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September 5, 2017

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

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Re: Request for Coordinated Nationwide PFAS Health Study and Testing and Notice of Intent to Sue

Ladies and Gentlemen:

Millions of people across the country have been exposed to highly fluorinated chemicals (per- and polyfluoralkyl substances, including PFOA and PFOS) collectively referred to as "PFAS," in their drinking water supplies. EPA acknowledged the risks posed by the entire family of PFAS in its "Long-Chain Perfluorinated Chemicals (PFCs) Action Plan," which was released over seven years ago, but has never been fully

implemented. (*See* Ex. A (excerpts).) EPA has, however, recently confirmed that at least one PFAS – PFOA – poses sufficient "potential adverse effects for the environment and human health based on its toxicity, mobility, and bioaccumulation potential" to support investigating and addressing its presence in drinking water under the federal Superfund law, codified in the Comprehensive Environmental Response and Liability Act of 1980, as amended, 42 U.S.C. § 9601 *et seq.* ("CERCLA"). (*See e.g.*, Ex. B (excerpts) at 9.) Through the authority granted to ATSDR under that same Superfund law, ATSDR has classified PFAS as a class of chemicals that meet the definition of "toxic substance" within the scope of ATSDR's purview.[1] Consequently, ATSDR has developed a draft toxicological profile for PFAS, issued various statements and guidance to impacted individuals and physicians dealing with certain PFAS exposures, and even agreed to partner with a handful of state or local entities investigating specific instances of specific types of PFAS drinking water contamination in specific communities. (*See e.g.*, Ex. C.) To date, however, ATSDR has not embarked on any coordinated, comprehensive nationwide study or investigation of the impacts on human health from the presence of the entire *class* of PFAS in drinking water, or associated testing of all such impacted individuals. We write to request that ATSDR move forward immediately with such a national study and testing.

As explained below, ATSDR has the clear power and authority to mandate a national study of PFAS health impacts and associated testing, has access to mechanisms to secure funding from responsible parties, and has a proven model to follow to implement such a study/testing. Based on our past decade of experience designing and overseeing a project to assess human health impacts from one such PFAS – PFOA – we stand ready to assist ATSDR in overseeing the design and implementation of a nationwide study and testing focusing on the entire class of PFAS chemicals through a program that could encompass and involve all affected parties, including PFAS manufacturers, PFAS users, impacted water supplies, impacted residents, and affected governmental entities/contractors and regulators, in a way that provides everyone with independent, credible scientific answers and certainty.

I. ATSDR Has The Authority To Require A National PFAS Health Study and Testing And Ability To Secure Full Funding For Such Work.

Under Section 104 of CERCLA, ATSDR shall "provide medical care and testing to exposed individuals, including but not limited to tissue sampling, chromosomal testing where appropriate, epidemiological studies, or any other assistance appropriate under the circumstances" in situations involving "public health emergencies caused or believed to be caused by exposure to toxic substances." (42 U.S.C. § 9604(i)(1)(D).) This is a non-discretionary mandate. Thus, under this provision of CERCLA, ATSDR (which, as noted above, already has classified PFAS as a "toxic substance") is not only

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[1] *See also* 42 U.S.C. § 9604(i)(18).

authorized to conduct epidemiological studies and testing in circumstances where there have been excessive PFAS exposures, but is required to do so.

EPA repeatedly has indicated that situations involving excessive levels of PFAS in drinking water qualify as public health emergencies mandating immediate alternate water supplies. For example, as early as 2002, EPA entered a consent order in which it found that levels of a PFAS (PFOA) exceeding the non-regulatory threshold used by EPA at that time presented a sufficient threat of "imminent and substantial endangerment" to warrant the provision "[a]s soon as practicable" of alternative drinking water to those exposed. (*See* Ex. D (excerpts).) EPA entered similar orders noting the threat of such "imminent and substantial endangerment" from excessive PFAS levels in drinking water, mandating immediate alternate drinking water supplies, after EPA adopted its first provisional health advisory guidelines for short-term exposures to two different PFAS materials (PFOA and PFOS) in 2009. (*See e.g.*, Ex. E (excerpts).) EPA reaffirmed this position as recently as January 2017 when it modified one of those same consent orders to require immediate clean water if levels of PFAS exceeded EPA's new long-term health advisory level of no more than 0.07 ppb for individual or combined levels of PFOA and PFOS. (*See* Ex. F.) EPA noted that these new, lower PFAS drinking water guidelines were based on EPA's review of "the best available peer-reviewed studies" indicating that exposure to these PFAS "may result in adverse health effects, including developmental effects to fetuses during pregnancy or to breastfed infants (e.g., low birth weight, accelerated puberty, skeletal variations), cancer (e.g., testicular, kidney) , liver effects (e.g., tissue damage), immune effects (e.g., antibody production and immunity), thyroid effects and other effects (e.g., cholesterol changes)." (Ex. G.)

ATSDR's actions to date confirm its recognition that studying PFAS contamination issues falls squarely within its broad authority. As recently as May 23 of this year, ATSDR released the results of its own assessment of whether an epidemiological study by the Agency of those exposed to PFAS contamination in their drinking water would be feasible. (Ex. H (excerpts).) ATSDR confirmed in the context of evaluating the feasibility of studying adverse health effects among the adults, children, and military personnel exposed to multiple PFAS compounds in drinking water at the Pease International Tradeport that undertaking such a study could generate important "scientific knowledge about the health effects of PFAS exposures, in particular, PFOS and PFHxS exposures," if the study could be designed to encompass a sufficiently large population of impacted people. (*Id.* at 2.) In order to properly and thoroughly study certain types of less common diseases (including cancer) associated with these PFAS exposures, ATSDR acknowledged that there would need to be far more than the couple hundred or even couple thousand anticipated study participants at that one site, which might be feasible if multiple sites were incorporated into the study. (*Id.* at 43.) ATSDR even listed over 100 sites identified to date across the country where PFOS and/or PFHxS have been confirmed to be present in drinking water at levels above EPA's reporting limit for the chemicals under EPA's Unregulated

Contaminant Monitoring Rule 3 ("UCMR-3"), which could provide the needed, larger pool of study participants. (*Id.* at Table A.1.)

II. A Proven Model Exists For Developing A National PFAS Health Study.

Settlement of a prior class action lawsuit in which we represented the plaintiff class resulted in the creation of an independent scientific panel that studied the effects of PFOA-contaminated drinking water among a class of approximately 70,000 people whose drinking water supplies in West Virginia and Ohio had been contaminated with quantifiable levels of the chemical (0.05 ppb at the time) attributable to releases from the Washington Works manufacturing plant then-owned by E. I. du Pont de Nemours & Company ("DuPont"). Through an innovative settlement with DuPont in that case (known as the "*Leach* Case"), we were able to secure sufficient funds to pay for: 1) blood testing of approximately 69,000 people through a "C8 Health Project"; 2) creation of a new "C8 Science Panel" of independent, world-class epidemiologists charged with confirming which diseases were linked to PFOA exposure among the class being studied; 3) the design and implementation by the C8 Science Panel of approximately a dozen extensive epidemiological studies and retrospective exposure modeling work, including class-wide studies of the exposed population; 4) provisions for immediate and long-term clean water/water filtration; and 5) medical monitoring/testing for all class members for each disease linked to their PFOA exposure. (*See* http://www.c8sciencepanel.org and http://C-8MedicalMonitoringProgram.com.) Through that settlement, we also were able to secure a binding agreement up front on how the results of the independent scientific work would be used in connection with future injury and compensation claims among the *Leach* Case class members, including the extent to which the independent scientific work would conclusively resolve issues of general causation as between the PFAS chemical at issue and the class member exposures. The settlement also included an agreement that all active litigation among the parties would be stayed and future filings barred (yet with all claims preserved and statutes of limitations tolled), pending the final outcome of the agreed scientific process.

The work of the C8 Science Panel (and the related C8 Health Project) under this prior class settlement involved only one PFAS compound (PFOA) and only one responsible party (DuPont). There is no reason, however, why this same model cannot be expanded to the current situation facing communities across the United States involving one or more (or a combination of) the other PFAS compounds in their drinking water, potentially attributable to the actions of multiple responsible parties. In fact, expanding the model to include multiple responsible parties and regulators provides the opportunity for creating a much bigger pool of funds and the opportunity to spread costs among a much bigger and more diverse group. Likewise, addressing the issue within the context of a national class provides the opportunity for the responsible parties to fashion common, global remedies that allow for uniform, consistent relief and treatment of impacted parties and greater financial, scientific, and regulatory certainty.

ATSDR already has acknowledged the significance and utility of the C8 Science Panel/C8 Health Project model and work for addressing health issues related to PFAS exposures. As noted by ATSDR in its May 23, 2017, draft feasibility assessment for studies at the Pease International Tradeport, the C8 Science Panel's/C8 Health Project's work, which focused on human impacts from PFOA contamination in drinking water, allows ATSDR to focus future PFAS studies on the effects from exposure to other PFAS compounds, such as PFOS and PFHxS, and the synergistic/combined effects of multiple PFAS compounds (including PFOA) being present in drinking water at the same time. (*See* Ex. H at 3.) In short, the C8 Science Panel and C8 Health Project work allows ATSDR to start from what is already known and addressed by the C8 Science Panel and C8 Health Project with respect to the adverse effects of PFOA, and direct its resources toward studying the effects of having one or more (or combination) of the other PFAS materials in drinking water.

III. Now Is The Time To Act.

It is imperative that ATSDR take action now to respond to this ongoing, imminent and substantial threat to the health of millions of Americans across this country. Every day, another community somewhere in the United States wakes up to news that one or more (or some combination) of an ever-expanding class of PFAS compounds (some being identified for the first time as even existing) are poisoning the drinking water that they and their families rely upon. Every day another community is being told not to drink its water or to immediately get on bottled water because the concentration of PFAS exceeds current EPA guidelines or other health benchmarks. Residents, water suppliers, local, state and national elected officials, governmental entities, NGOs, business leaders, scientists – all are demanding credible, scientific answers to exactly what this mix of PFAS compounds in the water will do to people over time– especially those who have had long term exposures over many years or may be in sensitive subpopulations, such as infants, the elderly, or the infirm. Recently, the leaders of the health departments in five states – New York, Michigan, Pennsylvania, New Hampshire, Vermont, and Alaska – all signed a joint letter specifically asking ATSDR to undertake a national PFAS health study. (Ex. I.) In the meantime, an ever-growing number of lawsuits are being filed by a variety of lawyers asserting a myriad of different claims and theories against multiple parties under varying state laws and standards.

ATSDR is uniquely endowed with the legal authority and ability to fashion a response that addresses this problem in a comprehensive, coordinated, national basis among all necessary parties. ATSDR also has the rare ability and power to require those deemed responsible for such PFAS contamination of the country's drinking water supplies, including any military or other governmental entities, to pay for and/or fund such work. (*See e.g.*, 42 U.S.C. §§ 9604(i)(5)(D), 9607(a)(4)(D).[2]) Given ATSDR's own recognition of the feasibility, importance, and need to study the effects of multiple PFAS

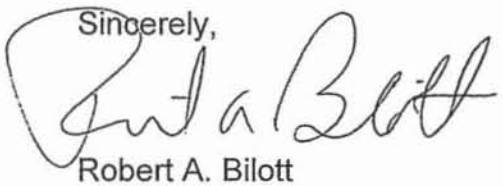
[2] *See also* 42 U.S.C §§ 9604(i)(17), 9620.

exposures in drinking water and its statutory authority and authorization to do so, ATSDR's continuing failure to do so provides a basis for a national class of all those negatively impacted by unstudied PFAS contamination of their drinking water supplies to bring a citizens' suit against ATSDR to force such action in the United States District Court for the District of Columbia, sixty days after ATSDR receives written notice of its failure to comply with this statutory mandate. (*See id.* § 9659.)

This letter serves as such a notice to ATSDR on behalf of our client, Dr. Arlo Paul Brooks, Jr., 92 Bella Vista Drive, Vienna, West Virginia 26105 (304-481-2946), as a representative of a national class of all persons whose primary source of residential drinking water for at least one year or more has been found to contain one or more PFAS chemicals at a concentration above the Method Reporting Limit (MRL) for such PFAS chemical(s) established by EPA for purposes of UCMR-3, excluding any such water supply where the only PFAS found above such MRL is PFOA or is a water supply falling within the scope of the *Leach* Case settlement. ATSDR has identified in Table A1 to Exhibit H attached hereto over 100 such water supplies across the country meeting this definition, including the municipal water supply for Vienna, West Virginia, which Dr. Brooks has used as his primary source of residential drinking water for many years. (*See* Ex. H Table A1.)

Dr. Brooks was one of the founding partners of Brookmar – the entity that designed, managed, and implemented the highly successful C8 Health Project. Dr. Brooks stands ready to share his unparalleled experience with ATSDR to help the Agency move forward with the type of national PFAS study that is now required. We remain hopeful that this matter can be resolved within the next sixty days without the need for pursuing any citizens' suit. We are available to meet with you to discuss and fashion a Consent Order or other document that will allow the matter to be addressed and resolved in a coordinated, uniform manner among all impacted parties, using the prior C8 Science Panel/C8 Health Project and related settlement model.

