

Guide to Targeted
Quantification
and Screening of
PFAS Compounds
in Environmental
Matrices



Introduction

From nonstick cookware to fire-fighting foam, per- and polyfluoroalkyl substances (PFAS) have been some of the most widely used chemicals in industry and manufacture for the last 70+ years. These human-made chemicals do not break down easily and thus are extremely pervasive in the environment and the body.

Guide to Targeted Quantification & Screening of PFAS Compounds in Environmental Matrices explores the basics of PFAS analysis and the regulatory framework for PFAS analysis. Both laboratories new to PFAS analysis and experts alike will learn best practices for PFAS analysis and how to future-proof their lab for this ever-evolving area of environmental analysis.

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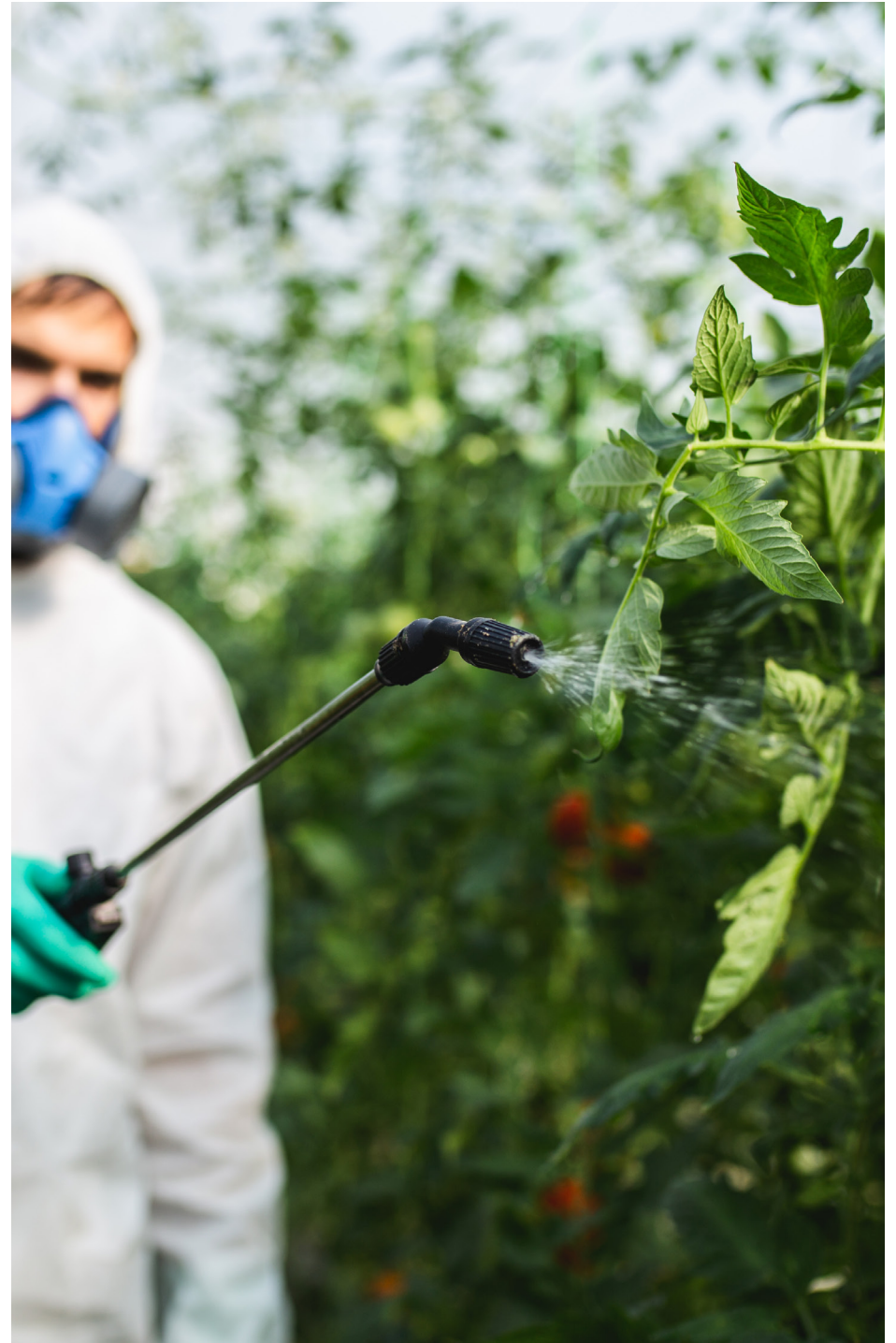
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PFAS: The Forever Chemical

What are PFAS and why are they important?



Per- and polyfluoroalkyl substances (PFAS) are known as “forever chemicals” due to their ubiquity and inability to break down. Their toxic effects are a cause for concern and have resulted in regulatory guidance for water and soil, as well as accelerated monitoring and identification. Agilent offers PFAS analysis workflow solutions to get the lab up to speed on extraction, quantification, and reporting of PFAS in the environment. We also offer in-laboratory, classroom, and online training to ensure your analysts have the skills necessary to be successful.

Q: What are PFAS?

A: Per- and polyfluoroalkyl substances (PFAS) are a group of >4,000 manmade chemicals that includes PFOA, PFOS, GenX, and more, according to the United States Environmental Protection Agency (EPA). They have been widely used since the 1940s, including applications such as nonstick cookware, stain-repellent clothing, food packaging materials, detergents, cleaning products, and firefighting foams. The carbon-fluorine bonds in PFAS impart high thermal stability and resistance to degradation, making them useful in many products. However, they are persistent and bio accumulative, meaning they don't break down in the environment.

Q: How do PFAS end up in our soil and water, and how are consumers exposed to PFAS?

A: PFAS are popular in industrial and commercial products because of their extremely stable chemical structure and unique chemical properties. Manufacturing of domestic and industrial products discharges PFAS into drinking water and wastewater treatment plants/waste streams and then further into the environment. Since they don't break down, consumers ingest them either directly or through contamination of the water used in an agricultural process. Their wide use in everyday household products (think food contact materials and personal care products) provides further exposure. However, drinking water is one of the most common routes of exposure. Their use in firefighting foams is one of the major ways PFAS enter the environment (1).

According to the US EPA, certain PFAS chemicals are no longer allowed to be manufactured in the United States, including PFOA and PFOS. While they are still used in some countries, certain PFAS chemicals in surface coatings cannot be manufactured or imported into the United States without EPA notification and review under the Toxic Substances Control Act (TSCA). However, several other PFAS currently in manufacture are still not regulated and can be used in commercial and domestic products.

¹ <https://www.epa.gov/pfas>

“Robust analytical techniques that provide reliable, unbiased quantitative and qualitative data on PFAS pollutants at trace levels are necessary for understanding their environmental fate, ecological impacts, and impacts on public health.”

