Human Health Effects of Drinking Water Exposures to Per- and Polyfluoroalkyl Substances (PFAS) at Pease International Tradeport, Portsmouth, NH

(The Pease Study)

New Information Collection Request

Supporting Statement Part A –

Justification

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Glossary of Per- and Polyfluoroalkyl Substances

PFAS - Per- and Polyfluoroalkyl Substances to be Studied	
PFOA	perfluorooctanoic acid n-PFOA - linear isomer Sb-PFOA - serum branched isomer
PFOS	perfluorooctane sulfonic acid n-PFOS – linear isomer Sm-PFOS – serum branched
PFHxS	perfluorohexane sulfonic acid
PFOSA	perfluorooctane sulfonamide
Me-PFOSAA	2-(N-methyl-perfluorooctane sulfonamido) acetic acid
Et-PFOSAA	2-(N-ethyl-perfluorooctane sulfonamido) acetic acid
PFBS	perfluorobutane sulfonic acid
PFHpA	perfluoroheptanoic acid
PFNA	perfluorononanoic acid
PFDA	perfluorodecanoic acid
PFUnDA	perfluoroundecanoic acid
PFDoA	perfluorododecanoic acid

Part A. Justification

Goal of the study: The main goals of the research study are to: 1) evaluate the study procedures and methods to identify any changes to the design or protocol that need to be made before embarking on a multi-site study; and 2) examine associations between a limited number of health outcomes for which statistical power is adequate and measured and historically reconstructed serum levels of PFAS.

Methods to be used to collect: ATSDR will employ a cross-sectional design using a convenience sample of persons exposed to PFAS-contaminated drinking water from the Pease International Tradeport vs. a referent group from other parts of Portsmouth, NH. Methods include health and exposure questionnaires, urine and blood measurements to assess exposure to PFAS compounds, requests for records to validate self-responses, and requests for water system records for historical reconstruction of drinking water exposures.

Subpopulation to be studied: ATSDR will enroll a convenience sample of 1,625 participants (1,100 adults and 525 children and their parents). For the exposure group (n=1,350), ATSDR will enroll 1,000 adults and 350 children. Eligible participants had to work at, live on, or attend childcare at the former Pease Air Force Base or the Pease International Tradeport, or live in a nearby home that was served by a PFAS-contaminated private well. For the referent

A.1. Circumstances Making the Collection of Information Necessary

Per- and polyfluoroalkyl substances (PFAS) are a family of environmentally and biologically persistent chemicals used in industrial applications such as aqueous film-forming foam (AFFF), used to extinguish flammable liquid fires. Since the 1970s, military bases in the U.S. have used AFFF with PFAS constituents for firefighting training as well as to extinguish fires. At some military bases, AFFF use has resulted in the migration of PFAS chemicals through soils to ground water and/or surface water sources of drinking water for bases and/or surrounding communities. In 2016, the U.S. Environmental Protection Agency (USEPA) issued a lifetime health advisory level of 0.07 total micrograms of perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) combined per liter of drinking water (µg/L).

In response to growing awareness of the extent of PFAS contamination across the U.S., Section 8006 of the Consolidated Appropriations Act, 2018 (Public Law 115-141) authorized the Agency for Toxic Substances and Disease Registry (ATSDR) to conduct a study on the human health effects of PFAS contamination in drinking water (**Appendix A1**).

The Agency for Toxic Substances and Disease Registry (ATSDR) is requesting a three-year Paperwork Reduction Act (PRA) clearance for a new information collection titled "Human Health Effects of Drinking Water Exposures to Per- and Polyfluoroalkyl Substances (PFAS) at Pease International Tradeport, Portsmouth, NH (The Pease Study)." The Pease Study will serve as a proof-of-concept model for a multi-site study of PFAS health effects. The existence of a large body of state and local environmental monitoring and population blood testing data makes the Pease community in Portsmouth, NH, particularly suitable as ATSDR's initial PFAS research study site.

From approximately 1970 until 1991, the Air Force used AFFF for firefighting and training at Pease Air Force Base. The base closed in 1991, and was converted to a large business and aviation industrial park in 1993, the Pease International Tradeport. In 2014, measured PFAS concentrations in the Haven Well, one of the three supply wells serving the Pease drinking water system, were 0.35 µg/L PFOA and 2.4 µg/L PFOS. In addition, perfluorohexane sulfonate (PFHxS) was measured in the Haven Well at 0.96 µg/L. Based on the contribution of each of the three wells to the Pease water system, the estimated geometric mean PFOA, PFOS and PFHxS levels in the drinking water system in 2014 were 0.18 µg/L, 1.29 µg/L, and 0.44 µg/L, respectively (ATSDR 2019). The combined PFOA and PFOS levels estimated in the Pease drinking water system (1.47 µg/L) was well above what was to become the USEPA lifetime health advisory level (0.07 µg/L PFOA/PFOS). In May 2014, the Haven Well was shut down.

From June 2014 onward, the combined levels of PFOA and PFOS in the Pease distribution system ranged from non-detect to 0.016 µg/L and the levels of PFHxS ranged from non-detect to 0.019 µg/L (ATSDR 2019).

In 2015-7, the New Hampshire Department of Health and Human Services (NH DHHS) offered a PFAS blood testing program to the community. The blood testing program showed that the respondents had serum PFOS and PFHxS geometric means that were two to three times higher than national estimates in the 2013-2014 NHANES (Daly et al 2018). PFOS and PFHxS were the primary PFAS contaminants in the Haven Well, which supplied about 50% of the Pease Tradeport drinking water from at least 2003 until the well was shut down in May 2014.

ATSDR and the Centers for Disease Control (CDC) National Center for Environmental Health (NCEH) were mandated to conduct research on PFAS contamination in drinking water in Section 8006 of the Consolidated Appropriations Act, 2018 (PL 115-141) (**Appendix A1**).

ATSDR has the general authority to conduct research under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) as amended by the Superfund Amendments and Reauthorization Act of 1986 (SARA) (42 U.S.C. 9601, 9604); and the Resource Conservation and Recovery Act of 1976 (RCRA) as amended in 1984 (42 U.S.C. 6901) (**Appendix A2**).

NCEH is generally authorized to conduct research under Public Health Service Act, Section 301, "Research and Investigation," (42 U.S.C. 241); and Sections 304, 306 and 308(d) which discuss authority to maintain data and provide assurances of confidentiality for health research and related activities (42 U.S.C. 242 b, k, and m(d)) (**Appendix A3**).

The 60-day Federal Register Notice was published on 08/27/2018 (**Appendix B**) and is further discussed in Section A.8.

A.2. Purpose and Use of the Information Collection

<u>Study Design and Research Goals</u>

The Pease Study will be cross-sectional in design, drawing from a convenience sample of people with and without exposure to PFAS-contaminated drinking water from the former Pease Air Force Base or the Pease International Tradeport, or live in a nearby home that was served by a PFAS-contaminated private well. The main goals of the research study are to: 1) evaluate the study procedures and methods to identify any changes to the design or protocol that need to be made before embarking on a multi-site study; and 2) examine associations between a limited number of health outcomes for which statistical power is adequate and measured and historically reconstructed serum levels of PFAS. The Pease Study includes two separate age-

group studies: the Adult Study for those 18 years and older and the Child Study for those 4 to 17 years of age at enrollment (**Pease Study Protocol**).

In 2017, ATSDR conducted a feasibility assessment and literature review to identify candidate designs and health outcomes for the Pease Study and a multi-site study (**Appendix C**) (ATSDR 2017). Based on the assessment, ATSDR has selected a cross-sectional design for the Pease Study. Cross-sectional studies are especially suitable for assessing the prevalence of effect biomarkers and the prevalence of nonfatal diseases, in particular, diseases with no clear point of onset (Checkoway 2004).

Cross-sectional studies can provide insight regarding the potential associations between environmental or occupational exposures and effect biomarkers such as pulmonary function, immune function, liver and kidney function, and so forth. Cross-sectional studies are methodologically sound and have provided important information on the health effects of PFAS exposures. For example, cross-sectional studies, such as those conducted in the mid-Ohio region, known as the "C8 studies" (C8 Science Panel 2009, Frisbee 2009&2010), and those based on NHANES data (Gleason 2015, Humblet 2014, Webster 2016), have provided many insights into the potential human health effects of PFAS exposures. The Pease Study, which is modeled after the C8 studies, will, to the extent to which there is adequate statistical power, test hypotheses and generate new hypotheses for future research.

