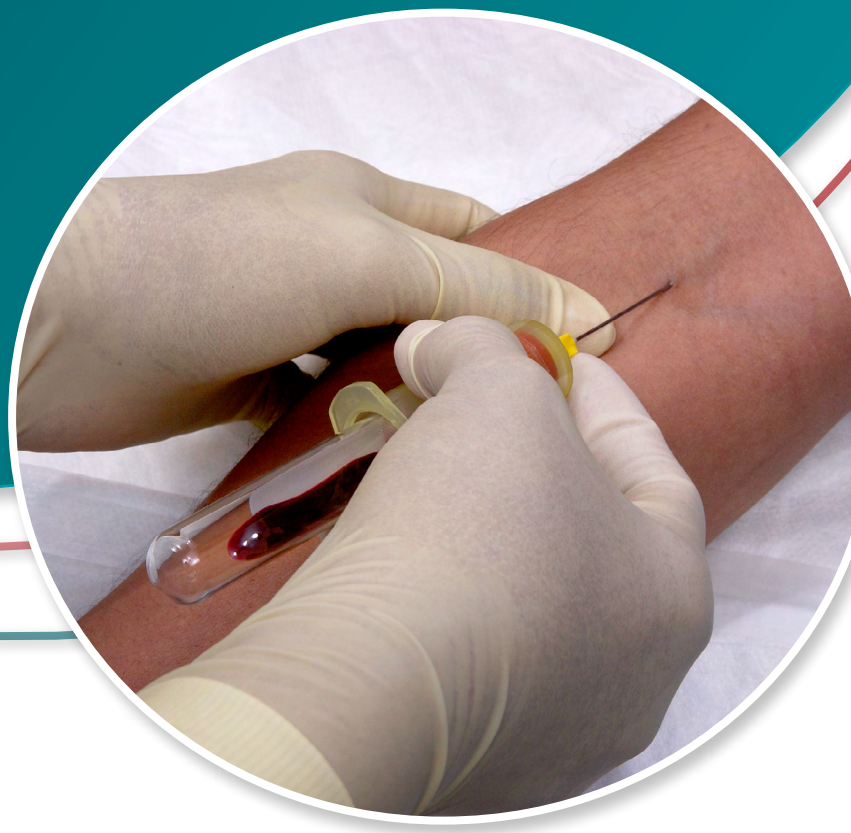
Enhancing PFAS Testing Infrastructure

APHL Recommendations for Clinical Specimens



APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®

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Introduction

Due to growing concerns about per- and polyfluoroalkyl substances (PFAS) contamination and associated health impacts, many laboratories and environmental health partners have initiated PFAS testing and intervention activities. An overarching challenge in formulating a comprehensive PFAS response is the volume of ever-increasing PFAS-related information and initiatives. These efforts can appear to be a patchwork of projects at the local, state and national level, but this approach promotes innovation and allows programs and jurisdictions to prioritize resources focused on problems they deem most important. A considerable amount of data has been produced by these combined efforts; however, identifying the most current and comprehensive data to inform decisions related to policy and practice is difficult and leads to concerns about potential gaps or duplication of effort. Ideally, the positive aspects of current strategies are preserved while developing accurate, consistent and reproducible actions to address human exposure concerns in a timely and efficient manner.

Regardless of a laboratory's current experience and expertise in PFAS testing, it is important for laboratory leadership to understand the recommendations articulated in the 2022 National Academies of Science, Engineering, and Medicine (NASEM) guidance and to identify potential gaps and challenges in their work. The Association of Public Health Laboratories (APHL) has crafted this report to address issues specifically related to PFAS testing in clinical specimens.

Background Reports

In the past two decades, many initiatives and reports about PFAS have been developed to inform public health initiatives. Such work has substantial implications for environmental monitoring and human biomonitoring for PFAS compounds. Examples of this work include:

NASEM: Guidance on PFAS Exposure, Testing and Clinical Follow-Up (2022)

- The Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute of Environmental Health Sciences (NIEHS) funded NASEM to provide an objective review of the current evidence regarding human health effects of PFAS.
- NASEM categorized the strength of evidence for various health effects for PFAS as a class. In addition to the health effects listed by ATSDR, NASEM also found epidemiologic associations with additional health effects.

ATSDR: PFAS Information for Clinicians (2024)

- Overall, significant investment in the infrastructure of public health is necessary to fully address PFAS, including development of expertise in vital disciplines including laboratory science, epidemiology and toxicology.
- A strategy to coordinate ongoing PFAS response efforts and incorporate new initiatives at local, state, and federal levels is needed to improve community resiliency and reduce or eliminate future exposures.
- ATSDR will continue to review the science and periodically update this information.

EPA: Final PFAS National Primary Drinking Water Regulation Fact Sheet

- On April 10, 2024, the US Environmental Protection Agency (EPA) announced the final National Primary Drinking Water Regulation (NPDWR) for six PFAS. To inform the final rule, EPA evaluated over 120,000 comments submitted by the public in response to the proposed rule and considered input received during multiple consultations and stakeholder engagement activities held both prior to and following the proposed rule. EPA expects that over many years the final rule will prevent PFAS exposure in drinking water for approximately 100 million people, prevent thousands of deaths and reduce tens of thousands of serious PFAS-attributable illnesses.
- The Bipartisan Infrastructure Law helps states and territories implement PFAS testing and treatment at public water systems and to help owners of private wells address PFAS contamination via EPA's Emerging Contaminant in Small and Disadvantaged Communities state and territories grant program, providing $5 billion in fiscal years 2022-2026.