Q: Why is it important to analyze for PFAS?

A: Providing scientists with measurement and identification technology solutions to accurately analyze PFAS chemicals is a critical first step for estimating exposure and potential risk. PFAS are measured in air, drinking water, soils, etc. and can be measured at low parts per trillion level. However, we still have much to learn about these chemicals.

Robust analytical techniques that provide reliable, unbiased quantitative and qualitative data on these PFAS pollutants at trace levels are necessary for understanding their environmental fate, ecological impacts, and impacts on public health. These analytical techniques and the fundamental data they generate will allow scientists and regulators to make informed assessments about PFAS use and future regulation in modern society.

Q: How do you analyze for PFAS?

A: PFAS analysis can be complex and requires a combination of good sample preparation, analysis, and reporting. PFAS must be measured at such low levels (down to about 1 ng/L) that LC/MS is typically required to achieve highest-quality data. Agilent provides complete end-to-end workflows for extraction, quantification, and reporting of PFAS in the environment. These workflows include sample containment, sample preparation tools, extraction products, and ultrahigh performance liquid chromatography (UHPLC) coupled to triple quadrupole mass spectrometry systems.

References and Resources

[Combating PFAS “The Forever Chemical” Contamination](#)

[Early Life Exposure to Per- and Polyfluoroalkyl Substances \(PFAS\) and Latent Health Outcomes. Toxicology](#)

[How Do you Solve a Problem like PFAS?, WaterWorld](#)

[Michigan PFAS 2019: Scientific and Policy Assessment for Addressing Per- and Polyfluoroalkyl Substances \(PFAS\) in Drinking Water](#)

[Per- and Polyfluoroalkyl Substances: An Emerging Contaminant of Concern, Annu. Rev. Nurs. Res.](#)

[PFAS – The Forever Chemical](#)

[PFAS – The Problem That Won't Go Away...](#)

[PFOA, PFOS, and other PFAS](#)

[The World's Water Supply](#)

The Regulatory Framework for PFAS Analysis

How PFAS analysis regulations differ worldwide.



It can be difficult for laboratories to keep abreast of the ever-changing regulatory landscape for PFAS analysis. An extra layer of complexity lies in the fact that each guidance can have different PFAS listed in differing matrices and with different regulatory levels. What follows is an overview of some of the guidance that exists worldwide for PFAS analysis and the key differentiators among them.

Q: What is the current regulatory framework for PFAS analysis?

A: In short, the current regulations around PFAS are complicated. Among the thousands of commercial PFAS substances, the toxicity is understood for only a few. Various regulatory initiatives specify their acceptable levels in environmental matrices including drinking water, surface water, soil, air, and biota. However, as newer PFAS are identified in the environment and more toxicological information becomes available, further regulations are almost certain. The rapidly developing regulatory landscape varies by country, state, region, and specific matrix. Vigilant surveillance by analytical laboratories is required to achieve compliance (see Figure 1). A brief summary of the global regulatory framework illustrates the diversity of policies and their continuing evolution:

- In 2009, perfluorooctanesulfonic acid (PFOS) and its salts were listed as persistent organic pollutants (POPs) under the Stockholm Convention. Since then, all parties have been required to eliminate the release of these compounds into the environment.

- The European Union (EU) Water Framework Directive lists PFOS as a priority hazardous substance that poses a “significant risk to the aquatic environment” ([Directive 2013/39/EU](#)). It has established an annual average environmental quality standard (AA-EQS) of 0.65 ng/L in inland surface waters, and an AA-EQS of 0.13 ng/L for other surface waters. The EU Drinking Water directive, which became adopted in December 2020, requires routine monitoring of up to 20 PFAS compounds in drinking water. EU members states have up to two years to comply.
- The UK Chemical Investigation Program requires the measurement of PFOS and perfluorooctanoic acid (PFOA) down to 0.09 ng/L. Similarly, in October 2018, the EU Parliament approved a proposal to recast its Drinking Water Directive with revised limits for monitoring PFOS and PFOA in drinking water. The new limits are 100 ng/L, with combined PFAS concentrations not to exceed 500 ng/L (COM (2017) 753 1.2.2018).

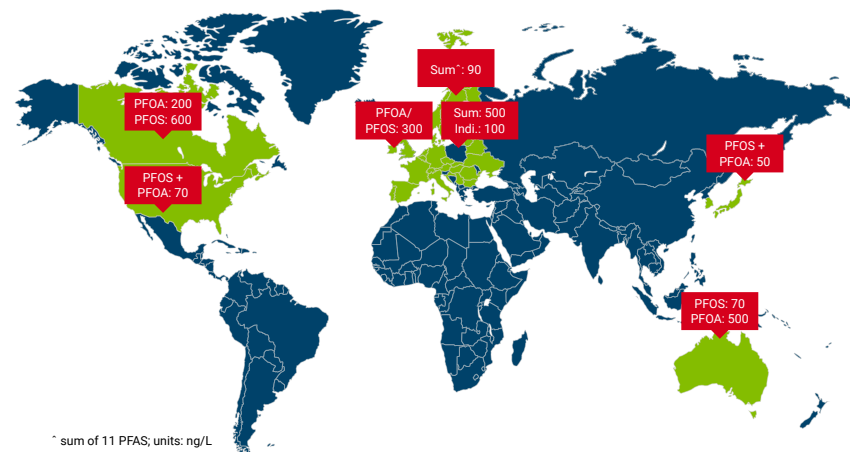


Figure 1. Global PFAS drinking water guidelines.

- Several European countries, including the Nordic region, have guidance levels for PFAS in drinking water and surface water. In Sweden, recommended levels for a sum of 11 PFAS in drinking water should not exceed 90 ng/L.
- In the United States, the US Environmental Protection Agency (EPA) has established a drinking water health advisory level for PFOS and PFOA at a combined 70 ppt (ng/L). Over 20 states have their own advisories for PFOA, PFOS, and other PFAS, such as perfluorononanoic acid (PFNA) and GenX, at the low ppt range in drinking water (see Figure 2). Other initiatives to regulate PFAS are also in the works. These initiatives include the PFAS Action Act (Jan 2019), the US EPA PFAS Plan (Feb 2019), and the US EPA Commitment to PFAS Drinking Water Standards (Feb 2019).
- Australia, China, and several other countries are implementing restrictions (or establishing maximum amounts) for drinking water and receiving water regulations for PFOA, PFOS, and newer PFAS detected at low ng/L to pg/L levels.

“Robust analytical methodologies for PFAS are difficult to develop. As reporting levels are lowered, new compounds are added to regulatory lists. Different regions develop diverse guidelines and the complexity of PFAS analysis increases.”

