

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

Principal Investigator: Marian Pavuk, MD, PhD

Title: Senior Epidemiologist

ATSDR Division of Toxicology and Human Health Sciences

Email: fsh8@cdc.gov

Phone: 770-488-3671

Fax: 770-488-1541

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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 issues that need to be addressed before embarking on a national multi-site study; and 2) examine associations between health outcomes and measured and historically reconstructed serum levels of PFAS.

Intended use of the resulting data: ATSDR will examine the association between PFAS compounds and 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 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.

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.

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 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.

How data will be analyzed: ATSDR staff will calculate descriptive statistics to identify the presence and distribution of PFAS and effect biomarker analytes in the Pease participants and their referent groups. Statistical methods will include multiple linear regression of continuous effect biomarkers on continuous PFAS serum levels and categorized PFAS serum levels, and logistic regression of categorized effect biomarkers or disease prevalence on continuous and categorical PFAS serum levels. ATSDR staff will use restricted cubic spline methods (or generalized additive models using cubic regression splines) for linear and logistic regression to obtain flexible, smoothed exposure-response curves. To identify risk factors that may act as confounders for a particular health outcome, the analysis will implement a “10% change in the estimate” rule.

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 ($\mu\text{g}/\text{L}$). 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**).

In response, 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 national 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, PFAS drinking water concentrations were detected (0.35 $\mu\text{g}/\text{L}$ PFOA and 2.4 $\mu\text{g}/\text{L}$ PFOS) at levels well above what was to become the USEPA lifetime health advisory level (0.07 $\mu\text{g}/\text{L}$ PFOA/PFOS). 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 Pease population had concentrations of some types of PFAS that were two to three times higher than national estimates.

ATSDR and the Centers for Disease Control (CDC) National Center for Environmental Health (NCEH) were mandated the authority 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

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 Pease. The main goals of the research study are to: 1) evaluate the study procedures and methods to identify any issues that need to be addressed before embarking on a national multi-site study; and 2) examine associations between health outcomes and measured and historically reconstructed serum levels of PFAS.

In 2017, ATSDR conducted a feasibility assessment and literature review to identify candidate designs and health outcomes for the Pease Study and a national 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 effect biomarkers and the prevalences of nonfatal diseases, in particular, diseases with no clear point of onset (Checkoway 2004). ATSDR does acknowledge inherent limitations, as the cross-sectional study concurrently measures 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). ATSDR aims to incorporate historically reconstructed serum levels PFAS to partially address this limitation. The initial results of the Pease Study and the national multi-site study may justify prospective PFAS studies in the future, which can be much more costly than cross-sectional designs.

Based on the feasibility assessment (ATSDR 2017), ATSDR will examine the association between PFAS compounds and 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 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. Adults will be 18 years or older, and children will be 4-17 years of age at enrollment.

Reasons that ATSDR selected the Pease community in Portsmouth, NH, as a suitable proof-of-concept model site for a national 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.
- The 2015-7 NH DHHS PFAS blood testing program was offered to address the health 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.
 - 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 the 2015-7 NH DHHS PFAS blood testing program.
- NCEH DLS will also perform blood and urine PFAS analyses for the Pease Study. Thus issues of inter-laboratory variability are avoided.
 - ATSDR will seek consent to access 2015-7 PFAS blood testing results from applicable Pease Study participants (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.

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

ATSDR will use information technology to reduce burden for over 36 percent of the information collections.

Attachment No.	Form Name	Mode of Collection	No. Responses	Total Burden (in hours)
6c	Wave One Eligibility Screening Script	CATI	526	88
7c	Wave Two Eligibility Screening Script	CATI	66	16
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			1,797	442
Pease Study Total			4,519	1,199
Improved Technology Percent			39.8%	36.9%

Computer Assisted Telephone Interviews (CATIs) and Computer Assisted Personal Interviews (CAPIs) programmed into Epi Info™¹ 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 ICR submission to OMB.

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

2005-2013

¹ <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. Given that the primary PFAS released by the chemical manufacturer was C8 (PFOA), the “probable link” to health outcomes are extremely informative for the Pease Study, but does not address all the PFAS constituents found in Pease drinking water.

2017

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 (**Attachment 3**).

2018

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.