- Through the NPDWR EPA established legally enforceable levels, called Maximum Contaminant Levels (MCLs), for six PFAS in drinking water: PFOA, PFOS, PFHxS, PFNA and HFPO-DA as contaminants with individual MCLs, and PFAS mixtures containing at least two or more of PFHxS, PFNA, HFPO-DA and PFBS using a Hazard Index MCL to account for the combined and co-occurring levels of these PFAS in drinking water. EPA also finalized health-based, non-enforceable Maximum Contaminant Level Goals (MCLGs) for these PFAS (**Table 1**).

Table 1. 2024 National Primary Drinking Water Regulation (NPDWR) Maximum Contaminant Levels (MCL) and Maximum Contaminant Level Goals (MCLG) for PFAS

Compound	Final MCLG	Final MCL (enforceable levels)
PFOA	Zero	4.0 parts per trillion (ppt) *Also expressed as ng/L*
PFOS	Zero	4.0 ppt
PFHxS	10 ppt	10 ppt
PFNA	10 ppt	10 ppt
HFPO-DA *Commonly known as GenX Chemicals*	10 ppt	10 ppt
Mixtures containing two or more of: PFHxS, PFNA, HFPO-DA or PFBS	1 (unitless)	1 (unitless)
	Hazard Index	Hazard Index

- In early 2025, EPA announced their intent to update the rule based on industry and community feedback. The revised rule projected for fall 2025, is expected to maintain the MCLs for PFOA and PFOS but delay implementation and reconsider the other facets of the rule.

EPA National PFAS Testing Strategy: Identification of Candidate PFAS for Testing (2021)

EPA Report Excerpt: "Phase IA is focused on human health data collection. EPA will initiate Phase IA by the end of 2021 using TSCA Section 4 authorities. Then, in Phase IB, EPA will refine the initial structural categories using mechanistic and toxicokinetic data from EPA Office of Research and Development (ORD) as well as further evaluation of degradation products and exposure data (e.g., environmental monitoring, biomonitoring). The EPA expects to issue further Toxic Substances Control Act (TSCA) Test Orders after the categories are refined. The process for refining and issuing Test Orders will be an iterative process as testing data is submitted to the Agency. In the second Phase of the Strategy (Phases IIA and IIB), EPA expects to use the category approach described above to inform ecological toxicity testing needs."

EPA Unregulated Contaminant Monitoring Rule (UCMR 5)

Published on December 27, 2021, the UCMR 5 requires sample collection for 30 chemical contaminants between 2023 and 2025 using analytical methods developed by the EPA and consensus organizations. This action provides the agency and other interested parties with scientifically valid data on the national occurrence of these contaminants in drinking water. UCMR 5 will provide new data that will improve the agency's understanding of the frequency that 29 PFAS and lithium are found in the nation's drinking water systems, and at what levels.

EPA/APHL: Centers of Emerging Contaminants Testing (Proposal)

The formation of a small, coordinated network of qualified principal state laboratories working together with EPA programs and regional laboratories has been proposed to bridge the gap between EPA work and utility and commercial laboratories.

EPA: Proposal to List Nine Per- and Polyfluoroalkyl Compounds as Resource Conservation and Recovery Act Hazardous Constituents

On February 8, 2024, EPA proposed changes to the Resource Conservation and Recovery Act (RCRA) regulations by adding nine specific per- and polyfluoroalkyl compounds, their salts, and their structural isomers, to its list of hazardous constituents in Title 40 of the Code of Federal Regulations Part 261 Appendix VIII. These nine PFAS are:

- Perfluorooctanoic acid (PFOA or C8)
- Perfluorooctanesulfonic acid (PFOS)
- Perfluorobutanesulfonic acid (PFBS)
- Hexafluoropropylene oxide-dimer acid (HFPO-DA or FRD-903)
- Perfluorononanoic acid (PFNA)
- Perfluorohexanesulfonic acid (PFHxS)
- Perfluorodecanoic acid (PFDA)
- Perfluorohexanoic acid (PFHxA)
- Perfluorobutanoic acid (PFBA)

CDC/ATSDR: PFAS Exposure Assessments

The US Centers for Disease Control and Prevention (CDC) and ATSDR conducted exposure assessments (EA) in communities known to have had PFAS contamination in their drinking water. The amount of PFOA and PFOS in the drinking water in these communities, located near current or former military bases, exceeded the EPA's 2016 health advisory of 70 parts per trillion and/or applicable state guidelines in the past. The primary goal of these EAs was to provide information to communities about levels of PFAS in their bodies. Results allow CDC/ATSDR to provide recommendations to reduce exposure. CDC/ATSDR will also use the data collected from these EAs to help inform future studies on PFAS exposure.

National Biomonitoring Network (NBN) Laboratories

- Many state programs conducting biomonitoring for PFAS compounds have done so as part of a response that includes site-specific investigations based on identification of environmental contamination through environmental monitoring or through other avenues.
- In some cases, state biomonitoring programs have included PFAS compounds as part of their population-based surveillance for potentially harmful environmental exposures.

DoD: PFAS DATA—Cleanup of PFAS

- The US Department of Defense (DoD) investigates potential releases of PFAS from current or former US Military installations and determines the appropriate cleanup actions based on risk.
- Through September 30, 2024, the DoD has determined that 722 active military installations, Base Realignment and Closure (BRAC) locations, National Guard facilities, and Formerly Used Defense Sites (FUDS) properties require an assessment of PFAS use or potential release. DoD is performing Preliminary Assessments/Site Inspections (PA/SIs) at these installations, which is the first phase of the cleanup process and may take two to three years to complete.
- As of September 30, 2024, DoD has completed the PA/SI phase at 712 installations. The Department has determined that no further action is required at 131 of these installations, while 581 are proceeding to the next step in the CERCLA process.
- DoD will prioritize sites to move to the next phase in the cleanup process (i.e., Remedial Investigation (RI)) and determine appropriate cleanup actions based on risk.