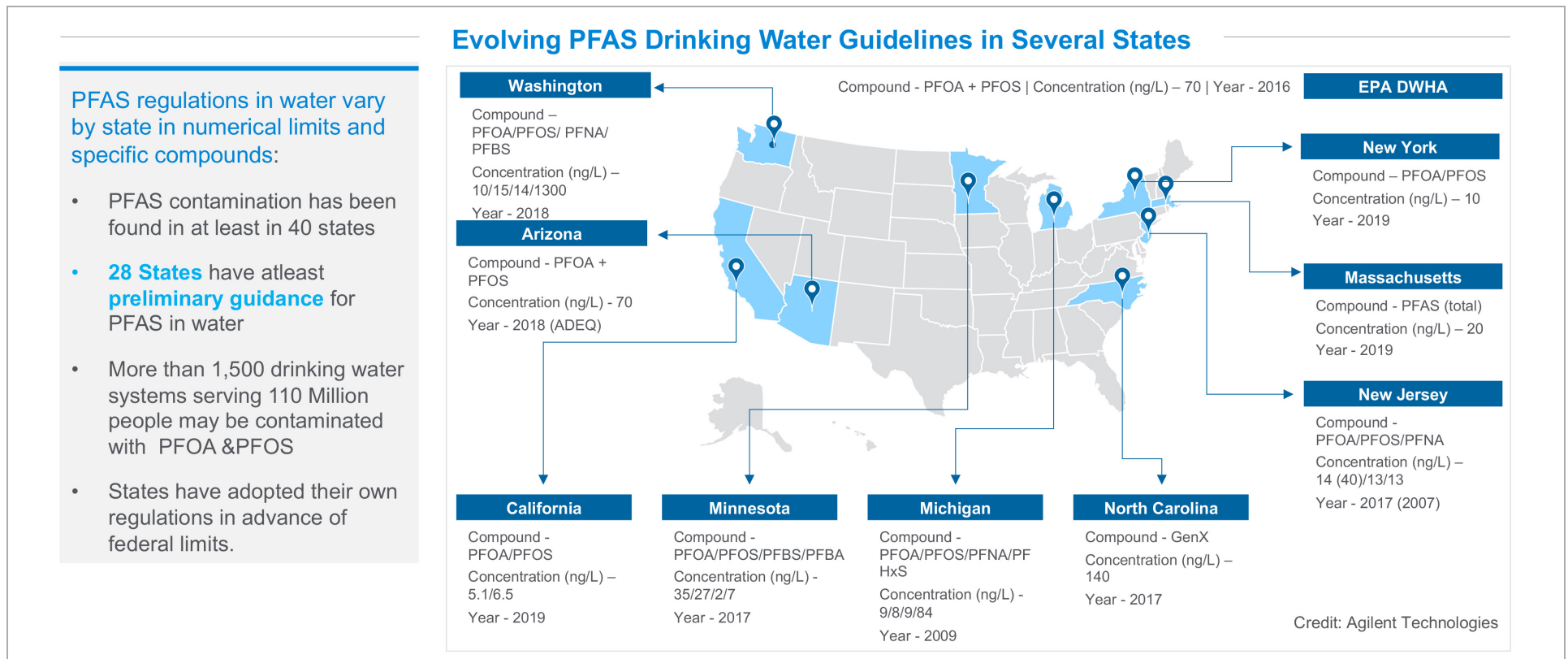


Figure 2. Global PFAS drinking water guidelines.

Q: What does this mean for labs developing analytical methods?

A: Labs developing analytical methods must be vigilant to make sure they are in compliance with ever-evolving regulatory methods and standards. Labs also require capabilities to rapidly monitor for more PFAS if their customers have specific needs. Robust analytical methodologies for PFAS are difficult to develop. As reporting levels are lowered, new compounds are added to regulatory lists. Different regions develop diverse guidelines and the complexity of PFAS analysis increases. This complexity makes it extremely challenging for laboratories to keep up with the regulatory changes while trying to develop comprehensive analytical methods in different matrices.

For example, the current EPA safe drinking water guidelines require PFOS and PFOA not to exceed 70 ng/L. However, several regions within the United States now require monitoring and detection of PFAS at low single-digit ng/L levels in water and soil. Analytical laboratories are challenged with monitoring all regulations relevant to their jurisdiction and adapting their methods to suit regulative modifications as they arise. In other regions of the world, performance-based methods may be acceptable. Labs have to strive for the lowest detection limits while maintaining high reproducibility and reliability, and ensuring highest-quality data.

Q: What are the current regulatory and consensus methods available for testing PFAS?

A: The current methods involve the quantification of PFAS in several different matrices (see Table 1) with many others expected soon. Regulatory and consensus methods differ in several areas including type and number of PFAS, matrices they are applicable for, detection limits and sample preparation choice. Although there is some overlap, the methods encompass many PFAS compounds, with different numbers of analytes, various matrices, allowable technology, reporting limits, and more. Thus, it is essential for analysts to understand the scope of each method and its applicability.

In the US, there are currently two standard methods to monitor and quantify PFAS in drinking water specifically (EPA 533 & 537/537.1). Both methods employ solid phase extraction (SPE) followed by liquid chromatography (LC) coupled to tandem mass spectrometry (MS/MS) for low ng/L detection of PFAS. EPA 537, which highlights a method for the analysis of 14 PFAS in drinking water, has been upgraded to EPA 537.1, which encompasses 18 PFAS compounds. In 2019, the US EPA introduced EPA 533 to address some of the challenging compounds in EPA methods 537 and 537.1 for C4 and C5 acids and sulfonates, while limiting chain length to C12 acids and adding some emerging PFAS. Twenty-five compounds are included, such as the C4 to C12 acids, C4 to C8 sulfonates, fluorotelomers, and mono/poly perfluorinated ethers. Ten of the 14 compounds in Method 537 are included, plus four more compounds in Method 537.1.

Table 1. Current standards and consensus methods for PFAS analysis in the environment.

Method	Matrix Trend	No. of Analytes	Sample Prep Procedure	Quantification Technique
EPA 533	Drinking water	25	Solid phase extraction	Isotope dilution
EPA 537	Drinking water	14	Solid phase extraction	Internal standard correction
EPA 537.1	Drinking water	18	Solid phase extraction	Internal standard correction
EPA 8327 (draft)	Surface water, groundwater, wastewater influent and effluent	24	Dilute and shoot	External calibration (isotope dilution also allowed)
ASTM 7979	Surface water, groundwater, wastewater influent and effluent	21	Dilute and shoot	External calibration (isotope dilution also allowed)
ASTM 7968	Soil and solids	21	Organic extraction with MeOH	External calibration
ISO/DIS 21675	Drinking water, seawater, fresh water, wastewater (<0.2% solids)	30	Solid phase extraction	Internal standard correction

EPA 537 and 537.1 use internal standard correction for quantification. EPA 533 differs by including isotope dilution analogs to assess recoveries through the sample preparation as well as internal standard addition for the native compounds. Branched and linear perfluorohexane sulfonate (PFHxS) and PFOS isomers are summed in the calibration and quantification of these analytes. Agilent application notes [5991-7951EN](#) and [5994-1628EN](#) include descriptions for the analysis of PFAS in drinking waters. The studies use a ZORBAX® Eclipse Plus C18 LC column and the 6470 triple quadrupole (TQ) MS for compliance with EPA 537 and 533, respectively. [5991-7951EN](#) includes an extra 16 PFAS of concern that are not yet regulated but their monitoring may be required in the future. In addition, details for analyzing PFAS for both EPA 537.1 and 533 on the Ultivo LC/TQ with a Poroshell EC-120 LC column and 10 minute run times can be found in [application note 5994-1920EN](#). This method offers faster analysis while being compliant for testing these drinking water methods. All the analyses in the application notes easily meet the criteria for sensitivity, precision, accuracy, and recoveries.