Sincerely,



Robert A. Bilott

RAB:
Encls. (Exs. A-I)
Cc: Dr. A. Paul Brooks, Jr. (w/encls.)

EXHIBIT A

Long-Chain Perfluorinated Chemicals (PFCs) Action Plan

I. Overview

Long-chain perfluorinated chemicals (PFCs)[1] are found world-wide in the environment, wildlife, and humans. They are bioaccumulative in wildlife and humans, and are persistent in the environment. To date, significant adverse effects have not been found in the general human population; however, significant adverse effects have been identified in laboratory animals and wildlife. Given the long half-life of these chemicals in humans (years), it can reasonably be anticipated that continued exposure could increase body burdens to levels that would result in adverse outcomes.

Since 2000, the Agency has taken various actions to help minimize the potential impact of PFCs on human health and the environment, including the publication of three Significant New Use Rules on perfluoroalkyl sulfonate (PFAS) chemicals and the review of substitutes for long-chain PFCs as part of its review process for new chemicals under EPA's New Chemicals Program. Although such actions are important steps to reducing exposure to these chemicals, EPA continues to be concerned with long-chain PFCs. Consequently, EPA intends to propose actions in 2012 under the Toxic Substances Control Act (TSCA) to address the potential risks from long-chain PFCs.

EPA intends to consider initiating TSCA section 6 rulemaking for managing long-chain PFCs. If EPA can make certain findings with respect to these chemicals (further analysis of the information will be performed as part of TSCA section 6 rulemaking), TSCA section 6 provides authority for EPA to ban or restrict the manufacture (including import), processing, and use of these chemicals. A rule addressing the PFAS sub-category could expand beyond the reach of the SNURs that the Agency has promulgated over the past decade. For example, the rule could address PFAS-containing articles. A rule addressing the perfluoroalkyl carboxylate (PFAC) sub-category could expand the reach of the 2010/15 PFOA Stewardship Program beyond the eight participating companies and further address the concerns for potential PFAC exposure through the use of PFAC-containing articles. EPA will develop more detailed assessments to support the TSCA section 6(a) "presents or will present an unreasonable risk" findings. If these more detailed assessments indicate that a different approach to risk management is appropriate, EPA will consider additional approaches.

Long-chain PFCs are a concern for children's health. Studies in laboratory animals have demonstrated developmental toxicity, including neonatal mortality. Children's exposures are greater than adults due to increased intakes of food, water, and air per pound of body weight, as well as child-specific exposure pathways such as breast milk consumption, mouthing and ingestion of non-food items, and increased contact with the floor. Biomonitoring studies have found PFCs in cord blood and breast milk, and have reported that children have higher levels of

[1] The terms long-chain PFCs, long-chain perfluoroalkyl sulfonate (PFAS), and long-chain perfluoroalkyl carboxylate (PFAC) chemicals in this document refer only to chemicals described in the chemical identity section, including certain polymers that contain perfluorinated moieties. They do not include other PFCs, particularly those having shorter chain lengths.

some PFCs compared to adults. Thus, given the pervasive exposure to PFCs, the persistence of PFCs in the environment, and studies finding deleterious health effects, EPA will examine the potential risks to fetuses and children.

II. Introduction

As part of EPA's efforts to enhance the existing chemicals program under the Toxic Substances Control Act (TSCA)[2], the Agency identified an initial list of widely recognized chemicals, including PFCs, for action plan development based on their presence in human blood; persistent, bioaccumulative, and toxic (PBT)[3] characteristics; use in consumer products; production volume; and other similar factors. This Action Plan is based on EPA's initial review of readily available use, exposure, and hazard information[4] on PFCs. EPA considered which of the various authorities provided under TSCA and other statutes might be appropriate to address potential concerns with PFCs in developing the Action Plan. The Action Plan is intended to describe the courses of action the Agency plans to pursue in the near term to address its concerns. The Action Plan does not constitute a final Agency determination or other final Agency action. Regulatory proceedings indicated by the Action Plan will include appropriate opportunities for public and stakeholder input, including through notice and comment rulemaking processes.

III. Scope of Review

Continuing contributions of PFAS/PFAC to the environmental/human reservoir are best addressed using a category approach.

The PFAS/PFAC precursors may be polymers that are coated on a specific substrate. This action is considering only the contribution of precursors as a source of PFAS/PFAC, and not the inherent toxic effects of the polymer or exposure to dust that contains fluorinated polymers.

Long-Chain Perfluoroalkyl Sulfonate (PFAS) Sub-Category

The PFAS sub-category includes perfluorohexane sulfonic acid (PFHxS)[5], perfluorooctane sulfonic acid (PFOS)[6], and other higher homologues. The category also includes the acid salts and precursors.

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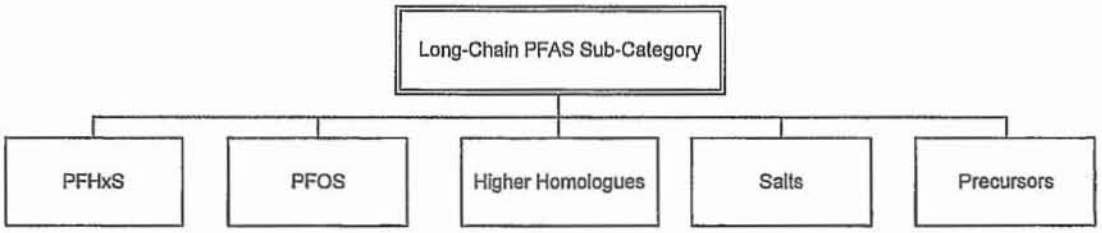
[2] 15 U.S.C. §2601 *et seq.*

[3] Information on PBT chemicals can be found on the EPA website at http://www.epa.gov/pbt/.

[4] Information sources customarily employed include Inventory Update Reporting (IUR) submissions; Toxic Release Inventory (TRI) reporting; data submitted to the HPV Challenge Program; existing hazard and risk assessments performed by domestic and international authorities including but not limited to U.S. Federal government agencies, the Organization for Economic Cooperation and Development, the Stockholm Convention on Persistent Organic Pollutants, Health and Environment Canada, the European Union; and others. Action plans will reference specific sources used.

[5] CF_3-$(CF_2)_5$-SO_3H; CAS RN: [355-46-4].

[6] CF_3-$(CF_2)_7$-SO_3H; CAS RN: [1763-23-1].



The similarities of the chemicals within the PFAS sub-category can be established when reviewing representative structures of the different category member compounds:

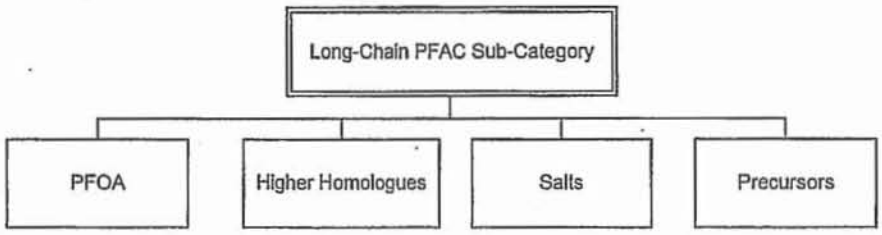
a. $CF_3(CF_2)_n$-SO_3^-M where $M = H^+$ or any other group where a formal dissociation can be made; and

b. $CF_3(CF_2)_n$-$S(=O)_y$-X where $y = 0 - 2$ and X is any chemical moiety.

where $n > 4$.

Long-Chain Perfluoroalkyl Carboxylate (PFAC) Sub-Category

The PFAC sub-category includes perfluorooctanoic acid (PFOA) [7] and other higher homologues. The category also includes the acid salts and precursors.



These similarities within the PFAC sub-category can be established by reviewing representative structures of the different category member compounds:

a. $CF_3(CF_2)_n$-COO^-M where $M = H^+$ or any other group where a formal dissociation can be made;

b. $CF_3(CF_2)_n$-$CH=CH_2$;

c. $CF_3(CF_2)_n$-$C(=O)$-X where X is any chemical moiety;

d. $CF_3(CF_2)_m$-CH_2-X where X is any chemical moiety; and

e. $CF_3(CF_2)_m$-Y-X where Y = non-S, non-N hetero atom and where X is any chemical moiety.

[7] CF_3-$(CF_2)_6$-COOH; CAS RN: [335-67-1].

where $n > 5$ or $m > 6$.

IV. Uses and Substitutes Summary

Production Volume

PFAS Chemicals

Commercial production of PFAS chemicals began over half a century ago. Total production from 1970 to 2002 was estimated to be about 100,000 tons (Paul A.G., 2009). By 2003, PFOS chemicals were no longer manufactured by 3M, the principal U.S. producer. However, production of PFOS-related chemicals is still ongoing in other countries, though to a much smaller extent than before 2003 (POPRC, 2007). As PFOS-based products became more strictly regulated in developed countries, production shifted to other countries. For example, manufacturers in China began large scale production in 2003 at the advent of 3M's 2002 global PFOS phase-out. China had an annual production in 2004 of less than 50 tons, but has increased production dramatically in recent years, with an estimated production of more than 200 tons in 2006. Approximately 100 tons of that amount is designated for export (POPs, 2008).

PFAC Chemicals

World-wide production of fluorotelomers was estimated at 20 million pounds in 2006. The United States accounts for more than 50 percent of world-wide fluorotelomer production. Textiles and apparel account for approximately 50 percent of the volume, with carpet and carpet care products accounting for the next largest share in consumer product uses. Coatings, including those for paper products, are the third largest category of consumer product uses.

Fluorotelomer release sources, and consequent exposure to fluorotelomers, can be explained through the examination of the life cycle of this category of chemicals:

Manufacture of Monomers → Manufacture of Polymers → Processing and Use → Product Life

The manufacture of non-polymeric chemicals (surfactants, wetting agents, cleansers, etc.) is included in the manufacture of monomers. Some residual monomers are present in the various raw materials and final products of the different steps of manufacturing. Because each intermediate contains the same R_f moiety, the polymers also contain this moiety. The 2010/15 PFOA Stewardship Program encourages the elimination of PFAC precursors in product content. Companies reporting under PFOA Stewardship Program differentiate between the amounts of PFAC precursors present in the final polymer product as residuals and the amount present in the polymer as R_f moities. The availability of PFAC precursor from the content of residuals in fluorotelomer based polymer products (FTBP) would be small in comparison to the amount released should polymeric materials biodegrade in the environment. Potentially all monomeric, not just the small amounts of residual monomers and other monomer raw material and intermediates released at each of the four steps in the sequence above, could be PFAC precursors.

Uses

PFCs are substances with special properties that have thousands of important manufacturing and industrial applications. They impart valuable properties, including fire resistance and oil, stain, grease, and water repellency. For example, they are used to provide non-stick surfaces on cookware and waterproof, breathable membranes for clothing, and are used in many industry segments, including the aerospace, automotive, building/construction, chemical processing, electronics, semiconductors, and textile industries.

PFAS Chemicals

PFAS are synthetic chemicals that do not occur naturally in the environment. Long-chain PFAS chemicals, as defined in this action plan, are no longer manufactured in United States. However, there is a limited set of existing uses for which alternatives are not yet available, and which are characterized by low volume, low exposure potential, and low releases.

The existing SNUR regulations on PFAS chemicals do not affect the continued use of existing stocks of the listed chemicals that had been manufactured or imported into the United States prior to the effective date of the SNURs. Existing products and formulations already in the United States containing these chemicals – for example, PFOS-based fire fighting foams produced before the rules took effect in 2002 – can also still be used without providing notice to the Agency. Because the PFAS SNURs exempt articles, PFOS may be imported or processed as part of an article without the Agency receiving prior notice.

PFAC Chemicals

PFAC are synthetic chemicals that do not occur naturally in the environment. PFOA is manufactured for use primarily as an aqueous dispersion agent [as the ammonium salt] in the manufacture of fluoropolymers, which are substances with special properties that have thousands of important manufacturing and industrial applications.

PFOA also be produced unintentionally by the degradation of some fluorotelomers, which are not manufactured using PFOA but could degrade to PFOA. Fluorotelomers are used to make polymers that impart soil, stain, grease, and water resistance to coated articles. Some fluorotelomer based products are also used as high performance surfactants in products where an even flow is essential, such as paints, coatings, cleaning products, and fire-fighting foams for use on liquid fuel fires. Fluorotelomer-based products can be applied to articles both at the factory and by consumers and commercial applicators in after-market uses such as carpet treatments and water repellent sprays for apparel and footwear.

Fluoropolymers, such as polytetrafluoroethylene (PTFE), which may contain some PFAC contamination, or that use PFOA as an emulsion stabilizer in aqueous dispersions, have a large U.S. market. The wire and cable industry is one of the largest segments of the fluoropolymer market, accounting for more than 35 percent of total U.S. fluoropolymer use. Apparel makes up about 10 percent of total fluoropolymer use, based on total reported production volume. Fluoropolymers are used in a wide variety of mechanical and industrial components, such as

plastic gears, gaskets and sealants, pipes and tubing, O-rings, and many other products. Total U.S. demand for fluoropolymers in 2004 was between 50,000 and 100,000 metric tons. The United States accounted for less than 25 percent of the world consumption of PTFE in 2007, and between 25 and 50 percent of the world consumption of other fluoropolymers. PTFE is the most commonly used fluoropolymer, and the United States consumed less than 50,000 metric tons of PTFE in 2008.