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

Medical practices and schools may be defined as small businesses or small entities.² The annual time burden for medical and educational record abstraction is estimated to be 122 hours for adult records and 116 hours for children's records. The portion of the time burden for medical and school record abstractions (125 + 58 + 60 = 243 hours) represents 20.3 percent of the total hours requested (243/1,199 x 100).

The time to complete the school record abstraction form and the adult and child medical record abstraction forms is 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.

² 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.

- 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. 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).
 - 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.

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. We are requiring the following:

- 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.
 - Justification for reporting frequency greater than quarterly is provided in **Sections A.5 and A.6.**
- The 2015-7 NH DHHS PFAS blood testing program recruited a convenience sample. As the proof of concept model for a national multi-site study, ATSDR will use this existing recruitment frame 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 for selection bias, ATSDR will compare the demographics of the convenience sample of Pease Study participants with U.S. Census estimates of the Pease community and of the City of Portsmouth, NH.

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 11 public comments, two were posted in duplicate, and 7 were substantive comments. The ATSDR response is provided **Appendix B1**.
- B. The following persons outside and inside the agency were consulted (**Attachment 1**).

Table A.8.1. ATSDR External Consultations, 2018

Name	Title	Affiliation	Phone	Email/Date of Consultation
<i>OUTSIDE CONSULTANTS</i>				
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 - per CERCLA requirements for research, four independent peer reviewers			
Matthew P. Longnecker, MD, ScD	Consultant	Ramboll Group A/S Consultants	(919) 765-8029	m-longnecker@ramboll.com 05/31/2018
Mark Strynar, PhD	Physical Scientist	US EPA National Research Exposure Laboratory (NERL)	(919) 541-3706	strynar.mark@epa.gov 09/06/2018
<i>ACADEMIC INSTITUTIONS</i>				
Kyle Steenland, PhD	Professor, Epidemiologist	Emory University	(404) 712-8277	ksteenl@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

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 Breyse, 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	hbb9@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 Sciences (DTHHS), Acting	(770) 488-3807	atr0@cdc.gov

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 questionnaire; 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 card.

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 C**).

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. Further discussion on the collection of Social Security Number (SSN) is found in **Section A.11**:

- | | |
|--|---|
| <input type="checkbox"/> Name | <input type="checkbox"/> Biological Specimens |
| <input type="checkbox"/> Date of Birth | <input type="checkbox"/> Email Address |
| <input type="checkbox"/> Social Security Number (SSN) | <input type="checkbox"/> Education Records |
| <input type="checkbox"/> Mailing Address | <input type="checkbox"/> Military Status |
| <input type="checkbox"/> Phone Numbers | <input type="checkbox"/> Employment Status |
| <input type="checkbox"/> Medical Information and Notes | |

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.

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.
 - Release of de-identified data to outside investigators must be approved by ATSDR. 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 non-exempt human subjects' research under 45 CFR 46. The CDC IRB approval memo is found in **Appendix E**.

The CoC approval also is found in **Appendix E**. A CoC is automatically issued 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 diagnoses of 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 20b**) 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 regulations set aside, to protect the privacy and confidentiality of participants' private information (**Attachment 14**).

As stated in **Section A.10**, ATSDR wishes to collect Social Security Numbers (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 1,199 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. In addition to the 95 percent eligibility rate, we assume that ATSDR will have an 80 percent response rate. We use these two assumptions to calculate estimated annualized respondent counts for eligibility screening and for study enrollment, starting with the existing number in the NH DHHS blood testing cohort and the target sample sizes in the research protocol.

Table A.12.1. Estimated Number of Respondents for Eligibility Screening and Enrollment

	ESTIMATED RESPONDENT COUNTS (assuming 95% eligibility and 80% response)						
	EXPOSURE GROUP				REFERENT GROUP		STUDY PARTICIPANTS
	WAVE ONE PER YEAR	WAVE TWO PER YEAR	TOTAL PER YEAR	THREE-YEAR TOTAL	WAVE THREE PER YEAR	THREE YEAR TOTAL	THREE YEAR TOTAL
No. Screened for Eligibility	526 (1,578/3 years)	66 [592-526]	592 [1,776/3 years]	1,776 [1,350* (100/95)* (100/80)]	121 [362/3 years]	362 [275* (100/95)* (100/80)]	2,138 [1,625* (100/95)* (100/80)]
	NOTE: 1,578 is the total number of NH DHHS blood testing program participants.	or [50* (100/95)* (100/80)]	or [450* (100/95)* (100/80)]		or [92* (100/95)* (100/80)]		
No. Eligible and	400 [526*(95/100)*]	50 [450-400]	450 (333)	1,350 (1,000)	92 (34 adults;	275 (100 adults;	1,625 (1,100 adults;