EPA 533, 537, and 537.1 are the only methods developed specifically for drinking water. The international ISO/DIS 21675 method pertains to seawater, fresh water, and wastewater in addition to drinking water. The method includes 30 analytes, and similar to EPA 537 and 537.1, specifies sample preparation by SPE and quantification with internal standards. EPA 8327 and ASTM 7979 both relate to surface water, ground water, and wastewater influent and effluent. Both methods use “dilute and shoot” large volume sample introduction instead of SPE and external calibration by LC-MS/MS. ASTM 7979 includes 21 analytes, whereas the new EPA 8327 covers 24. Agilent’s [application note 5994-0678EN](#) features a method for measuring 28 listed PFAS (including all in EPA 8327 and ASTM 7979) in nonpotable waters with good specificity, linearity, accuracy, and precision.

For analyzing PFAS in soil and solids, ASTM 7968 lists 21 analytes which are prepped using methanol extraction and quantified using external calibration by LC-MS/MS. [Agilent application note 5994-2999EN](#) includes optimized LC and MS conditions for meeting the requirements of this method, as well as best practices for sample handling, preparation, and storage. For all the different matrices, Agilent can help analysts navigate the ever-changing regulatory landscape and the many challenges of PFAS analysis.

As the number of analytes continue to increase and reporting limits decrease, it is essential for labs to be able to do the analyses expediently, with the highest data quality and robustness.

References and Resources

[Analysis of Per- and Polyfluoroalkyl Substances in Soil Extracts](#)

[Analysis of Per/Polyfluoroalkyl Substances \(PFAS\) in Drinking Water by EPA 537.1 and EPA 533 Using the Agilent Ultivo Triple Quadrupole LC/MS](#)

[Analysis of Per/Polyfluoroalkyl Substances \(PFASs\) in Drinking Water Using the Agilent Ultivo Triple Quadrupole LC/MS](#)

[Analysis of Per/Polyfluoroalkyl Substances in Water Using an Agilent 6470 Triple Quadrupole LC/MS](#)

[EPA Method 533 for Analysis of PFAS in Drinking Water Using Agilent 6470 LC/MS/MS](#)

[Quantification of Per- and Polyfluorinated Alkyl Substances in Water with Minimal Sample Preparation](#)

Instrumentation and Challenges with PFAS Analysis

Top challenges with PFAS analysis.



Laboratories face several challenges in the analysis of PFAS for a whole host of reasons. What follows is an overview of some powerful tools to help analytical laboratories overcome these issues.

Q: What is the preferred instrument for targeted analysis of PFAS?

A: The gold standard for the quantification of PFAS is liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) using electrospray ionization (ESI). Triple quadrupole (TQ) mass spectrometers provide robust, sensitive targeted data, while high-resolution mass spectrometers (HRMS) like quadrupole time-of-flight (Q-TOF) are required for the identification of new and unknown PFAS compounds. Solid phase extraction (SPE) with an anion exchange resin is typically used for the extraction of PFAS from drinking water samples.

Agilent offers four instruments that address targeted analysis of PFAS in environmental matrices. For routine quantification, the Ultivo triple-quadrupole LC-MS/MS instrument offers excellent specificity, accuracy, and precision. The Ultivo's extremely small footprint and early maintenance feedback features make it a great choice for novice LC/MS analysts. The instrument's demonstrated sensitivity compared to the current EPA reporting levels makes it amenable to EPA Methods 537.1 and 533. The Ultivo is designed for users with limited LC/MS experience, as it contains features such as guided maintenance to simplify operations. Agilent recently developed a streamlined protocol for analysis of PFAS in drinking water using the [Ultivo LC/TQ system](#). This system is ideal for drinking water and methods that involve solid phase extraction.

Enhanced sensitivity and outstanding robustness are found in the 6470 triple-quadrupole LC-MS/MS, which offers the performance required for trace-level quantification. Suitable for "dilute and shoot" methods, the 6470's robustness handles

large volume injections and high matrix samples with little clean up. The instrument can easily achieve the low nanogram per liter detection limits for PFAs required in the EPA 8327 and ASTM methods. These innovations maximize ionization, minimize instrument downtime, and reach low levels of detection, while achieving a wide linear dynamic range. The enhanced sensitivity of the 6470 future-proofs analytical labs against dropping regulatory limits and reporting levels that are expected for many PFAS. The 6470 LC/TQ system interfaced with a PFAS-free 1290 Infinity II LC has been used by researchers, contract-testing labs and government agencies for many years in analyzing PFAS. [The 6470 has been shown to exceed performance requirements for EPA 8327 and ASTM methods for nonpotable waters in validation studies](#). The instrument has also been used with weak anion exchange SPE for the quantification of 30 PFAS in eight different classes. The quantification included all 14 PFAS in EPA Method 537, using a single analytical method.

When labs are chasing the lowest reporting limits for many PFAS or want to skip the extraction step, direct injection requires a mass spectrometer with the utmost sensitivity and selectivity such as the 6495 triple quadrupole LC-MS/MS. As the highest performance LC/TQ available, its limits of quantification (LOQs) are often in the sub-ng/L range for PFAS in water. This enhanced sensitivity allows labs to run many different classes of PFAS in a single injection. The 6495's sensitivity allows users achieve low detection limits despite making compromises in MS conditions to accommodate different PFAS into a single run. [A method was developed for analyzing >50 PFAS in a single method spanning 14 different subclasses using the 6495 with sub- or low ng/L method reporting limits for all analytes](#).

"The enhanced sensitivity of the 6470 [triple-quadrupole LC-MS/MS] future-proofs analytical labs against dropping regulatory limits and reporting levels that are expected for many PFAS."

“Sample preparation also has the potential to introduce contamination if it is not performed carefully.”

Q: What are some of the challenges of analyzing PFAS in environmental samples?