Substitutes

EPA is reviewing substitutes for PFOS, PFOA, and other long-chain PFCs under the New Chemicals Program. EPA established the program under section 5 of TSCA to help manage the potential risk from chemicals new to the marketplace.

EPA's review of alternatives to long-chain PFCs has been ongoing since 2000 and is consistent with the approaches to alternatives encouraged under the PFOA Stewardship Program. Through 2009, EPA has received and reviewed over 100 perfluorinated alternatives of various types. EPA reviews the new substances against the range of toxicity, fate, and bioaccumulation issues that have caused past concerns with perfluorinated substances, as well as any issues that may be raised by new chemistries (EPA, 2009b).

V. Hazard Identification Summary

The information used by EPA for this Action Plan includes the Organisation for Economic Co-operation and Development's (OECD) assessments of PFOS (OECD, 2002) and PFOA (OECD, 2006), EPA's Office of Pollution Prevention and Toxics' (OPPT) draft risk assessment of PFOA (EPA, 2009d), Environment Canada's assessment (Canada, 2006), the assessment of PFOS by the Stockholm Convention on Persistent Organic Pollutants (POPs, 2009), and other sources. The summary of the toxicity information is based on these previous assessments, and where appropriate, additional information on short- and long-chain lengths is provided.

World-Wide Distribution of PFAS and PFAC

Presence in Humans

PFAS and PFAC have been detected in human blood samples throughout the world. Blood samples have been collected in countries world-wide including the United States, Japan, Canada, Peru, Colombia, Brazil, Italy, Poland, Germany, Belgium, Sweden, India, Malaysia, Korea, China, and Australia. In addition, PFAS and PFAC have been detected in breast milk, liver, umbilical cord blood, and seminal plasma. In most cases, the analytes most often detected in human matrices, and usually in the highest concentrations, were PFOS, PFOA, and PFHxS. Other PFAS and PFAC detected in human tissue include perfluorooctane sulfonamide (PFOSA), 2-(N-methyl-perfluorooctane sulfonamido) acetic acid (Me-PFOSA-AcOH), 2-(N-ethylperfluorooctane sulfonamido) acetic acid (Et-PFOSA-AcOH or PFOSAA), perfluoroheptanoic acid (PFHpA), perfluorononanoate (PFNA), perfluorodecanoic acid (PFDeA or PFDA), perfluoroundecanoic acid (PFUA), perfluorododecanoic acid (PFDoA),

perfluoropentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), and perfluorobutane sulfonate (PFBS).

National Health and Nutrition Examination Survey (NHANES) data show that mean levels of PFOS, PFOA and PFHxS in the general U.S. population older than 12 years declined between the sampling period of 1999-2000 and 2003-2004 (Calafat, 2007). In addition, 3M reported a decline of the same chemicals from 2000 to 2006 in a group of 600 adult American Red Cross (ARC) blood donors (G. W. Olsen, Mari DC, Church TR, Ellefson ME, Reagen WK, Boyd TM, Herron RM, Medhdizadehkashi Z, Nobiletti JB, Rios JA, Butenhoff JL, Zobel LR 2008). The biggest drop reported in both surveys was in PFOS (~30% in NHANES and ~60% in the ARC study). Both reported ~25% decline in PFOA. NHANES reported a 10% decrease in PFHxS while the ARC study reported a 30% drop. Conversely, PFNA increased by approximately 50% over 4 years in NHANES and by 100% over 6 years in the ARC study. 3M also reported a 100% increase in PFDeA, while the increase in NHANES was 60%. 3M reported an 80% increase in PFUA.

It appears that most of PFAS and PFAC do not vary much across adolescents participating in NHANES; however, pooled data from 2001-2002 indicate that most of the levels of perfluorinated compounds are higher in children ages 3-11 years compared to adults (individual samples 2001-2002), especially for PFHxS (Kato, 2009). More recent data on children are not available.

It is clear that there are individuals who have been exposed to perfluorinated compounds at levels much higher than the majority of the population. Recent data indicate that individuals living near a U.S. facility that uses PFOA may have much higher PFOA serum concentrations than those currently reported for the general population (Calafat, 2007; Emmett, 2006).

Presence in the Environment and Wildlife

Water

Log K_{ow} values for PFOA, PFOS and other commercially available ammonium salts range from -0.52 to > 6.8 (De Silva, 2008; Tomlin, 2005) and have water solubilities that range from 0.10 to > 500,000 (Hekster, 2003; Kissa, 2001). Long-chain PFAC have been measured in surface waters of remote areas such as the north shore of Lake Superior, the Hudson Bay region of Northeastern Canada, tributaries of the Pearl River in Guangzhou, China and the Yangtze River. Ice surface samples in the Canadian Arctic (Northwest Territories and Nunavut) had levels of that ranged from 5-246 pg/L for C9-C11 compounds.

Multiple studies have reported a global distribution of PFAC and PFAS that have been reported in wildlife tissue and blood samples. PFAS have also been found in a variety of aquatic organisms. Most recently, four perfluorinated analytes (PFOS and PFAS: C10, C11, and C12) were found in fillets from bluegill in selected rivers in Minnesota and North Carolina (Delinsky, 2009). In general, the highest concentrations in wildlife have been found in the livers of fish-eating animals close to industrialized areas.

Soil and Sediment

PFOA and PFOS are considered to be resistant to degradation in soil. Levels of C9-C11 PFAC have been found in remote Arctic region sediment ranging from 0.68 µg/kg – 2.58 µg/kg. PFAC are known to increase over time in sediment as observed in a 22-year study (1980-2002) of the Niagara River discharge. Sediment dwelling invertebrates such as amphipods, zebra mussels, and crayfish have also been found to have PFOA concentrations ranging from 2.5 – 90 ng/g ww in the Raisin, St. Clair, and Calumet Rivers (MI)(Kannan, 2005). At the 3M Decatur, AL site, PFOA concentrations in Asiatic clams ranged from 0.51 ng/g to 1.01 ng/g. Mussels and oysters in Tokyo Bay were found to contain PFOA concentrations 0.660 ng/g ww and worms from the Ariake Sea in western Japan had concentrations of PFOA of 82 ng/g ww.

PFAS and PFAC are Persistent, Bioaccumulative, and Toxic

Persistence and Bioaccumulation in Humans and Laboratory Animals

Animal studies of the straight-chain PFAS and PFAC have shown that these compounds are well absorbed orally, but poorly eliminated; they are not metabolized, and they undergo extensive uptake from enterohepatic circulation. Studies of PFOS and PFOA have shown that these compounds are distributed mainly to the serum, kidney, and liver, with liver concentrations being several times higher than serum concentrations; the distribution is mainly extracellular. Both compounds have a high affinity for binding to B-lipoproteins, albumin, and liver fatty acid-binding protein. Studies have reported PFOS, PFOA, and several other PFAS and PFAC in umbilical cord blood indicating these chemicals cross the placenta.

The elimination half-lives of several PFAS and PFAC are summarized in Table 1. In general, the rate of elimination decreases with increasing chain length, although the half-life of PFHxS (C6) is longer than the half-life of PFOS (C8) in humans. There is a tremendous species difference in elimination, and elimination is greatly reduced in humans. Thus, the half-life of PFOS is 7 days in rats, 150 days in monkeys, and 5.4 years in humans. There is a gender difference in the elimination of PFOA and other PFAC in laboratory animals. Studies of PFOA in rats have shown that the gender difference is developmentally regulated, and the adult pattern is achieved by sexual maturation. The reason for the species and gender differences in elimination are not well understood. These differences are hormonally controlled, and may also be due to the actions of organic anion transporters. A gender difference has not been found in humans, although uncertainty exists due to the small sample size.

Table 1. Comparative Rates of Elimination*

Serum Half-life	PFHxS (C6)	PFOS (C8)	PFOA (C8)	PFNA (C9)	PFDA (C10)
Rat		7 days	2-4 hours 6-7 days	2 days 31 days	59 days 40 days
Mouse			16 days 22 days	41 days 64 days	
Monkey	87 days 141 days	150 days	30 days 21 days		

Human	8.5 years	5.4 years	2.3-3.8 years		

***Red – females; blue - males**

Regardless of chain length, it is critical to note that the half-lives of these compounds are measured in hours to days to months in rats, mice and monkeys, but years in humans. This means that these compounds will persist and bioaccumulate in humans, and comparatively low exposures can result in large body burdens. The gender and species differences in elimination also indicate that comparisons of toxicological effects must utilize some measure of body burden rather than administered dose.

Persistence and Bioaccumulation in the Environment

PFOS and longer chain PFAC (> C8) bioaccumulate and persist in protein-rich compartments of fish, birds, and marine mammals such as carcass, blood, and liver (Conder, 2008). Studies have found fish bioconcentration factor (BCF) values for C8 to C14 PFAC ranging from 4 – 40,000 in rainbow trout (Martin, 2003). Fish BCF values for C8-C11 PFAS are relatively lower (4-4900). There are two BCF study results for long chain PFAC with BCF values from 4,7000 to 4,800 for perfluorohexadecanic acid (C16) in carp and BCF values from 320 to 430 for perfluorooctadecanoic acid (C18) in carp (Martin, 2003). Available evidence shows the likely potential for bioaccumulation or biomagnifications in marine or terrestrial species. This is due to conformational changes into a helical structure in the molecule resulting in a smaller cross-sectional diameter as chain length increases which can lead to the ability to accumulate in organisms (NITE, 2002a, 2002b). Additional evidence that C14 and C15 PFAC bioaccumulate and are bioavailable is their presence in fish, invertebrates, and polar bears. The bioaccumulation of PFOS and PFAC (C8 through C14) in air-breathing animals (e.g., birds and mammals) is thought to represent biomagnification due to high gastrointestinal uptake and slow respiratory elimination (B. Kelly, MG Ikonomou, JD Blair, B Surridge, F Hoover, R Grace, APC Gobas 2009; B. C. Kelly, Ikonomou MG, Blair JD, Morin AE, Gobas APC, 2007). In addition, Conder et al. state that the bioaccumulation and bioconcentration potential of PFAC are directly related to the length of the perfluorinated chain, and PFAS are more bioaccumulative than PFAC of the same chain length (Conder, 2008).

Within the PFAC and PFAS categories, the perfluorinated carboxylic and sulfonic acids (R_f from C5 to C20) are persistent chemicals that are resistant to degradation under environmental conditions. Even the reaction of PFAS/PFAC precursors with hydroxyl radicals in the atmosphere are considered to be so slow that long range transport is considered a viable exposure pathway (Hurley, 2004; G. W. Olsen, DC Mari, WK Reagen, ME Ellefson, DJ Ehresman, JL Butenhoff, LR Zobel, 2007).

Toxicity in Humans

Until recently, epidemiological and medical surveillance studies have been conducted primarily in the United States on workers occupationally exposed to POSF-based fluorochemicals. These studies specifically examined PFOS or PFOA exposures and possible adverse outcomes. One occupational study of exposures to a PFNA surfactant blend was

undertaken. The studies on PFOS and PFOA include mortality and cancer incidence studies, a study examining potential endocrine effects, an "episodes-of-care" study evaluating worker insurance claims data, and worker surveillance studies examining associations between primarily PFOS and/or PFOA serum concentrations and hematology, hormonal and clinical chemistry parameters. The PFNA study examined liver enzymes and blood lipid levels. In general, no consistent association between serum fluorochemical levels and adverse health effects has been observed.

Toxicity in Laboratory Animals

PFOA

The toxicity of PFOA has been extensively studied. Repeated-dose studies in rats have shown reduced body weight, hepatotoxicity, reduced cholesterol, and a steep dose-response curve for mortality. Due to gender differences in elimination, adult male rats exhibit effects at lower administered doses than adult female rats. Thus, dietary exposure for 90 days resulted in significant increases in liver weight and hepatocellular hypertrophy in female rats at 1000 ppm (76.5 mg/kg-day) and in male rats at doses as low as 100 ppm (5 mg/kg-day). Studies in nonhuman primates have shown similar effects at doses as low as 3 mg/kg-day, although the reduction in cholesterol has not been observed.

The carcinogenic potential of PFOA has been investigated in two dietary carcinogenicity studies in Sprague-Dawley rats, and has been shown to induce hepatocellular adenomas, Leydig cell tumors, and pancreatic acinar tumors. It has not been shown to be mutagenic in a variety of assays. There is sufficient evidence to indicate that PFOA is a PPARα-agonist and that the liver carcinogenicity (and toxicity) of PFOA is mediated by PPARα in the liver in rats. There is no evidence that the liver toxicity in nonhuman primates is due to PPARα-agonism. There is controversy over the relevance of this particular mode of action for humans. The mode of action for the Leydig cell tumors and pancreatic acinar tumors has not been established, and therefore these are assumed to be relevant for humans.

