for all known PFAS. Human exposures to PFAS are generally not from individual PFAS but from a complex mixture (Schaider et al. 2017), and analytical techniques are limited for determining which PFAS constituents are in a given mixture. Hence, the full extent of PFAS contamination could be underestimated when targeted analytical methods are used to quantify PFAS concentration. The complexity of PFAS, the production of commercial mixtures, and the tendency to generate intermediate transformation products (Guelfo et al. 2018) present a performance challenge for current targeted methods.

Another complex challenge is the study of PFAS in the human body. Reviews and studies conducted by Luz et al, (2019)[1] indicated that short-chain PFAS product such as perfluorohexanoic acid (PFHxA) are less toxic or hazardous to human health than the long chain PFAS (e.g. PFOA). Anderson et al. (2019)[1] in their review of PFHxA concluded that PFHxA and related short-chain fluorotelomers present a low human health risk to the general population. However, Brendel et al, (2018) in their study of short-chain PFAAs concluded that short-chain PFAAs are as persistent as long-chain PFAAs, and highlights the concern of short-chain PFAAs as replacement for long-chain PFAAs. There is insufficient information on the toxicity of short-chain PFAAs to exclude sub-lethal long-term effects (Lilienthal et al, 2017). The majority of the estimated 4,700 PFAS currently on the world market have very limited or no toxicity information (Wang et al., 2017), indicating a critical data gap on the full extent of PFAS.

Studies have indicated that scientists are using techniques that focus on measuring the total exposure of all PFAS instead of one or a limited set of PFAS substances. This is important to gain a better understanding of exposures to PFAS as a class (Hartmann et al.2107; Poothong et al. 2017).

In a published study by the Nordic Council of Minister on the analysis of PFAS and total organic fluorine (TOF) in product (Borg et al. 2017). Comparison between analysed individual PFAS and TOF concentration showed that individual PFAS constitute a small proportion of the TOF. It indicates a data gap relative to the "unknown "or potentially uncharacterized PFAS by conventional analytical techniques. Schultes, et al. (2019), also compared CIC based EOF to target PFAS measurement in food packaging samples by liquid chromatography-tandem mass spectrometry that revealed large amounts of unidentified organic fluorine not captured by compound-specific analysis.

<u>Measuring PFAS as a class (total PFAS) due to their persistent nature and toxicity is probably a more appropriate way for assessing exposure and risk to human health and the environment</u>.

In addressing PFAS, the California Department of Toxic Substances Control (DTSC) Safer Consumer Products has labeled the entire class of PFAS as a "priority chemical" and is drafting work plans to evaluate these chemicals in products such as carpet and rug textiles and treatments (DTSC 2018). In treating PFAS as a class, formal PFAA regulations as hazardous wastes or hazardous substances have been promulgated in Vermont, New York, New Jersey, Colorado and Alaska for PFAA.

Non-standard analytical techniques for measuring PFAS

McDonough et al. (2018) evaluated analytical techniques for measuring total (bulk) organo-fluorine developed for the study and quantification of unidentified fractions of PFAS in environmental and biological samples. These methods or techniques vary in applicability to different sample matrices, and in their selectivity and sensitivity. These techniques include:

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[1] Funded by the FluoroCouncil.

Combustion ion chromatography (CIC) methods

Combustion ion chromatography mineralizes and then measures organic fluorine from the extractable organic fluorine (**EOF**) and adsorbable organic fluorine (**AOF**) assay. Samples are combusted between 900 -1000 degree Celsius (C) to convert organic fluorine to hydrofluoric acid, which is then absorbed into solution of sodium hydroxide (McDonough et al. 2018). The total concentration of the fluoride is subsequently measured by ion chromatography (IC) after calibration with sodium fluoride. The choice of sample preparation is important in isolating organic fluorine from fluoride prior to CIC analysis since CIC will not differentiate between organic and inorganic fluorine, and does not identify individual PFAS.