A: The analysis of PFAS compounds is challenging for numerous reasons, including their ubiquity in everyday life. Their myriad applications have led to the detection of PFAS in environmental matrices around the globe. These 4000+ persistent chemicals are found on analysts’ clothing, as well as in laboratory supplies and even inside analytical instrumentation. Due to their ubiquity, these sources produce can have unacceptable background concentration and contamination in PFAS measurements.

Sample preparation also has the potential to introduce contamination if not performed carefully. Complex matrices, such as biosolids, add intricacy to the sample preparation as well. Besides, some PFAS can adsorb onto glass containers and pipettes causing low recoveries. Biases can result from sample preparation and instrument conditions, such that it can be difficult to determine whether all the PFAS in a sample have been captured and measured accurately. Thus, in addition to following stringent preparation protocols, analysts must understand the behavior of PFAS in their instrument to evaluate a method’s effectiveness. Also, it is critical that labware and sample preparation and extraction products be PFAS free for accurate and reliable quantification. Finally, PFAS contamination may occur in the LC/MS instrument too due to impurities present in fluoropolymers that are commonly used. This contamination needs to be characterized and potential sources in the instrument also need to be addressed.

As regulations evolve, the list of target compounds grows, and many minimum reporting levels (MRLs) are reduced. These requirements complicate method development, which is already difficult due to the multitude of compounds combined with the need for low detection limits for every analyte. The low detection limits demand well-trained analysts and sensitive instrumentation in addition to meticulous sample preparation. As ionization efficiencies may change with temperature, the analysis of each compound should be evaluated at high and low temperature during method optimization. Yet another burden stems from the fact that there are few validated reference materials for the various matrices; thus, their validation is left up to the analysts.

Unknown PFAS must be identified using high-resolution accurate mass untargeted analysis. This analysis requires a skilled analyst who is experienced with the operation of high-performance instrumentation as well as the chemistry involved. Once the new PFAS are characterized, they can be added to the targeted list of analytes. Also, previous data may need to be retroactively mined for the newly identified compounds using software tools.

Q: What are the best ways to overcome background PFAS contamination in the lab?

A: The pervasiveness of PFAS compounds makes their analysis a challenge. In addition to solvents, most laboratory supplies and equipment include at least one component comprising a fluorinated compound: vial caps, fluoropolymer tubing in sample preparation devices, and other general labware. PFAS-containing materials are included in most modern LC/TQ instruments as well. Liquid chromatographs contain per- and polyfluorinated compounds (PFCs) due to their chemical inertness, which enables the compatibility of the LC instruments with a broad range of acids, bases, and organic solvents. However, when running analyses at the ppb level and below, the PFAS leaches from the LC and causes an increase in background noise. This contamination can have a deleterious effect on the LOQs and limits of detection (LODs) so that the acquired data will not meet regulatory requirements. As such, users must pursue ways to minimize the potential for the introduction of PFAS impurities from the analytical process.

Identification and elimination of PFAS contamination requires diligent evaluation of all processes in the workflow for analysis in the lab. Care must be taken to use labware, sample containment, filters, extraction, and preparation products that are free of PFAS. Agilent offers a full range of supplies, including solvents and sample preparation products that have been tested to be free or below detection level for many common PFAS.

To mitigate PFAS background in the LC/MS, aim to remove as many sources of contamination as possible and design the experiment to separate the sample PFAS from the background PFAS. It is vital to avoid components containing polytetrafluoroethylene (PTFE). When setting up the HPLC system for PFAS analysis, analysts must replace all PTFE tubing with PEEK tubing. They must also remove PTFE filters present in the inline filters, and bypass the degasser, which contains several PTFE components. In addition, a delay column should be used between the autosampler and the pump head to separate the system’s background PFAS contamination peaks from the sample peaks. Conveniently, Agilent offers a PFC-free HPLC conversion kit specifically for eliminating PFAS background from the LC/MS.

“To mitigate PFAS background in the LC/MS, remove as many sources of contamination as possible and design the experiment to separate the sample PFAS from the background PFAS.”

The ready-to-use kit includes replacements for all critical parts of the LC system that contain organic fluorine compounds, as well as a delay column with InfinityLab Quick Connect fittings. The kit addresses PFAS materials in the bottle head assembly, pump head outlet connector, inline filter, and multisampler tubing parts. The kit is designed for an Agilent 1290 Infinity II LC with a high-speed pump (G7120A) and an Agilent 1290 Infinity II Multisampler (G7167B) with multiwash option. These LC modules provide the best possible performance for PFAS analysis applications.

Figure 3 illustrates the dramatic reduction of background noise that is achieved by the PFC-free HPLC conversion kit. The left panel shows the intense signal obtained from a blank when using a standard LC setup. A significant decrease in the signal is observed after replacing PFAS materials in the LC with the substitutes from the conversion kit. The cumulative effect of the delay column combined with PFAS-containing parts removal in the LC is demonstrated in the right side of the figure. The large blank signal from the standard LC configuration has been reduced to zero in the range of the PFAS sample's retention time by using the conversion kit. This effect optimizes the method's limits of detection and quantification to produce reliable PFAS results.

It is also critical for analysts to check the mobile phase for contaminants before analysis, as high-purity solvents are often filtered through PTFE filters. For removing impurities in unfiltered solvents, use of the InfinityLab Solvent Filtration assembly is recommended before PFAS analysis.

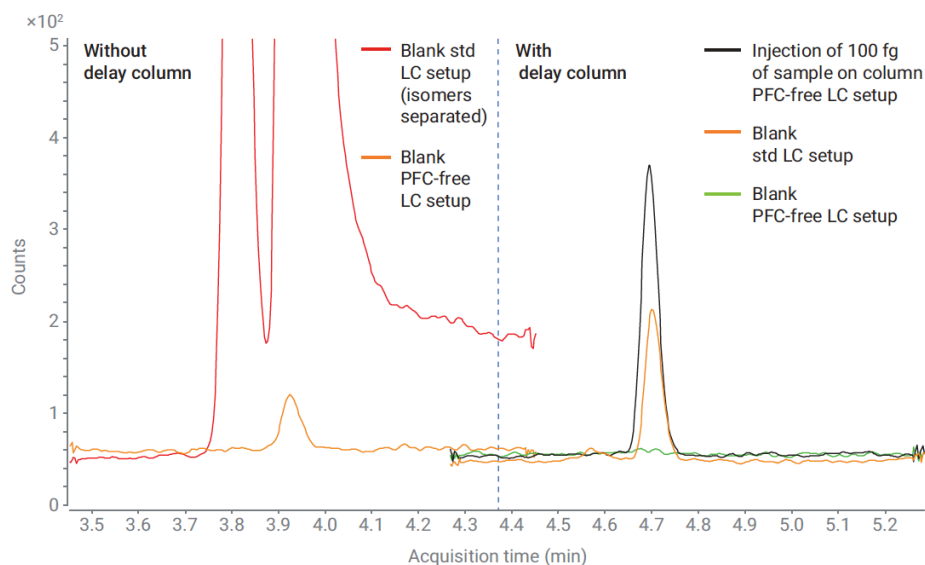


Figure 3. Reduced background noise with the PFC-free HPLC conversion kit.

