Docket No. ATSDR-2018-0008 - Proposed Data Collection Submitted for Public Comment and Recommendations

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

No.	Comment No.	Submitted by:	Mode of Submission	Agency Response
B1a	ATSDR-2018-0008-0002	Anonymous	online	ATSDR appreciates the comments from the submitter. The comments are outside the scope of this docket.
B1b	ATSDR-2018-0008-0003	Karandeep Lachhar	online	ATSDR appreciates the comments of Karandeep Lachhar.
B1c	ATSDR-2018-0008-0004	Karandeep Lachhar	online	Posted in duplicate
B1d	ATSDR-2018-0008-0005	Jimmy Chuong	online	ATSDR appreciates the comments from Jimmy Chuong. The purpose of including a Portsmouth area referent group in this study is to provide information on background PFAS serum levels as well as background levels of effect biomarkers (e.g., liver, kidney, thyroid and immune function) among those unexposed to PFAS-contaminated drinking water. Medical records will not provide this information. According to consumer confidence reports, the Pease Tradeport and City of Portsmouth drinking water systems have been in compliance with EPA safe drinking water regulations, so there are no other toxic chemicals of concern in the water supply besides PFAS. It is possible that study participants may be exposed to other toxic chemicals at their residences or workplaces, but confounding should be minimal because these other exposures will likely not be associated with PFAS serum levels. The questionnaire does obtain occupational history so that occupational exposures can be taken into account in the analyses. Analyses will be adjusted for age of the participant. The study will obtain medical history including dates of diagnosis and the use of medications. A study of mother-infant pairs is beyond the scope of the Pease study. This requires a special study design.
B1e	ATSDR-2018-0008-0006	Robert Bilott	letter	ATSDR appreciated the comments from Robert Bilott. In November 2017, ATSDR published a feasibility assessment for epidemiological studies at Pease International Tradeport that provided sample size calculations for a wide range of diseases and effect biomarkers. The assessment concluded that a children's study at Pease that included 350 exposed and 175 referents would have

				evaluate lipids, kidney function, growth hormone deficiency and obesity. Other outcomes that might be effectively evaluated included thyroid function, sex hormones, neurobehavioral effects, asthma, and rhinitis. An adult study that included 1,000 exposed at Pease could effectively evaluate lipids, kidney function, cardiovascular disease, and osteoarthritis. The assessment clearly stated that health outcomes in children such as ADHD, thyroid disease and cancers, and health outcomes in adults such as kidney and liver disease, ulcerative colitis, and cancers, could not be effectively evaluated in a study limited to the Pease population but would require a multi-site study. Nevertheless, the Pease study will collect information on these outcomes. As a "proof of concept", a key purpose of the Pease study is to evaluate procedures that will also be used in a multi-site study, so that any problems that may arise can be identified and resolved prior to conducting the multi-site study. Unlike the exposure assessments, the Pease proof of concept is an epidemiological study whose findings can be generalized to other sites where exposures to PFAS- contaminated drinking water occurred. Moreover, since the study will evaluate specific PFAS serum levels, the results will also be relevant to anyone with similar PFAS serum levels. The data from the Pease study will be integrated in a database with data from the other sites included in the multi-site epidemiological study. The proposed multi-site study will include data from a total of at least 2,000 children and 6.000 adults. The sites that will be included in the multi-site will not necessarily be the sites included in the EA. With a sample size of at least 6,000 adults and categorizing PFAS serum levels into exposure quartiles, there would be sufficient statistical power to detect the relative risk for ulcerative colitis observed in the C8 study. The multi-site study proposal will be submitted to the Federal Register for a 60-day public comment period in 2019. ATSDR is aware of concerns about PFAS contamination around fire training centers and fire stations, and recognizes that firefighters and emergency responders are at risk of PFAS exposures due to the use of AFFF and possibly through protective equipment treated with chemicals that include PFAS. However, the Pease Proof of Concept Study is focused on PFAS exposures via the consumption of contaminated drinking water at the Pease International Tradeport.

