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PFAS Testing: LC/MS/MS and Other Techniques Take on the Challenge

PFAS testing has rapidly grown in recent years as scientific studies, regulatory scrutiny and public concern have brought attention to the chemicals. LC/MS/MS is a one of the primary methods for testing for PFAS compounds. As the US EPA takes steps to regulate the contaminant in drinking water under the Safe Drinking Water Act (SDWA), LC/MS/MS testing methods are front and center. Additionally, they are also playing a part of in the need to test for LC/MS/MS in other environmental samples, such as wastewater, biosolids and air. How are and will new US PFAS testing requirements affect demand for LC/MS/MS? ***IBO*** spoke with PACE Analytical, a national testing laboratory, and two LC/MS/MS manufacturers, Agilent Technologies and Shimadzu Scientific Instruments (SSI), to find out.

Last year was a major year for PFAS regulatory developments at the federal level, as the EPA took a number of actions indicating its aim to increase evaluation, testing and regulation of PFAS chemicals. Among these actions, the agency released its "PFAS Strategic Roadmap" for 2021–24. The roadmap indicates that a national primary drinking water regulation (NPDWR) for PFOS and PFOA, two PFAS chemicals, will be proposed by fall 2022. A final regulation is scheduled for fall 2023 and would set a maximum contaminant level. States currently have set their own limits. This would mark the first enforceable PFAS regulation of any type by the federal government.

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The NPDWR designation is a sign of the EPA's commitment to regulating PFAS chemicals. "EPA is intent on adding PFOA and PFAS to the Safe Drinking Water Act [SDWA] maximum contaminant level list with enforceable limits," stated Paul Jackson, Program Manager, Specialty Analytical Services for PACE Analytical. "Every public water system in the country fairly soon will be compelled to routinely test it for at least those two compounds every time they go out and do compliance sampling, just like we're doing now for mercury and arsenic and benzene [and] whatever is regulated under the SDWA right

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now." The plan also indicates that the EPA will publish multi-lab validated analytical methods for 40 PFAS compounds by fall 2022, and update to PFAS analytical methods to monitor drinking water by fall 2024.

In addition, this year, PFAS was added to the list of contaminants to be monitored between 2023 and 2025 in drinking water systems nationwide as part of the fifth Unregulated Contaminant Monitoring Rule (UCMR) cycle, which provides information on the occurrence of a contaminant. Although PFAS compounds were tested as part of UCMR 3, UCMR 5 is expected to provide more extensive information as labs will be testing more compounds (29) and at lower quantitation limits (2 ppt depending on the compound, including 4 ppt for PFOA and PFOS). UCMR 5 will be major source of PFAS exposure data and will assist in guiding future EPA regulatory decisions.

PACE Analytical will be among the testing labs participating in UCMR 5 and also took part in PFAS testing as part of UCMR 3. The company has invested heavily in LC/MS/MS starting with UCMR 3. "We analyzed probably 100,000 drinking water samples during UCMR 3, and every single one of those samples got tested for PFAS," commented Mr. Jackson. Regarding preparations for UCMR 5, he told IBO, "We are acquiring additional LC/MS/MS for our labs. We already have more on the books for 2022 and more planned for 2023."

LC/MS/MS manufacturers also noted increased interest in solutions for PFAS testing for drinking water for several years. "We have seen PFAS instrument demand significantly increase for the last four to five years driven by proposed changes to EPA regulations," observed Tarun Anumol, Director, Global Environment and Food Markets, Agilent Technologies. "The decision of whether to purchase an instrument or not has been influenced by the knowledge that UCMR5 could probably include PFAS, even from before the EPA announced the final rule," noted Ruth Marfil-Vega, PhD, Senior Market Manager, Environmental, SSI.

Under UCMR5, two LC/MS/MS methods will be used to measure PFAS in drinking water: 537.1 (Determination of Selected Per- and Polyfluorinated Alkyl Substances in Drinking Water by Solid Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry) and the newer 533.1 (Determination of Per- and Polyfluoroalkyl Substances in Drinking Water by Isotop1e Dilution Anion Exchange Solid Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry). As Mr. Jackson explained, "530 7.1 has some inherent limitations that mean we can't detect some of the newer PFAS chemicals at low enough detection limits. As a result, EPA developed 533."

Besides being able to test measure PFAS compounds, LC/MS/MS also enabled detection limits to be reduced. Compared to UCMR 3, when detection limits were set at 40 ppt and 20 ppt for PFAS and PFOA, respectively, UCMR 5 will test at lower detection limits. "Now we're detecting PFAS down to a reporting limit that is pretty standard amongst the labs to do it, not just at PACE, of 2 ppt. So, EPA is including [PFAS] again, but they want to study them at lower levels to potentially ratchet down to even lower-level enforcement limits." PACE's own method detection limit, as opposed to the method detection limit, for PFAS is less than 1 ppt.