An inherent limitation of the cross-sectional studies is that they concurrently measure the exposure and the outcome (i.e., the disease or effect biomarker). Concurrent measures make it difficult to determine whether the exposure caused the outcome or whether the outcome influenced the measured exposure level (Flanders 1992, 2016). Similar to the C8 studies, in addition to evaluating measured PFAS serum levels, the Pease study will also estimate both the historical PFAS concentrations in the drinking water at Pease as well as individual-level historical PFAS serum levels.

To better understand the extent to which the biological measures of exposure reflect cumulative drinking water exposures, historical reconstruction modeling approaches (e.g., PFAS contaminant source characterization, and ground water PFAS contaminant fate and transport and drinking water distribution system models) and pharmacokinetic (or physiologically-based pharmacokinetic) modeling will be used. These models will draw on the approach used in the C8 studies, which attempted to estimate both cumulative PFAS serum levels as well as PFAS serum levels at past points in time. These estimates (e.g., lagged cumulative PFAS serum levels) can be used to generate hypotheses regarding the temporality between the time of PFAS exposure relative to the incidence of health and behavioral outcomes of interest. The initial results of the Pease Study and the multi-site study may inform decisions regarding the value of prospective PFAS studies in the future.

ATSDR has also considered the potential for selection bias associated with using of the pre-existing convenience sample conducted at Pease. For selection bias to occur, participation must be associated not only with the outcome of interest but also with the exposure of interest. In the Pease Study, the exposures of interest are the measured PFAS serum level and the estimated cumulative PFAS serum level. The participants in the 2015-7 Pease PFC Blood Testing Program knew they were likely exposed since the program was restricted to those who worked or attended day care at Pease. However, it is less likely that they knew the magnitude of their exposure at the time of enrollment. So among the participants in the blood testing program, their participation is not likely to be strongly associated with their PFAS serum levels. The plan of the Pease Study is to invite all of the blood testing participants who meet the study's eligibility criteria (as described in detail in **Section B.1 - Respondent Universe and Sampling Methods**). Participants, who already know their initial blood testing results, may worry about the potential health impacts of PFAS exposure. They may over-report their health or behavioral outcomes in the questionnaire. To address the potential for such recall bias, the key outcomes of interest will be objective measures of effect obtained through clinical tests and the neurobehavioral test battery (NBT). In addition, health conditions and childhood developmental disorders reported in the questionnaire will be confirmed via a review of medical and educational records. The clinical biomarkers and diagnostic indicators should not be affected by recall bias.

For the children study, it is necessary, especially for younger children, that the parent provide information about the child as well as information on factors that might have affected the child's PFAS serum levels (e.g., exposures during the pregnancy with the child and from breastfeeding). This information is best provided by the biological mother or primary caretaker during infancy. The parent will not be providing a blood sample for analyses of PFAS or effect biomarkers unless the parent is also enrolled in the adult study. The adult study will not preferentially recruit female participants. It will attempt to recruit all adults who were previously enrolled in the NH DHHS biomonitoring program and who meet the study's eligibility criteria as described in the protocol.

<u>Recruitment Plan</u>

The study is built around three waves of recruitment as described in detail in the **Protocol, Section 3.5** and in **Section A.12** and **Section B.1** of these Supporting Statements.

> <u>Wave One Recruitment</u>: ATSDR will recruit from the 1,836 individuals who participated in the NH DHHS Pease biomonitoring program in 2015-2017. The NH DHHS program's consent form did not obtain permission to recontact the participant for future studies. Therefore, ATSDR will not directly contact the biomonitoring program participants for Pease Study recruitment. Instead, NH DHHS, which manages the Pease biomonitoring records and possesses the recruitment frame for the Pease Study, will send out an introductory letter indicating its support for, and encouraging its former participants to

contact ATSDR to take part in the ATSDR Pease Study. The letter will provide a toll-free line that the interested person can call ATSDR to request participation in the study and/or ask any questions about the study.

Wave Two Recruitment: It is anticipated that the Wave One recruitment will not achieve the required sample size for children and adults exposed to the PFAS-contaminated drinking water at Pease. Therefore, ATSDR will conduct a second wave of recruitment focused on individuals who were eligible for the NH DHHS Pease biomonitoring program (i.e., who were exposed to the Pease contaminated drinking water while working or attending daycare at Pease, or were exposed to the Pease contaminated drinking water in utero or via breastfeeding from a mother who worked at Pease) but who did not participate in the program. ATSDR will launch a media campaign to announce Wave Two. A recruitment flyer will be sent to parents of children identified as attending daycare centers at Pease before June 2014 who didn't participate in biomonitoring in 2015-7. Advertisement in local public media and through the Portsmouth Development Authority (PDA) and the Tenants Association of Pease Tradeport (TAP) will encourage other eligible adults to participate in the study. The flyers and advertisements will provide a toll-free number that interested recruits can call ATSDR to request participation in the study and ask any questions about the study.

Wave Three Recruitment: ATSDR will recruit children and adults who were never exposed to the PFAS-contaminated drinking water at Pease to achieve the required sample size for the child and adult referent groups. To recruit child referents, ATSDR will conduct outreach to the Portsmouth schools and day care centers. To recruit adult referents, ATSDR will conduct outreach to Portsmouth community organizations, colleges and local government employees. Wave 3 can occur concurrently with Wave 1 and with Wave 2, if needed to reach recruitment goals.

Health Endpoints

ATSDR conducted an extensive literature review for its Pease feasibility study (**Appendix C** - summarized on pages 14-15, and detailed beginning on page 77). The literature review focused on the epidemiological results for PFOA, PFOS and PFHxS since these were the major contaminants detected in the Pease Tradeport Haven Well during the April and May 2014 sampling as well as the elevated PFAS in the serum of those tested in the NH DHHS Pease testing program. The purpose of the literature review was to identify the health-related endpoints that have been evaluated in at least one epidemiological study, and to assess the extent of the epidemiological research on the health effects of PFHxS and PFOS. The literature review was also used to derive sample size estimates for the Pease Study.

The literature review found that less information was available about the potential health effects of PFOS exposures, and very little information was available on the potential health

effects of exposures to PFHxS. Because the primary contaminants in the drinking water at the Pease Tradeport were PFOS and PFHxS, epidemiological studies of the Pease populations have the potential to fill key knowledge gaps and address the community's concerns (**Appendix C**). ATSDR plans to analyze 14 serum PFAS in its biochemical analytical plan (**Glossary** and **Attachment 3**).

Based on the literature review conducted for the 2017 ATSDR Feasibility Assessment (ATSDR 2017), ATSDR decided it was most productive and feasible to examine associations between PFAS compounds and the health endpoints in its multi-site study: lipids, renal function and kidney disease, thyroid hormones and disease, liver function and disease, glycemic parameters and diabetes, as well as immune response and function in both children and adults. In addition, ATSDR will investigate if PFAS exposure is related to differences in sex hormones and sexual maturation, vaccine response, and neurobehavioral outcomes in children. In adults, additional outcomes of interest include cardiovascular disease, osteoarthritis, osteoporosis, endometriosis, and autoimmune disease. The underlying justifications for the selected research hypotheses were: (1) to follow-up a suggestive positive result (e.g., OR or RR >1.2) for a disease or effect biomarker in one or more PFAS epidemiological studies of children aged 4 or older and/or adults; or (2) to follow-up a finding for a disease or biomarker in the C8 studies and/or PFAS studies utilizing NHANES data; and/or 3) to study a biomarker or disease for which a multi-site study of individuals aged 4 years or older would have sufficient statistical power but for which there is a lack of data on the effect of PFHxS exposure on the disease or biomarker.

For the Pease study, we will collect many of these variables to explore "proof of concept" for the multi-site study. The statistical power and sampling frame of this proof of concept study limits our ability to detect moderate differences in many of these variables. Those for which ATSDR estimated it has sufficient statistical power in the Pease Study to detect meaningful differences among children are lipids, kidney function, insulin-like growth factor - 1 (IGF-1) and thyroid-stimulating hormone (TSH). Among adults, ATSDR estimated it has sufficient statistical power in the Pease study to detect meaningful differences for lipids, kidney function, thyroid function, and hypertension. For other variables, we would need to see very large differences between the higher PFAS serum levels and reference PFAS serum levels.

