Per- or Polyfluoroalkyl Substances Exposure Assessments (PFAS EAs)

OMB Control No. 0923-0059 (Exp. Date 06/30/2022)

Information Collection Request –Revision

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, the Agency for Toxic Substances and Disease Registry and the National Center for Environmental Health (ATSDR/NCEH) are requesting a three-year revision information collection request (ICR) titled *Per- or Polyfluoroalkyl Substances Exposure Assessments (PFAS EAs)* (OMB Control No. 0923-0059, exp 6/30/2022).

The initial ICR was used to complete PFAS EAs authorized in *Section 8006 of the Consolidated Appropriations Act, 2018*.[1] The initial ICR allowed ATSDR/NCEH to fulfill the EA requirements of the Act at military installations in a timely fashion. Up to 15 EAs was allowed, and eight were completed.

The current revision ICR will allow up to nine additional EAs to be conducted over the next three years using lessons learned from the completed eight EAs, including revisions to the recruitment strategy and questionnaire. The revisions are detailed in **Section A.15.**

ATSDR/NCEH will use statistical methods to identify participants at Department of Defense (DoD) or non-DoD locations known to have PFAS contamination in drinking water, groundwater, or other water sources.

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**).[2] 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**).

[1] General ATSDR authorities to conduct EAs are found in the *Comprehensive Environmental Response, Compensation, and Liability Act* of 1980 (CERCLA), commonly known as the "Superfund" Act, as amended by the *Superfund Amendments and Reauthorization Act* (SARA) of 1986 (**Attachment 1a**). NCEH is generally authorized under the *Public Health Service Act* to perform EAs related to public health (**Attachment 1b**).

[2] 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 Restart Plan that allowed ATSDR/NCEH to continue data collection during the COVID-19 pandemic (**Appendix J**).
- The crosswalk tables that detail the modifications to the protocol as a result of lessons learned by conducting the eight EAs is provided as **Appendix K**.

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**).

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

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 completed EAs were 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 was 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/NCEH guidance (PFAS EA **Protocol - Appendix I**).

PFAS EA Information Collection and Sampling Steps: The ICR will allow ATSDR/NCEH to identify, recruit, consent and question eligible EA respondents. A protocol has been prepared that will be used for all EAs (**PFAS EA Protocol**).[3] The additional nine EAs will be conducted in accordance with the PFAS EA Protocol, with modifications made to the recruitment strategy and questionnaire, as indicated in **Appendix K** of the PFAS EA Protocol.

The EAs will be conducted by trained ATSDR/NCEH staff and contractors. The steps in the information collection and sampling include:

1. A public meeting will be held within each EA community that will provide information on the EA process. A Community Event Evaluation Survey (**Appendix A1**) will be provided to the attendees to assess ATSDR/NCEH's PFAS public health messaging, the EA enrollment process and to gauge local feelings toward the ATSDR PFAS EA project. The survey will help the EA team members adjust and enhance public health messaging and EA project information in real time.
2. Potentially eligible households within each EA community will be identified using one-stage cluster sampling **(PFAS EA Protocol**).
3. A recruitment letter and fact sheets will be sent to the randomly-selected households within the statistical sampling frame (**Appendix A2**).
4. All eligible people in the household will be invited to participate. Eligibility criteria (**Appendix A2**) include people that:
    a. Have lived in the home for one year or longer before the PFAS was removed from the drinking water,
    b. Are aged 3 years or older, and
    c. Do not have a bleeding disorder that would preclude a blood draw.
5. If participants do not contact ATSDR/NCEH to make an appointment as a result of the recruitment letter, ATSDR/NCEH will attempt to reach them by phone (a maximum of three attempts; Appendix A3) or an in-person visit will be attempted.

[3] 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 the **PFAS EA Protocol**, which is extended to assess PFAS in urine and in environmental media (drinking water and indoor dust).

