Per- or Polyfluoroalkyl Substances Exposure Assessments (PFAS EAs)

New Information Collection Request

Supporting Statement Part B –

Collections of Information Employing Statistical Methods

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Part B. Collections of Information Employing Statistical Methods

As indicated in Part A, this new information collection request (ICR) is intended to complete per- or polyfluoroalkyl substances exposure assessments (PFAS EAs) authorized in *Section 8006 of the Consolidated Appropriations Act, 2018*.

The Agency for Toxic Substances and Disease Registry and the National Center for Environmental Health (ATSDR/NCEH) will use statistical methods to identify participants on or near current or former domestic military installations known to have PFAS contamination in drinking water, groundwater or other water sources. A minimum of eight EAs will be completed to assess exposure to PFAS in the environment at these locations.

A protocol has been prepared that will be used for all of EAs that will be conducted by trained ATSDR/NCEH staff and contractors (**PFAS EA Protocol**).[1] The protocol includes:

- The specific details of the statistically based recruitment design and sample size goals.
- All recruitment materials, consent forms and questionnaire forms (**Appendices A,B, and F**)
- Sampling and analytical methods that will be used to determine levels of PFAS in biological and environmental samples (**Appendices C to E**).
- Results letters that will be provided to respondents with their individual results (**Appendix G**).
- A Site Health and Safety plan for the EAs (**Appendix H**).
- A Data Management Plan for the EAs (**Appendix I**).

A community report will be written detailing the results of the EA when completed. **Attachment 4** provides an example report from a previous ATSDR PFAS exposure investigation (EI).

B.1 Respondent Universe and Sampling Methods

To identify potential participants, one-stage cluster sampling will be conducted to estimate PFAS exposure at the chosen current or future military installations (**PFAS EA Protocol**).

[1] As another resource, NCEH has developed a PFAS Exposure Assessment Technical Tool (PEATT) that provides a framework for state health departments to assess exposure to PFAS in drinking water by testing PFAS in serum (**Attachment 3**). ATSDR/NCEH has adapted the PEATT methodology for its EA protocol, which is extended to assess PFAS in urine and in environmental media (drinking water and indoor dust).

A one-stage cluster sample — where each household in the area receiving impacted water is a cluster and all individuals in a selected household are included in the sample — will be used to identify participants for each EA. Clusters (households) will be randomly selected from the sampling frame. This sampling design is representative of the impacted population, allowing for inferences to be made on the entire sampling frame. A step-by-step approach for the one-stage cluster sampling is described below.

1. **ESTABLISH THE SAMPLING FRAME**

   A geographic area where PFAS exposure is known or expected will be defined and a complete list of all exposed/affected households in this area will be identified. This list comprises the sampling frame. Depending on the operations of the water system, the geographic area may be defined by the service boundaries of specific municipal water systems. The geographic area may also be defined as the area with impacted private drinking water wells.

   For simple water systems expected to deliver drinking water with consistent PFAS concentrations to all end users (e.g. municipal drinking water systems with one ground water supply well, or municipal drinking water systems with a surface water source), the sampling frame will consist of all households served by the impacted water system.

   The list of households served by municipal water systems can be obtained from the water company or from local municipal water supply billing information.

   Sequential numbers will be assigned to each household (1, 2, 3,…N) in the sampling frame.

2. **CALCULATE SAMPLE SIZE**

   The required sample size of independent individuals in each community for blood sampling is given by:

$$m = \left[\frac{z_{\frac{\alpha}{2}} \cdot \sigma}{E} \right]^2$$

   Where,

   m = sample size (individuals)
   z = Z value (e.g. 1.96 for 95% confidence level)
   α = level of significance
   E = maximum error
   σ = standard deviation of the logarithm of measured PFAS levels.

If local biomonitoring data are available to determine the standard deviation of the natural logarithm of measured PFAS levels, this data can be used. If these data are not available, national data from NHANES will be used to calculate the necessary sample size, as described below.