ATSDR will interpret the findings from this study based on the magnitude of the effect estimates (e.g., the linear regression coefficient for continuous outcomes or the odds ratio for categorical outcomes) of the exposure-response relationship, consistency with findings from other studies, and the possible sources of bias (Rothman 2014). The analyses will construct confidence intervals to indicate the level of precision (or uncertainty) in the effect estimates. The studies will use statistical significance testing to interpret findings but will not use it as a sole factor in determining scientific and public health significance (Rothman et al. 2008, 2010; Stang et al. 2010).

Data Collection

Details about the data collection procedures, which will include both adults and children, are provided in **Section A.12**. A summary is provided here.

The data collection will occur as follows:

- Eligibility Screening: Interested community members will be invited to call ATSDR to volunteer for the study in three recruitment waves.
    - Exposure group recruitment
        - Wave One – former participants in the New Hampshire Department of Health and Human Services PFC Blood Testing Program, 2015-17.
        - Wave Two – If sample size goals are not met for the exposure group, ATSDR will open Wave Two to recruit persons who were eligible for the NH PFC Blood testing Program but did not participate in 2015-17.
    - Referent group recruitment
        - Wave Three – participants will be drawn from the surrounding Portsmouth, NH, area, and must not have exposure to PFAS-contaminated drinking water from the Pease Tradeport or from private wells.
    - Once deemed eligible and willing to participate, a study appointment will be scheduled for the participant.
- A study appointment will be scheduled and completed by trained study staff:
    - Study staff will remind prospective participants of their upcoming appointment.
    - At the appointment, participants will provide informed consent to be formally enrolled in the research study, and the following information will be collected:
        - Contact information Update, if needed
        - Medication list
        - Body (height and weight) and blood pressure measurements
        - Blood draw and urine collection
        - Questionnaires
        - Neurobehavioral test battery for the child. A parent will also provide his or her assessment of the child.
- During the informed consent process, ATSDR will ask for permission to request record abstractions from the participants. After the study appointment is over, ATSDR will send out requests for:
    - School records to verify a child's neurobehavioral test battery results.
        - School administrators will receive these individual requests from ATSDR
        - Education specialists will fill out the school record abstraction form from the child's school records.

- Medical records to verify self-reported health conditions on the participant's questionnaire.
  - Medical office administrators will receive these individual requests from ATSDR.
  - Medical record specialists will fill out the medical record abstraction form from the adult's or child's medical records.

Site Selection

Reasons that ATSDR selected the Pease community in Portsmouth, NH, as a suitable proof-of-concept model site for a multi-site study, include the ability to leverage and maximize a great deal of existing state and local data.

- In 2013-4, the New Hampshire Department of Environmental Services (NH DES) worked with NH DHHS to characterize and remediate the PFAS contamination of drinking water among the supply wells that serviced the former Pease Air Force Base, now the Pease International Tradeport.
  - Using this existing monitoring data, ATSDR would like to perform water contamination modeling to inform pharmacokinetic (PK) or physiologically based pharmacokinetic (PBPK) modeling.
- ATSDR is currently conducting a Health Consultation of the Pease Tradeport Public Water System. As part of this effort, ATSDR has obtained from the City of Portsmouth, Department of Public Works, the historical pumping information for the three public water supply wells serving the Pease Tradeport. This pumpage data is necessary for estimating historical PFAS concentrations in the drinking water at Pease. https://www.atsdr.cdc.gov/HAC/pha/pease/Pease-Tradeport-Public-Water-PFAS-HC-508.pdf.
- The 2015-7 NH DHHS Pease PFAS Blood Testing Program[1] was offered to address the concerns of the Pease community members. The program drew a convenience sample and documented that human exposure was occurring at levels two to three times higher than national NHANES estimates.
  - The program provides a readily available recruiting frame for the Pease Study exposure group (Wave One).
  - With a few restrictions, ATSDR is using the same eligibility criteria as NH DHHS.

[1] The initial Pease PFC Blood Testing Program in 2015 enrolled 1,578 participants for which ATSDR is using as a baseline for this research because much more information about this cohort is available in the final report at https://www.dhhs.nh.gov/dphs/documents/pease-pfc-blood-testing.pdf.

NH DHHS expanded PFC blood testing in 2016-2017 for a number of southern New Hampshire communities, including testing for an additional 258 Pease Tradeport residents. Their results were consistent with the 2015 Pease PFC Blood Testing Program. ATSDR will also invite these additional 258 participants in Wave One; however, the age information is not readily available to allow us to estimate the number of adults and children for the blood testing expansion in Table B.1.2. See https://www.bedfordnh.org/DocumentCenter/View/2472/PFC-Blood-Testing-Aggregate-Results-Overview_FINAL_100517.

    - NH DHHS is supporting the Pease Study by sending out invitation letters for its past participants to enroll in the research study.
- NCEH has an existing collaboration with NH DHHS. The NCEH Division of Laboratory Sciences (DLS) performed PFAS blood analyses as a technical assistance, at the state's request, for 49 percent of the serum samples for the 2015-7 Pease PFC Blood Testing Program.[1]
- NCEH DLS will perform all blood and urine PFAS analyses for the Pease Study. Thus issues of inter-laboratory variability are avoided.
    - ATSDR plans to seek consent from participants to access to their 2015-7 PFAS blood testing results (Wave One).
        - ATSDR would like to use both sets of lab results to look at changes of PFAS levels over time, if possible.
        - ATSDR would like to reconstruct historic serum PFAS concentrations by estimating half-lives and elimination rates.

Proof of Concept Study Goals

As a proof of concept study, the purpose of the Pease Study, in addition to addressing research questions for the Pease community, is to understand if the proposed methods for data collection will be suitable for a multi-site study of the health effects of PFAS exposure through drinking water. A summary of the Pease Study research goals are discussed in the **Protocol Section 1.1.4.**

Although all facets of the research methods and operations will be monitored for proposed improvements, the following are key issues that the study investigators plan to assess for feasibility, efficiency, cost, and effort for the multi-site study:

- Proposed recruitment strategies: ATSDR plans to work closely with community-based organizations, such as the Pease Community Assistance Panel (CAP) and the NH DHHS, to maximize recruitment efforts (**Attachment 5 – Communication Plan** and **Attachment 6 – NH DHHS Invitation Letters**). Throughout the recruitment period, the investigators will monitor and identify areas of improvement necessary to achieve the desired sample size goals.
- Proposed sample sizes: The current power and sample size assumptions are summarized in **Section B.1**, and discussed in **Protocol Section 3.3.1 and 3.3.2.**, and in **Attachment 4**. The sample sizes proposed for the Pease Study are acknowledged by the investigators to be sufficient for some outcomes; however, the sample sizes for other outcomes of interest will require the larger sample sizes afforded in the multi-site study to answer other research questions.

- Proposed inclusion of a referent group: ATSDR will assess whether an external "unexposed" referent group will be recommended for the multi-site study (**Protocol Section 1.1.4)**. ATSDR plans to recruit 100 adults and 175 children from parts of Portsmouth, NH, who have not been exposed to drinking water from Pease, as a comparison group. The ATSDR investigators also plan to use cutpoints to establish PFAS exposure categories. For example, ATSDR may create PFAS exposure groups with low, medium, and high tertiles of serum PFAS concentrations, using the low tertile as the internal "low exposed" referent group. Using both types of referent groups will provide information on whether external "unexposed" referent groups for the multi-site study will be recommended.
- Proposed biospecimen collection: ATSDR aims to determine if it is necessary to change the proposed blood and urine collection volumes, processing, shipment, and analysis so that they will be sufficient to meet the goals of the biochemical analytic plan for the multi-site study (**Attachment 3**). Objective measures of PFAS exposure and proposed health effects are critical in this study design.
- Proposed medical and educational record abstractions: As previously stated, reliance on objective measures of health and behavioral outcomes is a key strategy to reduce the potential for self-reported recall bias among participants (**Attachments 19,19a&19b** and **Attachments 20,20a&20b**). The use of objective measures will allow ATSDR to understand if recall bias is occurring, and whether the reliance on clinical testing, record abstractions, and NBT measures are justified and feasible.
- Proposed reconstruction of historic PFAS concentrations in drinking water: ATSDR aims to use historical reconstruction of PFAS concentrations in drinking water as previously demonstrated in the C8 studies (**Protocol Section 3.9**). In order to achieve this objective, ATSDR will request pertinent information from the US Air Force, the NH Department of Environmental Services, and the City of Portsmouth Department of Public Works. For example, ATSDR will request information on the annual amount of AFFF used at Pease Air Force Base, accidental releases, training locations, soil and groundwater characteristics, and drinking water production logs. ATSDR will use the proof of concept study to assess how difficult it will be to obtain necessary environmental records.
- Proposed reconstruction of historic PFAS serum concentrations: In addition to the above reconstruction of drinking water concentrations, ATSDR will use current and past PFAS serum measurements, questionnaire data on participants' water consumption, NHANES estimates, and physiologically based pharmacokinetic (PBPK) models to estimate each participant's cumulative PFAS serum level (**Protocol Section 3.9**). ATSDR will use the proof of concept study to explore necessary methods for cumulative PFAS serum estimates.