Several studies have shown that PFOA is immunotoxic in mice. PFOA causes thymic and splenic atrophy, and has been shown to be immunosuppressive in both *in vivo* and *ex vivo* systems. Studies using transgenic mice showed that the PPARα was involved in causing the adverse effects to the immune system.

Standard prenatal developmental toxicity studies in rats and rabbits in which pregnant animals are exposed only during gestation and sacrificed prior to the birth of the pups have not shown many effects. Thus, there was no evidence of developmental toxicity after exposure to doses as high as 150 mg/kg-day in an oral prenatal developmental toxicity study in rats. In a rat inhalation prenatal developmental toxicity study, the NOAEL and LOAEL for developmental toxicity were 10 and 25 mg/m3, respectively. In a rabbit oral prenatal developmental toxicity study there was a significant increase in skeletal variations after exposure to 5 mg/kg-day, and the NOAEL was 1.5 mg/kg-day.

However, the potential developmental toxicity of PFOA is evident when the pups are evaluated during the postnatal period. Thus, a two-generation reproductive toxicity study in rats

showed a reduction in F1 pup mean body weight during lactation at 30 mg/kg-day group and during the post-weaning period at 10 mg/kg-day. In addition, there was a significant increase in mortality mainly during the first few days after weaning, and a significant delay in the timing of sexual maturation for F1 male and female pups at 30 mg/kg-day.

Due to the rapid elimination of PFOA in female rats, many researchers have examined the developmental toxicity of PFOA in mice. These studies have shown a pattern of developmental effects similar to those observed with PFOS. Full liter resorptions were noted at 40 mg/kg-day and the percent of live fetuses and fetal body weight were reduced at 20 mg/kg-day. The most notable effect of prenatal exposure to PFOA was the severe compromise of postnatal survival at doses as low as 5 mg/kg-day, and the postnatal growth impairment and developmental delays noted among the survivors; the BMD_5 and $BMDL_5$ for neonatal survival were estimated at 2.84 and 1.09 mg/kg-day, respectively. Additional studies in mice have shown that PFOA exposure causes a significant reduction in mammary gland differentiation in the dams and stunted mammary gland development in the female pups.

Several studies have examined the mode of action for the developmental effects. These have shown that exposure to a dose of 20 mg/kg-day for 2 days late in gestation is sufficient to cause the neonatal mortality in mice. Studies with PPARα knockout mice have shown that the PPARα is required for the neonatal mortality and expression of one copy of this gene is sufficient. This is in contrast to the studies showing that PPARα is not involved in the neonatal mortality associated with PFOS exposure. Although there is controversy over the human relevance of the PPARα-agonist hepatotoxicity observed in rodents, the role of PPARα in development and particularly in the PFOA-induced neonatal mortality observed in mice is unknown; therefore this mode of action is assumed to be relevant for humans.

Other PFAC Chemicals

Although there is an extensive database for PFOA, few studies have examined the toxicity of the shorter or longer chained PFAC. However, the data suggest that the toxicity profile is quite similar to that of PFOA, albeit at different dose levels presumably due to the differences in elimination half-life.

Although standard repeated-dose toxicity studies have not been conducted on the PFAC with chain lengths greater than PFOA, many studies have been conducted examining the potential for hepatomegaly and peroxisome proliferation (a marker for the activation of PPARα). Kudo et. al. found that PFOA, PFNA, and PFDA induced the activity of peroxisomal B-oxidation in male rats (2000). Kudo et al. showed that all PFAC with six- to nine-carbon length chains induced hepatomegaly and peroxisomal B-oxidase activity in mice, and the potency was in the order of PFNA > PFOA > perfluoroheptanoic acid (2006). Permadi et al. also showed that PFDA induces hepatomegaly and hepatic peroxisomal palmitoyl-CoA oxidase (1993). Thus, these studies indicate that the PFAC with a carbon chain length of eight and greater activate PPARα. The differences in potency probably reflect the differences in the half-life of the varying chain lengths. Despite the lack of traditional toxicity studies, it is reasonable to conclude that these compounds would likely produce similar effects as those observed with PFOA.

With respect to the potential developmental effects of PFAC with carbon chain lengths greater than C8, EPA is completing a developmental toxicity study of PFNA in mice (C. Lau, personal communication, 2009). Maternal body weight gain was reduced at 3 mg/kg-day, and severe toxicity was observed at 10 mg/kg-day. Neonatal survival was compromised at 5 mg/kg-day, and significant lags in neonatal growth were observed at 3 mg/kg-day. Thus, this study shows a pattern of effects very similar to those observed with PFOA. It is likely that PFAC with carbon chain lengths greater than nine would also result in similar effects, and that the potency would be dependent on the half-life of the compound.

PFOS

The toxicity of PFOS has also been extensively studied and was summarized in OECD report (2002) and by Lau et al. (2006). Repeated-dose studies in rats and nonhuman primates have shown reduced body weight, hepatotoxicity, reduced cholesterol, and a steep dose-response curve for mortality. These effects occur in nonhuman primates at doses as low as 0.75 mg/kg-day, and in rats at 2 mg/kg-day.

The carcinogenic potential of PFOS has been investigated in a dietary carcinogenicity study in Sprague-Dawley rats, and has been shown to induce hepatocellular adenomas at 20 ppm. In addition, thyroid follicular cell adenomas were observed in male rats that had been allowed to "recover" for a year following treatment for one year; the reason for this is unclear. However, thyroid follicular tumors have also been observed in rats exposed to N-EtFOSE, a major precursor of PFOS. PFOS has not been shown to be mutagenic in a variety of assays. Although PFOS can activate PPARα, the data are not sufficient to establish a PPARα-agonist mode of action for the liver tumors.

A standard prenatal developmental toxicity study in rats has shown a significant decrease in fetal body weight and significant increase in external and visceral anomalies, delayed ossification, and skeletal variations; a NOAEL of 1 mg/kg-day and a LOAEL of 5 mg/kg-day for developmental toxicity were indicated. In rabbits, significant reductions in fetal body weight and significant increases in delayed ossification were observed; a NOAEL of 1.0 mg/kg-day and a LOAEL of 2.5 mg/kg-day for developmental toxicity were indicated.

A two-generation reproductive toxicity study in rats showed neonatal mortality. All F1 pups at the highest dose of 3.2 mg/kg-day died within a day after birth, while close to 30% of the F1 pups at 1.6 mg/kg-day died within 4 days after birth. As a result of the pup mortality in the two top dose groups, only the two lowest dose groups, 0.1 and 0.4 mg/kg-day, were continued into the second generation. The NOAEL and LOAEL for the F2 pups were 0.1 mg/kg-day and 0.4 mg/kg-day, respectively, based on reductions in pup body weight.

The results of this study prompted additional research. Studies in which pregnant rats and mice were dosed during gestation and the pups were followed postnatally provided a BMD_5 and $BMDL_5$ for neonatal survival of 1.07 and 0.58 mg/kg-day in rats, respectively, and 7.02 and 3.88 mg/kg-day in mice, respectively. Studies have shown that the critical period of exposure is during late gestation. Mode of action studies initially focused on the lung and found significant histological and morphometric differences in the lungs of pups treated with PFOS. However,

subsequent studies did not find any effect on lung phospholipids and rescuing agents failed to mitigate the neonatal mortality. Thus, the mortality does not appear to be related to lung immaturity. In contrast to PFOA, studies with PPARα knockout mice have shown that the PPARα is not involved in the neonatal mortality. Current research is focusing on the possibility that the physical properties of PFOS may interfere with the normal function of pulmonary surfactant, leading to neonatal mortality.

Other PFAS Chemicals

A combined reproductive/developmental toxicity study of PFHxS has been conducted in rats. In the parental males there was a significant reduction in cholesterol at doses as low as 0.3 mg/kg-day, and hepatotoxicity at doses as low as 3 mg/kg-day. There was no evidence of developmental or reproductive toxicity at doses as high as 10 mg/kg-day.

Toxicity to Wildlife

Adverse effects on exposed populations of organisms have been observed with exposure to perfluorinated compounds in the parts per million range. Studies have shown a reduction in hatchability of chickens when they were exposed *in ovo* to PFOS, and a reduction in survival in 14-day old Northern bobwhite quail from hens exposed to 10 ppm of PFOS in the diet. In addition, a delay in growth and metamorphosis in the Northern leopard frog exposed to 3 mg/L of PFOS has been reported, as well as reduced cumulative fecundity and fertility effects in fathead minnows exposed to 0.1 mg/L PFOS. Further evidence of potential reproductive effects has been observed with exposure to C9-C11 PFAC. A significant induction of vitellogenin in rainbow trout was observed in a dose-dependent manner at concentrations of C10 PFAC 0.0256-2000 μg/g in the diet as well as a weak affinity demonstrated for the hepatic estrogen receptor from C9-C12 PFAC.

Mortality in sediment dwelling organisms such as the nematode, *Caenorhabditis elegans* has been observed with concentrations of C9 up to 0.66 mM and subsequent effects in offspring generations were found at concentrations up to 1nM as evidence by a 70 % decline in fecundity.

VI. Fate Characterization Summary

The PFAS and PFAC acids are strong acids that exist in equilibrium between the neutral form and the anionic form. Both the anionic and neutral forms of PFOA are soluble in water. While the Henry's law constant values suggests partitioning to air for the neutral, protonated form, predicting the amount that partitions into air is complicated because there is uncertainty over the degree to which carboxylic and sulfonic acids partition from the water to atmosphere. The uncertainty arises with regard to the value of the acid dissociation constant (i.e., pK_a), or the fraction of the acid form present at environmentally relevant pH. PFAC and PFAS have been detected in air, water, and soil samples collected throughout the world. The oceans have been suggested as the final sink and route of transport for perfluorinated carboxylic and sulfonic acids, where they have been detected on the surface and at depths > 1,000 meters (Yamashita, 2005).

Some PFAS/PFAC have the potential for long-range transport. They are transported over

long distances (i.e., long-range transport) by a combination of dissolved-phase ocean and gas-phase atmospheric transport; however, determining which is the predominant transport pathway is complicated by the uncertainty over water to atmosphere partitioning. Furthermore, there is evidence that transport and subsequent oxidation of volatile alcohol PFAS/PFAC precursors may contribute to the levels of PFAS / PFAC in the environment.

Studies by industry and academic researchers have shown that fluorotelomer alcohols (FTOH) can be degraded by microorganisms and by abiotic processes. 8-2 FTOH and FTOH of other chain lengths, and related chemicals in mixed microbial cultures, activated sludge and soil systems have been shown to be easily degraded to form PFOA and related perfluorinated acids. Some studies have also shown that $-CF_2-$ groups can be mineralized, forming shorter chain perfluoro acids. If FTOH are absorbed from ingestion, inhalation, dermal or ocular exposure or formed in vivo by from other compounds they can be metabolized by mammals and other organisms to form perfluorinated acids and other fluorinated compounds. FTOH can be degraded by abiotic processes in water and air to produce PFAC and various intermediates. FTOH are fairly volatile. Based on atmospheric half-lives determined in chamber studies, FTOH can be transported globally. Deposition or degradation in areas far from the source can result in PFAC contamination in high latitudes and other remote locations and contribute to global background levels of PFAC and PFAS.

Data submitted by industry and in the open literature show that perfluorooctane sulfonyl fluoride (POSF) and its derivatives can be degraded under environmental conditions to form perfluoroalkyl sulfonates and carboxylic acids. Reaction of POSF ($CF_3(CF_2)_n-SO_2F$) with methyl or ethyl amines is used to produce N-ethyl or N-methyl perfluorooctane sulfonamidoethanols (FOSE). Similar reactions are used to make shorter and longer chain analogs to POSF and POSF derivatives. FOSE compounds, (or $CF_3(CF_2)_n-SO_2N(R1)(R2)$, where R1 and R2 can be hydrogen, methyl or longer alcohols or other organic chains), such as N-methyl and N-ethyl FOSEs can be degraded though a series of intermediates to form both perfluoro carboxylic acids and perfluoroalkyl sulfonates. Data on the degradation of individual intermediates has been used to identify these pathways and has confirmed that these compounds can be degraded by a number of microbial and abiotic mechanisms. Reaction with other chemical intermediates produces other FOSA derivatives, including phosphate esters, fatty acids esters, silanes, carboxylates, and polymers with acrylate, urethane and other linkages. Longer and shorter chain perfluoro sulfonyl derivatives have also been produced intentionally and as unintended reaction products. Based on existing data from the open literature and CBI data, it is expected that that most, if not all, of these POSF and other chain length sulfonyl fluorides and their derivatives will be degraded to carboxylic acids and/or sulfonate over time. Most of these compounds will have environmental and metabolism half-lives of weeks to months. Some will be degraded faster and some will degrade more slowly, but all will eventually be degraded.

Very little data is available on the behavior of other perfluorochemicals in the environment and in vivo but the existing data suggest that they will also be degraded to form PFAC. For example, recent studies have shown that ingested mono and di polyfluoroalkyl phosphates (PAPs) can be degraded in rats to form PFOA and other PFAC in the body. They can also be degraded by microbial processes in soil and wastewater to form perfluorinated acids (D'eon, 2007).