Analysts should also keep in mind that proper sample cleanup and concentration are essential to robust, accurate analysis. The sample collection apparatus must be PFAS-free and the use of glass or aluminum foil avoided. In addition, samples should be stored below 6 °C. The analyst's skin and clothing may also affect PFAS measurements. Personal care products such as sunscreen and hand creams, as well as waterproof and stain-repellent clothing and shoes should not be worn. Well-washed lab coats and nitrile lab gloves are recommended.

Q: How do I get my lab up and running quickly to analyze for PFAS?

A: Rather than spending weeks or months doing method development, most analytical laboratories aspire to start using their new LC/TQ as soon as possible. Fortunately, Agilent can help labs get up and running quickly several ways.

In addition to the convenient HPLC PFC-free conversion kit, Agilent offers a range of supplies that help overcome background contamination issues common in PFAS analysis. These supplies simplify the buying decision and provide confidence when performing a new analysis. For example, as most common syringe filters contain PFAS, Agilent offers Captiva premium RC syringe filters as suitable replacements. Filtration is a critical element in the sample preparation workflow, and the Captiva filters are free from background interferences and sorption losses. Demonstration of their excellent performance can be found in [application note 5994-2151EN](#). Captiva disposable syringes also enable high-quality results for PFAS analysis without extensive cleaning. [Application note 5994-2247EN](#) illustrates their benefits of time and cost savings regarding solvent use and waste disposal.

For drinking water extractions, Agilent offers a weak anion exchange (WAX) cartridge for offline SPE along with a well-defined modified extraction procedure that is comparable to EPA Method 537. As documented in [application note 5994-0250EN](#), the protocol achieved excellent recoveries for 30 PFAS in both LC-grade water and tap water when analyzed on the 6470 LC/MS/MS system. All Agilent products are tested under strict conditions for reliable analysis of PFAS.

Agilent has also developed two electronic tools that accelerate implementing or developing a PFAS analysis. The first, the PFAS Water e-method, offers laboratories complete start-to-finish workflows for extraction, screening, quantification, and reporting of analytes in water and environmental samples. The ready-to-run e-method accelerates the lab's startup time by condensing the vast amounts of technical information and optimized analytical methods into a downloadable, digital information package. Agilent has already done all the hard work (Figure 4). The PFAS e-method comes with information on the 6470 LC/TQ instrument configuration, columns and supplies, including solvents, calibration standards, and sample preparation protocols. Optimized methods for sample introduction, chromatographic separation, detection, and data analysis are also included.

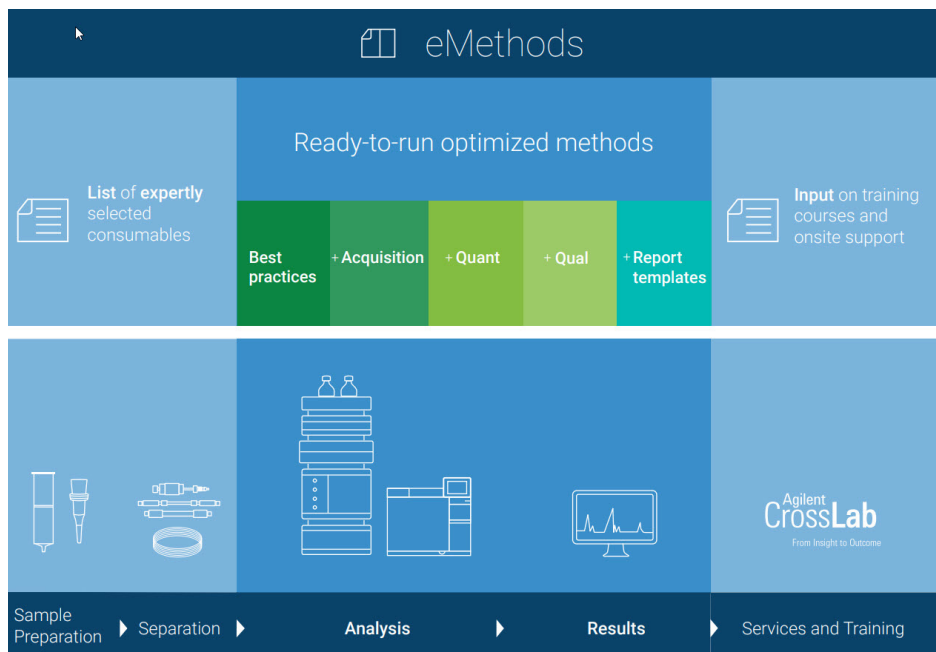


Figure 4. Agilent e-methods provide comprehensive workflows. The Agilent e-method covers the full scope of a PFAS testing setup, from the consumables needed for sample preparation to templates for result reporting. What's more, Agilent can provide you with information on training and onsite support relevant to your analysis.

Agilent also offers a multiple reaction monitoring (MRM) database for the analysis of more than 100 native and isotopically labeled PFAS compounds on the Ultivo, 6470B, and 6495C LC/TQ instruments. Analysts can quickly build targeted screening and quantification methods using the PFAS MRM database. Whether creating a PFAS method or expanding an existing one, laboratories will never have to worry about falling behind on the latest regulations.

The curated database includes:

- Intrinsic properties and identifiers such as compound name, molecular formula, and CAS number.
- MRM parameter settings for the acquisition of 72 native and 36 isotopically labeled analytes from several PFAS groups.
- Retention time information derived from an optimized chromatographic method.

“The PFAS measurement method was very time-saving and easy to establish, so that our routine procedures and the productivity of the laboratory could continue as usual and without disruptions.

We were able to start routine measurement of more than 50 PFAS compounds in a very short time using the Agilent PFAS MRM database on our Agilent 1290 Infinity II/6495-QQQ system.

The PFC-free HPLC elimination kit was easy to install and allowed us to significantly reduce PFAS blank values.

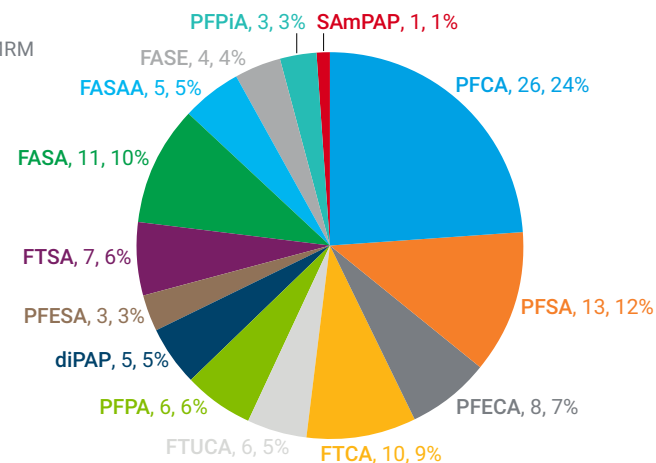
Thanks to the collaboration with Agilent, we were able to provide our customers with a very reliable and highly accurate analysis of PFAS analytes in a very short time.”