A.3. Use of Improved Information Technology and Burden Reduction

ATSDR will use information technology to reduce burden through electronic modes of information collection. The estimated percentages of total number of responses and total number of burden hours to be collected by electronic means are shown in **Table A.3.1**; where we estimate that 34.4 percent of responses will be by electronic means and 29.8 percent of time burden will be by electronic means.

Computer Assisted Telephone Interviews (CATIs) and Computer Assisted Personal Interviews (CAPIs) programmed into Epi Info™[2]will reduce burden by incorporating computer-generated skip patterns, and improve data quality by automating data entry. Also, ATSDR is offering the child questionnaire short form (**Attachment 17a**) to parents who will enroll as adults themselves. Responses to the short form will reduce duplication of effort and a parent's burden by half.

Screenshots of CATI and CAPI forms will be submitted to OMB as a non-substantive change request after PRA clearance for the Pease Study is granted, unless the CAPIs and CATIs are ready at the time of the information collection request (ICR) submission to OMB.

Table A.3.1. Information Collection by Electronic Means

Attachment No.	Form Name	Mode of Collection	No. Responses	Total Burden (in hours)
6c	Wave One Eligibility Screening Script	CATI	612	102
7c	Wave Two Eligibility Screening Script	CATI	57	14
7c	Wave Three Eligibility Screening Script	CATI	121	30
10	Appointment Reminder Telephone Script	CATI	542	45
17	Child Questionnaire – Long Form	CAPI	140	70
17a	Child Questionnaire – Short Form	CAPI	35	9
18	Adult Questionnaire	CAPI	367	184
		Improved Technology Total Counts	1,874	454
		Pease Study Total Counts	5,440	1,521
		Improved Technology Percent	34.4%	29.8%

A.4. Efforts to Identify Duplication and Use of Similar Information

2005-2013

[2] https://www.cdc.gov/epiinfo/index.html

The most notable PFAS research in the U.S. to date was the C8 Health Project (see http://www.c8sciencepanel.org/). C8 is a trade name given to PFOA, manufactured in Parkersburg, WV. Extensive migration of C8 into the environment and subsequently into drinking water affected many people in the Mid-Ohio Valley in Ohio and in West Virginia. The purpose of the C8 Health Project was to collect health data from almost 70,000 Class Members of a lawsuit through written questionnaires and a battery of blood tests, including a test to measure C8 in the blood. As part of the Settlement Agreement, the C8 Science Panel released a series of "probable cause" reports linking C8 exposure to health outcomes (from a legal standard, not an epidemiologic standard). Given that the primary PFAS released by the chemical manufacturer was C8 (PFOA), the legal "probable link" to health outcomes are extremely informative for the Pease Study where PFOA is also a contaminant of interest, but not sufficient to provide the level of rigor regarding likely causal associations that anticipated multi-site investigation for which Pease is a "proof of concept."

The NH DHHS Pease biomonitoring program included a total of 1,836 individuals during 2015-2017. Of these, 1,578 were tested during 2015 and the results were published in a NH DHHS report and a peer-reviewed journal article (Daly et al., 2018). The abstract for the journal article stated the results: "Geometric mean serum concentrations of PFOS, PFOA, and PFHxS were 8.6 µg/L (95% CI:8.3–8.9), 3.1 µg/L (95% CI: 3.0–3.2), and 4.1 µg/L (95% CI: 3.9–4.3), respectively, which were statistically higher than the general U.S. population. Significant associations were observed between PFAS serum concentrations and age, time spent in the affected community, childcare attendance, and water consumption." Among the 1,578 participants in 2015, 1,181 were 20 years of age or older, 31 were 12-19 years of age, and 366 were 11 years of age or younger. The program used 2011-2012 NHANES serum data for PFOA, PFOS and PFHxS for comparison.

Also, under Section 8006 of the Consolidated Appropriations Act, 2018 (PL 115-141), CDC/ATSDR will also be conducting exposure assessments in communities near current or former military bases and that are known to have had PFAS in their drinking water. The primary goal of these exposure assessments is to provide information to communities about levels of PFAS in their bodies. People in each of these communities will be randomly selected to participate in these exposure assessments.

A.5. Impact on Small Businesses or Other Small Entities

The purpose of the review of medical and school records is to verify health conditions and developmental disabilities reported in the questionnaires (see **Section A.12).** Medical practices

and schools may be defined as small businesses or small entities.[3] The annual time burden for medical and educational administrative review and record abstraction is estimated to be 553 hours (250 hours for adult records and 303 hours for children's records. The portion of the time burden for medical and school record abstractions represents 44.2 percent of the total hours requested (553/1,521 x 100).

The time for school and medical office administrators to review and approve the individual requests for school record abstractions and adult and child medical record abstractions is estimated to take 20 minutes per request. The time to complete the school record abstraction form and the adult and child medical record abstraction forms is also estimated to take 20 minutes per response. It is likely that the average time per response and the total number of record verifications will be less because:

- ATSDR anticipates that only a portion of children will have applicable education records of interest; however, once identified, it will be important that education specialists verify those that do.
- Most participants will report a smaller subset of the full complement of outcomes of interest on their questionnaire; therefore, medical record specialists will be able to find and abstract the medical outcomes within their practice specialties, and will not need to review patient records for every diagnosis or treatment on the list.

The number of outcomes of interest has been held to the absolute minimum required for the intended use of the research data. In order to reduce burden on, and if permitted by, the businesses or entities, ATSDR may offer to send trained study staff and contractors to assist in record abstraction.

A.6. Consequences of Collecting the Information Less Frequently

There are three types of respondents.

- The *Pease Study participants* (1,100/3 = 367 adults per year and 525/3 = 175 children and their parents per year) will respond to the information collection once.
- ATSDR is requesting two types of record abstractions to verify children's behavioral assessments and to verify adults' and children's self-reported medical histories (**Attachments 9b, 19, 19a, 19b, & 20b)**. We estimate the following:
    - Across school districts, ATSDR estimates up to 15 *education specialists* will each abstract 12 student records per year (n=525 children/15 specialists/3 years).

[3] OMB FORM 83-I: A small entity may be (1) a small business which is deemed to be one that is independently owned and operated and that is not dominant in its field of operation; (2) a small organization that is any not-for-profit enterprise that is independently owned and operated and is not dominant in its field; or (3) a small government jurisdiction which is a government of a city, county, town, township, school district, or special district with a population of less than 50,000.

- Across medical practices, ATSDR estimates up to 25 *medical record specialists* will each abstract 15 adult and 7 child medical records per year (n=1,100 adults/25 specialists/3 years; n=525 children/25 specialists/3 years).
- To reduce burden on school districts and medical practices, ATSDR may send trained study staff and contractors to assist with this effort. ATSDR's contractor on the study has experience abstracting medical and school records. Their staff will abstract the necessary data if school districts or medical practices are unable to abstract the data.

If the collection is not conducted or is conducted less frequently, the validity of the study results, by relying on self-reported outcomes alone, will be subject to recall bias. Therefore, records verification at the estimated frequency is needed to address and to understand the extent of this potential source of bias.

There are no technical or legal obstacles to reducing burden.