A limited number of studies on the degradation of fluorotelomer-based polymers have been submitted in support of PMN submissions and existing chemicals, and published in the open literature. Based on studies, some fluorotelomer-based polymers are subject to hydrolysis, photolysis and biodegradation to some extent. Studies have shown half-lives of a few days to hundreds of years.

In addition, preliminary research on degradation of fluorotelomers has shown that some urethanes and acrylates biodegrade; however, half-lives and kinetics of the fluorotelomers are not yet well-defined. Ongoing research by EPA's Office of Research and Development (ORD) research is designed to generate high quality data that will help the Agency address some key uncertainties in pathways of exposure and potential risks from PFOA (Washington, 2009).

These studies have shown that the perfluorinated portion of some polymers is released as the polymer is degraded by microbial or abiotic processes to form telomer alcohols or other intermediates and that they eventually form PFAC. Polymers based on POSF and other chain length chemistries show similar degradation rates and release intermediates that further degrade to form perfluorinated acids and sulfonates. Studies have shown that some polymers can undergo indirect photolysis in soil and in aquatic systems and be degraded with half-lives of days to several years.

VII. Exposure Characterization Summary

The pattern of PFAS and PFAC contamination varies with location and among species, which suggests multiple sources of emission and patterns of migration into environmental media from the sources of emission. Major pathways that enable PFOA and PFOS to get into human blood in small quantities are not yet fully understood. Manufacturing releases are known to have contaminated local drinking water supplies in the immediate vicinity of some industrial plants, leading to localized elevated blood levels. The widespread presence of PFOA and PFOS precursors in human blood samples nationwide suggests other pathways of exposure, possibly including long range air transport, and the release of PFOA and PFOS from treated articles.

Summary of Exposure to Consumers and Children from PFCs in Indoor Environments

PFCs in Articles of Commerce

EPA's ORD has conducted research on 116 articles of commerce documenting that PFCs contained in articles of commerce have the potential to be released from those articles. Articles tested and found to contain the highest levels of PFAC were carpet and carpet treatment products, various types of apparel, home textiles, thread sealant tape, floor wax and other sealants, and food contact paper and paper coatings. Carpet and carpet treatment products contained individual PFAC in levels from 0.04-14100 ng/g; food contact paper and paper coatings: 0.05-160,000 ng/g; thread sealant tape and apparel: ND (non-detect)-3488 ng/g and ND-4640ng/g respectively; floor wax and sealer: 0.03-3720 ng/g; and home textiles: ND-519 ng/g. Some of the more commonly found PFAC measured in these articles were PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFOA and PFOS. Inhalation levels of PFOA and total PFCs

measured in carpet were 5385 pg/cm^3 and 32500 pg/cm^3 respectively (Guo, 2009).

Children are particularly susceptible to exposure from inhalation of PFC off-gassing from carpet and carpet protectants during their earliest years when they are lying, crawling and spending large amounts of time playing on the carpet. The significantly high levels of PFC found by ORD in carpet and carpet protectants pose an exposure concern for children through this pathway. Adults can also be exposed to PFCs in carpets through inhalation and dermal contact. Consumers and children may also be exposed to PFCs in apparel, home textiles, thread sealant tape, floor wax, contact paper and paper coatings. Some of these articles such as paper coatings for foods cannot be ruled out for the ingestion exposure pathways for children and adults depending upon how the PFCs in the paper contacts the food and subsequently humans.

PFCs in Indoor Air

Another source of PFCs to the indoor environment is dust containing not only PFAC and PFAS but also fluorotelomer alcohols. Maximum indoor dust air measurements of 6:2 FTOH were found at 804 ng/g in the house dust of eastern United States (Strynar, 2008). The PFAS (ET-FOSA, Et-FOSE, MeFOSE) chemicals were measured at 646 ng/g, 75440 ng/g, and 8860 ng/g respectively in indoor air in Canada (Shoeib, 2005). PFOA was found at 3700 ng/g in Japanese household vacuum cleaner dust (Moriwaki, 2003).

Summary of Exposure to the General Population

PFCs in Groundwater, Freshwater, Saltwater, and Rainwater

PFAC and PFAS have been found in many countries as well as in Unites States in untreated groundwater, rivers, streams, bays, estuaries, oceans and rain water. Levels of PFAC in groundwater near the 3M Cottage Grove, MN industrial site have been measured as high as 846,000 ng/l (PFOA) and in freshwater as high as 178,000 ng/l (PFBA) (Department of Health and Human Services, 2005). PFOS has been found near Cottage Grove, MN in groundwater at levels of 371,000 ng/l and in freshwater at 18,200 ng/l. PFAC in rainwater has been measured in the United States between 0.1 and 1006 ng/l (PFHpA) (Scott BF, 2006).

Saltwater levels of PFOS have been measured in the Pacific Ocean at 57,700 ng/l and in precipitation from snow and rain in China at 545 ng/l (Liu W, 2009; Yamashita, 2005). While the general population may not directly ingest these groundwater, freshwater and saltwater levels as drinking water, the ground water and freshwater containing PFCs may discharge to surface waters from which municipalities withdraw drinking water. The general population may also experience dermal, ingestion and inhalation exposures when coming into contact with freshwater containing PFCs. Rainwater containing PFCs may contribute PFCs to vegetables and fruits in home gardens, crops grown on commercial crop lands, drinking water reservoirs, and surface waters from which drinking water is withdrawn.

PFCs in Freshwater and Saltwater Fish

Freshwater fish have been found to contain levels of PFAS and PFAC. The highest levels

of PFAS measured in the United States to date were near the 3M Cottage Grove, MN site (Oliaei F, 2006). Liver samples of bass, walleye and carp ranged from 130-6350 ng/g PFOS wet weight. Blood samples of these same fish ranged from PFOS levels of 136-29600 ng/ml in serum. Total PFCs for the blood of freshwater fish in the same area was measured at 32248 ng/ml serum. The highest levels of PFAC for freshwater fish were found near the 3M Cottage Grove, MN site and were measured for blood samples of bass, walleye, and carp in the range of 2.53-210 ng/ml serum. For comparison, saltwater fish in Danish seas had measured levels of PFOS up to 156 ng/g and saltwater fish in Charleston Harbor South Carolina were found with PFOS levels up to 101 ng/g (Bossi R, 2005; Houde M, 2006).

VIII. Risk Management Considerations

Current Risk Management Summary

PFAS Chemicals

Following the voluntary 3M phase-out of PFAS chemicals in the United States in 2002, EPA issued SNURs to control the reintroduction of these chemicals into the U.S. market. Final rules were published on March 11, 2002 (EPA, 2002b) and December 9, 2002 (EPA, 2002a), to limit any future manufacture or importation of 88 PFAS chemicals specifically included in that phase-out. On October 9, 2007, EPA published another SNUR on 183 additional PFAS chemicals (EPA, 2007). Those actions were necessary because data showed that certain alkyl chain lengths of the PFAS chemicals are toxic to human health, bioaccumulate, and are persistent in the environment. PFAS chemicals are no longer manufactured in United States. However a limited set of existing uses was excluded from the SNURs because alternatives were not yet available.

Similar to the PFAS SNURs in United States, PFOS has also been restricted in the European Union, Canada, Australia and other countries, and has been nominated for inclusion in the Stockholm Convention and the Convention on Long-Range Transboundary Air Pollution (LRTAP) Persistent Organic Pollutants (POPs) protocol. At the fourth Conference of the Parties (COP) to the Stockholm Convention on POPs, held in May 2009, delegates agreed to add PFOS, its salts, and perfluorooctane sulfonyl fluoride (PFOSF) to Annex B, subjecting it to restrictions on production and use. Parties agreed that while the ultimate goal is the elimination of PFOS, production of the chemical may continue for limited purposes, including coatings for semiconductors, firefighting foam, photo imaging, aviation hydraulic fluids, metal plating, and certain medical devices. Countries must notify the Convention Secretariat whether they intend to continue production for acceptable purposes. Countries can also ask for specific exemptions allowing the production of PFOS for use in the production of chemical substances used in goods such as carpets, leather and apparel, textiles, paper and packaging, coatings, and rubber and plastics (POPs, 2009).

PFAC Chemicals

OPPT's core strategy for working towards the elimination of PFAC chemicals has been through the PFOA Stewardship Program. Under the program, eight major companies operating

in the United States committed to reduce global facility emissions and product content of PFAC chemicals by 95 percent by 2010, and to work toward eliminating emissions and product content by 2015 (EPA, 2009a). Companies provide annual progress reports, and most companies have reported significant progress in meeting program goals.

On March 7, 2006, EPA published a proposal to amend the polymer exemption rule to exclude polymers containing certain perfluoroalkyl moieties from eligibility for the exemption (EPA, 2006). Under this proposal, polymers containing these perfluoroalkyl moieties would need to go through the pre-manufacture notification (PMN) review process so that EPA can better evaluate these polymers for potential effects on human health and the environment. This change to the current regulation is necessary because, based on current information, EPA can no longer conclude that these polymers "will not present an unreasonable risk of injury to health or the environment" under the terms of the polymer exemption rule, which is the determination necessary to support an exemption under section 5(h)(4) of TSCA. This amendment to the polymer exemption rule is a necessary complement to the PFOA Stewardship Program and will give EPA the necessary tools to review and control risk of PFC-based and related polymers, including those PFAS and PFAC containing polymers.

In January 2009, EPA's Office of Water (OW) developed Provisional Health Advisory (PHA) values for PFOA and PFOS to mitigate potential risk from exposure to these chemicals through drinking water (EPA, 2009c). Due to limited information on the toxicity of PFCs other than PFOA and PFOS, no attempt was made by OW at that time to develop PHA values for the other PFCs. OPPT and OW are working together to determine whether revised health advisory values are needed for PFOA and PFOS.

In October 2009, EPA's Office of Solid Waste and Emergency Response (OSWER) used OW's PHA's to derive sub-chronic R_fD values for PFOA and PFOS. These values may be used in the Superfund program's risk-based equations to derive Removal Action Levels and/or Screening Levels for water and other media, as appropriate.

EPA has taken the leadership role in raising the profile of PFCs at an international level stemming from Agency concerns about the role of long range transport in the environmental distribution of PFCs, and U.S. importation of products containing these chemicals (UNEP, 2009b). As a result of these activities, in May 2009, during the International Conference on Chemicals Management (ICCM2), delegates to the Strategic Approach to International Chemicals Management (SAICM) agreed to consider the development of stewardship programs and regulatory approaches to reduce emissions and content of PFAC and PFAS chemicals in products and to work towards their elimination, where feasible (UNEP, 2009a).

Remaining Issues and Concerns

PFAS Chemicals

PFAS chemicals are no longer manufactured in the United States but continue to be manufactured outside of the United States. Although the PFAS SNURs are an important step toward controlling any future manufacture or import of PFAS chemicals, these chemicals may

continue to be imported into United States in articles, such as carpets, leather and apparel, textiles, paper and packaging, coatings, and rubber and plastics.

Possible scenarios of concern:
- Direct releases to the environment from U.S. facilities as a result of few existing uses.
- Direct releases to the environment from non-U.S. facilities, resulting in transboundary environmental transport to United States.
- Articles containing PFAS chemicals. Recent research by EPA's ORD has shown that consumer articles could release PFCs, significantly increasing the magnitude and duration of exposure to humans and the environment to these chemicals.

PFAC Chemicals

Although the 2010/15 PFOA Stewardship Program is expected to eliminate the production of C8-based fluorotelomers by the eight participating companies by 2015, the potential remains for continued environmental and human loading of PFAC in the United States. This is in part because companies not participating in the PFOA Stewardship Program may follow the market opportunity presented when the eight PFOA Stewardship Program companies leave the PFAC market by 2015. This occurred with PFAS production in some Asian countries after the 3M 2002 phase-out of PFAS chemicals in United States (Wenya, 2008).

Possible scenarios of concern:
- Direct releases to the environment from U.S. facilities not participating in PFOA Stewardship Program.
- Direct releases to the environment from non-U.S. facilities not participating in PFOA Stewardship Program, resulting in transboundary environmental transport to United States.
- Articles, including imports, containing PFAC chemicals. These articles could release PFAC as a result of their residual content in fluorotelomer-based products and/or as the fluorotelomers-based polymers in articles biodegrade.

IX. Next Steps

To date, significant adverse effects have not been found in general human population; however, significant adverse effects have been identified in laboratory animals and wildlife. Given the long half-life of these chemicals in humans (years), it can reasonably be anticipated that continued exposure could increase body burdens to levels that would result in adverse outcomes. Consequently, EPA intends to propose actions in 2012 under TSCA to address the potential risks from long-chain PFCs.

EPA intends to consider initiating TSCA section 6 rulemaking for managing long-chain PFCs. If EPA can make certain findings with respect to these chemicals (further analysis of the information will be performed as part of TSCA section 6 rulemaking), TSCA section 6 provides authority for EPA to ban or restrict the manufacture (including import), processing, and use of these chemicals. A rule addressing the PFAS sub-category could expand beyond the reach of the SNURs that the Agency has promulgated over the past decade. For example, the rule could address PFAS-containing articles. A rule addressing the PFAC sub-category could expand the

reach of the 2010/15 PFOA Stewardship Program beyond the eight participating companies and further address the concerns for potential PFAC exposure through the use of PFAC-containing articles. EPA will develop more detailed assessments to support the TSCA section 6(a) "presents or will present an unreasonable risk" findings. If these more detailed assessments indicate that a different approach to risk management is appropriate, EPA will consider additional approaches.

