

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 B –

Collections of Information Employing Statistical Methods

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Part B. Collections of Information Employing Statistical Methods

B.1. Respondent Universe and Sampling Methods

Statistical methods will not be used to recruit participants for the Pease Study.

The respondent universe and the rationale for using convenience sampling methods are described in the **Pease Study Protocol**. 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.

Respondent Universe: In summary, ATSDR will enroll 1,625 participants (1,100 adults and 525 children and their parents). The study populations and eligibility are discussed in the **Pease Study Protocol Section 3.2**. Statistical justification for desired sample sizes is provided in **Pease Study Protocol Section 3.3** and in more detail in **Attachment 4**.

Adults will be 18 years or older, and children will be 4-17 years of age at enrollment. Ideally, the parent should be the mother, who can best answer some survey questions about the child's exposures and about the mother's pregnancy and breastfeeding history. A parent can enroll with more than one child. In this case, ATSDR will enroll each child separately along with his or her parent. Parents, if eligible, may also enroll in the adult study.

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.

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. Drinking water exposures must have occurred at some time between 2004 and May 2014, after which remediation of the public water supply occurred.

For the referent group (n=275), ATSDR will enroll 100 adults and 175 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.

Sampling Methods: 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. Recruitment methods are described in the **Pease Study Protocol Section 3.5**. No statistical methods will be employed for recruitment. The Pease Study builds off the existing state and local PFAS exposure assessments during the 2015-7 NH DHHS PFAS blood testing program, which employed convenience sampling to address community concern. See further discussion in **Section A.2 of Supporting Statement A - Justification**.

Trained study staff and contractors from ATSDR will recruit, screen for eligibility, and enroll in three waves (**Attachments 6c&7c**). ATSDR assumes that 5 percent of the people who volunteer will not meet eligibility requirements.

- Due to the substantial community, state, and Congressional interest in the Pease Study, ATSDR estimates that 90 percent of the exposure group will be enrolled in Wave One (n=1,215), that is, will be past participants of the 2015-7 NH DHHS PFAS blood testing program. NH DHHS will assist ATSDR by sending out letters of invitation to its former blood testing program participants (**Attachments 6a&6b**).
 - Assuming that all of the blood testing program cohort will respond to the NH DHHS letters of invitation (**Attachments 6a&6b**), ATSDR will screen the 1,578 people from the NH DHHS PFAS blood testing program in Wave One. Of the past participants of the NH DHHS PFAS blood testing program, 1,499 persons will be eligible.
 - If 1,215 enroll in Wave One that will result in a response rate to the NH DHHS letter of invitation of 81 percent.
- Wave Two and Wave Three recruits will call to volunteer after ATSDR opens those waves to enrollment.
 - To achieve the desired sample size, the other 10 percent of the exposure group (n=135) will be recruited in Wave Two (**Attachments 7a&7b**). These will be people who were eligible for the PFAS blood testing program but did not take part.
 - ATSDR will screen at least 142 exposed people in Wave Two to get 135 eligible.
 - The referent group will be recruited in Wave Three (n=275), which can occur concurrently with Wave One and Wave Two (**Attachments 7d&7e**).
 - ATSDR will screen at least 289 unexposed people in Wave Three to get 275 eligible.

Steps in screening are:

- Administer the eligibility screening scripts and schedule appointments (**Attachments 6c&7c**).

- Begin tracking the recruitment process (**Attachment 8**).
- Mail out appointment packets (**Attachment 9**), which will contain the following documents to keep and read before their appointments:
 - Appointment reminder cards (**Attachment 9a**), with instructions on how to prepare for the appointment
 - Informed consent packets (**Attachment 9b**),
 - Privacy Act Statement (**Attachment 9b1**)
 - Parental Permission and Child Assent Forms (**Attachment 9b2**)
 - Parental Consent to Release Student Information (**Attachment 9b3**)
 - Adult Consent Form (**Attachment 9b4**)
 - Parent/Child/Adult Permission for Medical Record Abstraction (**Attachment 9b5**)
 - Study Fact Sheet (**Attachment 9c**)
- Encourage participation with appointment reminder calls (**Attachments 10&11**).