A.7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The following special circumstance(s) apply to this information collection. The number of responses per respondent is discussed in detail in **Section A.12**. We are requiring the following:

- School and medical office administrators will review requests for individual record abstractions more often than quarterly because of the number of Pease Study participants for whom records will be abstracted.
- Education specialists and medical records specialists will report information to the agency more often than quarterly because of the number of Pease Study participants for whom records will be abstracted. ATSDR assumes that there will be a fixed number of specialists to perform records abstractions (n=15 education and n=25 medical). The number of educational records for children (n=175) will be abstracted by 15 specialists, or n=175/15=11.7 rounded to 12 records per educational specialist. ATSDR estimates up to 25 medical record specialists will each abstract 15 adult and 7 child medical records per year (n=1,100 adults/25 specialists/3 years; n=525 children/25 specialists/3 years).
    - Justification for reporting frequency greater than quarterly is provided in **Sections A.5** and **A.6**.
- The 2015-7 Pease PFC Blood Testing Program recruited a convenience sample. As the proof of concept model for a multi-site study, ATSDR will use this existing recruitment frame (a fixed cohort) established by the NH DHHS for Wave One. ATSDR will also recruit convenience samples in Waves Two and Three.

  Although the use of convenience samples may affect the generalizability of the results to all persons exposed and not exposed to PFAS-contaminated drinking water from

Pease, given the existence of this recruitment frame and the large amount of existing data, ATSDR believes this is the best approach.

To gauge the potential and magnitude of possible selection bias and information biases, two approaches will be taken. First, quantitative methods described in Lash et al (2009) will be used to estimate the possible magnitude of selection and informational biases. Second, "negative control" diseases will be used to also estimate the potential and magnitude of these biases (Lipsitch et al 2010). Negative control diseases are those diseases not known to be associated with the exposures of interest. In the Pease study, the exposures of interest are PFAS serum levels. Based on a literature review of the epidemiological studies of PFAS exposures, ATSDR selected negative control diseases for children and adults. The selected negative control diseases for children are celiac disease, scleroderma, lupus, and Crohn's disease. In addition to these diseases, the selected negative control diseases for adults are Parkinson disease, emphysema, chronic bronchitis, multiple sclerosis, and fibromyalgia.

A.8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

A. A 60-day Federal Register Notice was published in the *Federal Register* on 08/27/2018, Vol. 83, No. 166, pp. 43685 (**Appendix B**).

   - ATSDR received a total of 12 public comments, two were posted in duplicate, and 7 were substantive comments. The ATSDR response is provided in **Appendix B1**.

B. The following persons outside and inside the agency were consulted.

Table A.8.1. ATSDR External Consultations, 2018-2019

Name	Title	Affiliation	Phone	Email/Date of Consultation
OUTSIDE CONSULTANTS				
Benjamin P. Chan, MD	NH State Epidemiologist	NH DHHS	(603) 271-5325	benjamin.chan@dhhs.nh.gov Ongoing since 2016
Pease Community Assistance Panel (CAP)	see https://www.atsdr.cdc.gov/sites/pease/cap.html			Ongoing since 2016
External Peer Reviewers	Spring 2018 – the research protocol was reviewed by four independent peer reviewers as part of the Agency clearance process.			
Matthew P. Longnecker, MD, ScD	Consultant	Ramboll Group A/S Consultants	(919) 765-8029	mlongnecker@ramboll.com 05/31/2018
Mark Strynar, PhD	Physical Scientist	US EPA National Research Exposure	(919) 541-3706	strynar.mark@epa.gov 09/06/2018

		Laboratory (NERL)		
ACADEMIC INSTITUTIONS				
Kyle Steenland, PhD	Professor, Epidemiologist	Emory University	(404) 712-8277	nsteenl@sph.emory.edu 03/27/2018
Elsie M. Sunderland, PhD	Associate Professor	Harvard University	(617) 496-0858	ems@seas.harvard.edu 05/10/2018
Alan Ducatman, MD, MSc	Professor	West Virginia University	(304) 293-3693	aducatman@hsc.wvu.edu 05/17/2018
Philippe Grandjean, MD, DMSc	Professor; Adjunct Professor	University of Southern Denmark; Harvard University	617-384-8907	pgrand@hsph.harvard.edu 10/11/2018
OTHER FEDERAL AGENCIES				
Interagency Scientific Reviewers	April 2018 – along with four external peer reviewers, the research protocol was reviewed by National Institute of Environmental Health Sciences (NIEHS) as part of the Agency clearance process.			
	February 2019 – the ICR was submitted to OMB for PRA clearance.			
	March 2019 – OMB initiated an interagency scientific review of the protocol			

Table A.8.2. Ongoing Consultations within CDC/ATSDR, 2018

Name	Title	Affiliation	Phone	Email
Antonia Calafat, PhD	Chief	NCEH Organic Analytical Toxicology Branch, Division of Laboratory Sciences (OATB/DLS)	(770) 488-7891	aic7@cdc.gov
Matthew Maenner	Epidemiologist	NCBDDD Division Of Congenital And Developmental Disorders (DCDD) Developmental Disabilities Branch (DDB)	(404) 498-3072	xde8@cdc.gov
NCEH/ATSDR PFAS Steering Committee				
Patrick Breysse, PhD, Chair		NCEH/ATSDR Director	(770) 488-0604	pjb7@cdc.gov
Donna Knutson, PhD*		NCEH/ATSDR Deputy Director	(770) 488-0673	dbk2@cdc.gov
Yulia Carroll, MD*		NCEH/ATSDR Associate Director for Science, Acting	(770) 488-3912	eya3@cdc.gov
Pamela Protzel-Berman, PhD, MPH		NCEH/ATSDR Associate Director for Policy	(770) 488-3016	pxp5@cdc.gov
Christopher Reh, PhD, MS		ATSDR Associate Director	(770) 488-xxxx	xxxx@cdc.gov
Heather Bair-Brake, DVM, MS		NCEH/ATSDR Associate Director for Communications	(404) 639-3323	hhb9@cdc.gov
John Decker, MS, RPh, CIH		Director, NCEH Division of Environmental Health Science and Practice (DEHSP), Acting	(404) 498-2582	jad4@cdc.gov
James Pirkle, MD		Director, NCEH Division of Laboratory Sciences (DLS)	(770) 488-7950	jlp1@cdc.gov
Angela Ragin, PhD		Deputy Director, ATSDR Division of Toxicology and Human Health	(770) 488-3807	atr0@cdc.gov

Sciences (DTHHS), Acting
* No longer in this position as of 06/2019.

In efforts to increase cross-government coordination, ATSDR and NCEH/ATSDR senior leadership attended the PFAS National Leadership Summit, sponsored by U.S. EPA in Washington, D.C. on May 22-23, 2018 (see https://www.epa.gov/pfas/pfas-national-leadership-summit-and-engagement). During the summit, participants worked together to:

- Share information on ongoing efforts to characterize risks from PFAS and develop monitoring and treatment/cleanup techniques
- Identify specific near-term actions, beyond those already underway, that are needed to address challenges currently facing states and local communities
- Develop risk communication strategies that will help communities to address public concerns with PFAS

The list of confirmed organizations in attendance is found here: https://www.epa.gov/sites/production/files/2018-05/documents/pfas_summit_list_of_confirmed_organizations_5.22.18.pdf.

External Peer Review and Interagency Scientific Review Requirements for ATSDR Research: As required by statute and by the regulations (PL 96-510 or 42 CFR part 90.11), research protocols and resulting reports of research conducted by ATSDR "shall be reported or adopted only after appropriate peer review." **Table A.8.1** shows that the research protocol had completed external peer review by four independent reviewers plus an interagency scientific review by NIEHS prior to ICR submission to OMB for PRA clearance in Spring 2018. The ICR was submitted to OMB during February 2019. On March 8, 2019, OMB initiated an interagency scientific review, inviting representatives from several federal agencies to meet with ATSDR and provide comments on the study design and protocol.

A.9. Explanation of Any Payment or Gift to Respondents

As a token of thanks for participation, ATSDR will offer gift cards according to the following schedule:

- $25 for body and blood pressure measures, and for blood and urine collection;
- $25 for completed in-person questionnaire, body measures, and biospecimen collection in the study office; and
- $25 for child/parent completion of the neurobehavioral test battery.

If all parts of the study are completed, adult participants will receive $50 and children and their parents will receive $75 in gift cards.

Trained study staff will document provision of gift cards on the hard copy form (**Attachment 14**). As part of the exit procedures, the participant will sign this form to document receiving the gift cards.

A.10. Protection of the Privacy and Confidentiality of Information Provided by Respondents

Privacy Act Determination: On 12/11/2018, the CDC Chief Privacy Officer reviewed this submission and determined that the Privacy Act does apply (**Appendix D**).