EPA will continue with the 2010/15 PFOA Stewardship Program to work with companies toward the elimination of long-chain PFCs from emissions and products. EPA will also continue to evaluate alternatives under EPA's New Chemicals Program and collaborate with other countries on managing PFCs.

As part of the Agency's efforts to address these chemicals, EPA also intends to evaluate the potential for disproportionate impact on children and other sub-populations.

X. References

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EXHIBIT B

Bilott, Robert A.

From: US Environmental Protection Agency <noreply-subscriptions@epa.gov>
Sent: Monday, July 31, 2017 11:23 AM
To: Bilott, Robert A.
Subject: EPA Adds Saint-Gobain Performance Plastics Site in Hoosick Falls, N.Y. to the Federal Superfund List

U.S. ENVIRONMENTAL PROTECTION AGENCY

NEWS RELEASE

WWW.EPA.GOV/NEWSROOM

EPA Adds Saint-Gobain Performance Plastics Site in Hoosick Falls, N.Y. to the Federal Superfund List

Contact: Elias Rodriguez, (212) 637-3664, rodriguez.elias@epa.gov

(New York, N.Y. – July 31, 2017) The U.S. Environmental Protection Agency has added the Saint-Gobain Performance Plastics site in the Village of Hoosick Falls, N.Y. to its Superfund National Priorities List (NPL) of the country's most hazardous waste sites. Groundwater at the Saint-Gobain Performance Plastics facility, located at 14 McCaffrey Street, and in other locations in Hoosick Falls is contaminated with Perfluorooctanoic Acid (PFOA) and Trichloroethylene (TCE). Adding the site to the federal Superfund list will allow the EPA to work with New York State to ensure that the contamination is cleaned up and that people's health is protected.

"My goal as Administrator is to restore the Superfund program to its rightful place at the center of the agency's core mission. Today, we are adding sites to the Superfund National Priorities List to ensure they are cleaned up for the benefit of these communities," said EPA Administrator Scott Pruitt, "When we clean up these sites, we make communities healthier places to live and clear the way for development and increased economic activity."

The McCaffrey Street facility was built in 1961, and had been used to manufacture circuit board laminates, polytetrafluoroethylene (PTFE)-coated fiberglass and other PTFE products. In 1999, Saint-Gobain Performance Plastics purchased the facility and began operations there, using PFOA in its manufacturing process. PFOA belongs to a group of chemicals used to make household and commercial products that resist heat and chemical reactions and repel oil, stains, grease and water. PFOA was widely used in non-stick pots and pans, stain-resistant carpets, and water-resistant outerwear. In 2006, the EPA reached a nationwide agreement with eight manufacturers to phase out the production and use of PFOA. These manufacturers stopped using PFOA in 2015. PFOA is persistent in the environment and can pose adverse effects to human health and the environment. TCE is a volatile organic compound widely used as an industrial solvent. Exposure to TCE can have adverse health impacts, including liver damage and increased risk of cancer.

After PFOA was discovered in the public drinking water supply, a carbon filtration system was installed on the Village of Hoosick Falls water supply wells to treat the water and protect consumers. PFOA was also discovered in private wells, and special systems called "point of entry treatment systems," or POETS, have been installed on a number of private drinking water wells. The New York State Department of Environmental Conservation (NYSDEC) and Department of Health, with input from the EPA, have overseen measures to address the drinking water contamination.

- In January 2016, the NYSDEC added the Saint-Gobain site to New York State's Superfund list and requested that the EPA include the site on EPA's federal Superfund list.
- In April and May 2016, the EPA installed monitoring wells to sample groundwater at and around the Saint-Gobain Performance Plastics facility (McCaffrey Street facility) and sampled the Village water supply wells. The EPA also collected soil samples from the McCaffrey Street facility, Village ballfields and recreational areas.
- In June 2016, the NYSDEC entered into a legal agreement with Saint-Gobain Performance Plastics Corporation and Honeywell International Inc. and initiated a study of the nature and extent of contamination at the site.
- In September 2016, the EPA proposed adding the Saint-Gobain Performance Plastics site to the federal Superfund list.

The EPA has determined that the appropriate course of action to address contamination from the Saint-Gobain facility is to list the site on the NPL. The EPA took public comment and considered public input before finalizing the decision. The EPA is coordinating all investigation and cleanup efforts with New York State. To learn more about the Saint-Gobain Performance Plastics Superfund site, please visit:

https://www.epa.gov/ny/hoosick-falls-water-contamination

For Federal Register notices and supporting documents for final and proposed sites, visit: https://www.epa.gov/superfund/current-npl-updates-new-proposed-npl-sites-and-new-npl-sites

Today's NPL update follows the announcement of the Superfund Task Force recommendations to improve the Superfund program.

The task force's recommendations focused on five overarching goals: expediting cleanup and remediation, reinvigorating cleanup and reuse efforts by potentially responsible parties, encouraging private investment to facilitate cleanup and reuse, promoting redevelopment and community revitalization and engaging with partners and stakeholders.

Work to prioritize and reinvigorate the program by the task force has been initiated and will be ongoing into the future. The Superfund Task Force Recommendations can be viewed at https://www.epa.gov/superfund/superfund-task-force-recommendations.

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17-049

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United States Environmental Protection Agency

OLEM/OSRTI
Washington, DC 20460

NATIONAL PRIORITIES LIST (NPL)

****NPL Site****

July 2017

SAINT-GOBAIN PERFORMACE PLASTICS | **Village of Hoosick Falls, New York**
Rensselaer County

Site Location:

The Saint-Gobain Performance Plastics (SGPP) site is located at 14 McCaffrey Street in the Village of Hoosick Falls, Rensselaer County, New York. The facility is situated in the southwest corner of Hoosick Falls and along the east side of the Hoosic River.

Site History:

SGPP manufactures plastic materials, tapes, and foams and has operated in Hoosick Falls from 1999 to the present. The McCaffrey Street facility was originally built in 1961 and was used for manufacturing extruded tapes, circuit board laminates, polytetrafluoroethylene (PTFE)-coated fiberglass, and molded and extruded PTFE intermediates before SGPP began operations. The facility used perfluorooctanoic acid (PFOA)-containing materials in their manufacturing process until they began phasing them out in 2003.

Site Contamination/Contaminants:

Ground water underlying the SGPP facility and withdrawn by the public supply wells for the Village of Hoosick Falls is contaminated with PFOA above the Health Advisory and with chlorinated solvents, such as trichloroethylene (TCE) and vinyl chloride.

Potential Impacts on Surrounding Community/Environment:

The public supply wells in the Village of Hoosick Falls, which serve approximately 4,000 people as the main source of drinking water, are contaminated with PFOA at concentrations above the EPA Health Advisory. In addition, PFOA has been found in several private wells.

Response Activities (to date):

Saint-Gobain Performance Plastics installed a carbon filtration system. Drinking water now meets all federal and state standards.

Need for NPL Listing:

Ground water contaminated with PFOA in the public supply wells requires cleanup to protect human health and the environment. NPL listing has been determined to be the most effective approach for cleanup. The EPA received a letter of support for placing the site on the NPL from the state of New York.

[The description of the site (release) is based on information available at the time the site was evaluated with the HRS. The description may change as additional information is gathered on the sources and extent of contamination. See 56 FR 5600, February 11, 1991, or subsequent FR notices.]

For more information about the hazardous substances identified in this narrative summary, including general information regarding the effects of exposure to these substances on human health, please see the Agency for Toxic Substances and Disease Registry (ATSDR) ToxFAQs. ATSDR ToxFAQs can be found on the Internet at https://www.atsdr.cdc.gov/toxfaqs/index.asp or by telephone at 1-800-CDC-INFO or 1-800-232-4636.

SITE SUMMARY

The Saint-Gobain Performance Plastics (SGPP) site as scored consists of soil and ground water contaminated with trichloroethylene (TCE), vinyl chloride (VC), polychlorinated biphenyls (PCBs), and perfluorooctanoic acid (PFOA) as a result of historical releases from the SGPP facility located at 14 McCaffrey Street in Hoosick Falls, NY. Sampling and analysis of soil and ground water by EPA in April–May 2016 document the presence of TCE in facility soils, and TCE, VC, and PFOA in ground water at concentrations that meet the criteria for observed release by chemical analysis [see **Section 3.1.1 of this HRS documentation record**]. Sampling and analysis by EPA of the Village of Hoosick Falls municipal water supply in May 2016 document Level I actual contamination of drinking water wells with VC and Level II actual contamination with PFOA that is attributable at least in part to the site [see **Section 3.3.2**]. In addition, information provided by SGPP to EPA in December 2014 documents an observed release by direct observation of PFOA to the aquifer of concern [see **Section 3.1.1**]. A Site Location Map is presented in Figure 1.

For the SGPP site, EPA is evaluating the ground water migration pathway. The source is evaluated as soil contaminated with cis-1,2-dichloroethylene (DCE), TCE, and PCBs (Source 1) as further discussed in **Section 2.4.1**. *Sampling and analysis by EPA in April and May 2016 showed the presence of PFOA in SGPP facility soil; however, due to laboratory quality control issues, the data are considered unusable and will not be evaluated in this HRS Documentation Record Package.*

The facility that currently houses SGPP was originally built in 1961 for Dodge Fibers Corp. and was used first for producing extruded tapes and then circuit board laminates; prior to 1961 the property was vacant land [Ref. 39, p. 23]. Oak Materials Group (a.k.a. Oak Electronetics; a.k.a. Oak Industries) purchased the property from Dodge Fibers between 1969 and 1971 [Ref. 39, p. 23]. Oak Industries operated the facility until 1987 when it was sold to Allied Signal Fluorglas [Ref. 39, p. 23]. The property was sold to Furon Company in February 1996 [Ref. 40, p. 24]. Allied Signal Fluorglas and Furon Company used the facility to manufacture polytetrafluoroethylene (PTFE)-coated fiberglass, and molded and extruded PTFE intermediates [Ref. 40, p. 24]. Manufacturing processes at the facility included the use of certain non-stick coatings [Ref. 40, p. 24]. Fluoropolymers used to manufacture non-stick coatings are known to include PFOA [Ref. 13, p. 20; 52, p. 1].

SGPP has operated at 14 McCaffrey Street (Tax Map/Parcel No. Section 37.6, Block 3, Lot 1) since 1999 [Ref. 4, p. 1; 18, p. 2]. SGPP is a Paris-based multinational corporation which manufactures a variety of polymer-based products [Ref. 14, pp. 1–2]. The McCaffrey Street facility manufactures high-performance polymeric films and membranes, as well as foams for bonding, sealing, acoustical and vibrational damping, and thermal management; the facility previously used PFOA in its manufacturing processes [Ref. 4, p. 1; 14, pp. 4, 7, 9]. The facility is situated near the southwest corner of Hoosick Falls and along the east side of the Hoosic River [**Figure 1**; Ref. 4, p. 1; 5, p. 1].

The McCaffrey Street facility historically used PFOA or raw materials containing PFOA in its manufacturing processes; since 2003, the facility has participated in the industry's voluntary PFOA phase-out effort by purchasing raw materials with decreasing levels of PFOA as an ingredient. [Ref. 4, p. 1; 19, p. 1]. PFOA is a man-made chemical that belongs to a group of fluorine-containing chemicals called perfluorinated chemicals (PFC) [Ref. 12, p. 2; 15, p. 2]. PFOA was once widely used in nonstick cookware, in surface coatings for stain-resistant carpets and fabric, and in paper and cardboard food packaging [Ref. 12, p. 2]. PFOA was also used in fire-fighting foam and in many products for the aerospace, automotive, building/construction, and electronic industries [Ref. 12, p. 2]. PFOA and related compounds are persistent in water and soil, and resistant to typical environmental degradation processes [Ref. 15, p. 3]. PFOA poses potential adverse effects for the environment and human health based on its toxicity, mobility, and bioaccumulation potential [Ref. 15, pp. 1, 3-4]. PFOA exists as a white powder or waxy white solid at room temperature, and it is water-soluble and can readily migrate from soil to ground water [Ref. 15, pp. 2–3].

Former employees of the McCaffrey Street facility describe a powder-like smoke plume that was routinely discharged to the air from the facility's smokestacks and settled in the valley surrounding the plant [Ref. 4, p. 1]. The powder was observed to cover equipment and other surfaces within the facility as well [Ref. 4, p. 1]. After approximately 15 years of unfiltered emissions, filters were installed in the facility's smokestacks in the early 1980s [Ref. 4, p. 1]. A former employee stated that the filters and other equipment contacted by the white powder were cleaned weekly by washing them on a hillside outside the plant [Ref. 4, p. 1].