PFAS Related Litigation

- 'Forever chemicals' were everywhere in 2023. Expect more litigation in 2024 (December 2023 (*Reuters*): Lawsuits accusing major chemical companies of polluting US drinking water with toxic PFAS chemicals led to over $11 billion in settlements in 2023, with experts predicting that new federal regulations and a growing awareness of the breadth of PFAS contamination in the US will spur more litigation and settlements in the year ahead [2024].
- Mass tort litigation to watch in 2025 (December 2024, *Reuters):* Thousands of personal injury claims remain pending by people who say they developed cancer from exposure to PFAS, mostly from people exposed to firefighting foam that contains the chemicals and is widely used in training exercises, either while working as firefighters or at airports where firefighters train. Most of the claims are centralized in federal court in South Carolina, where the first bellwether trials are scheduled to begin next year [2025].

US GAO: Persistent Chemicals: Technologies for PFAS Assessment, Detection and Treatment

From the US Government Accountability Office (2022):

- Current and promising technologies and methods could accelerate assessment of human health effects caused by PFAS and improve the detection and treatment of PFAS in the environment. Technologies that may accelerate assessment of PFAS health effects include high-throughput assays—automated testing methods that rapidly evaluate many chemicals—and machine learning, which may help improve on technologies that predict health effects based on the effects of similar molecules. New detection methods include high-resolution mass spectrometry (HRMS) and total fluorine analysis.
- However, these technologies and methods face key challenges that hinder effective management of PFAS. PFAS chemical structures are diverse and difficult to analyze for health risks, and machine learning requires extensive training data that may not be available. Researchers lack analytical standards for many PFAS, limiting the development of effective detection methods.

Laboratory Analysis for PFAS Testing

Quality laboratory analyses are a cornerstone of both environmental public health and clinical practice. While both disciplines share the goal of improved health, whether it be for a community or for an individual patient, the context around specimen collection and application of results is distinctive and therefore definitions of the various techniques used are necessary.

Public health practice benefits from employing biomonitoring. Biomonitoring is the assessment of individual and population exposures to environmental contaminants by measuring the concentration of chemicals and/or their metabolites in human specimens. Biomonitoring identifies and quantifies chemicals in the human body to provide scientific evidence of the degree of exposure to a particular chemical. When combined with subsequent trend analysis, demographic, and other contextual information, this information improves understanding of the relationship between exposure to environmental chemicals and their impact on health so that comprehensive exposure assessments may be developed. These assessments may help identify potentially harmful exposures, and this information can then lead to a reduction or elimination of these exposures.

Clinical medicine relies on laboratory analyses such as clinical screening or diagnostic testing. While clinical testing is similar in technique to biomonitoring, the utility of clinical testing differs based on the questions a test is designed to help answer. Screening tests are typically administered in cases where an association exists between a particular test result and a potential increased risk for an adverse health outcome in persons who are not currently displaying any signs or symptoms of that adverse condition. Conversely, a diagnostic test is administered to a symptomatic individual to help rule-in or rule-out a possible cause.

When used within the proper context, each of these practices—biomonitoring, screening and diagnostic testing—all provide valuable information to answer important health questions.

Project Scope and Design

In August 2023, consulting work began on behalf of APHL to coordinate and assist with PFAS recommendations for environmental public health laboratories. The project's intent was to draft an analytical testing plan for public health laboratories regarding clinical PFAS testing in response to increasing needs, articulated in the 2022 NASEM guidance.

One component of the project was a review of current PFAS response activities and related references, including NASEM's 2022 *Guidance on PFAS Exposure, Testing, and Clinical Follow-Up* and ATSDR's 2024 *PFAS Information for Clinicians*.

Additional project information came through online interviews and conference calls with state and federal experts on biomonitoring and PFAS-related activities. A request was made at the October 23, 2023 NBN Quarterly Conference Call through an informal survey inquiring as to current PFAS testing capabilities of NBN laboratory members and soliciting opportunities to discuss these activities including gaps and challenges. This request led to several state programs offering support for the project. Members of the NBN Steering Committee (NBNSC) also agreed to assist with the project.

Significant input was obtained at the 2024 National Biomonitoring Meeting (NBM), held in Honolulu, Hawai'i in January 2024. At this meeting draft recommendations were presented to attendees, followed by a series of roundtable discussions intended to identify information gaps and known challenges in PFAS response activities. Afterward, the NBNSC reviewed and discussed input from the NBM roundtable discussions to refine recommendations and PFAS biomonitoring action items.

Likewise, the joint meeting for APHL's Environmental Health and Environmental Laboratory Sciences Committees in March 2024 afforded another opportunity to promote discussion and elicit expert input related to these recommendations.

The feedback and input obtained through the avenues described above and an opportunity to meet and discuss this information with the NBNSC proved valuable and significant. This information was reviewed, discussed and assimilated into this final report, the main deliverable for this APHL project.

Recommendations

Seven APHL recommendations for expanding and improving PFAS testing of clinical specimens are followed by sections of supporting information, including related referenced guidance content from two primary source documents, NASEM's *Guidance on PFAS Exposure, Testing, and Clinical Follow-Up* and ATSDR's *PFAS Information for Clinicians*. The recommendations may be categorized into areas of funding investments, quality management systems, testing activity coordination, method and data harmonization and data accessibility.