The applicable Privacy Act System of Records Notices (SORN) are:

- No. SORN 09-19-0001 ATSDR "Record of Persons Exposed or Potentially Exposed to Toxic or Hazardous Substances." ATSDR will file and retrieve Information in identifiable Form (IIF) by the name of the individual and Social Security Number.
- No. SORN 09-20-0136 "Epidemiologic Studies and Surveillance of Disease Problems." NCEH will file and retrieve IIF by the name of the individual and Study ID number.

The following IIF Categories apply to this information collection:

❑ Name
❑ Date of Birth
❑ Social Security Number (SSN)
❑ Mailing Address
❑ Phone Numbers
❑ Medical Information and Notes
❑ Biological Specimens
❑ Email Address
❑ Education Records
❑ Military Status
❑ Employment Status

SSNs will be used to verify self-reported health outcomes by retrieving and abstracting some study participants' existing medical records. For example, for cancers, full SSN is key to matching with state cancer registry data. In addition, SSN is needed to track and trace individuals who consent to be re-contacted for future longitudinal studies at Pease. Longitudinal studies at Pease have been strongly advocated by community representatives at Pease. The most effective way to track participants over time is to use their SSN with external parties like Lexus Nexus or credit agencies. In particular, persons who change their names are

difficult to trace without SSN. Further discussion on the collection of Social Security Number (SSN) is found in **Section A.11.**

Safeguards: The following special safeguards are provided to protect the records from inadvertent disclosure:

- Authorized Users: A database security package is in place for CDC's technology infrastructure to control unauthorized access to the system. Attempts to gain access by unauthorized individuals are automatically recorded and reviewed on a regular basis. Access to records is granted to only a limited number of physicians, scientists, statisticians, and designated support staff of ATSDR or its contractors, as authorized by the system manager to accomplish the stated purposes for which the data in this system have been collected.
- Physical Safeguards: Questionnaires, log books, and other source data are maintained in locked cabinets in locked rooms, and security guard service in buildings provide personnel screening of visitors. Access to CDC facilities housing technology infrastructure is controlled by a cardkey system. The facilities are protected by an automatic sprinkler system, numerous automatic sensors (e.g., water, heat, smoke, etc.) are installed, and a proper mix of portable fire extinguishers is located throughout the facility. The system is backed up on a nightly basis with copies of the files stored off site in a secure fireproof safe. Computer workstations, lockable personal computers, and automated records are located in secured areas.
- Procedural Safeguards: Protection for computerized records includes programmed verification of valid user identification code and password prior to logging on to the system, mandatory password changes, limited log-ins, virus protection, and user rights/file attribute restrictions. Password protection imposes user name and password log-in requirements to prevent unauthorized access. Each user name is assigned limited access rights to files and directories at varying levels to control file sharing. There are routine daily backup procedures and secure off-site or cloud storage is available for backup files.
- Non-disclosure review plan for dataset shared outside of ATSDR are described in detail in **Appendix F (Data Sharing and Disclosure Review)**.

Retention and Disposal**:** Records are retained and disposed of in accordance with the CDC Records Control Schedule (B-321) and the ATSDR Comprehensive Records Control Schedule (B-371). Current CDC and ATSDR procedures allow the system manager to keep the records for 20 years unless needed for further study. Retention periods vary depending on the type of record. Source documents for records are disposed of when no longer needed in the study as

determined by the system manager, and as provided in the signed consent form, as appropriate.

Privacy Impact Assessment: ATSDR will collect, maintain, and disseminate IIF in flat files stored in encrypted share drive. The CDC NCEH Division of Environmental Health Science and Practice (DEHSP) Lead Poisoning Prevention and Environmental Health Tracking Branch (LPPEHTB) will receive files from forms that do not collect IIF. The NCEH/ATSDR Information Systems Security Officer (ISSO) has determined that a full Privacy Impact Assessment (PIA) is not required as the information collection does not have a single dedicated IT system. It uses various authorized CDC IT systems for the collection, processing, analysis, and storage of the data. The submission date was 11/16/2018 (**Appendix D**).

The system's Security Plan defines the process for handling security incidents. The system's team and OCISO share the responsibilities for event monitoring and incident response. All incidents involving a suspected or confirmed breach of IIF must be reported to OCISO according to the policy titled "OCISO/CDC Standard for Responding to Breaches of Personally Identifiable Information (PII)." The team will direct reports of suspicious security or adverse privacy-related events to the NCEH/ATSDR ISSO, CDC helpdesk, or to the CDC Incident Response team. The CDC OCISO reports to the HHS Secure One Communications Center, which reports incidents to US-CERT as appropriate.

The participant will be informed about the security measures for privacy protections. The advisement information on privacy protections is contained in the consent information (**Attachment 9b**) and the study fact sheet (**Attachment 9c**).

- The participant will be informed that, under the requirements of the 2016 21st Century Cures Act and Section 301 of the Public Health Service Act, ATSDR will issue a 301(d) Certificate of Confidentiality (CoC) (**Appendix E**).
- The ATSDR plans for data ownership and data sharing are found in the **Pease Study Protocol** (**Section 3.8.5**).
    - Coded research datasets and specimens will be available to ATSDR study investigators listed in **Attachment 1**.
        - Coding with a study ID means that datasets and specimens are still identifiable to investigators.

- ATSDR will produce coded datasets by removing the following: name, SSN, date of birth, address, former address (es), phone number, and date of completion of the blood draw and questionnaire.
    - SSN will be collected at enrollment for linkage to medical records and school records. Once the linkage has occurred, the SSN will be kept with other PII in a separate access restricted secure database. ATSDR may use SSN for tracking and tracing Pease Study participants for future studies.
    - Age will replace date of birth in the data analysis file because it is the necessary variable in exposure and health outcome analyses.
- Specimen collection tubes provided to performing laboratories will be coded with study ID only.
- ATSDR PIs will maintain the identifying links as described in the consent information (**Attachments 9b&9c**):
    - To report results for the Pease Study and any future research studies, if necessary, by ATSDR.
    - To recontact Pease Study participants to take part in future research studies.

o Release of de-identified data to outside investigators must be approved by ATSDR (**Appendix F**). A data use agreement (DUA) will be prepared, detailing the condition of use of the data and proposed analyses for each outside project. The DUA condition of use will specify that ATSDR will not release the link between the study IDs and the participants' PII to the outside researchers. Through the DUA, the data are no longer coded, but are effectively de-identified to the outside researchers. The DUA will also specify that:

- After the approved project with the outside researchers is completed, further or secondary analyses of electronic datasets can only be undertaken with additional approval(s) from ATSDR.
- Written confirmation of understanding the conditions of use will be required from the lead scientist and institution. Copies of statistical code and datasets used in statistical analyses by the outside investigators will be kept by ATSDR.

A.11. Institutional Review Board (IRB) and Justification for Sensitive Questions

The Pease Study has been determined to be subject to human subjects' research under 45 CFR 46. The CDC IRB approval memo is found in **Appendix E**.

The issuance of a Certificate of Confidentiality (CoC) also is found in **Appendix E**. A CoC is automatically issued under Subsection 301(d) of the Public Health Service Act, because the Pease Study will collect sensitive identifiable information from the study participants, including school records and medical records. ATSDR considers school and medical records verification necessary to maximize the quality and accuracy of the study results; otherwise, reliance on self-reported outcomes alone would be subject to recall bias. The participants will be asked to consent for ATSDR to access these records during the informed consent process (**Attachments 9b&9c**). The participant will be informed that his or her response is voluntary (**Attachments 9b&9c**).

A portion of participants may view self-reporting medical conditions that may affect employability or insurability (e.g., heart disease, cancer) as sensitive, as well as special education requirements, developmental disabilities, occupation, race, and ethnicity data (**Attachments 17, 17a, and 18**). Accidental disclosure, when linked to a person's identity, such as the medications list (**Attachment 13**) or medical records abstraction forms (**Attachment 19a&19b**) may be sufficient to discern a participant's health history. Accidental disclosure of

school records abstraction forms (**Attachment 20c**) may be damaging to a child's reputation and social standing. For all these reasons, all study staff and contractors will be trained to understand the need, and the regulatory requirements to protect the privacy and confidentiality of participants' private information (**Attachment 14**).

As stated in **Section A.10**, ATSDR wishes to collect SSNs. The following information appears on the Privacy Act Statement that the participants can keep (**Attachment 9a**), which includes: 1) the statute which authorizes ATSDR to solicit the SSN; 2) how the SSN will be used; and 3) whether the respondent's disclosure of the SSN is mandatory or voluntary.