B.2. Procedures for the Collection of Information

At the appointment, enrollment and data collection procedures are described in the **Pease Study Protocol Section 3.5.3, Section 3.6**, and in the Manual of Procedures for staff and contractor training (**Attachment 14**). Steps in enrollment are:

- Administration of informed consent, parental permission, and child assent (**Attachment 9b**).
- Update participant contact information, if needed (**Attachment 12**).
- Record participant medication list (**Attachment 13**).
- Take body and blood pressure measures (**Attachment 15**).
- Collect blood and urine biospecimens (**Attachment 16**).
- Administer questionnaire (**Attachment 17, 17a, 18**).
- (For children and parents) Administer the neurobehavioral test battery (**Attachment 20**).

After the appointment, ATSDR will seek:

- Medical record verification for self-reported conditions noted in the questionnaire (**Attachment 19, 19a, 19b**).

- Education record verification to compare to the results of the children's neurobehavioral assessments and their parents' assessments of their children (**Attachment 20b**).

B.3. Methods to Maximize Response Rates and Deal with Non-response

The **Pease Study Protocol Section 3.2.1** describes the estimated number of eligible children and assumptions about participation rates needed to achieve statistical goals:

“Assuming that a minimum of about 500 children attended the two day-care centers at Pease before June 2014 and would be aged 4–17 years in 2018, we would require a participation rate of about 70% to recruit 350 Pease children into the study. Such a participation rate is possible given the high visibility of the study, strong interest in the community, and the commitment of the Pease CAP and associated organizations to conduct outreach for the study.

It would also be feasible to recruit at least 175 children in the same age range from the schools in Portsmouth, NH, who were unexposed to the PFAS-contaminated drinking water at the Pease Tradeport and whose parents did not work at the Pease Tradeport or have occupational exposures to PFAS.”

The **Pease Study Protocol Section 3.2.2** describes the estimated number of eligible adults and assumptions about participation rates needed to achieve statistical goals:

“Apart from the occupational exposure exclusion, the study will recruit adults who participated in the Pease biomonitoring program. Adults who did not participate in biomonitoring program but meet eligibility criteria could also enroll in the current study in order to meet sample size requirements. About 1,430 adults have participated in this program. A participation rate of 70% would result in a sample size of about 1,000. In addition, for some of the outcomes of interest, e.g., serum level of total cholesterol, hyperuricemia, and cardiovascular disease, a sample size of 1,000 would be sufficient for PFAS serum levels categorized into quartiles.

The study will recruit a comparison population of 100 adults, unexposed to the contaminated drinking water at Pease, consisting of adults aged ≥ 18 years, taking into account the age distribution of the adults who participated in the Pease biomonitoring program.”

In order to maximize participation in the Pease Study, ATSDR will provide the flexibility to schedule or re-schedule office or home visits within the study period (**Pease Study Protocol Section 3.5.3**).

- Interested recruits who are unable or unwilling to come to the study office, will be offered an in-home appointment by trained study staff to complete the study. Interested recruits who request or require a home interview, blood draw, and urine collection, must reside within a one-hour drive from the study office.
- Study staff will give the interested recruit a reminder telephone call one to two days before the scheduled appointment (**Attachment 10**).
 - The study staff will make up to five contact attempts to an interested recruit who misses an appointment in order to reschedule the appointment and maximize the number of completed appointments (**Attachment 11**).

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

The **Pease Study Protocol** will serve as the proof of concept research study. One of the main goals of the research study is to evaluate the study procedures and methods to identify any issues that need to be addressed before embarking on a national multi-site study.