The geometric mean for serum PFOS was 4.72 µg/L for the US population in 2015–2016 NHANES. The corresponding 95% confidence interval (4.40, 5.07) and the NHANES sample size of 1,993 are used to estimate the standard deviation of the ln (values). Using the upper limit of the confidence interval:

$$\hat{\sigma} = \frac{\sqrt{1993} \cdot \left[\ln(5.07) - \ln(4.72)\right]}{1.96} = 1.63$$

Then, the sample size of independent individuals to estimate the mean with precision 15% of the ln (geometric mean), and 5% level of significance is:

$$m = \left[\frac{1.96 \cdot 1.63}{0.15 \cdot \ln(4.72)}\right]^2 = 188$$

Since data are collected using a cluster design, individuals within a household are not independent. The lack of independence must be accounted for by incorporating the design effect (DE) into calculation of the required sample size. The required sample size for a cluster sample is the sample size for an independent sample multiplied by DE.

$$DE = 1 + ICC * (k - 1)$$

Where,

DE = design effect
ICC = intra-cluster correlation coefficient
k = cluster size

A pilot of representative biomonitoring for PFAS conducted by the New York State Department of Health and the Pennsylvania Department of Health resulted in retrospective calculations of the intra-cluster correlation coefficient (ICC) for PFAS in serum ranging from 0.39 to 0.54 (unpublished data from New York State Department of Health and Pennsylvania Department of Health, 2019). To be conservative, we assume an ICC of 0.54 for our calculation of the design effect.

The average household (cluster) size for the communities selected as exposure assessment sites ranges from 2.4 to 3.0 individuals per household. To be conservative, we assume a household (cluster) size of 3 for our calculation of the design effect.

Using these values, the design effect is:

$1+0.54*(3-1)=2.1$

As a conservative assumption, we use a design effect of 2.1 to calculate our required sample size.

$sample ¿ m \cdot DE$

This results in a sample size of 2.1*188=395 individuals accounting for intracluster correlation. To be conservative, we will use this design effect for all communities, even when a smaller average household size would result in a lower design effect.

Assuming all individuals from each selected household are included in the sample, the required number of households that should be contacted for recruitment is given by

$$n = sample ¿ \left(\frac{N}{M}\right)$$

Where,

n = required number of households
N = the total number of households in the sampling frame
M = the total number of individuals in the sampling frame

In the Hampden County community (the first exposure assessment site) m = 395, N = 2,882, M = 7,665 so a sample of n = 149 households is needed. Values for N and M taken from 2010 census data for census tract 8125 in Hampden County, MA. At the pilot sites, a within household response rate of 85% was achieved for households in which at least one person participated. Assuming this response rate applies at all sites, the total number of households that need to be contacted in order to get 395 individuals to participate is 269 households. This value is based on an 85% household participation rate (149/0.85 = 175) and a general response rate of 65% (175/0.65 = 269).

Sample size estimate will be adjusted to ensure adequate precision despite non-participating households, using an estimated household response rate of 65%. In Hampden County, n = 175/0.65 = 269 households will be contacted. The number of households contacted in each community will be based on the total number of households and total number of individuals in the sampling frame but will use the same sample size of individuals for all sites. The sample size of 188 independent individuals (based on the original NHANES calculation) will be used for all sites and will be modified by response rate, design effect and required household sample size.

Sampling weights for both households and children are needed to calculate prevalence estimates and make inferences about the entire population of children three years of age or older. Sampling weights can be adjusted to account for unequal probabilities of selection that may have occurred due to non-response from potential participants. Complex survey procedures in SAS/SUDAAN software or EpiInfo software will be used to account for unequal weighting, stratification and clustering in the sample (SAS Institute, Inc., Cary, NC; RTI International, Research Triangle Park, NC).

3. **Select Households**

Each household in the sampling frame will be assigned a number (1, 2, 3,…N). A random number generator will be used to create a list of random numbers equal in size to the number of households in the sampling frame. Households will be contacted for recruitment into the EA based on estimated household size in the community and using an estimated response rate. If the response rate is lower than estimated, a reserve sample of households will be contacted for recruitment into the EA to reach the target sample size. If the reserved sample is used, households within the reserve sample will be given equal opportunity to participate as households initially invited to participate.

B.2. Procedures for the Collection of Information

ATSDR/NCEH will recruit all eligible household members from selected households to participate in the study (PFAS EA **Protocol - Appendix A**). Recruitment will occur by mail and phone beginning in the Spring of 2019. The principal investigator or team will be identified by name, along with qualifications or experience in conducting EAs in these materials.

NCEH has developed a PFAS Exposure Assessment Technical Tool (PEATT) that provides a framework for state health departments to assess exposure to PFAS in drinking water by testing PFAS in serum (**Attachment 3**). The PEATT provides guidance on a statistically based approach to recruit, measure and evaluation community exposures to PFAS including:

- Biomonitoring (serum testing)
- Identifying exposure source(s), and
- Administering questionnaires to provide an assessment of exposure source(s) along with the magnitude and distribution of exposure to the community.