				The study will be estimating cumulative PFAS serum levels, as was done in the C8 studies. By evaluating estimated PFAS serum levels in addition to measured PFAS serum levels, the study can avoid issues such as confounding and reverse causation that can occur when factors that affect a specific health outcome (or the outcome itself) also affect measured PFAS serum levels. Moreover, the estimation of PFAS serum levels facilitates the evaluation of specific periods of exposure (exposure windows) as well as lagged exposures (e.g., to account for latency periods). Estimating cumulative PFAS serum levels using pharmacokinetic models and the historical reconstruction of the Pease drinking water contamination will be difficult but doable for PFOA, PFOS and possibly PFHxS. However, without detailed information about PFAS exposures that occurred via occupation as a firefighter or to a worker in an industrial process that uses or manufactures PFAS, it would be impossible in this study to factor these occupational PFAS exposures into the estimates of cumulative PFAS serum levels. Additionally, it is likely that the firefighters also experienced occupational exposures to other toxic substances that would be difficult to take into account in the analyses, such as PAHs, benzene, asbestos, formaldehyde, cadmium, dioxins, and PCBs. Firefighters at airports and military bases may also have been exposed to high levels of jet fuel (JP-4). These confounding variables make it difficult to determine whether the health outcome is related to PFAS exposure or exposure to a different substance.
B1f	ATSDR-2018-0008-0007	Robert Bilott	letter	Posted in duplicate
B1g	ATSDR-2018-0008-0008	Diane Cotter	email	The Agency appreciates the comment from Diane Cotter. ATSDR is aware of concerns about PFAS contamination around fire training centers and fire stations, and recognizes that firefighters and emergency responders are at risk of PFAS exposures due to the use of AFFF and possibly through protective equipment treated with chemicals that include PFAS. However, the Pease Proof of Concept Study is focused on PFAS exposures via the consumption of contaminated drinking water at the Pease International Tradeport. The study will be estimating cumulative PFAS serum levels, as was done in the C8 studies. By evaluating estimated PFAS serum levels in addition to measured PFAS serum levels, the study can avoid issues such as confounding and reverse causation that can occur when factors that affect a specific health outcome (or the outcome itself) also affect measured PFAS serum levels. Moreover, the estimation of PFAS serum levels facilitates the evaluation of specific periods of

				exposure (exposure windows) as well as lagged exposures (e.g., to account for latency periods). Estimating cumulative PFAS serum levels using pharmacokinetic models and the historical reconstruction of the Pease drinking water contamination will be difficult but doable for PFOA, PFOS and possibly PFHxS. However, without detailed information about PFAS exposures that occurred via occupation as a firefighter or to a worker in an industrial process that uses or manufactures PFAS, it would be impossible in this study to factor these occupational PFAS exposures into the estimates of cumulative PFAS serum levels. Additionally, it is likely that the firefighters also experienced occupational exposures to other toxic substances that would be difficult to take into account in the analyses, such as PAHs, benzene, asbestos, formaldehyde, cadmium, dioxins, and PCBs. Firefighters at airports and military bases may also have been exposed to high levels of jet fuel (JP-4). These confounding variables make it difficult to determine whether the health outcome is related to PFAS exposure or exposure to a different substance.
B1h	ATSDR-2018-0008-0009	Martha Roy	online	Comments also Included in ATSDR-2018-0008-0013. Please see below for responses.
B1i	ATSDR-2018-0008-0010	Bryan Lindauer	online	ATSDR appreciates the comments of Bryan Lindauer and agrees that exposure to PFAS is a public health concern.
B1j	ATSDR-2018-0008-0011	Anonymous	online	ATSDR appreciates the comments from the submitter. The comments are outside the scope of this docket.

B1k	ATSDR-2018-0008-0012	Steve Risotto	online	The Agency appreciates the comments from Stephen Risotto. In November 2017, ATSDR published a feasibility assessment for epidemiological studies at Pease International Tradeport that provided sample size calculations for a wide range of diseases and effect biomarkers. The assessment concluded that a children's study at Pease that included 350 exposed and 175 referents would have sufficient statistical power to effectively evaluate lipids, kidney function, growth hormone deficiency and obesity. Other outcomes that might be effectively evaluated included thyroid function, sex hormones, neurobehavioral effects, asthma, and rhinitis. An adult study that included 1,000 exposed at Pease could effectively evaluate lipids, kidney function, cardiovascular disease, and osteoarthritis. The assessment clearly stated that health outcomes in children such as ADHD, thyroid disease and cancers, and health outcomes in adults such as kidney and liver disease, ulcerative colitis, and cancers, could not be effectively evaluated in a study limited to the Pease population but would require a multi-site study. Nevertheless, the Pease study will collect information on these outcomes. As a "proof of concept", a key purpose of the Pease study is to evaluate procedures that will also be used in a multi-site