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But the EPA's two validated methods for testing PFAS in drinking water have drawbacks. "A challenge that customers are facing, especially in the US, is the limited flexibility incorporated into the methods published by the EPA, so, in some cases, customers cannot take advantage of technological advances," explained Dr. Marfil-Vega. "An example: EPA method 533 and 537.1 require up to a 250-fold sample concentration; however, modern LC/MS/MS systems, such as the Shimadzu LCMS-8060NX, have enough sensitivity to perform the analysis without sample preconcentration." She added, "Eliminating the sample preconcentration step would shorten the analysis time and reduce sources of error. Additionally, methods would be greener and safer as less volume of organic solvents are required."

Agilent has also addressed the sample prep time of the methods. "[C]urrently one of the biggest bottlenecks of PFAS analysis in water is the time and labor required for the sample preparation process to extract the PFAS out of water, and into a suitable organic solvent for analysis on an LC/MS/MS … that can take hours," said Mr. Anumol. "We have developed an online SPE method for automated analysis of PFAS and have seen a good demand for this solution, particularly in labs that are doing PFAS research and want to quantify many PFAS in a fast turnaround time, since this workflow is significantly faster than traditional EPA methods that include offline SPE."

In addition, not all PFAS compounds can be measured using the two methods. "There are four commonly tested PFAS chemicals on the 537.1 list that we can't detect sufficiently well with 533." But Mr. Jackson does expect these four chemicals to be regulated any time soon. "I think it's quite likely or not unlikely that 533 will become the dominant method at some point, especially if those four 537.1 compounds stay low down on the totem pole of potential regulation," he noted.

But what presents greater analytical challenges for PFAS testing is sample types besides drinking water. Here, method development is still ongoing, promising even more demand for LC/MS/MS solutions. "For the first bunch of years the only major matrix we tested was drinking water," observed Mr. Jackson. "But since then PFAS has exploded on the environmental landscape. Now we're testing wastewater influent, effluent, sludge, biosolids, leaching, groundwater, surface water, soil, biota, [and] in fact, concentrated aqueous film forming foam (AFFF), the Class B chemical firefighting foam."

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Testing of PFAS compounds in sample types is being driven by both government and industry, especially in light of regulatory plans. "Public concern has also prompted industry testing due to the potential of PFAS in raw materials or finished products," said Mr. Anumol. "We expect this trend to continue as EPA regulates PFAS with national primary drinking water limits as well as a large demand for testing PFAS in other media like wastewater, soil, air, food and materials where regulation is under consideration."

Other federal agencies besides the EPA have tested for PFAS in other sample types for years and thus have worked to develop LC/MS/MS methods. One of the most significant efforts to develop analytical methods for matrixes such as AFF has been led by the Department of Defense (DoD). "There has long been demand for a standard method to analyze for PFAS in wastewater and soils since the EPA action plan has some new requirements for PFAS monitoring in industrial discharges and also reporting of PFAS which are in wastewater," explained Mr. Anumol. "This along with requirement for the DoD to test water (and soil) on their sites that have historically been contaminated by fire-fighting exercises, and as mandated by certain sections of the National Defense

Authorization Act passed by Congress, is driving demand. The Draft EPA 1633 offers a standardized protocol for wastewater and soil testing of PFAS."

Capable of detecting 40 compounds, Draft 1633 (Analysis of Per- and Polyfluoroalkyl Substances (PFAS) in Aqueous, Solid, Biosolids, and Tissue Samples by LC-MS/MS) is expected to be finalized this year. "The DoD has mandated the use of EPA Draft 1633 from February 2022 for all its contracts so that will increase demand," noted Mr. Anumol. "However, it must be stressed that this method is a DRAFT that is only validated by a single lab and very likely that changes to this method will be made in the next few months as a multi-lab validation is performed."

Draft 1633 will harmonize testing across labs, an important step forward for PFAS testing according to Mr. Jackson. "The only finalized EPA method for PFAS analysis in any matrix are for drinking water," observed Mr. Jackson. "The problem with not having an EPA finalized method for non-potable water, or soil, sludge, etc., is that it leads to variability in the data between labs," he observed. "1633 will enable us to detect 40 [compounds]. So it has 40 PFAS chemicals on that list, but 533 has 25 and 537.1 has 18." He added, "When it becomes a final test method, it will sweep away all of the lab-specific SOPs and modified methods that we've all been using," stated Mr. Jackson. "We'll all immediately switch to using 1633 across the board for the major matrixes for which it is applicable, for which it's critical. That includes non-potable water, soil, sludge [and] biota".

Although new methods advance LC/MS/MS testing of PFAS chemicals, regulatory changes are most important for stimulating instrument purchases, said Dr. Marfil-Vega. "It's important to reiterate that product demand is more driven by regulatory changes than simply the publication of new methods."