Extractable organic fluorine (EOF) - In EOF, the organic fluorine fraction is isolated by ion pairing methods and total organic fluorine (TOF) is measured by CIC. The EOF assay is the most commonly used assay found in literature for total organic fluorine measurement in different environmental matrices, human blood (Miyake et al. 2007, Yeung et al. 2013), and in marine mammals (Yeung et al. 2009).

Adsorbable organic fluorine (AOF) - Wagner et al. (2013) described the AOF assay, and differs in the way the organo-fluorine is extracted from the sample matrix. In AOF, the sample is passed through cartridges containing synthetic polystyrenedivinylbenzene-based activated carbon (AC). Residual fluoride is removed with a sodium nitrate washing solution, and the AC absorbent is then analyzed by CIC. AOF has only been applied to waters/wastewater (Wagner et al. 2013, Dauchy et al. 2017).

Particle-induced gamma ray emission (PIGE)

PIGE is a non-destructive analytical technique that takes advantage of the unique gamma-ray wavelength emission of fluorine when impacted with a proton ion beam. The technique is not compound specific but it is able to assess total fluorine content of a variety of materials isolated on a thin surface. Fluorine can be detected to a depth of approximately 200 um, but the precise value varies by substrate type. (Ritter et al. 2017). The sample is secured in the instrument and bombarded ex vacuo under a 3.4 MeV beam with an intensity of 10 nA for approximately 180 s. Two gamma rays characteristic of the decay of the ^{19}F nucleus (110 keV and 197 keV) are measured and the responses integrated. PIGE has recently been quantitatively applied to the measurement of PFAS impacted samples by creating calibration standards consisting of textiles soaked in solution of a known organofluorine (Ritter et al. 2017).

PIGE has primarily been used for solid-phase samples such as textiles, paper and food packaging (Lang et al. 2016, Robel et al. 2017, Schaider et al.2017). PIGE is a rapid screening technique to measure fluoride, PFAS, and other fluorine containing compounds in the samples. PIGE does not differentiate between inorganic fluorine and organic fluorine. It is important to understand whether there are significant sources of both organic and inorganic fluorine in a sample. There are techniques to remove inorganic fluorine that can make it specific for organofluorine if the sample does not contain significant amount of fluoride or if the inorganic fluoride has been removed from the sample.

PIGE can detect a wide range of fluorine treatment chemicals including polymeric fluorine treatments such as polytetrafluoroethylene, side-chain fluorinated polymers and small molecule products.

Total oxidizable precursors (TOP) assay

Houtz and Sedlak (2012) developed the total oxidizable precursor (TOP) assay method. The TOP assay was developed to infer and indirectly quantify the total amount of chemical "precursors" to PFAAs in a sample by comparing the concentrations of specific PFAAs before and after oxidation of the sample by an excess of hydroxyl radicals (Houtz and Sedlak 2012). It is the most selective of PFAS surrogate analytical methods, in that it selects only PFAS compounds that can be oxidized to form targeted PFAAs (McDonough et al., 2018). The same procedure of sample preparation is followed as traditionally used for targeted LC-MS/MS analysis. The assay is useful with compounds that oxidize to form LC-amenable hydroxyl radical resistant PFAS, however, these oxidation products must then also be detectable by LC-MS/MS. Some oxidation products, such as very short chain PFAS, will not be detected by standard post-assay detection approaches such as EPA method 537.

The assay is subject to low and variable recoveries that may lead to false negatives, especially in samples that have very low levels of PFAS (Robel et al., 2017). The limitation of the TOP assay is that it does not easily differentiate between precursors that contain telomer or sulfonamide functionalities, as all of these precursors are chemically oxidized primarily to perfluoroalkyl carboxylates. The TOP assay has not been demonstrated on large molecular weight polymer compounds or newer ether-linked PFAS like GenX; it is unknown if the oxidative process would liberate PFAAs from these types of compounds.