1: Identify public health laboratory roles in coordinating and harmonizing PFAS testing for more complete exposure assessments

Challenges to Implementation

- Available literature on PFAS documents many sources of PFAS exposure that can vary widely between communities and individuals depending on environmental contamination, location, occupation and lifestyle choices. Therefore, identifying the comprehensive scope of potential and actual external exposure is difficult.
- Biomonitoring of individuals to identify which compounds are present and in what concentration helps identify potentially harmful exposures when paired with robust demographic, occupational and recreational exposure information. Currently, funding levels are insufficient to support a robust PFAS biomonitoring response in affected jurisdictions or to support environmental health surveillance.
- Private residence drinking water wells are not typically included in state and federal drinking water or other environmental monitoring, leading to gaps in exposure data for a significant number of US communities.

Consequences for Not Implementing or Pursuing

- A key outcome in assessing and identifying environmental exposures is identification of the source of contamination followed by targeted contamination reduction or elimination efforts. Without assessment and identification of the contamination source, exposures will continue unmitigated with the potential to negatively impact health outcomes.
- Inadequate exposure assessments can lead to a diminished ability to prioritize limited resources for an appropriate PFAS community response.
- Conducting exposure assessments is needed for identifying and addressing community concerns.
- Without sufficient foundational exposure data, it is difficult to make a case for additional and ongoing resources for testing to identify and mitigate risks.

Potential Implementation Strategies

- Define environmental exposure assessment practices and the role of public and environmental health programs, including biomonitoring and environmental monitoring, to facilitate partnership with the medical community and enhance awareness of environmental health issues and strategies .
- Utilize individual exposure assessment data to enhance personal knowledge for informed personal decision making that can reduce or eliminate exposures to PFAS compounds.
- Collect, compile, and analyze data from community-level exposure assessments to formulate public health recommendations that are communicated to community leaders and policy makers.
- Identify public health laboratory roles in coordinating and harmonizing PFAS testing for more complete exposure assessments.

- Support funding to increase quality, capability and capacity for initiating and maintaining PFAS analyses. This includes the following areas:
    - Biomonitoring
    - Environmental Monitoring
        - Water (e.g., drinking water, source water, wastewater)
        - Private well water (separate because typically not regulated)
        - Air
        - Food
        - Consumer products
- Include guidelines for harmonizing data and coordinate monitoring and access to provide a comprehensive picture for any given affected community and between affected communities to prevent disparities or environmental justice concerns.
- Identify and outline the various roles of public health laboratories (both environmental monitoring and biomonitoring) in environmental exposure assessments or otherwise informing communities and potentially exposed individuals about external and internal exposure levels.
- Increase and improve coordination of monitoring efforts, in both environmental and clinical matrices, within and between jurisdictions to address data and information gaps.
- Provide data necessary for identifying and responding to community concerns.
- Establish a comprehensive PFAS testing and evaluation plan to identify exposures to help secure and prioritize funding and other resources.
- Provide technical assistance regarding quality management practices for laboratories considering clinical screening.

Related Referenced Guidance Content

- **NASEM Recommendation 4-1:** Clinicians advising patients on PFAS exposure reduction should begin with a conversation aimed at first determining how they might be exposed to PFAS (sometimes called an environmental exposure assessment) and what exposures they are interested in reducing. This exposure assessment should include questions about current occupational exposures to PFAS (such as work with fluorochemicals or firefighting) and exposures to PFAS through the environment. Known environmental exposures to PFAS include living in a community with PFAS-contaminated drinking water, living near industries that use fluorochemicals, serving in the military, and consuming fish and game from areas with known or potential contamination.
- **ATSDR Exposure History:** The goals of an exposure history are to:
    - Identify current and past pfas exposures
    - Assess the duration, magnitude, and routes of exposure
    - Help patients understand how they have been exposed
    - Determine if current exposures can be reduced.

2: Improve partnerships between environmental health and public health programs and clinical medicine

Challenges to Implementation

- Historical disconnect between environmental public health and clinical practice has led to gaps in understanding and addressing the clinical manifestations of environmental health issues.
- Increased input is needed from biomonitoring programs to develop comprehensive educational materials for clinicians. Such information should include testing methods, access to relevant environmental data on potential exposures, relevant biomonitoring investigations results and conclusions.
- The lack of sufficient testing leads to a gap in achieving a comprehensive "one health" response to contaminated communities to address major and minor sources of exposure such as food, water, air and occupational exposures.
- PFAS biomonitoring informs approaches to other environmental contamination incidents and public and environmental health responses and therefore may alert the medical community of potential exposures and emerging health issues.

Consequences for Not Implementing or Pursuing

- Failure to improve the healthcare community's understanding of environmental public health exposures and associated risks perpetuates information gaps and limits the ability to work cooperatively to improve public and individual health.
- To address the extensive nature of PFAS contamination, exposures and potential health effects, an improved relationship between environmental public health and the healthcare community is necessary for success.
- Future responses to chemical contamination events will be affected by the willingness to address and improve the current relationship between environmental health and healthcare.