Enrolled	(80/100)]		adults; 117 children) [1,350/3 years]	adults; 350 children) (Target sample size)	58 children) [275/3 years]	175 children) (Target sample size)	525 children) (Target sample size)
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The estimates for the number of respondents in Table A.12.1 are described in the following sections.

Eligibility Screening. The estimated annual number of respondents to be screened for eligibility are based on the protocol sample size goals ($n=713=526+66+121$). The total annual time burden for eligibility screening is 134 hours.

Exposure Group Screening. For the exposure group ($n=1,350$), ATSDR will enroll 1,000 adults and 350 children. Annualized estimates are 450 exposed participants (333 adults and 117 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. 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 Wave One, NH DHHS will assist ATSDR by sending out letters of invitation to its 1,578 former blood testing program participants (**Attachments 6a&6b**). Therefore, ATSDR will screen 526 people from the NH DHHS PFAS blood testing program per year ($n=1,578/3$ years).

ATSDR will screen at least 198 exposed people in Wave Two ($n=66$ per year) (**Attachment 7a&7b**). These will be people who were eligible for the NH DHHS PFAS blood testing program but did not take part.

The annual number of respondents who will be screened for Wave Two eligibility ($n=66$) was derived indirectly from the sample size goal of 1,350 exposed participants. We assumed 95 percent eligibility and 80 percent response of the total number of respondents in the exposure group to be screened [$n=1,776=1,350*(100/95)*100/80$]. The total annual number of respondents to be screened for eligibility in the exposure group is 592. Therefore, the annual number of Wave Two respondents for eligibility screening is 66 ($n=592-526$).

Referent Group Screening. For the referent group ($n=275$), ATSDR will enroll 100 adults and 175 children. 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.

The referent group will be screened and recruited in Wave Three (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.

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=400+50+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 adults and 350 children. Annualized estimates are 450 exposed participants (333 adults and 117 children; 400 Wave One and 50 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 compare adults’ and children’s medical histories with their medical records (**Attachments 19a&19b**). 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). The annualized time burden for medical record abstraction is 183 hours.

ATSDR will also ask for permission to check children’s school records to compare their behavioral assessment results (**Attachment 20b**). 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). The annualized time burden for school record abstraction is 60 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	526	1	10/60	88
	Wave Two Eligibility Screening Script	66	1	15/60	16
	Wave Three Eligibility Screening Script	121	1	15/60	30
	Appointment Reminder Telephone Script	542	1	5/60	45
	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
Education Specialists	Child School Record Abstraction Form	15	12	20/60	60
Medical Record Specialists	Medical Record Abstraction Form - Adult	25	15	20/60	125
	Medical Record Abstraction Form - Child	25	7	20/60	58
Total					1,199

The total annualized cost burden requested is \$28,401.63. Estimates of the annualized cost to respondents were based on the Department of Labor “May 2017 National Occupational Employment and Wage Estimates, United States” (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	\$24.34
Education Specialists	25-9099	Education, Training, and Library Workers, All Other	\$22.69
Medical Record Specialists	29-2071	Medical Records and Health Information Technicians	\$20.59

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	526	1	10/60	88	\$24.34	\$2,133.81
	Wave Two Eligibility Screening Script	66	1	15/60	16	\$24.34	\$401.61
	Wave Three Eligibility Screening Script	121	1	15/60	30	\$24.34	\$736.28