The TOP assay process converts fluorotelomer-based compounds including PFAA precursors into a mixture of PFAA products (Houtz & Sedlak 2012). The increase in PFAAs measured after the TOP assay, relative to before, is a conservative estimate of the total concentration of PFAA precursors present in a sample, because not all PFAS present will be subject to quantitation or reaction, and will remain as undetected PFAS. The PFAAs generated have perfluoroalkyl chain lengths equal to, or shorter than, the perfluoroalkyl chain lengths present in the precursors (Houtz et al. 2013; Houtz and Sedlak 2012; Weber et al. 2017; Dauchy et al. 2017). The TOP assay has been applied to a number of environmental matrices such as effluent wastewater, stormwater runoff, river and ground waters as well as soil. Applications of the TOP assay have been published by Houtz and Sedlak, 2012; Houtz et al.,2013, 2016; McGuire et al., 2014; Harding-Marjanovic et al., 2015.

Challenges of analytical method selection and conclusion

Detailed descriptions of the non-standard analytical techniques for measuring PFAS are referenced in TOP (Houtz and Sedlak 2012), PIGE (Ritter et al. 2017), EOF (Miyake et al. 2007) and AOF (Wagner et al. 2013). These methods enable measurement of total precursors, total fluorine, and total organic fluorine, respectively. Which method you choose depends on the selectivity and inclusivity for a given application. McDonough et al. (2018) indicated that methods that are highly inclusive, such as PIGE that does not differentiate between organic and inorganic fluorine, are impractical for measuring PFAS related organofluorine. However, EOF has a unique advantage over other methods as its selectivity can be adjusted depending on the sample preparation and fractionation method, and can be used to measure PFAS related organofluorine present in a sample. EOF and AOF may have sufficient sensitivity to measure

total PFAS in water (Miyake et al. 2007), while the sensitivity of PIGE may be limited by fluoride interferences.

Among these methods, the TOP assay is the most sensitive for individual PFAS (Houtz and Sedlak 2012), as it utilizes LC-MS/MS of targeted precursors. However, it is limited in its ability to account for emerging PFAS of concern such as GenX and ADONA that do not oxidize. It is also prone to selectivity concerns with reverse phase liquid chromatography, meaning that compounds that are not retained by the LC columns such as short-chain PFAS are lost.

Although, progress has been made in the analysis of PFAS, significant challenges remain from the fact that the complete list of PFAS relevant to environmental and human health exposure scenarios is still unknown. As more research and studies are completed in identifying novel PFAS and precursor transformation products, effective comprehensive technique capable of quantitative non-target analysis remains elusive (Nakayama et al, 2019).

The full extent of PFAS contamination may be underestimated unless non-targeted methods are used for PFAS analysis. The lack of available analytical standards means that precursors, degradation products and transformation products will not be quantified (D 'Agostino and Mabury, 2018).

McDonough et al. (2018) recommended that total organofluorine measurements by EOF and/or TOP assay be combined with high-resolution mass spectrometer (HRMS) as well with targeted analytical methods (LC-MS/MS) to obtain a full characterization of PFAS composition, sources and health risk.

HRMS using technology such as quadrupole time of flight (QTOF) generates high mass accuracy data that can be used in identification of unknown compounds (Barzen-Hanson et al. 2017b; Strynar et al. 2015).

Although, this recommendation may be specific to water, TOF measurement has been applied to other matrices (Schultes, et al. 2019). Guelfo et al. (2018) suggested that coupling AOF/EOF, TOP or PIGE with LC-MS/MS could help provide a better understanding of the total PFAS load present in a sample but will not result in identification of all individual PFAS present.

The availability of these techniques (EOF, PIGE, and HRMS except TOP assay) are mostly limited to non-commercial research facility or laboratories, and the quantification of PFAS that lack standards remains a challenge.

Measuring PFAS as a class (total PFAS) due to their persistent nature and toxicity is probably a more appropriate way for assessing exposure and risk to human health and the environment. Due to the limitation of available standard methods, non-targeted analytical techniques that can measure the total PFAS concentration in multiple matrices is preferred. The selection of any non-targeted method depends on the selectivity and inclusivity for a given application.