				study, so that any problems that may arise can be identified and resolved prior to conducting the multi-site study. Analyses for specific diseases will be restricted to those self-reported cases that are confirmed by medical records. To minimize recall bias, analyses internal to the Pease population will be conducted as well as analyses comparing Pease to the referent group. However, the key outcomes are the effect biomarkers (e.g., lipids, kidney, liver, thyroid and immune function) that are not affected by recall biases and do not require medical record confirmation. The Pease study will incorporate age-, sex- and calendar year-specific historical background PFAS serum levels from NHANES for the historical reconstruction of PFAS serum levels in the Pease population. This approach will take into account PFAS sources other than the Pease drinking water. ATSDR has extensive experience conducting groundwater fate and transport modeling of contaminants (e.g., the Camp Lejeune study) as well as drinking water distribution system modeling (Toms River, NJ and Camp Lejeune studies) and historical reconstruction of drinking water exposures based on very limited contaminant sample data (Camp Lejeune study). The protocol for the Pease study has completed an independent peer review process and ATSDR intends to consult with independent experts to determine the best approach to historically reconstructing the PFAS concentrations in the Pease drinking water system. In addition to reconstruction of PFAS drinking water concentrations, ATSDR intends to estimate historical PFAS serum concentrations in participants. This approach was successfully implemented in the C8 study using historically reconstructed PFOA drinking water concentrations. PBPK models exist for PFOS, so it is also possible to historically reconstruct PFOS serum levels from PFOS drinking water concentrations. Currently, PBPK approaches for PFHxS are limited but ATSDR intends to consult with independent experts to determine the best approach to estimating PFHxS serum levels from PFHxS concentrations in drinking water. The study questionnaire includes a medical history, occupational history, and lifestyle/demographic questions. The information from the questionnaire can be used in the analyses to adjust for possible confounding. In addition, “negative controls” (i.e., diseases not known to be associated with PFAS

				bias and confounding. Confounding will also be minimized by conducting analyses internal to the Pease population since it is unlikely that PFAS serum levels will be associated with possible confounding factors. Finally, conducting analyses using estimating PFAS serum levels will avoid biases such as reverse causation and confounding due to factors (including the outcome under evaluation) that might affect measured PFAS serum levels. The document, “Human health effects of drinking water exposures to per- and polyfluoroalkyl substances (PFAS) at Pease International Tradeport, Portsmouth, NH” was submitted with the Federal Register Notice announcing the project and was available for review during the 60-day comment period. This document contains a detailed list of the PFAS to be studied in the project.

B1l	ATSDR-2018-0008-0013	Martha Roy	online	ATSDR appreciates the comments from Martha Roy, Town Administrator, and the Newington Selectmen. In the study recruitment's second wave, letters of invitation will be sent out to those eligible for the study, including Newington households served by private wells with measured PFOA + PFOS ≥70 parts per trillion (ppt). The recruitment's first wave will include those who participated in the NH DHHS Pease biomonitoring program because they have PFAS concentration available close to the time when wells were shut down. It is unlikely that the sample size goals will be achieved after completion of wave one recruitment, so Newington community members with private well contamination that exceeds the EPA Lifetime Health Advisory for PFOA + PFOS will likely be recruited during wave two. The time period of 2004-May 2014 is relevant to the Pease Tradeport. Newington residents with PFAS-contaminated private wells above the EPA advisory will be eligible for wave 2 recruitment if they were exposed anytime from 2004 onward. Newington residents who did not use private wells will be eligible for the referent group if they never consumed drinking water at the Pease Tradeport. Newington residents will be recruited for the referent group in a similar fashion as others in the Portsmouth area who never drank Pease drinking water. For adults, the study procedures should take about one hour plus time to review and sign a consent form to participate. For children, the study procedures will take about 2 hours and 30 minutes plus time for reviewing and signing a consent form. All participants will be asked to provide a blood and urine sample. Once all the PFAS analyses are completed, ATSDR will provide each participant with his/her PFAS results. While we understand community members' concerns about their individual PFAS serum levels, due to the study design participants should expect that it may take a year or longer from the time they provided the blood sample to the time they receive their PFAS results.