DoD has been especially instrumental in advancing PFAS compound testing using LC/MS/MS for samples other than drinking water. "Outside the EPA, the US DoD has also required extensive testing of environmental samples. Furthermore, testing at DoD locations where significant PFAS usage historically has resulted in contamination has also increased demand mainly in the contract labs through award of defense contracts," said Mr. Anumol. But action is taking place across government programs. He provided one example. "We have also recently seen an increase in demand as the EPA PFAS action plan aims to tackle PFAS in wastewater discharges through NPDES [National Pollutant Discharge Elimination System] and other media like air and soil."

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Interest in PFAS compounds in samples besides drinking water has also expanded the types of labs doing PFAS testing. As Dr. Marfil-Vega told ***IBO***, "Growth in demand of LC/MS for the analysis of PFAS from non-research environmental laboratories has been steadily increasing for the past three to five years, including laboratories conducting analysis of drinking water and other environmental samples, such as wastewater, soils, sediments and air.

In addition, market opportunity may lie in the application of more powerful LC/MS/MS techniques, including those for non-targeted analyses. "The most suitable techniques for the analysis of PFAS offered by Shimadzu include LC/MS/MS for accurate and sensitive quantitation of targeted PFAS, with the LCMS 8060NX being the newest instrument in this product line," noted Dr. Marfil-Vega. "We also offer a Q-TOF LCMS, the LCMS-9030, for the analysis of untargeted PFAS, including the discovery of new compounds. This analysis is normally done using suspect screening or non-targeted workflows. In addition, the LCMS-9030 is also suitable of quantitation of targeted PFAS and other contaminants."

Agilent also offers LC/MS techniques with higher sensitivity for expanded PFAS testing. "The use of LC-HRMS techniques like LC-Q/TOF is additionally proving to be a critical development for PFAS analysis and expected to increase in the future," explained Mr. Anumol. "These techniques allow simultaneous quantification of targeted PFAS with standards, but also screening of potentially thousands of PFAS without the need for analytical standards, with the help of databases and libraries along with computation in silico fragment predictors, retention-time models."

However, PFAS testing is not only benefiting demand for LC/MS/MS but also other analytical techniques. "PFAS is an interesting case since it is the first time in decades that EPA is considering adding national primary drinking water limits federally," commented Mr. Anumol. "It is also unique because PFAS is not one compound but a large class of compounds that require different analytical methods and potentially different instruments like LC/TQ, GC/TQ, LC-HRMS and GC-HRMS depending on the media, types of PFAS and detection limits required."

Agilent has also addressed PFAS through other consumables offerings. These include vials, columns, and LC/MS kits that reduce and eliminate PFAS contamination. "We have seen an increase in instrument demand but also in our specific PFAS consumables kits and PFAS applications consulting in these labs."

PACE is also working to develop other methods that do not use LC/MS/MS. "In conjunction with an instrument manufacturer, we've developed a method called Total Orgnao Fluorine (TOF)…It can provide you with a single number of the entirety of all PFAS chemicals that may be present in a sample. It's not LC/MS/MS, which is very much compound specific. It's ion chromatography," said Mr. Jackson. "We're currently under contract to develop a method called absorbable organic fluorine (AOF). The EPA is interested in using that test method potentially to regulate wastewater discharge for all PFAS."

"We also see an increasing demand for volatile PFAS testing especially in air where GC/MS techniques are required."

Among the opportunities to use techniques other than LC/MS/MS for PFAS testing is the testing of air using GC/MS. "We also see an increasing demand for volatile PFAS testing especially in air where GC/MS techniques are required. We also expect EPA to release GC/MS methods for PFAS in air and other media in the future which will drive demand for instruments, sample preparation tools and consumables," said Mr. Anumol. "GC/MS is ideal for measuring smaller and more volatile PFAS as these are hard to analyze by LC/MS. Another benefit is the easy and direct coupling of GC/MS to sample collection and introduction techniques like thermal desorption that allow large sampling and concentration of air in an automated manner."

Standardized methods could increase market opportunities. "EPA is looking into creating standard methods with GC/MS in air and water for these PFAS, so we expect demand to increase for both GC/MSD and GC/MS/MS instruments. This can also be extended into GC-HRMS like GC-Q/TOF that is already being used in research labs to identify newer volatile PFAS," noted Mr. Anumol.

SSI also sees GC/MS demand increased related to PFAS testing. "Shimadzu offers a full line of GCMS instruments, including single and triple quad models, for the analysis of PFAS precursors. And combining the GC/MS with a pyrolyzer or thermal desorption unit allows customers to analyze various PFAS in gas emissions, air and solid samples, like textiles and consumer products," commented Dr. Marfil-Vega. "Finally, Shimadzu is working on new approaches for a more comprehensive analysis of PFAS in diverse samples. But it is too early to share the information about this future alternative."

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Regulatory requirements and/or increased testing for PFAS analysis are also growing beyond environmental contaminants and compounds currently tested for, according to Dr. Marfil-Vega. "There is a lot of work being done on the standardization of methods for PFAS analysis to include more target compounds and types of samples," he said. "More than the changes in the methods, product demand will be driven by regulatory changes and the increased need to respond to the public about occurrence of PFAS in water, foods, consumer products, etc."