The EAs will be based on the methodology, consents, and questionnaires provided in the PEATT. The PEATT, however, only provides methodology for assessing PFAS in serum at locations that have been impacted by PFAS in drinking water. The EAs protocol has been expanded to include assessing PFAS in urine and in environmental media (tap water and indoor dust). The protocol provides methods for the sampling of these additional media.

ATSDR/NCEH will implement a Data Management Plan for the data collected for the EAs per ATSDR guidance (PFAS EA **Protocol - Appendix I**).

Quality Control Procedures

Prior to the interviews, the EA team members will be trained to administer the consent forms and questionnaire. The list of questions and individuals' answers will recorded using Epi Info™ and will be stored in a secure database. The EA protocol indicates that the privacy of the information given by respondents will be protected to the extent allowed by law, and that respondents can withdraw from EA participation at any time without penalty.

The EA team will give each respondent the following information: the name of the EA, a telephone number to call with questions, and the address of the ATSDR/NCEH website to access for more information about the EA, if applicable. All respondents will receive a copy of their personal results.

B.3. Methods to Maximize Response Rates and Deal with Nonresponse

PFAS EAs will follow several steps to maximize the response rates and thus decrease non-response bias:

A recruitment letter and fact sheets (PFAS EA **Protocol - Appendix A**) will be sent to all homes statistically identified for the EAs. Potential respondents will also be contacted by phone (PFAS EA **Protocol - Appendix A**) a maximum of three times for recruitment. It may not be possible to get household or individual participation, even after multiple contact attempts. Since those that do not choose to participate may be substantively different from those that do, replacing households or individuals that cannot be reached or choose not to participate may result in participation bias. In order to reduce participation bias, households that choose not to participate will not be replaced. However, if the household chooses to participate but no one in the household meets the eligibility criteria, the household will be replaced.

Appointments for biological and environmental sampling will be made during the recruitment phone call. EA respondents will receive information that confirms their participation and provides supplies and instructions for at-home urine collection, including a toll-free number for participants to call with any questions.

Respondents will receive free biological and/or environmental sampling, which may increase their interest in taking part in an EA. ATSDR/NCEH will not provide respondents other tokens of appreciation.

CDC/ATSDR will prepare a non-response bias analysis for each community. As the draft study protocol notes, ATSDR currently estimates a 65 percent response rate for its participant recruiting efforts. Characterizing the profile of non-responders within the sampling frame will be important to assess the extent of non-response bias. At a minimum, ATSDR anticipates having information on property ownership among non-responders. This will likely include the type of

household (e.g., single-family residence, multi-family residence, apartment building), the assessed value of the property, and the ownership status. The only other data that may be available for non-responders are answers to the questions to determine eligibility (i.e., number of years living in the community, age of household members, and whether household members have bleeding disorders). CDC/ATSDR plans to compare the profile of non-responders to that of responders to assess the magnitude and characteristics of non-response bias. This profile will include type of household, assessed value, ownership status, and number of years living in the community, if available. CDC/ATSDR will not use answers to eligibility questions based on age or presence of a bleeding disorder in preparing the non-response bias analysis.

B.4. Test of Procedures or Methods to be Undertaken

The EA team will use the questionnaires provided in the EA Protocol (**Appendix F)**. ATSDR has completed over 190 Exposure Investigations (EIs), which are used to fill data gaps at a site by conducting biological and/or environmental sampling, over approximately 10 years, Therefore, the procedures and methods used for evaluating community exposure are well-tested and based on the Agency's long experience working in communities with environmental contamination.

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Rachel Worley, MS, PhD, is the Principal Investigator of the EA protocol (**PFAS EA Protocol**). Dr. Worley is an ATSDR PFAS Subject Matter Expert (SME) and serves as the NCEH/ATSDR PFAS Coordinator. Mateusz Karwowski, MD, MPH is the Medical Officer on the EA team. They, and Ekta Choudary, PhD, MPH (the project officer for the PEATT, have reviewed this package and approve the adaptation of the PEATT methodology (**Attachment 3**) for use in PFAS EA protocol**.**

Trained statisticians and/or epidemiologists will be part of a probability-based design and sampling team. Additionally, investigators will, to the extent possible, collaborate with state and local health officials. Additional statistical resources are available at both ATSDR and CDC.

If resources outside of ATSDR and NCEH are used to collect or evaluate the data, the privacy of respondents and of their responses will be maintained to the extent practicable.

List of Attachments