– **Dr. rer. Nat Tobias Minuth**

Lower Saxony State Agency for Water Management, Coastal Defence and Nature Conservation [NLWKN - Hannover-Hildesheim - Dept. for Organic Trace Analysis](#).

For ease of use, the database allows for the customization of MRM submethods based on a target list of interest or standard methods, such as the EPA drinking water methods. Classification of the analytes in the database, denoted by group, number of PFAS, and percent of total PFAS is shown in Figure 5.

Figure 5. Classification of analytes in Agilent's PFAS MRM database.



Finally, Agilent offers customizable, in-laboratory Method and Application Services tailored to meet a lab's specific goals. Agilent's global team of experts use their deep knowledge of Agilent equipment and applications to help laboratories accelerate productivity and achieve desired outcomes, while saving time and resources. Agilent can assist with method development, optimization, and implementation based on one of our existing PFAS application notes or specific to a laboratory's analytical needs. Custom data analysis reporting, macro development, and sample preparation assistance can be included as well. The many ways to maximize operational efficiency in partnership with Agilent's experts can be found at www.agilent.com/crosslab.

The comprehensive scope of Agilent's e-method, MRM database, PFC-free conversion kit, PFAS-free consumables, application notes, and expert support ensures that laboratories can be up and running quickly and confidently. Agilent's PFAS solutions support analytical laboratories from start to finish.

Q: How do I identify the correct tools and products for different PFAS methods?

A: Finding the right parts and supplies for an application can be very time consuming. However, the PFAS Consumables Ordering Guide makes this process easy by providing a table of all the products required for each regulated method, from sample preparation to final separation. With a click of the mouse, the helpful MyList feature enables analysts to download the entire list of part numbers to their personalized Favorite products page on the Agilent online store. The list can be customized by easily adding or removing part numbers. Lists can be saved to an analyst's Favorite products page, making it convenient to re-order items without having to search for them again. This simplified approach to ordering saves considerable time and ensures that labs choose the appropriate consumables for their analyses.

A list of parts and supplies for EPA 533, taken from the [PFAS Consumables Ordering Guide](#), is shown in Table 2. The View MyList option is located in the table header to enable rapid addition of all the listed parts to the Favorite products page in the online store. Alternatively, analysts can click individual part numbers to add specific items from the table. The ordering guide's curated list of product recommendations based on regulatory methods helps streamline laboratory operations and eliminates confusion in the ordering process.

Table 2. EPA 533 or similar: Determination of PFAS in drinking water by SPE and LC/MS/MS (short-chain PFAS) [View MyList](#).

Product Category	Description	Part Number
Sample preparation	SampliQ WAX polymer 6 mL cartridges, 150 mg, 30 µm (30/pk)*	5982-3667
	Bond Elut Adapter cap for 1, 3 and 6 mL Bond Elut cartridges (15/pk)	12131001
	Bond Elut Empty SPE cartridge 60 mL (100/pk)	12131012
	15 mL centrifuge tubes and caps, 50/pk	5610-2039
	Collection rack and funnel set for 12 or 15 mL conical tubes, for Vac Elut SPS 24 Manifold	12234027
	Vac Elut SPS 24 Manifold with collection rack for 10 x 75 mm test tubes	12234003
Guard column	ZORBAX RRHD Eclipse Plus C18 2.1 x 5 mm, 1.8 µm guard	821725-901
Separation column	ZORBAX RRHD Eclipse Plus C18, 2.1x50mm, 1.8 µm	959757-902
PFC-free LC kit w/ delay column	InfinityLab PFC-free HPLC Conversion Kit	5004-0006
Delay column	InfinityLab PFC Delay Column, 4.6 x 30 mm, 1200 bar (replacement)	5062-8100
Other LC supplies	InfinityLab Quick Connect assembly, 0.12 x 105 mm, for column inlet connection on UHPLC	5067-5957
	InfinityLab Quick Connect assembly, 0.17 x 105 mm, for column inlet connection on UHPLC	5067-6166
	InfinityLab Quick Turn fitting, for column outlet	5067-5966
	Quick Turn capillary 0.12 x 280 mm, for connection from column to detector	5500-1191
	Kit of Stay Safe waste cap GL45 with 4 ports and waste can (6 L)	5043-1221
	Charcoal filter with time strip for waste container	5043-1193
	Stainless steel solvent inlet filter, 10 µm pore size	01018-60025
Solvent filtration assembly**	InfinityLab solvent filtration assembly, includes glass funnel, 250 mL, membrane holder glass base, glass flask, 1 L, and aluminum clamp	5191-6776
	Regenerated Cellulose Filter membrane 47mm, 0.20µm 100/pk	5191-4340
Sample containment	2 mL polypropylene snap style vials (100/pk)	5182-0567
	Clear snap style caps with polypropylene septa (100/pk)	5182-0542
	2 mL polypropylene screw style vials (100/pk)	5191-8150
	9 mm screw style cap with polypropylene/silicone screw septa (100/pk)	5191-8151
Solvents	InfinityLab Ultrapure LCMS Water	5191-4498

* For better recoveries rinse with 10 mL of the elution solvent (2% ammonium hydroxide in methanol) before conditioning with phosphate buffer.

** Prefiltered solvents can be a source of PFAS contamination. Use the InfinityLab Solvent Filtration assembly to filter non-filtered solvents for PFAS analysis.

Q: What about identifying new and emerging PFAS?

A: While there are potentially, >4,000 PFAS produced in commerce, only a few hundred are known and ones we have analytical reference standards to quantify using an LC/TQ. LC/TQs are ideal for the quantification of known PFAS that have standards, but are not capable of identifying PFAS without any prior knowledge. For untargeted analyses, the 6546 LC/Q-TOF high-resolution accurate mass instrument is ideal for suspect screening and identification of new and emerging PFAS compounds. Its high sensitivity, five orders of in-spectrum dynamic range, resolution up to 60,000 independent of acquisition speed, excellent isotope fidelity, and sub-ppm mass accuracy deliver high-quality data and confident identifications. Coupling that with the Agilent MassHunter and Mass Profiler Professional Software tools, identification of new PFAS is made much simpler. Capable of both qualitative and quantitative analyses, this Q-TOF's performance has earned its place as the centerpiece for untargeted PFAS analysis.