An important shortcoming of the non-targeted methods is that they are not standardized or multi-laboratory validated. The use of these methods is limited to research and investigation. Their result cannot be use for estimating toxicological effects, preventing the use of these methods for regulatory purposes.

EPA update on PFAS analytical method development and validation efforts

Currently, there are no standard EPA methods for analyzing PFAS in surface water, non-potable groundwater, wastewater, or solids. For non-drinking water samples, some U.S. laboratories are using modified methods based on EPA Method 537. These modified methods have no consistent sample collection guidelines and have not been validated or systematically assessed for data quality.

EPA labs tested an existing direct injection analytical protocol for preparing and analyzing 24 PFAS in groundwater, surface water, and wastewater. These methods will be included in the SW-846 updates.

Draft SW-846 Method 8327 Non-drinking water aqueous samples

Direct injection (DI) LC/MS/MS for non-potable waters based on EPA Region 5/Chicago Regional Lab Method

This method focuses on simplicity and robustness, and minimizes sample transfers and extraction. It is similar to the draft ASTM Method D7979.

- Phase 1: Six internal (EPA) lab validation trials (Completed December 2017)
- Phase 2: Ten external lab validation (ongoing)
- Initial demonstration of capability complete (7 labs "in" and 3 "out")
- August 2018: Shipped samples (60 unknowns: surface, ground, and waste waters)
- January 2019: Draft method posted for public comment (has not been posted, may be posted in March 2019)

EPA has also drafted a solid-phase extraction/isotope dilution (SPE-ID) method. This method is undergoing internal EPA validation.

Draft SW-846 Method 8328 Solid phase extraction (SPE) isotopic dilution method for non-potable waters and solid matrices (soils, sediments, waste)

Draft Method 8328 will include solid matrices in addition to non-drinking water aqueous matrices. Additionally, an analytical method for short-chain PFAS in drinking water is under development and planned for external validation and publication for public review by early 2019.

Method 8328 is a more complex method relative to direct injection, and will likely be more robust for complex matrices (e.g., wastewater influents, biosolids). Account for matrix effects (e.g., sorption) through isotopically marked standard recoveries. The method will:

- Meet DoD requirements.
- Allow users to perform a deeper dive based on screening (e.g. 8327) results.
- Same 24 PFAS analytes plus GenX chemical (HFPO-DA)
- Target Quantitation Limits of 10 nanogram/L
- Two internal lab validation started, and Ten external lab validation study planned

- Spring 2019 target for draft method

ASTM D-7968 Soil extraction/direct injection

EPA's office land management is in collaboration with ASTM for external multi-laboratory validation of ASTM D-7968 for 24 PFAS including all target analytes in EPA method 537.

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List of chemical acronyms

These are the chemical acronyms and names used in this chapter.

Acronym	Chemical Name
11Cl-PF3OUdS	11-chloroeicosafluoro-3-oxaundecane-1-sulfonic acid
9Cl-PF3ONS	9-chlorohexadecafluoro-3-oxanone-1-sulfonic acid
ADONA	4,8-dioxa-3H-perfluorononanoic acid
HFPO-DA (GenX)	Hexafluoropropylene oxide dimer acid
NEtFOSAA	N-ethyl perfluorooctanesulfonamidoacetic acid
NMeFOSAA	N-methyl perfluorooctanesulfonamidoacetic acid
PFAA	perfluorinated alkyl acid
PFAS	per- and poly-fluorinated alkyl substances
PFBS	perfluorobutane sulfonic acid
PFDA	perfluorodecanoic acid
PFDoA	perfluorododecanoic acid
PFHpA	perfluoroheptanoic acid
PFHxA	perfluorohexanoic acid
PFHxS	perfluorohexane sulfonic acid
PFNA	perfluorononanoic acid
PFOA	perfluorooctanoic acid
PFOS	perfluorooctane sulfonic acid
PFTA	perfluorotetradecanoic acid
PFTrDA	perfluorotridecanoic acid
PFUnA	perfluoroundecanoic acid