The Village of Hoosick Falls operates three public supply wells (Village Wells 3, 6, and 7); the well field is located

2.4.1 Hazardous Substances

As discussed above, soil samples collected by SGPP in August 2015 document the presence of PFOA in facility soils. Soil and ground water samples collected by EPA in April 2016 document the presence of TCE, cis-1,2-DCE, and PCBs in site soils and TCE and VC in the aquifer of concern. As all of these compounds are man-made chemicals and do not naturally occur in the environment, the data for the samples discussed above are being considered for source documentation and are presented in Tables 1–7. The source type is contaminated soil; therefore, background soil samples are used for comparison purposes. *Sampling and analysis by EPA in April and May 2016 showed the presence of PFOA in SGPP facility soil; however, due to laboratory quality control issues, the data are considered unusable and will not be evaluated in this HRS Documentation Record Package.*

TABLE 1. BACKGROUND AND SOURCE SAMPLE INFORMATION – cis-1,2-DCE and TCE

Field Sample ID	CLP ID	Sample Date	Sample Time	Depth (feet)	Solids (%)	References
Background Sample						
SGPP-S01	BD371	5/3/2016	1550	0–2	81.7	22, p. 29; 23, p. 112; 45, pp. 2, 78
Source Sample						
SGPP-SS07B	BD3B1	4/27/2016	1710	10–12	88.7	22, p. 24; 23, p. 84; 49, pp. 3, 168

TABLE 2. BACKGROUND AND SOURCE SAMPLE INFORMATION – PCBs

Field Sample ID	CLP ID	Sample Date	Sample Time	Depth (feet)	Solids (%)	References
Background Sample						
SGPP-S01	BD371	5/3/2016	1550	0–2	81.7	22, p. 29; 23, p. 112; 45, pp. 2, 1220
Source Sample						
SGPP-S07	BD3A9	4/27/2016	1650	0–2	78.3	22, p. 24; 23, p. 84; 49, pp. 3, 1200

TABLE 3. BACKGROUND AND SOURCE CONCENTRATIONS – cis-1,2-DCE and TCE

	Maximum Background Concentration		Source Concentration	
Field Sample ID	SGPP-S01		SGPP-SS07B	
Sample Date	5/3/2016		4/27/2016	
CLP Sample ID	BD371		BD3B1	
Depth (feet)	0–2		10–12	
	Result	**RDL***	**Result**	**RDL***
cis-1,2-DCE	5.1 U	5.1	8.4	4.2
TCE	5.1 U	5.1	160	4.2
References	22, p. 29; 23, p. 112; 33, p. 8; 41, pp. 2–6, 28, 122; 45, pp. 2, 78		22, p. 24; 23, p. 84; 32, pp. 3–6, 59, 160; 33, p. 8; 49, pp. 3, 168	

Concentrations reported in micrograms per kilogram (µg/kg).
RDL = Reporting Detection Limit.
U = The analyte was analyzed for, but was not detected at a level greater than or equal to the level of the adjusted Contract Required Quantitation Limit (CRQL) (i.e., SQL) for sample and method.
*The RDL for each result is the CRQL adjusted for sample and method [Ref. 33, p. 8]. Since the samples were analyzed through CLP, these adjusted CRQLs are used in place of the HRS-defined sample quantitation limit (SQL) [Ref. 1, Sections 1.1 and 2.3].

GW-Observed Release

Hazardous Substances Released:

Trichloroethylene (TCE)	CAS No. 79-01-6
Vinyl chloride (VC)	CAS No. 75-01-4
Perfluorooctanoic Acid (PFOA)	CAS No. 335-67-1

EXHIBIT C

ATSDR Agency for Toxic Substances and Disease Registry

Overview

Per- and Polyfluoroalkyl Substances (PFAS) are a large group of man-made chemicals that have been used in industry and consumer products worldwide since the 1950s. In the United States, making and using these chemicals in consumer products has greatly decreased during the last 10 years, but people can still be exposed to PFAS because they are still present in the environment. Scientists have studied how PFAS affect animals' health but are still trying to understand how exposure to PFAS affects human health. Over the last decade, interest in PFAS has been growing. ATSDR and our state health partners are investigating exposure to PFAS at a number of sites.

PFAS are heat, oil, grease, and water resistant.

The two best known groups of this family of chemicals are the perfluorocarboxylic acids (PFCAs), which include perfluorooctanoic acid (PFOA, sometimes called C8), and the perfluorosulfonates (PFSAs), which include perfluorooctane sulfonate (PFOS). PFCAs and PFSAs do not break down easily in the environment. They also bioaccumulate, or build up, in the blood and organs of exposed humans and animals and remain there for extended periods of time.

Some PFAS are precursors to PFCAs and PFSAs and can break down to those chemicals in the body or the environment.

The largest manufacturer of PFOS voluntarily stopped producing it in 2002. However, other countries still produce PFOS, and it can be imported into the United States in limited quantities. In 2006, EPA and major companies in the PFAS industry launched the 2010/2015 PFOA Stewardship Program. Companies participating in the program are working to stop producing PFOA and related chemicals by 2015. These companies include Arkema, Asahi, BASF Corporation (successor to Ciba), Clariant, Daikin, 3M/Dyneon, DuPont, and Solvay Solexis.

List of Perfluorosulfonates and Perfluorocarboxylic Acids and Their Abbreviations			
Chemical	Abbreviation	Chemical Abstracts Service Registry Number (CAS No.)	Chemical Formula
Perfluorosulfonates (PFSAs)			

Perfluorobutane sulfonate	PFBuS	375-73-5	$C_4HF_9O_3S$
Perfluorodecane sulfonate	PFDS	335-77-3	$C_{10}HF_{21}O_3S$
Perfluoroheptane sulfonate	PFHpS	375-92-8	$C_7HF_{15}O_3S$
Perfluorohexane sulfonate	PFHxS	432-50-7	$C_6HF_{13}O_3S$
Perfluorooctane sulfonate	PFOS	1763-23-1	$C_8HF_{17}O_3S$
Perfluorooctanesulfonamide	PFOSA	754-91-6	$C_8H_2F_{17}NO_2S$
Perfluorocarboxylic acids (PFCAs)			
Perfluorobutanoic acid	PFBA	375-22-4	$C_4HF_7O_2$
Perfluorodecanoic acid	PFDA	335-76-2	$C_{10}HF_{19}O_2$
Perfluorododecanoic acid	PFDoA	307-55-1	$C_{12}HF_{23}O_2$
Perfluoroheptanoic acid	PFHpA	375-85-9	$C_7HF_{13}O_2$
Perfluorohexanoic acid	PFHxA	307-24-4	$C_6HF_{11}O_2$
Perfluorononanoic acid	PFNA	375-95-1	$C_9HF_{17}O_2$
Perfluorooctanoic acid	PFOA	335-67-1	$C_8HF_{15}O_2$
Perfluoroundecanoic acid	PFUA	2058-94-8	$C_{11}HF_{21}O_2$

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Page last reviewed: September 18, 2015

Page last updated: May 26, 2016

Content source: Agency for Toxic Substances and Disease Registry (https://www.atsdr.cdc.gov)

ATSDR Agency for Toxic Substances and Disease Registry

Health Effects of PFAS

On this Page

How can PFAS affect people's health?

Scientists are not yet certain about the possible health effects resulting from human exposure to PFAS at levels typically found in our water and food. Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonate (PFHxS), and perfluorononanoic acid (PFNA) have been more widely studied than other PFAS. For the most part, laboratory animals exposed to high doses of PFOA or PFAS, including the PFAS mentioned above, have shown changes in the liver, thyroid, and pancreatic function, as well as some changes in hormone levels. Because animals and humans do not always process chemicals the same way, scientific methods are used to account for these differences and ensure their conclusions about chemicals are protective of the public.

Some PFAS accumulate in the human body and the levels decrease slowly over time. The ability of these compounds to be stored in the body, also known as body burden, increases concerns about the possible effects on human health.

Some, but not all studies in humans have shown that certain PFAS may:

- affect the developing fetus and child, including possible changes in growth, learning, and behavior.
- decrease fertility and interfere with the body's natural hormones,
- increase cholesterol,
- affect the immune system, and
- increase cancer risk.

At this time, there is not enough information to evaluate the health effects of exposures to mixtures of PFAS. Further studies are needed to understand whether the same effects are caused by the same mechanism of action.

How can people reduce the risk of exposure to PFAS?

PFAS are found in the blood of people and animals all over the world and are present at low levels in a variety of food products and in the environment (air, water, soil, etc.). Therefore, completely preventing exposure to PFAS is unlikely, and no effective recommendations can be made for reducing individual exposures in the general population. However, if you live near known sources of PFAS contamination, you can take steps to reduce your risk of exposure to PFAS.

Minnesota, Michigan, and Alabama have issued advisories cautioning consumers to either stop or limit eating fish from waters contaminated with PFOS or other PFAS. Check with your state public health and environmental quality departments for any advisories in place in your area and to learn the types and local sources of fish that are safe to eat.

A variety of consumer products such as non-stick coatings on cookware and surface-protective coatings on clothing, carpets, and paper packaging have contained different types of PFAS in the past. But recent efforts to remove PFAS in many of these products have reduced the likelihood of PFAS exposure. In addition, research has suggested that exposure from consumer products is usually low, especially when compared to the impact of exposure in contaminated drinking water or contaminated food such as fish.

You can contact CDC/ATSDR for updated information on this topic at 1-800-CDC-INFO.

If you have questions or concerns about the products you use in your home, contact the Consumer Product Safety Commission at (800) 638-2772.

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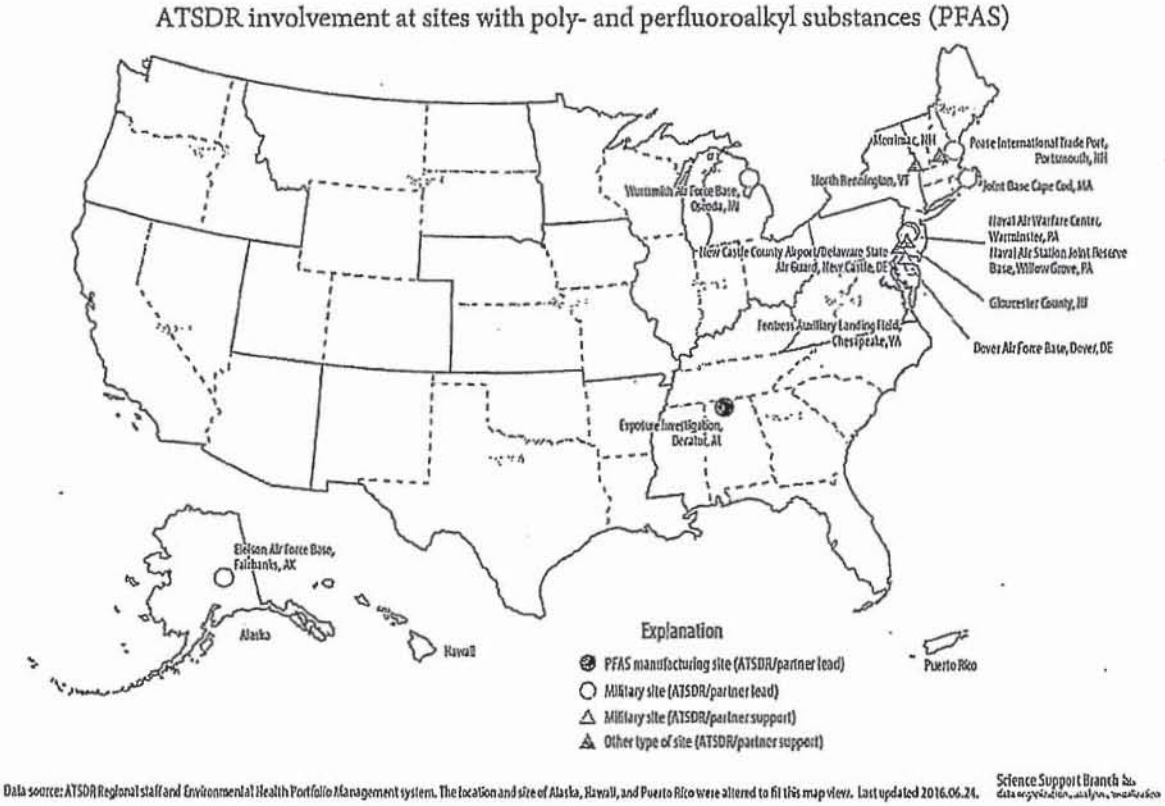
ATSDR Agency for Toxic Substances and Disease Registry

How is ATSDR involved investigating PFAS in the environment?

ATSDR is involved at a number of PFAS-related sites, either directly or thorough assisting state and federal partners (Figure 1). As of now, most sites are related to drinking water contamination connected with PFAS production facilities or fire training areas where aqueous film-forming firefighting foam (AFFF) was regularly used. We are working with one state partner on a site where consuming contaminated fish is the concern.



Data source: ATSDR Regional staff and Environmental Health Portfolio Management system. The location and size of Alaska, Hawaii, and Puerto Rico were altered to fit this map view. Last updated 2016.06.24. Science Support Branch, Division of Community Health Investigations

Figure 1. Perfluorinated compound (PFAS) sites with ATSDR, state health department, US Environmental Protection Agency, or Department of Defense involvement

Examples include:

Region 1

Joint Base Cape Cod, MA

Military activities have contaminated soil at the Joint Base Cape Cod facility and the aquifer below. The contaminated aquifer provides drinking water to some residents of Cape Cod. The MA Department of Health (MA DPH), under the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html), is evaluating whether people have been exposed to per- and polyfluoroalkyl substances (PFAS) in their drinking water at levels high enough to cause health effects. ATSDR will provide help as needed. For more information about PFAS in drinking water, visit the ATSDR PFAS website at https://www.atsdr.cdc.gov/pfc/index.html (https://www.atsdr.cdc.gov/pfc/index.html).

