1. Introduction

The Pease International Tradeport is located in Portsmouth, New Hampshire (NH) on land that was formerly the Pease Air Force Base. In 1993, companies began to operate at the Tradeport. It contains over 250 companies employing more than 9,525 people. Two day care centers are located at the Tradeport.

In April and May 2014, the three drinking water supply wells serving the Pease Tradeport were sampled for perfluoroalkyl substances (PFAS). The Haven Well, which supplied about half of the total drinking water at the Pease Tradeport at the time of the sampling, was found to have perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), and perfluorohexane sulfonate (PFHxS) levels averaging 2.5 micrograms per liter (µg/L), 0.34 µg/L, and 0.90 µg/L, respectively. While the Environmental Protection Agency has a lifetime health advisory for PFOS and PFOA, no regulatory standards by any federal agency have been promulgated for PFAS. Much lower levels of these contaminants were found in the other two wells serving the Pease Tradeport. The Haven well was shut down in May 2014.

The contamination of the drinking water wells was the result of the use of aqueous film forming foam (AFFF) at the former Pease Air Force Base for firefighting training and to extinguish flammable liquid fires. The firefighting foam contained PFAS. It was used at the base from approximately 1970 until the base closed in 1991. The AFFF likely leached into the soil and groundwater and migrated to the three drinking water supply wells that served the base and later served the Pease Tradeport. It is not known when these wells were contaminated with PFAS. However, it is possible that the contamination began when the base was still in operation and prior to the opening of the Tradeport in 1993.

During April – October 2015, a blood testing program for PFAS was conducted by the NH Department of Health and Human Services. The program was for those who may have been exposed to the contaminated drinking water at the Pease Tradeport or those who consumed water from contaminated private wells adjacent to the Tradeport. A total of 1,578 individuals volunteered to submit a blood sample. A report of the program found that the average levels of PFOS, PFOA and PFHxS in the blood of those tested were higher than national averages for these chemicals (http://www.dhhs.nh.gov/dphs/documents/pease-pfc-blood-testing.pdf).

The Agency for Toxic Substances and Disease Registry (ATSDR) evaluated the feasibility of conducting epidemiological studies of the populations at the Pease Tradeport. This assessment was in response to community health concerns and the community’s request for health studies. The purpose of the assessment was to determine whether studies are feasible to conduct at Pease given the size of the exposed populations, and whether data exist to conduct scientifically credible studies.
2. Approach

ATSDR used three criteria to determine whether health studies were feasible:

- **Meaningful and credible results** – a study should have sufficient validity and precision, be capable of detecting moderate as well as large health-related effects, and be as responsive as possible to the community’s questions and concerns.

- **Scientific importance** – a study should evaluate biologically plausible diseases and other health-related endpoints (also called “effect biomarkers”) and improve our understanding of possible health effects of PFAS exposures.

- **Public health significance** – a study should provide a strong basis for determining if PFAS exposures increase the risks of specific adverse health effects, and if so, what public health actions are necessary to reduce the risks. The study should also be relevant to other populations with similar exposures.

Feasibility was also assessed in terms of whether sufficient participation (sample size) could be obtained from within the Pease community, or whether the study would need to be expanded to other communities beyond the Pease population.

ATSDR reviewed published health studies to identify health-related endpoints that have been studied and the data gaps that exist. The review found that most information on potential health effects concerned exposures to PFOA, much less information was available for PFOS exposures, and very little information was available for PFHxS exposures. In general, there was limited information on the human health effects of PFAS exposures because research is still at an early stage. Because of this research gap, health studies of the Pease population might contribute to scientific knowledge about the health effects of PFAS exposure, in particular, PFOS and PFHxS exposure.

Based on its review, ATSDR concluded that several health-related endpoints could be considered for studies of the Pease population. However, whether it is feasible to study a specific health-related endpoint depends to a great extent on the size of the exposed population that can be recruited into a study. In order to determine the size of the exposed population required to study each health-related endpoint effectively, sample size calculations were made.

3. Feasibility of Possible Studies at Pease

a. Feasibility of a Children’s Health Study at Pease

To determine the population appropriate for a children’s study at Pease, ATSDR took into account the date when the Haven well was shut down, the length of time (e.g., “half-life”) that PFHxS and PFOS remain in the blood after exposure, and the age range appropriate for the health endpoints under consideration. ATSDR concluded that a study is feasible of children who attended a day care center at
Pease any time prior to June 2014 and who will be aged 4 – 16 years at the time the study begins. Because PFAS-contaminated drinking water exposures could occur to children in utero and during breastfeeding if the mother worked at the Pease Tradeport, the study would include these additional children if the exposures began prior to June 2014 and their ages are 4 – 16 years at the time the study begins.

The sample size calculations indicated that at least 350 exposed children were needed to be included in a study. The study would also require a comparison group of at least 175 children unexposed to the contaminated drinking water at the Pease Tradeport. Based on this sample size, health-related endpoints were grouped into three categories: 1) feasible to study, 2) possible to study in children at Pease (but likely will require recruiting a larger sample size than 350 exposed and 175 unexposed children from the Pease community), and 3) not feasible to study using the Pease children population unless additional populations from other communities exposed to PFAS-contaminated drinking water are included in the study.