A.12. Estimates of Annualized Burden Hours and Costs

The total annualized time burden requested is 1,454 hours.

ATSDR will recruit, screen for eligibility, and enroll in three waves (**Attachments 6c&7c**). To restrict this study to drinking water exposures, any adult occupationally exposed to PFAS will not be eligible for the study (i.e. ever firefighters or in chemical manufacture). Likewise, children whose birth mothers were occupationally exposed will not be eligible. This restriction applies to both the exposure and the referent group. ATSDR assumes that 5 percent of the people who are screened will not meet eligibility requirements based on available data about the number of firefighters who participated in the NH PFC Blood Testing Program.[4] In addition to the 95 percent eligibility rate, we assume that ATSDR will have an 70 percent response rate for Waves One (the fixed cohort). For Wave Two and Wave Three, we assume a response rate of 80 percent. We expect this response rate because these people are already interested in participating and will voluntarily call ATSDR to enroll. We are allowing that 1-in-5 (20 percent) may change their minds after hearing the consent information. We use these assumptions to calculate estimated annualized respondent counts for eligibility screening and for study enrollment, starting with the fixed number in the NH DHHS blood testing cohort (n=1,836) and the target sample sizes (n=1,625) in the research protocol.

Table A.12.1. Estimated Number of Respondents for Pease Study over Three Years (and Per Year).

[4] The initial Pease PFC Blood Testing Program in 2015 enrolled 1,578 participants. The final report is available at https://www.dhhs.nh.gov/dphs/documents/pease-pfc-blood-testing.pdf.

NH DHHS expanded PFC blood testing in 2016-2017 for a number of southern New Hampshire communities, including testing for an additional 258 Pease Tradeport residents. Their results were consistent with the 2015 Pease PFC Blood Testing Program. ATSDR will also invite these additional 258 participants in Wave One; however, the age information is not readily available to allow us to estimate the number of adults and children for the blood testing expansion in Table B.1.2. Since the demographics for the 258 cohort members are not reported by the NH DHHS, we assume the same proportion of adults to children as reported for the 2015 cohort (76.4% adults and 23.6% children), which results in 1,403 adults and 433 children screened for eligibility, or 1,836 screened for eligibility in all. See https://www.bedfordnh.org/DocumentCenter/View/2472/PFC-Blood-Testing-Aggregate-Results-Overview_FINAL_100517.

	Estimated Respondent Counts (Wave One 95% eligibility and 70% response rate) (Wave Two and Wave Three 95% eligibility and 80% response rate)					
	Exposure Group Wave One* (Per Year)	Exposure Group Wave Two (Per Year)	Total Exposure Group (Per Year)	Referent Group Wave Three (Per Year)	Total Referent Group (Per Year)	Total (Per Year)
No. Screened for Eligibility	**1,836 (612)**	*170 (57)*	*2,006 (669)*	362 *(121)*	362 *(121)*	*2,428 (809)*
No. Eligible and Enrolled	*1,221 (407)*	*129 (43)*	*1,350 (450)*	**275 (92)**	**275 (92)**	**1,625 (542)**

*All 1,836 cohort members of the 2015-17 Pease PFC Blood Testing Program are assumed to be screened and recruited in Wave One. **Bold** numbers indicate actual number of cohort members (n=1,836) or target sample sizes to be achieved (n = 1,625 = 1,350 exposed + 275 referent). *Italicized* numbers indicate numbers indirectly calculated and interpolated assuming 95% eligibility and 70% response for Wave One, and 95% eligibility and 80% response rate for Wave Two and Wave Three.

The estimates for the number of respondents in **Table A.12.1** are described in the following sections and in **Table A.12.3**. Assumptions for estimation broken down by adults and children are detailed in **Table B.1.2**.

Eligibility Screening. The estimated annual number of respondents to be screened for eligibility are based on the protocol sample size goals (n=790). The total annual time burden for eligibility screening is 146 hours.

> ***Exposure Group Screening.*** Eligible participants had to work at, live on, or attend childcare at the former Pease Air Force Base or the Pease International Tradeport, or live in a nearby home that was served by a PFAS-contaminated private well. Drinking water exposures must have occurred at some time between 2004 and May 2014, after which remediation of the public water supply occurred.
>
> The exposure group will be recruited in Waves One and Two. For eligibility screening for the exposure group (n=2,006), ATSDR will screen 1,491 adults and 515 children. Annualized estimates are 669 exposed participants (497 adults and 172 children; 612 in Wave One and 57 in Wave Two).
>
> For Wave One, NH DHHS will assist ATSDR by sending out letters of invitation to its 1,836 former blood testing program participants (**Attachments 6a&6b**). Therefore, ATSDR will screen 612 people from the NH DHHS PFAS blood testing program per year.
>
> ATSDR will screen at least 170 people in Wave Two (n=57 per year) (**Attachment 7a&7b**). These will be people who were eligible for the Pease PFC Blood Testing Program but did not take part. The annual number of respondents who will be screened for Wave Two eligibility was derived indirectly from the sample size goal of 1,350 exposed participants. The total annual number of respondents to be screened for eligibility in the exposure group is 669. Therefore, the annual number of Wave Two respondents for eligibility screening is 57 (n=669-612).

Referent Group Screening. The referent group will be screened and recruited in Wave Three (total n=362, or 121 per year), which can occur concurrently with Wave One and Wave Two (**Attachments 7d&7e**). Wave Two and Wave Three recruits will call to volunteer after ATSDR opens those waves to enrollment.

From the eligibility screening, ATSDR will enroll 100 adults and 175 children (n=275). Annualized estimates are 92 referent participants (34 adults and 58 children). Eligible participants, never exposed to PFAS-contaminated drinking water from Pease or never exposed to a private well contaminated by PFAS from the former Pease AFB, will come from other areas of Portsmouth, NH. Birth mothers of referent children likewise must never have had exposure to PFAS-contaminated drinking water at Pease or from a private well contaminated with PFAS from the former Pease AFB.

Enrollment. Over the course of the study, ATSDR will enroll a convenience sample of 1,625 eligible participants (1,100 adults and 525 children and their parents). The estimated annual number of respondents to be enrolled are based on the above protocol sample size goals (n=542=1,625/3 years=407+43+92 by Waves). The total annual time burden for appointment reminders is 45 hours (**Attachment 10**).

Exposure Group Enrollment. For the exposure group (n=1,350), ATSDR will enroll 1,000 eligible adults and 350 children. Annualized estimates are 450 exposed participants (333 adults and 117 children; 407 in Wave One and 43 in Wave Two).

Eligible participants had to work at, live on, or attend childcare at the former Pease Air Force Base or the Pease International Tradeport, or live in a nearby home that was served by a PFAS-contaminated private well. Drinking water exposures must have occurred at some time between 2004 and May 2014, after which remediation of the public water supply occurred.

Referent Group Enrollment. For the referent group (n=275), ATSDR will enroll 100 adults and 175 children. Adults will be 18 years or older, and children will be 4-17 years of age at enrollment. Annualized estimates are 92 referent participants (34 adults and 58 children).

Eligible participants, never exposed to PFAS-contaminated drinking water from Pease, will come from other areas of Portsmouth, NH. Birth mothers of referent children likewise must never have had PFAS drinking water exposure.

At enrollment, ATSDR will obtain adult consent, parental permission, and child assent before data collection begins (**Attachment 9b**). Each child will enroll with a parent, who ideally will be the child's birth mother, as ATSDR will ask details about the child's exposure, pregnancy, and breastfeeding history.

Study Data and Specimen Collection. ATSDR will take this opportunity to update each participant's contact information on hardcopy forms (**Attachment 12**; annualized time burden - 45 hours) and list out medications (**Attachment 13**; annualized time burden – 27 hours).

For each participant, ATSDR will take body measures and collect blood and urine samples for chemical and biomarker analysis (**Attachments 15 & 16**; annualized time burden – 45 and 90 hours, respectively).

ATSDR will administer a questionnaire on exposures and medical history to 1,100 adults (n=367 adults per year) (**Attachment 18**). For purposes of burden estimation for 525 child questionnaires (n=175 per year), ATSDR assumes that 20 percent of parents (n=105) will also enroll as adults; therefore, they will take the short form to reduce burden (n=35 per year) (**Attachment 17a**). The remaining 420 parents will take the long form child questionnaire (**Attachment 17**) (n=140 per year). The annualized time burden for questionnaire administration is 263 hours.