Potential Implementation Strategies

- Work towards improved partnerships between environmental health and public health programs and clinical medicine.
- Partner with other professional public health organizations (e.g., Association of State and Territorial Health Officials (ASTHO), National Association of County and City Health Officials (NACCHO), Environmental Council of the States (ECOS), Council of State and Territorial Epidemiologists (CSTE), etc.) and other professional groups (e.g., American Academy of Pediatrics (AAP), American Medical Association (AMA), American Nurses Association (ANA), etc.) to help establish national guidelines or expectations for a coordinated, interdisciplinary response to PFAS.
- Identify partners to explore awarding continuing education units (CEU) and continuing medical education (CME) credits for public and environmental health workshops focused on environmental exposures, exposure assessments, biomonitoring strengths and limitations, sources and interpretation of quality exposure related data (e.g., biomonitoring and environmental monitoring). APHL and NBN member laboratories should Identify partners to help develop and offer CME offerings on environmental health topics for medical providers.
- Identify ways clinical medicine can inform environmental and public health practice related to environmental exposures and an understanding of clinical practice patient engagement and follow-up (i.e., standard of care and biomarker of effect testing).
- Find ways for environmental health programs to partner with the medical community to provide education and promote important tools such as biomonitoring and clinical screening.
- Promote public health laboratory and biomonitoring activities more broadly in universities, schools of public health, and schools of medicine/clinical practice.
- Support efforts to reinstate required environmental health training in medical and public health education.

- Explore opportunities for NBN program members to serve as adjunct faculty for Environmental Public Health and Environmental Medicine programs within their jurisdictions.
- Outline core competencies related to biomonitoring and environmental monitoring to ensure environmental exposure assessments, public health laboratory testing processes, and results interpretation and application are well understood.

Related Referenced Guidance Content

- **NASEM Recommendation 5-1:** As communities with PFAS exposure are identified, government entities (e.g., CDC/ATSDR, public health departments) should support clinicians with educational materials about PFAS testing so they can discuss testing with their patients.
- **ATSDR:** Communities around the US have been concerned about possible health effects from PFAS exposure and have been looking to healthcare providers for counseling and support related to PFAS exposure.

3: Increase access to quality PFAS testing and ensure proper sample collection for exposed populations

Challenges to Implementation

- Testing of human specimens for PFAS is resource intensive and represents high complexity testing that requires an investment in laboratory instrumentation and equipment, and sufficient expertise in laboratory methods to provide sample collection guidance.
- Knowledge of partner disciplines such as epidemiology, toxicology and clinical medicine are necessary to provide results interpretation and reporting.
- Proper sample collection techniques and documentation are necessary to ensure sample and results integrity. Proper matrix selection is also vital to safeguard the accuracy and comparability of testing results within and between testing jurisdictions.

Consequences for Not Implementing or Pursuing

- Failure to address current limitations in testing capabilities and capacities may exacerbate health impacts and community concerns. Specifically, inaction could lead to disparities in access to health information and medical care.
- Laboratories not engaged in rigorous quality management practices such as those outlined in the NBN Strategy for Harmonization of Laboratory Measurements may generate unreliable testing results.

Potential Implementation Strategies

- Explain the distinction between biomonitoring, clinical screening, and diagnostic testing for PFAS.

From APHL Guidance (Biomonitoring):

- Work with biomonitoring programs to increase access to quality serum PFAS testing for exposed populations.
- CDC National Center for Environmental Health (NCEH) and NBN should establish and communicate a robust and comprehensive set of minimum requirements for performance-based methods including minimum Limit of Quantitation (LoQ), Quality Control (QC) and acceptance criteria for reporting harmonized data for an established PFAS analyte list based on National Health and Nutrition Examination Survey (NHANES).

- Quality Assurance (QA)/QC efforts need to address acceptable specimen types, sample collection materials and protocols to minimize contamination, ensure accurate measurements and emphasize data harmonization.
- Generalize the PFAS method and data harmonization criteria for other environmental contaminants.
- Promote the role of biomonitoring for response and biosurveillance activities and the benefits of biomonitoring to evaluate exposure mitigation and public health intervention efforts.
- Consider approaches of other networks (e.g., Laboratory Response Network for Chemical Threats (LRN-C), Human Health Exposure Analysis Resource (HHEAR), Human Biomonitoring for Europe/Partnership for the Assessment of Risks in Chemicals (HBM4EU/PARC)).
- Address additional testing capabilities and capacities in a way that scales up testing quantity and quality. Quality testing will yield data that is amenable to harmonization and sharing to improve individual and public health. The NBN should provide leadership and support to public health laboratories and other laboratories looking to add PFAS biomonitoring capabilities to not only provide the needed additional capacity, but also to harmonize data generated so that results can be compiled across jurisdictions.
- Expand PFAS testing capabilities and capacities in response to specific community investigations. There would be value in having this testing capacity then used for ongoing population-based PFAS surveillance to monitor trends and the effectiveness of exposure mitigation/public health intervention efforts.
- Consider ways to partner with the clinical practice/medical community to evaluate biomonitoring prioritization plans and to possibly triage groups of individuals for testing (e.g., patients identified/concerned over high environmental exposures).
- Partner with health departments and other programs working to address community concerns by identifying opportunities to offer biomonitoring to exposed and underserved communities.

Related Referenced Guidance Content

- **NASEM Recommendation 5-2:** Clinicians should offer PFAS testing to patients likely to have a history of elevated exposure. In all discussions of PFAS testing, clinicians should describe the potential benefits and harms of the testing and the potential clinical consequences (such as additional follow-up), related social implications, and limitations of the testing so that patient and clinician can make a shared, informed decision.