References and Resources

[Disposable Syringes for Analysis of Per- and Polyfluoroalkyl Substances in Environmental Extracts](#)

[Extraction of Per/Polyfluoroalkyl Substances in Water Using Agilent WAX Offline SPE](#)

[Filtration for the Analysis of Per- and Polyfluoroalkyl Substances in Environmental Extracts](#)

[Method & Application Services](#)

[Per- and Polyfluoroalkyl Substances \(PFAS\) Analysis - Consumables Ordering Guide](#)

[Poly- and Perfluoroalkyl Substances in Water: Challenges and Mitigating Strategies in Detection and Treatment](#)

[Reduce PFAS Background with the Agilent PFC-Free HPLC Conversion Kit](#)

The Future of PFAS Analysis

How to future-proof your lab for the changing landscape of PFAS analysis.



As PFAS regulations evolve, future-proofing your laboratory to adjust for these changes is extremely important. What follows are some best practices and tips to meet the needs of tomorrow's environmental lab.

Q: What might change for PFAS analysis in the future?

A: Regulations for PFAS are expected to continue evolving over the next several years. More compounds will be added to regulatory lists as their health concerns are identified, and detection limits for listed compounds will likely decrease. We anticipate these changes to be incremental, with small scope increases made year on year. To stay relevant, analytical laboratories must find solutions that are flexible and enable them to adapt to the shifting landscape on a continual basis.

Q: How can I future-proof my lab?

A: There are many aspects to “future-proofing” a laboratory for PFAS analysis. A lab needs to balance its current needs and cost to implement a new analysis with its expected future needs and possible future costs. Some points to consider include:

Instrumentation: Agilent's 6470 and 6495 triple quadrupole LC/MS and 6546 quadrupole time-of-flight LC/MS instruments provide the flexibility to meet changing requirements by offering exceptional sensitivity and dynamic range. The robust performance and sensitivity of the 6470 and 6495 LC-MS/MS will deliver reliable, compliant PFAS screening for years to come. The high resolution and mass accuracy of the 6546 LC/Q-TOF will continue to enable the confident characterization and identification of unknown PFAS.

Also, these models, as well as Agilent's other instrumentation, have a proven record of reliability and longevity for over 45 years in environmental labs. As such, laboratories with Agilent instruments can expect years of reliable and repeatable service from an instrument and can plan accordingly. Agilent's suite of instruments future-proof analytical laboratories in an ever-changing regulatory environment.

Sample preparation: Sample introduction may migrate more toward large volume direct injection or online SPE to provide faster and more accurate results. This change makes Agilent LC/TQ's even more advantageous due to their sensitivity plus the availability of a fully integrated commercial online SPE system. For time savings, analysts would like the benefit of combined targeted and untargeted runs. Although this is already possible on the 6470, it is not yet routine. Combined runs at a production level may be possible in the future, offering significant gains in efficiency.

Methodology: As regulations require more compounds or customers request expanded target lists, a laboratory must be flexible to stay relevant. One approach would be for the laboratory to take on the additional method development/ optimization work. This work includes investigating the expanding requirements, modifying the existing methodology to meet those needs, and finally verifying and deploying the expanded method. Depending on staff skill and changes required, the work could take a few days, a few weeks, or a few months—all of which is time not spent running samples for revenue. And this must be done each time the requirements change.

An alternate approach is to use either the PFAS MRM database or Water e-method (for water matrices) to quickly update an existing method as need arises. The PFAS MRM database, for example, currently includes optimized MRM transitions and ion source parameters for over 100 native and isotopically labeled PFAS compounds, a number well beyond current regulations. Using the database, it is simple to expand a 14, 24, or 35 compound method through integrated functionality provided with standard Agilent MassHunter software. This approach greatly reduces the investigation and experimentation time required and allows a laboratory to go directly to verification testing and then deployment of the expanded method.

The protocols and electronic methods provided with the PFAS Water e-method have been demonstrated effective for the low-level detection of up to 60 PFAS compounds. Whether a laboratory is using the e-method to analyze a subset of those compounds or wants to add the e-method to an existing instrument, its comprehensive scope allows labs to expand their analyses, without extensive method development. All the laborious development work has already been done, which offers new labs a head start on moving from setup to results.

Finally, in time, the use of isotope dilution for quantification of targeted analytes may increase. Its accuracy, along with decreased matrix influence and instrument effects are beneficial. The technique may also see increased use for monitoring recoveries from extractions. The sensitivity and robustness of Agilent's LC/TQ instruments are ideal for isotope dilution in PFAS analysis. The PFAS Water e-method, for example, uses isotope dilution already.

Partnering for the future: As a laboratory considers its future needs, this exercise should include identifying an instrument solution provider to partner with for continued success. As a supplier of environmental analytical instrumentation for over 45 years, Agilent has valuable PFAS-specific solutions for environmental laboratories. PFC-free consumables and supplies, robust, reliable, and sensitive instrumentation, and proven methodology are packaged for rapid deployment. A prime example of this is Method & Applications Services. In addition to helping a laboratory deploy a new instrument and train analysts, services can also update an existing method or train new analysts, helping laboratories over the life of their Agilent instrument-driven analysis.

Q: Do you anticipate ion mobility will be a bigger player in the future?

A: For deeper characterization of unknown PFAS, including forensic identification of sources of potential PFAS contamination, ion mobility mass spectrometry offers another dimension of separation in addition to the LC-Q/TOF. The technique, when coupled to LC-Q/TOF, can separate compounds of identical mass based on differences in structure and their cross-sectional size. This approach allows isomers to be distinguished, such as linear vs. branched PFAS compounds. As laboratories start to incorporate ion mobility into their untargeted workflows, the Agilent 6560 ion mobility Q-TOF LC/MS system delivers the required separation and selectivity. The instrument achieves this by combining chromatography, ion mobility, and mass spectrometry for complex samples.

Q: What about air analysis?

A: Currently, air as a matrix for PFAS is not as well characterized as water and soil matrices. However, recent studies have shown a large component of volatile PFAS may indeed escape into the air. Thus, the need for developing GC/MS methods to analyze and sample more volatile PFAS in air. Agilent's GC and GC/MS systems are capable of analyzing and detecting PFAS in air. Agilent's GC/TQ systems will provide low detection limits and robustness to overcome the analytical obstacles associated with extremely low detection limits and more specificity needed for quantifying PFAs in air.

No matter what the future brings, Agilent's suite of instruments, consumables, software, and support are ready to tackle the toughest challenges. Ultimately, scientists will have greater awareness of PFAS in the environment, as Agilent's comprehensive solutions deliver the answers needed today and tomorrow.

References and Resources

[Application of a MRM Database for the Quantitation of Per- and Polyfluoroalkyl Substances \(PFAS\) in Water Extracts](#)

[PFAS analysis, MRM transition database, PFOA, PFOS, PFC](#)

[Expert Discussion Forum—Analysis of PFAS: Strategies to Optimize Performance](#)

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