Parents and children (n=175 parent/child pairs per year) will also complete assessments of the child's attention and behaviors (**Attachments 20 & 20a**). The annualized time burden for the neurobehavioral test battery is 307 hours.

ATSDR will ask for permission to verify adults' and children's medical histories with their medical records (**Attachment 19**). Across an estimated 10 medical practices, ATSDR estimates up to 25 medical record specialists will each abstract 15 adult and 7 child medical records per year (n=1,100 adults/25 specialists/3 years; n=525 children/25 specialists/3 years) (**Attachments 19a&19b)**. The annualized time burden for medical record abstraction including the time for administrators to review the ATSDR requests for medical records is 336 hours.

ATSDR will also ask for permission to check children's school records to verify their behavioral assessment results (**Attachment 20b**). Across an estimated five schools, ATSDR estimates up to 15 education specialists will each abstract 12 student records per year (n=525 children/15 specialists/3 years) (**Attachment 20c**). The annualized time burden for school record abstraction including the time for administrators to review the ATSDR requests for school records is 120 hours.

Table A.12.2. Estimated Annualized Burden Hours

Type of Respondents	Form Name	Number of Respondents	Number of Responses per Respondent	Average Burden per Response (in hours)	Total Burden (in hours)
Pease Study Participants	Wave One Eligibility Screening Script	612	1	10/60	102
	Wave Two Eligibility Screening Script	57	1	15/60	14
	Wave Three Eligibility Screening Script	121	1	15/60	30
	Appointment Reminder	542	1	5/60	45

	Telephone Script				
	Update Contact Information Hardcopy Form	542	1	5/60	45
	Medication List	542	1	3/60	27
	Body and Blood Pressure Measures Form	542	1	5/60	45
	Blood Draw and Urine Collection Form	542	1	10/60	90
	Adult Questionnaire	367	1	30/60	184
	Child Questionnaire – Long Form	140	1	30/60	70
	Child Questionnaire – Short Form	35	1	15/60	9
	Parent Neurobehavioral Test Battery	175	1	15/60	44
	Child Neurobehavioral Test Battery	175	1	90/60	263
School Administrators	Request for Child School Record Abstraction	5	36	20/60	60
Education Specialists	Child School Record Abstraction Form	15	12	20/60	60
Medical Office Administrators	Request for Medical Record Abstraction	10	55	20/60	183
Medical Record Specialists	Medical Record Abstraction Form - Adult	25	15	20/60	125
	Medical Record Abstraction Form - Child	25	7	20/60	58
Total					1,454

The total annualized cost burden requested is $42,228.37.

Estimates of the annualized cost to respondents were based on the Department of Labor “May 2018 National Occupational Employment and Wage Estimates, United States” mean hourly wages. (https://www.bls.gov/oes/current/oes_nat.htm#00-0000).

ATSDR used the following occupation codes and hourly wage estimates to represent each respondent type in the burden table.

Table A.12.4. Mean Hourly Wages for Respondent Types

Respondent Type	Occupation Code	Occupation Title	Mean Hourly Wage
Pease Study Participants	00-0000	All Occupations	$24.98
School Administrators	11-9030	Education Administrators	$46.65
Education Specialists	25-9099	Education, Training, and Library Workers, All Other	$22.44
Medical Office Administrators	11-9111	Medical and Health Services Managers	$54.68
Medical Record Specialists	29-2071	Medical Records and Health Information Technicians	$21.16

Table A.12.4. Estimated Annualized Burden Costs

Type of Respondent	Form Name	Number of Respondents	Number of Responses per Respondent	Average Burden per Response (in hours)	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Pease Study Participants	Wave One Eligibility Screening Script	612	1	10/60	102	$24.98	$2,547.96
	Wave Two Eligibility Screening Script	57	1	15/60	14	$24.98	$355.97
	Wave Three Eligibility Screening Script	121	1	15/60	30	$24.98	$755.65
	Appointment Reminder Telephone Script	542	1	5/60	45	$24.98	$1,128.26
	Update Contact Information Hardcopy Form	542	1	5/60	45	$24.98	$1,128.26
	Medication List	542	1	3/60	27	$24.98	$676.96
	Body and Blood Pressure Measures Form	542	1	5/60	45	$24.98	$1,128.26
	Blood Draw and Urine Collection Form	542	1	10/60	90	$24.98	$2,256.53
	Adult Questionnaire	367	1	30/60	184	$24.98	$4,583.83
	Child Questionnaire – Long Form	140	1	30/60	70	$24.98	$1,748.60
	Child Questionnaire – Short Form	35	1	15/60	9	$24.98	$218.58
	Parent Neurobehavioral Test Battery	175	1	15/60	44	$24.98	$1,092.88
	Child Neurobehavioral Test Battery	175	1	90/60	263	$24.98	$6,557.25
School Administrators	Request for Child School Record Abstraction	5	36	20/60	60	$46.65	$2,799.00
Education Specialists	Child School Record Abstraction Form	15	12	20/60	60	$22.44	$1,346.40

Medical Office Administrators	Request for Medical Record Abstraction	10	55	20/60	183	$54.68	$10,024.67
Medical Record Specialists	Medical Record Abstraction Form - Adult	25	15	20/60	125	$21.16	$2,645.00
	Medical Record Abstraction Form - Child	25	7	20/60	58	$21.16	$1,234.33
Total							$42,228.37

A.13. Estimates of Other Total Annual Cost Burden to Respondents and Record Keepers

There are no required capital and start-up costs to respondents or record-keepers for the Pease Study. In addition, there are no cost requirements for operation, maintenance, and purchase of equipment or services for respondents or record-keepers.

A.14. Annualized Cost to the Federal Government

Pursuant to PL 115-141, ATSDR received funds from the Department of Defense to conduct the research on the health effects of PFAS in drinking water.

The annualized cost of the Pease Study is $1,912,122.70 . This estimate was based on the following table:

Table A.14.1. Annual Estimated Costs to the Federal Government

Staff	GS Level	Salary (2018)	% FTE	$ Cost
Study co-PI; Technical Officer	14	$140,765	50	$70,382.50
Study co-PI, Technical Officer	14	$140,765	70	$98,535.50
Project Officer, Health Scientist	12	$87,332	85	$74,232.20
Associate Service Fellow	11	$72,863	50	$36,431.50
Other Annualized Costs				$ Cost
Contracts				
Pease PFAS Health Study (for data collection and historical reconstruction of PFAS exposures)				$1,615,874.00
Travel				$16,667
Total				$1,912,122.70

A.15. Explanation for Program Changes or Adjustments

This is a new information collection.

A.16. Plans for Tabulation and Publication and Project Time Schedule

The 2018 National Defense Authorization Act (NDAA) (PL 115-91) was enacted on 12/12/2017, and serves as a guide for the scope of the study for which appropriations were authorized under the Consolidated Appropriations Act, 2018 (PL 115-141) (**Appendix A**). It specifies that "not later than 5 years after the date of enactment of this Act (or 7 years after such date of enactment after providing notice to the appropriate congressional committees of the need for the delay)," that ATSDR is to complete such study and make any appropriate recommendations; and submit a report to the appropriate congressional committees on the results of such study.

Therefore, ATSDR aims to complete the data collection by the end of 2021 (approximately 3 years), and to complete data analysis and reports by the end of 2023 (5 years). As required by statute and by the regulations (PL 96-510 or 42 CFR part 90.11), resulting reports of research conducted by ATSDR "shall be reported or adopted only after appropriate peer review" as a routine practice of the Agency.

Table A.16.1. Project Time Schedule

Activity	Time Schedule
Letters sent to respondents	1—4 months after OMB approval
Information/Data collection	5—30 months after OMB approval
Complete field work	31-32 months after OMB approval
Validation	31—37 months after OMB approval
Analyses	34—55 months after OMB approval
Publications	60 months after OMB approval

If unforeseen delays occur, ATSDR may submit a 2-year extension or revision, making the time to complete the report to Congress a total of 7 years.

A.17. Reason(s) Display of OMB Expiration Date is Inappropriate

The display of the OMB expiration date is appropriate.

A.18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification. These activities comply with the requirements in 5 CFR 1320.9.

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List of Appendices and Protocol Attachments

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