- **ATSDR:**
  - In deciding whether to order PFAS testing, clinicians can consider:
    - An individual's exposure history
    - Results of PFAS testing from the patient's water supply, food sources, or other exposure routes
    - Whether results can inform exposure reduction and health promotion.
  - PFAS Blood Testing:
    - Systematic, community-wide blood testing can enable public health officials to investigate and respond to community-wide exposures. Results from these tests can assess the types and blood levels of PFAS in the community. (Blood PFAS is the accepted biomarker of exposure for PFAS studies, but some investigations have also included urine testing.)
    - Clinicians can order PFAS blood levels through Clinical Laboratory Improvement Amendments of 1988 (CLIA)-certified* commercial clinical laboratories. Results (current levels of PFAS in the blood) could reflect recent exposures or past exposures in the case of PFAS with long half-lives.

4: Support appropriate use of NASEM and ATSDR guidance to improve current response to PFAS exposure and advance biomonitoring

Challenges to Implementation

- For environmental public health, the causal link between chemical exposures and adverse health outcomes remains a tenuous one. While PFAS have been and continue to be well studied both in controlled laboratory animal studies and epidemiological studies, the complex nature of chronic disease etiology leads to high degrees of uncertainty. The NASEM report demonstrates a reasonable approach for linking exposure with potential adverse health effects and lays out many of the processes used in decision making. However, some decisions, such as the summation approach may need further examination and explanation.
- Without an overarching federal agency endorsement, some biomonitoring programs, as well as some clinicians may be reluctant to fully implement this recommendation.
- The fact that the science of PFAS continues to evolve means that consideration needs to be given to not only how to implement this recommendation, but also how to do so in a manner that allows for enough flexibility to adjust the risk information as appropriate to account for new information.
- The summation method for the analytes included in this recommendation seems to be a novel approach that may require some additional explanation and evaluation. Another method that may be considered as more data on additional PFAS analytes becomes available is relative potency factor approach like that used to consider risk from other complex families of contaminants such as polycyclic aromatic hydrocarbons (PAHs).
- The ability to distinguish the highest exposed individuals within the investigated population to both best utilize response resources as well as intervene in part of the affected individuals is needed to improve community health and improve public and environmental health practice.
- Determination of the "level" of testing (biomonitoring vs. clinical screening vs. diagnostic testing, see APHL Recommendation 3) and testing stringency (e.g., Limit of Detection, Limit of Quantitation, Quality Assurance, and Quality Control) is needed to ensure that tested individuals will receive accurate and, if needed, actionable results.

Consequences for Not Implementing or Pursuing

- The NASEM report is a public report and programs that are biomonitoring for PFAS in affected communities may receive inquiries or feedback from study participants or community leaders asking why NASEM report recommendations are not being implemented as part of the study design.
- A needed step in the evolution of biomonitoring practice is the establishment of reference ranges and risk levels to put the concentration of measured biomarkers of exposure into a context related to potential health outcomes. While these NASEM levels may be open to debate, they do serve as a starting point derived from a robust set of data and through a reasonable and transparent expert committee process. Failure to incorporate and discuss this information in some constructive manner may result in fewer future efforts for organizations to develop these needed actionable levels. When copious data is being collected for PFAS, which is such an active level of concern and research, the question of what threshold needs to be met in order for biomonitoring and environmental public health programs to endorse using derived risk levels arises.

Potential Implementation Strategies

- Identify potential partners to develop and refine risk-based biomarkers of exposure to move the science and practice of environmental health forward to a more effective understanding of exposures and adverse health outcomes.
- Establish reference ranges and internal exposure risk levels to effectively identify at-risk individuals and communities and reduce or eliminate future exposures.

- There is an ever-growing body of information related to potential PFAS health effects including in vitro, laboratory animal, and human epidemiological studies. While the specific levels set may be the subject of debate, the committee has outlined a reasonable approach based on the available information and was transparent in their processes and decision making. More context on the potential major and minor sources of exposure is needed to help combine internal and external exposure levels into a more complete picture of risk. An appropriate use of these ranges as a link to adverse outcomes is an important next goal for biomonitoring practice.

Related Referenced Guidance Content

- **NASEM Recommendation 5-3:** Clinicians should use serum or plasma concentrations of the sum of PFAS* to inform clinical care of exposed patients, using the following guidelines for interpretation:
  - Adverse health effects related to PFAS exposure are not expected at less than 2 nanograms per milliliter (ng/mL).
  - There is a potential for adverse effects, especially in sensitive populations, between 2 and 20 ng/mL.
  - There is an increased risk of adverse effects above 20 ng/mL.
- **ATSDR:** Health effects potentially associated with PFAS exposure include increases in cholesterol levels, decreases in birth weight, lower antibody response to vaccines, kidney and testicular cancer, pregnancy-induced hypertension, preeclampsia and changes in liver enzymes. No concentration-based risk levels provided.

* Simple additive sum of MeFOSAA, PFHxS, PFOA (linear and branched isomers), PFDA, PFUnDA, PFOS (linear and branched isomers) and PFNA in serum or plasma. **Caution is warranted when using capillary blood measurements as levels may differ from serum or plasma levels.**

5: Explore scenarios for clinical testing of children to identify PFAS exposures

Challenges to Implementation

- Typically, biomonitoring studies that include children rely on non-invasive sample collection techniques such as those used for urine sample collections. Urine is not an appropriate specimen type for PFAS analysis. The challenges related to including children in studies relying on blood collection are well known.
- The NASEM report includes information suggesting potential risks for children with higher exposure to PFAS. Therefore, the general concerns related to biomonitoring in children may be reconsidered. However, anxiety over logistical challenges as well as study participation remain. In some jurisdictions where children have been recently given the opportunity to participate in biomonitoring studies there continues to be a low participation rate.
- Apart from a program like childhood blood lead, for many environmental contaminants, biomonitoring rarely includes children when the preferred sample is a blood collection.
- Results in children represent an exposure that has already occurred. Identifying exposed children can prevent further exposure to the same source. Additionally, improved exposure data will help assess how health is affected by exposures during developmental phases of life.