ATSDR will use the proof of concept study experience to refine questions, minimize burden, and improve utility. Some of the proposed data/information collection instruments have been based on those successfully used in the “Anniston Community Health Survey: Follow up and Dioxin Analyses (ACHS-II)” (OMB Control No. 0923-0049; discontinued 11/12/2015) (**Attachments 12, 13, 15, 16**).

The Pease Study questionnaires (**Attachments 17, 17a, 18**) were developed specifically for the unique PFAS exposure scenarios at Pease; therefore, ATSDR will use this proof of concept experience to see if questionnaire refinement will be recommended for the multi-site protocol. Additionally, eligibility screeners (**Attachments 6c, 7c**), medical records abstraction forms (**Attachments 19a, 19b**), and the school records abstraction form (**Attachment 20b**) are new forms to be tested for ease of use and utility.

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

Table B.5.1. Personnel Consulted on Statistical Design

Name	Title	Affiliation	Phone	Email
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FEDERAL AGENCY				
Marian Pavuk, MD, PhD	Senior Epidemiologist, PI Pease Study	ATSDR	(770) 488-3671	fsh8@cdc.gov
Frank Bove, DSc	Senior Epidemiologist, PI Pease Study	ATSDR	(770) 488-3809	fjb0@cdc.gov

Table B.5.2. Personnel Responsible for Collection and Analysis of Information

Name	Title	Affiliation	Phone	Email
Marian Pavuk, MD, PhD	Senior Epidemiologist, PI Pease Study	ATSDR	(770) 488-3671	fsh8@cdc.gov
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References

Agency for Toxic Substances and Disease Registry (ATSDR). Feasibility Assessment for Epidemiological Studies at Pease International Tradeport. Portsmouth, New Hampshire. November 2017. **Appendix C** 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

Attachment 1. Investigators and Key Study Personnel

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

Attachment 3. Biochemical Analytical Plan in Children and Adults

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

Attachment 7a – Wave Two Flyer to Recruit Additional Exposed Children

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

Attachment 7c – Wave Two or Wave Three Eligibility Screening Script

Attachment 7d – Wave Three Child Flyer for Referent Recruitment

Attachment 7e – Wave Three Adult Flyer for Referent Recruitment

Attachment 8 – Recruitment Tracking Form

Attachment 9 – Appointment Packet

- Attachment 9a – Appointment Reminder Card
- Attachment 9b – Informed Consent Packet
 - Attachment 9b1 – Privacy Act Statement
 - Attachment 9b2 – Parental Permission and Child Assent Forms
 - Attachment 9b3 – Parental Consent to Release Student Information
 - Attachment 9b4 – Adult Consent Form
 - Attachment 9b5 – Parent/Child/Adult Permission for Medical Record Abstraction
- Attachment 9c – Study Fact Sheet

Attachment 10 – Appointment Reminder Telephone Script

Attachment 11 – Appointment Tracking Form

Attachment 12 – Update Contact Information Hardcopy Form

Attachment 13 – Medication List

Attachment 14 – Manual of Procedures

Attachment 15 – Body and Blood Pressure Measures Form

Attachment 16 – Blood Draw and Urine Collection Form

Attachment 17 – Child Questionnaire – Long Form

- Attachment 17a – Child Questionnaire – Short Form

Attachment 18 – Adult Questionnaire

Attachment 19 – Letter to Provider for Record Abstraction

- Attachment 19a – Medical Record Abstraction Form - Adult
- Attachment 19b – Medical Record Abstraction Form - Child

Attachment 20 – Child/Parent Neurobehavioral Test Battery

- Attachment 20a – NBT Time Estimation Table, by Age in Years
- Attachment 20b – Child School Record Abstraction Form

Attachment 21 – Body and Blood Pressure Measurements Report

Attachment 22 – Advance Reporting Script for Clinical Tests

- Attachment 22a – Advance Clinical Test Report Tracking Form
- Attachment 22b – Letter Report of Critical Values

Attachment 23 – Clinical Test Results Report

Attachment 24 – PFAS Results Report

- Attachment 24a – ATSDR PFAS Factsheet