**Health-related endpoints feasible to study in children at Pease:**

- Mean difference in lipids (total cholesterol, LDL, HDL, triglycerides)
- Mean difference in estimated glomerular filtration rate (eGFR), a measure of kidney function
- Insulin-like Growth Factor – 1 (a measure of growth hormone deficiency)
- Overweight/Obesity

**Health-related endpoints that may be possible to study in children at Pease** (although a larger sample size from the Pease community will likely be needed):

- Mean difference in uric acid
- Elevated total cholesterol (hypercholesterolemia)
- Elevated uric acid (hyperuricemia)
- IQ/neurobehavioral
- Thyroid function
- Sex hormones
- Asthma and atopic dermatitis (Immune function)
- Rhinitis (stuffy, runny nose)
- Antibody response to rubella, mumps and diphtheria vaccines

**Health-related endpoints not feasible to study using the Pease children population** (in order to address these health endpoints, populations from other sites beyond the Pease community with PFAS-contaminated drinking water would need to be included along with the Pease children population):

- Attention deficit/hyperactivity disorder (ADHD)
- Autism spectrum disorder
- Delayed puberty
- Thyroid disease
- Childhood cancers
b. Feasibility of an Adult Health Study at Pease

Based on the date when the Haven well was shut down and the length of time (e.g., “half-life”) that PFHxS and PFOS remain in the blood after exposure, ATSDR concluded that an adult study at Pease of adults aged ≥18 years who worked anytime at the Pease Tradeport during January 2008 - May 2014 is feasible.

The sample size calculations indicated that at least 1,500 exposed adults needed to be included in a study. The study would also require a comparison group of at least 1,500 adults unexposed to the contaminated drinking water at the Pease Tradeport. Based on this sample size, health-related endpoints were grouped into three categories: 1) feasible to study, 2) possible to study at Pease (but likely will require recruiting a larger sample size than 1,500 exposed and 1,500 unexposed adults from the Pease community), and 3) not feasible to study using the Pease adult population unless additional populations from other communities exposed to PFAS-contaminated drinking water are included in the study.

**Health-related endpoints feasible to study at Pease:**

- Mean difference in lipids (total cholesterol, LDL, HDL, triglycerides)
- Elevated total cholesterol (hypercholesterolemia)
- Mean difference in uric acid
- Elevated uric acid (hyperuricemia)
- Thyroid disease (unconfirmed)
- Cardiovascular disease
- Hypertension
- Osteoarthritis and osteoporosis
- Mean differences in serum immunoglobin (IgA, IgE, IgG, IgM), and C-reactive protein (an indicator of inflammation); increase in antinuclear antibodies (an indicator of autoimmune reaction); alterations in specific cytokines

**Health-related endpoints that may be possible to study at Pease** (although a larger sample size from the Pease community may be needed):

- Liver function
- Thyroid disease (confirmed)
- Thyroid function
- Endometriosis
- Pregnancy-induced hypertension
Health-related endpoints not feasible to study using the Pease adult population (i.e., populations from other sites beyond the Pease community with PFAS-contaminated drinking water would need to be included to make the study feasible):

- Liver disease
- Kidney disease
- Ulcerative colitis
- Rheumatoid arthritis
- Lupus
- Multiple sclerosis
- Kidney cancer (and other adult cancers)

c. Study of former military service and civilian workers at the Pease Air Force Base

Based on sample size considerations, ATSDR concluded that it is not feasible to conduct a mortality or cancer incidence study that is limited to the military service and civilian workers who were stationed or worked at the Pease Air Force Base. Such studies would require, in addition to the Pease Air Force Base populations, several thousands of exposed populations from military bases where PFAS-contaminated drinking water occurred, as well as several thousands of comparison populations from military bases that did not have drinking water contamination.

4. Conclusions

The feasibility assessment concluded that it is possible to evaluate some health-related endpoints if a sufficient number of children and adults from the Pease population participate. Other health-related endpoints would require larger numbers of exposed individuals and would require the inclusion of populations from other sites who were exposed to PFAS-contaminated drinking water. The feasibility assessment concluded that a third study design, a mortality and cancer incidence study of former military service and civilian worker personnel, would not be feasible solely with the population at Pease.

No single study of the Pease population will provide clear answers to the community about whether their exposures to the PFAS-contaminated drinking water caused their health problems. All epidemiological studies of environmental exposures and health outcomes have limitations and uncertainties. Whether a study will find an association between an environmental exposure and health effects cannot be known prior to conducting the study. The ability of a study of the Pease population to provide useful information will depend to a great extent on the success of recruiting sufficient number of study participants.

The feasibility assessment is still a draft. It will be finalized once the Pease Community Assistance Panel (CAP) and the larger Pease Tradeport community have the opportunity to review and make comments on the assessment. ATSDR will then revise the assessment based on the comments received. The feasibility of successfully evaluating particular health-related endpoints (or effect biomarkers) could change depending on final study design and goals.