Consequences for Not Implementing or Pursuing

- The benefit of including children depends on what the measured results might show regarding exposure levels and whether there is a way to follow highly exposed children prospectively. Good PFAS laboratory data on children is lacking; if we do not move forward to include children in biomonitoring these data gaps will remain. Given the potential for PFAS health effects, not informing children/parents of higher exposures may have long term consequences, especially if absence of data results in a lack of sufficient exposure mitigation activities.

- As work continues to better understand potential adverse health effects from PFAS exposures in all age groups, the question of the benefit for including children in PFAS biomonitoring studies may shift in favor of testing to follow up and intervene prior to adulthood.
- Biomonitoring results are a snapshot of exposure at the time of specimen collection. For compounds with longer biological half-lives (e.g., PFAS), biomonitoring results can also represent a snapshot of an individual's historical exposures. However, it may still be of value to identify those within highest exposure groups for which their exposures occurred at key developmental stages, such as those impacting the developing fetus and during early childhood. The impacts of PFAS on childhood and early adulthood development need additional study, as well as the potential for latent adverse health effects following early life exposures.

Potential Implementation Strategies

- **Collect an additional specimen at the time blood is collected for medically indicated testing.**
- Test children to identify PFAS exposures in areas of known PFAS contamination. This may be of greater importance in areas where resources are limited for families with children to invest in home-based water filtration or access to known sources of PFAS-free water.
- Explore the impact of children's environmental exposures and possible associated adverse health effects related to PFAS and other contaminants further.

Related Referenced Guidance Content

- **NASEM Recommendation 5-4:** The National Health and Nutrition Examination Survey should begin collecting and sharing more data on children younger than 12 years of age and pregnant people to generate reference populations for those groups.
- **ATSDR:** PFAS can be found in human breast milk. Due to the many benefits of breastfeeding, CDC and the American Academy of Pediatrics recommend that most nursing people continue to breastfeed. More information on breastfeeding is available from:
    - ATSDR: Breastfeeding and PFAS
    - CDC: About Breastfeeding

6: Consider the value of including biomarkers of effect in addition to biomarkers of exposure

Challenges to Implementation

- Additional resources are needed to provide these "biomarker of effect" tests; biomonitoring programs would need increased expertise to interpret and provide the results to study participants and patients.
- Most "biomarkers of effect" are non-specific to a particular chemical exposure and need to be properly interpreted as part of a comprehensive clinical assessment.

Consequences for Not Implementing or Pursuing

Without these follow up test results, data gaps will continue to exist between exposure data and potential adverse health outcomes.

Potential Implementation Strategies

- Biomonitoring practices include the measure of biomarkers of exposure and related context. One way to link environmental exposures to adverse health outcomes is to better understand the relationship between these biomarkers of exposure and biomarkers of effect.
- How might an increased or otherwise improved understanding of this relationship between these markers of exposure and effect be informed by biomonitoring data?
- These NASEM recommendations focus on clinical practice. Of interest for biomonitoring is that some of the potentially used tests seem to straddle the concepts of "biomarkers of exposure" versus "biomarkers of effect," such as thyroid function tests, blood pressure screening, cholesterol, or liver enzyme measurements. Some public health laboratories might be testing or considering testing for these additional parameters (internally or through subcontracting with clinical laboratories). It may be of value to identify how these additional test results might inform exposed populations regarding medical follow up and long-term evaluation. Information related to these additional tests for biomarkers of effect might lead to potential changes to questionnaires used in study design.
- The Partnership for the Accurate Testing of Hormones (PATH) testing guidelines would be helpful if public health laboratories are considering this type of measurement .

Related Referenced Guidance Content

- ***NASEM Recommendations 6-1, 6-2, 6-3:*** *Clinical follow-up and management based on biomonitoring measurement results.*
- **ATSDR:** Patients and clinicians can discuss the potential risks and benefits of using PFAS blood testing results to guide clinical management. Considerations include:
  - Factors unique to the patient, including the patient's risk for disease
  - Whether health screening beyond the usual standards of care is appropriate
  - The potential for unnecessary further testing and treatment related to false positives from additional screening tests.

7: Increase access to PFAS testing data to better identify and reduce exposures in individuals and affected communities

Challenges to Implementation

- Required reporting is resource intensive and requires sufficient infrastructure to not only accurately and securely record and store the data, but also to evaluate the information and make it accessible for appropriate purposes.
- Improved exposure surveillance for PFAS (or other environmental contaminants) would improve public and environmental health practice, but a cost-benefit analysis of utilizing resources needed to make a test result reportable needs to be assessed.
- The number of resources required to generate relevant environmental exposure data needs to be matched by resources earmarked for making the data compatible and accessible so all communities-at-risk may be identified, their concerns addressed, and the exposures mitigated.
- Data from multiple laboratories would need to be harmonized to ensure results are consistent and comparable. Sufficient metadata would need to be captured to provide context and identify and track sample collection and types, methodology, instrumentation, and technology, LOQ, etc.