6. If potential respondents are eligible and willing, an appointment to conduct the biological testing will be made during the phone call.
7. The Household Recruitment Phone Script (**Appendix A3**) also includes a question regarding whether the residents use tap water as a source of drinking water. After all respondents are identified for biological testing, households that were found to be eligible for environmental sampling (i.e., those that use tap water for drinking water) will be randomly selected and offered environmental sampling via a second phone call (**Appendix A4**). The environmental sampling will occur during the same time period that the biological testing will occur, but will be a separate appointment. The appointment for the environmental sampling will be made during the phone call.
8. Once respondents are identified, information will be sent to households confirming participation and providing urine collection supplies and instructions for urine collection and transport to the blood collection location. On the day of testing, a first morning urine sample will be brought to the centralized blood draw location and given to EA personnel.
9. At the centralized location, the respondents will be consented (**Appendices B1 to B4**), administered the appropriate questionnaire (**Appendices F1 and F2**) and a blood sample will be taken. Participants will be tracked throughout the process with a biological testing tracking form (Appendix B6) to ensure all steps of the EA are completed.
10. Environmental sampling will be conducted at the time scheduled with the respondents (10% of eligible households). A consent form for the environmental testing will be completed (Appendix B5).

In addition to the forms cited above, the protocol includes:

1. The specific details of the statistically based recruitment design and sample size goals.
2. Sampling and analytical methods that will be used to determine levels of PFAS in biological and environmental samples.
    - A federal team leader with appropriate training will oversee all environmental and biological sampling.
    - Trained EA personnel and contractors, with assistance from federal, state and local partners, will collect samples and ship them directly to the appropriate laboratories for analysis.
    - Trained personnel, such as registered nurses (RNs), will collect biological samples and documentation and ship them directly to qualified laboratories for analysis.
    - ATSDR, NCEH, contractors, and partner states will prepare and implement appropriate Quality Assurance Plans as appropriate.
3. Results letters that will be provided to respondents with their individual results (**Appendices G1 and G2**).
4. A Site Health and Safety plan for the EAs (**Appendix H**).

5. A Data Management Plan for the EAs (**Appendix I**).
6. A Restart Plan that was completed to allow data collection to occur during the COVID-19 pandemic (**Appendix J**).

Administration of Questionnaires

Prior to administration of questionnaires, 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.

The information to be collected during biological and environmental sampling events include:

- Demographic and residential history
- Occupational history
- Water source and household filtration system
- Age and activity patterns for respondents
- Basic health status information (e.g., kidney disease, pregnancy status) that will allow the individual blood results to be assessed for each respondent.
- Location of environmental samples taken, where appropriate

The samples will be sent to an accredited laboratory and the resultant data will be analyzed and presented to the community in a report when completed. **Attachment 4** provides an example report from a completed ATSDR PFAS EA.

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. In the event participants cannot be reached by phone, ATSDR/NCEH will conduct door-to-door recruitment as needed. 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.

ATSDR/NCEH will prepare a non-response bias analysis for each community. In the original PFAS EA protocol, an estimated response rate of 65 percent was used for recruitment of participants using the recruitment letters. For the eight completed EAs, a response rate of approximately 10% was found, so this rate will be used for the additional EAs. 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/NCEH 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). ATSDR/NCEH 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. ATSDR/NCEH 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/NCEH completed eight EAs and approximately 200 Exposure Investigations (EIs), which are used to fill data gaps at a site by conducting biological and/or environmental sampling, over approximately 15 years, Therefore, the procedures and methods used for evaluating community exposure are well-tested and based on the ATSDR’s long experience working in communities with environmental contamination.

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

Karen Scruton, MS, is the Principal Investigator of the EA protocol (**PFAS EA Protocol**). Ms. Scruton is the Section Chief for the Exposure Investigations team and is an ATSDR PFAS Subject Matter Expert (SME) on PFAS EAs. Michelle Zeager, DO, MPH, FAAP is a Medical Officer on the EA team and has provided support to EA communities for the eight completed EAs. They have reviewed this package and approve the modifications to the protocol based on lessons learned while conducting the eight completed EAs**.**

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 NCEH.

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.