	Appointment Reminder Telephone Script	542	1	5/60	45	\$24.34	\$1,099.36
	Update Contact Information Hardcopy Form	542	1	5/60	45	\$24.34	\$1,099.36
	Medication List	542	1	3/60	27	\$24.34	\$659.61
	Body and Blood Pressure Measures Form	542	1	5/60	45	\$24.34	\$1,099.36
	Blood Draw and Urine Collection Form	542	1	10/60	90	\$24.34	\$2,198.71
	Adult Questionnaire	367	1	30/60	183	\$24.34	\$4,466.39
	Child Questionnaire - Long Form	140	1	30/60	70	\$24.34	\$1,703.80
	Child Questionnaire - Short Form	35	1	15/60	9	\$24.34	\$212.98
	Parent Neurobehavioral Test Battery	175	1	15/60	44	\$24.34	\$1,064.88
	Child Neurobehavioral Test Battery	175	1	90/60	263	\$24.34	\$6,389.25
Education Specialists	Child School Record Abstraction Form	15	12	20/60	58	\$22.69	\$1,361.40
Medical Record Specialists	Medical Record Abstraction Form - Adult	25	15	20/60	125	\$20.59	\$2,573.75
	Medical Record Abstraction Form - Child	25	7	20/60	60	\$20.59	\$1,201.08
Total							\$28,401.63

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 \$1,629,467.70. This estimate was based on the following table:

Study Co-PI, Technical Officer	14	\$140,785	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				\$ Cost
Contracts (list out all types)				
Pease PFAS Health Study (PR #: 000HJAAM-2019-29724; PIIN: 200-2018-01410)				\$1,333,219
Travel (PR #: 000HJAAM-2019-29724; PIIN: 200-2018-01410)				\$16,667
Total				\$1,629,467.70

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

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.

References

- Agency for Toxic Substances and Disease Registry (ATSDR). Feasibility Assessment for Epidemiological Studies at Pease International Tradeport. Portsmouth, New Hampshire. November 2017. Available at:
https://www.atsdr.cdc.gov/sites/pease/documents/Pease_Feasibility_Assessment_November-2017_508.pdf
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- Flanders WD, Klein M, Mirabelli MC. Conditions for valid estimation of causal effects on prevalence in cross-sectional and other studies. Ann Epidemiol 2016;26:389-394.

List of Appendices and Protocol Attachments

Appendix A. Authorizing Legislation

Appendix B. 60-day Federal Register Notice

Appendix B1. Public Comments and Program Responses

Appendix C. ATSDR Pease Feasibility Assessment

Appendix D. Privacy Impact Assessment

Appendix E. IRB Approval Memo

Pease Study Protocol and Attachments

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Attachment 2. PFAS Serum Levels, Pease vs. External Populations

Attachment 2a. Pease serum PFAS levels in $\mu\text{g/L}$, by age groups, 2018

Attachment 2b. Serum PFAS levels in $\mu\text{g/L}$, children aged <12 years, Pease vs. comparisons

Attachment 2c. Serum PFAS levels in $\mu\text{g/L}$, aged ≥ 12 years, Pease vs. NHANES

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Attachment 4. Justification for Sample Size Calculations

Attachment 4a. Sample Size for Child Study

Attachment 4b. Sample Size for Adult Study

Attachment 5 – Pease Study Communication Plan

Attachment 5a. Pease Study Communication Plan Objectives

Attachment 5b. Pease Study Overarching Communication Messages

Attachment 5c. Pease Study Press Release – Launch

Attachment 5d. Pease Study Website Flyer

Attachment 5e. Pease Study Public Service Announcement

Attachment 6 – Wave One - NH DHHS Invitation Letters for Study Roll Out

Attachment 6a – NH DHHS Child Invitation Letter

Attachment 6b – NH DHHS Adult Invitation Letter

Attachment 6c – Wave One Eligibility Screening Script

Attachment 7 – Waves Two and Three Recruitment Materials

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Attachment 7b – Wave Two Flyer to Recruit Additional Exposed Adults

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Attachment 7d – Wave Three Child Flyer for Referent Recruitment
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Attachment 9b1 – Privacy Act Statement
Attachment 9b2 – Parental Permission and Child Assent Forms
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Attachment 10 – Appointment Reminder Telephone Script
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Attachment 13 – Medication List
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Attachment 17 – Child Questionnaire – Long Form
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Attachment 19a – Medical Record Abstraction Form - Adult
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Attachment 20 – Child/Parent Neurobehavioral Test Battery
Attachment 20a – NBT Time Estimation Table, by Age in Years
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Attachment 21 – Body and Blood Pressure Measurements Report
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Attachment 22b – Letter Report of Critical Values
Attachment 23 – Clinical Test Results Report
Attachment 24 – PFAS Results Report

Attachment 24a - ATSDR PFAS Factsheet