> **"The reason for collecting, analyzing and disseminating information on a disease is to control that disease. Collection and analysis should not be allowed to consume resources if action does not follow."**
>
> Foege, et. al., Int J of Epidemiology 1976; 5:29-37

Consequences for Not Implementing or Pursuing

- Data are central to decision-making and funding requests. The lack of a central repository for biomonitoring data related to PFAS exposures results in knowledge gaps related to risk and geography. This could lead to inconsistencies in response such as lack of funding for all exposed communities in need of mitigation activities.
- Lack of access to quality harmonized PFAS data is essentially the same as if the data were not generated at all. Ensuring that environmental and public health professionals, clinical practitioners, and community officials have access to the information needed to make informed decisions should be a prioritized effort.

Potential Implementation Strategies

- Develop a comprehensive registry of PFAS exposure data to move the response to these environmental contaminants forward. Centralizing data collection, storage, and access is paramount to ensuring that the scope of the increasing amount of human biomonitoring data related to PFAS exposures can be captured and communicated. With testing for PFAS not only increasing at federal and state environmental public health laboratories, but also from commercial laboratories, using an established mechanism such as the EPH Tracking Network is needed to address the need for collated, quality, curated data. However, EHPTN is designed as a public health surveillance tool and currently relies on standardized data for exposures. That data is based on sources such as EPA standard methods from ongoing regulatory programs and standard reporting of health effects from clinical practice. The challenge for including biomonitoring data in such a repository, is that it includes the testing purpose (biomonitoring—community investigation, environmental health surveillance or clinical screening) different methodologies, analyte lists and reporting limits. Additionally, some biomonitoring is used for ongoing population surveillance and sometimes for site or community specific investigations or studies.
- Utilize an existing network such as the NBN and supporting processes such as setting results reporting requirements and or establishing an exposure or disease registry to help identify trends regionally and at the national level.
- Consider ways to work with commercial laboratories to provide results to appropriate jurisdictions like the use of commercial laboratories for childhood blood lead testing with results reported to state level programs.

- Consider the strengths and challenges of potentially exposed and affected individuals gaining access to testing. Ensuring consistent, comparable, and quality testing results are obtained so that they can be shared is a challenge. There are recognized strengths in a shared network approach such as NBN, LRN-C or HHEAR, but there are also recognized challenges in data harmonization and sharing.
- Define scenarios when a PFAS exposure registry might inform not only individual follow-up, but also the broader understanding and association of any potential latent/chronic health effects (e.g., the NIOSH Firefighter registry, 9/11 registry).

Related Referenced Guidance Content

- **NASEM Recommendation 8-1:** Laboratories conducting PFAS testing of serum or plasma should report the results to state public health authorities, following the respective states' statutes and reporting regulations. This reporting would improve PFAS exposure surveillance; it could be linked with CDC's environmental public health tracking network and help build capacity for improvements in the state-based national biomonitoring network.
- **ATSDR:** No specifications for reporting of PFAS testing results from clinical recommendations.

Conclusion

State public health authorities currently lack the infrastructure, resources and authority to require reporting of PFAS results but could implement them with sufficient support and will.

The culmination of this project is a series of recommendations that can be implemented to help expand and improve response efforts at local, state, regional, and national levels to identify and reduce PFAS-related exposures. The report's recommendations are intended to address gaps and challenges identified in the current system. The recommendations fall into the following categories: funding investments, quality management systems, testing activity coordination, method and data harmonization, and data accessibility. The focus of this report is to address issues specifically related to PFAS testing. However, these compounds serve as a model for investing in and establishing improved laboratory testing practices in general, thus ultimately expanding and enhancing the response to environmental contamination and human exposures.

Appendix

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List of Acronyms

AAP: American Academy of Pediatrics

AMA: American Medical Association

ANA: American Nurses Association

APHL: Association of Public Health Laboratories

ASTHO: Association of State and Territorial Health Officials

ATSDR: Agency for Toxic Substances and Disease Registry

BRAC: Base Realignment and Closure

CDC: Centers for Disease Control and Prevention

CEU: Continuing Education Unit

CLIA: Clinical Laboratory Improvement Amendments

CME: Continuing Medical Education

CSTE: Council of State and Territorial Epidemiologists

DOD: Department of Defense

ECOS: Environmental Council of the States

EH: Environmental Health

EPA: Environmental Protection Agency

FUDS: Formerly Used Defense Sites

HBM4EU: Human Biomonitoring for Europe

HHEAR: Human Health Exposure Analysis Resource

HRMS: High-Resolution Mass Spectrometry

IARC: International Agency for Research on Cancer

LOQ: Limit of Quantitation

LRN-C: Laboratory Response Network for Chemical Threats

NACCHO: National Association of County and City Health Officials

NASEM: National Academies of Sciences, Engineering, and Medicine

NBM: National Biomonitoring Meeting

NBNSC: National Biomonitoring Steering Committee

NCEH: National Center for Environmental Health

NIEHS: National Institute of Environmental Health Sciences

NPDWR: National Primary Drinking Water Regulation

ORD: Office of Research and Development

PAH: Polycyclic aromatic hydrocarbons

PARC: Partnership for the Assessment of Risks in Chemicals

PATH: Partnership for the Accurate Testing of Hormones

PA/SI: Preliminary Assessments/Site Inspections

PFAS: Per-and polyfluoroalkyl substances

PFBA: Perfluorobutanoic acid

PFBS: Perfluorobutanesulfonic acid

PFDA: Perfluorodecanoic acid

PFNA: Perfluorononanoic acid

PFOA: Perfluorooctanoic acid

PFOS: Perfluorooctanesulfonic acid

PH: Public Health

QA: Quality Assurance

QC: Quality Control

RCRA: Resource Conservation and Recovery Act

RI: Remedial Investigation

TSCA: Toxic Substances Control Act

Association of Public Health Laboratories

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