MA DPH has reviewed PFAS in recreational waters. The MA DPH fact sheet about PFAS in recreational waters is at http://www.mass.gov/eohhs/docs/dph/environmental/investigations/cape/jbcc-rec-wtr-fact-sheet.pdf (http://www.mass.gov/eohhs/docs/dph/environmental/investigations/cape/jbcc-rec-wtr-fact-sheet.pdf)

North Bennington, VT

The Vermont Department of Environmental Conservation (VDEC) has found perfluorooctanoic acid (PFOA) in private well water samples collected in North Bennington. PFOA is one of the chemicals in theper- and polyfluoroalkyl substances (PFAS) family. VDEC is testing private wells within a 1.5 mile radius of the former ChemFab site, which is the source of the PFOA, to see how widespread the contamination is. The Vermont Department of Health (VDH) asked NCEH/ATSDR for technical support in addressing health issues.

Visit the VT DPH for more information about PFOA at http://healthvermont.gov/enviro/pfoa.aspx (http://healthvermont.gov/enviro/pfoa.aspx) . For more information about PFAS in drinking water, visit the ATSDR PFAS website at http://www.atsdr.cdc.gov/pfc/index.html (http://www.atsdr.cdc.gov/pfc/index.html)

Merrimack area of southern NH

The New Hampshire Department of Environmental Services (NHDES) tested public and private drinking water supplies in the Merrimack area. Some of the wells are contaminated with perfluorooctanoic acid (PFOA). The sources of PFOA are factories in the area. The New Hampshire Department of Health and Human Services (NH DHHS) is attending public meetings to address residents' health concerns. ATSDR is helping the NH DHHS address health issues through the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html). NHDES collected water samples from public and private drinking water supplies. ATSDR is evaluating the test results to determine if drinking the water may harm people's health and will provide the findings in a written report. For more information about PFAS in drinking water, visit the ATSDR PFAS website at https://www.atsdr.cdc.gov/pfc/index.html (https://www.atsdr.cdc.gov/pfc/index.html)

Pease International Tradeport, Portsmouth, NH

The City of Portsmouth, working with the NH Department of Environmental Services and the NH Department of Health and Human Services, tested the Pease International Tradeport drinking water wells for chemicals in May 2014. One of three wells had elevated levels of perfluorooctane sulfonic acid (PFOS); the City of Portsmouth took the well off-line. Other PFAS were also found in well water samples, and in some residential private wells located near the site. Firefighting foam used at the former Pease Air Force Base is the presumed source of PFAS. Approximately 8,000 people work at or visit the Pease Tradeport daily. Two daycare centers operate on the property.

The New Hampshire Department of Health and Human Services (NH DHHS), through the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html), asked NCEH/ATSDR to help them evaluate how drinking water contaminated with PFOS may affect people's health. ATSDR is working with NH DHHS to answer these questions and to make recommendations to protect people from further PFAS exposure. NH DHHS will write two reports, one evaluating PFAS exposure in water at the Pease Tradeport, and one evaluating exposure from private water wells. The reports will answer the question if drinking PFAS contaminated water at these sites could harm people's health.

NH DHHS has released a report on the blood testing results. A copy of the report is at http://www.dhhs.nh.gov/dphs/documents/pease-pfc-blood-testing.pdf (http://www.dhhs.nh.gov/dphs/documents/pease-pfc-blood-testing.pdf) . ATSDR has created a Community Assistance Panel (CAP) to receive input about the potential of having future health studies using data from the site. For more information, visit the CAP website at http://www.atsdr.cdc.gov/sites/pease/cap.html (https://www.atsdr.cdc.gov/sites/pease/cap.html). The NH DHHS provides information about the site at http://www.dhhs.nh.gov/dphs/investigation-pease.htm (http://www.dhhs.nh.gov/dphs/investigation-pease.htm) .

Region 2

Community Water Systems (CWS) and Private Wells, Gloucester County, New Jersey

The Delaware River Keeper Network petitioned ATSDR to investigate whether residents of Gloucester County, NJ were exposed to harmful levels of perfluorononanoic acid (PFNA) and other PFAS in their drinking water.

The New Jersey Department of Health, through the ATSDR Cooperative Agreement Program (http://www.atsdr.cdc.gov/states/index.html), is reviewing public and private water sample results to see if people have been exposed to PFAS and if the exposure could harm their health. For more information about PFAS in drinking water, visit the ATSDR PFAS website at https://www.atsdr.cdc.gov/pfc/index.html (https://www.atsdr.cdc.gov/pfc/index.html).

Region 3

Naval Air Station Joint Reserve Base, Willow Grove, PA

Groundwater at the Willow Grove Air Station Joint Reserve Base is comtaminated with per- and polyfluoroalkyl substances (PFAS) (mainly perfluorooctane sulfonic acid, PFOS for short, and perfluorooctanoic acid, PFOA for short).\ Some public water supply wells in Horsham and Warrington, and some private wells nearby are also contaminated with PFOS and PFOA. PFAS in the groundwater are likely a result of past use of aqueous film-forming firefighting foams (AFFF) in the area. The Department of Defense asked the Environmental Protection Agency (EPA) to test private well water at the site. Public water utilities are collecting water samples from their systems.

EPA asked ATSDR to evaluate PFAS water test results to see if drinking water contaminated with these levels of PFAS could harm people's health. ATSDR is evaluating the available water test results. For more information about PFAS in drinking water visit the ATSDR PFAS website at https://www.atsdr.cdc.gov/pfc/index.html (https://www.atsdr.cdc.gov/pfc/index.html).

ATSDR is working with the Mid Atlantic Center for Children's Health and the Environment to answer the community's health questions and to educate local health professionals about possible health effects caused by exposure to PFAS. ATSDR continues to work with the PA Department of Health, through the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html), to summarize available cancer statistics for this area because community members are concerned about cancer in their community. The cancer data review for selected zip codes of Warminster, Warrington, and Horsham, PA is available at http://www.atsdr.cdc.gov/HAC/pha/CancerDataReviewPA/CancerDataReview_PA_508.pdf (http://www.atsdr.cdc.gov/HAC/pha/CancerDataReviewPA/CancerDataReview_PA_508.pdf).

Naval Air Warfare Center, Warminster, PA

Groundwater at the former Naval Air Warfare Center Warminster site is contaminated with per- and polyfluoroalkyl substances (PFAS) (mainly perfluorooctane sulfonic acid, PFOS for short, and perfluorooctanoic acid, PFOA for short). Some public water supply wells in Warminster, and some private wells nearby are contaminated with PFOS and PFOA. PFAS in the groundwater are likely from past use of aqueous film-forming firefighting foams (AFFF) in the area. The Department of Defense asked EPA to test private well samples at this site. Public water utilities are collecting water samples from their systems.

The Environmental Protection Agency (EPA) asked ATSDR to evaluate PFAS levels in the drinking water supplies to see if exposure to PFAS in drinking water could harm people's health. ATSDR evaluated the available off-site water test results. The report is available at http://www.atsdr.cdc.gov/HAC/pha/NavalAirWarfareCenter/Naval_Air_Warfare_Center_LHC_01-20-2016_508.pdf (http://www.atsdr.cdc.gov/HAC/pha/NavalAirWarfareCenter/Naval_Air_Warfare_Center_LHC_01-20-2016_508.pdf).

ATSDR is working with the Mid Atlantic Center for Children's Health and the Environment to answer health questions and to educate local health professionals about potential health effects caused by exposure to PFAS. In addition, ATSDR has worked with the PA Department of Health, through the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html), to summarize available cancer statistics for this area. The cancer data review for selected zip codes of Warminster, Warrington, and Horsham, PA is available at http://www.atsdr.cdc.gov/HAC/pha/CancerDataReviewPA/CancerDataReview_PA_508.pdf (http://www.atsdr.cdc.gov/HAC/pha/CancerDataReviewPA/CancerDataReview_PA_508.pdf).

Dover Air Force Base, Dover, DE

Groundwater at the Dover Air Force Base is contaminated with per- and polyfluoroalkyl substances (PFAS), but no off-base drinking water contamination has been found at this time. The Department of Defense sampled onsite and most off-site wells, and asked EPA to test one off-site well. PFAS in the groundwater are likely a result of past use of aqueous film-forming firefighting foams (AFFF) in the area.

The Environmental Protection Agency (EPA) asked ATSDR to address public health issues at this site. For more information about PFAS in drinking water, visit the ATSDR PFAS website at https://www.atsdr.cdc.gov/pfc/index.html (https://www.atsdr.cdc.gov/pfc/index.html).

Naval Auxiliary Landing Field Fentress, Chesapeake, VA

The groundwater at the Naval Auxilliary Landing Field Tentress site is contaminated with per- and polyfluoroalkyl substances (PFAS) and in nearby private drinking water wells. PFAS in the groundwater are likely a result of past use of aqueous film-forming firefighting foams (AFFF) in the area. The U.S. Navy is testing groundwater samples at this site.

The U. S. Navy asked ATSDR to answer health questions. ATSDR is working with the VA Department of Health, through the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html), and with local health departments to answer health questions from residents and health professionals. For more information about PFAS in drinking water, visit the ATSDR PFAS website at https://www.atsdr.cdc.gov/pfc/index.html (https://www.atsdr.cdc.gov/pfc/index.html).

New Castle County Airport/Delaware State Air Guard, New Castle, DE

Groundwater in the New Castel area,and some of the city public water supply wells, are contaminated with per- and polyfluoroalkyl substances (PFAS. The source of the PFAS is unknown. The state and EPA are testing groundwater samples at this site.

EPA asked ATSDR to address public health issue. For more information about PFAS in drinking water, visit the ATSDR PFAS website at http://www.atsdr.cdc.gov/pfc/index.html (http://www.atsdr.cdc.gov/pfc/index.html).

Region 4

Decatur (vicinity), AL -Biological Sampling of Per- and Polyfluoroalkyl Substances (PFAS) in the Vicinity of Lawrence, Morgan, and Limestone Counties, Alabama

In 2007, a PFAS manufacturer in Decatur, AL notified the EPA that it had discharged PFAS into the Decatur Utilities wastewater treatment plant, resulting in environmental contamination. In 2009, the Environmental Protection Agency (EPA) asked ATSDR to conduct an investigation to see if people who live in the vicinity of Decatur, Alabama, downstream of PFAS factories have been exposed to PFAS.

In 2010, ATSDR tested residents' blood and found that some of their blood contained PFCs (now called PFAS). ATSDR conducted follow-up blood and urine testing in 2016. Information about ATSDR's activities can be found below.

- PFAS Serum and Urine Sampling – 2016 Exposure Investigation Report (https://www.atsdr.cdc.gov/HAC/pha/BiologicalSampling/Biological_Sampling_of_Substances_in_Alabama_EI%20-Report_11-28-2016_508.pdf)
- Perfluorochemical Serum Sampling - 2013 Exposure Investigation Report (https://www.atsdr.cdc.gov/HAC/pha/Decatur/Perfluorochemical_Serum%20Sampling.pdf)
- Blood PFC Testing and Health Information Summary, Morgan, Lawrence and Limestone Counties, Alabama (https://www.atsdr.cdc.gov/HAC/pha/decatur/Blood%20PFC%20Testing%20and%20Health%20Information.pdf)
- Information update to the ATSDR Health Consultation Exposure Investigation Report: Perfluorochemical Serum Sampling in the vicinity of Decatur, Alabama - Morgan, Lawrence, and Limestone Counties dated April 1, 2013, (https://www.atsdr.cdc.gov/HAC/pha/decatur/InformationupdatetotheATSDRExposureInvestigationReportFINALDRAFTadditionalcomment31JAN14.pdf)

For more information about PFAS, visit the ATSDR PFAS website at http://www.atsdr.cdc.gov/pfc/index.html (http://www.atsdr.cdc.gov/pfc/index.html).

Region 5

Wurtsmith Air Force Base, Oscoda, MI

The Michigan Department of Health and Human Services (MDHHS), through the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html), is evaluating people's exposures to PFAS in the environment. Releases of PFAS from activities at the former Wurtsmith Air Force Base have resulted in contamination of groundwater and surface water. Sampling by the Michigan Department of Environmental Quality and the U.S. Air Force has identified elevated levels of PFAS contamination in some locally caught fish and drinking water wells. MDHHS has conducted health education in the community, installed fish advisory signs, and helped the local health department provide an alternate water supply to the community. More information is available at http://www.michigan.gov/mdhhs/0,5885,7-339-71551_2945_5105-285528--,00.html (http://www.michigan.gov/mdhhs/0,5885,7-339-71551_2945_5105-285528--,00.html) . For more information about PFAS, visit the ATSDR PFAS website at Perfluoroalkyl Substances and Your Health (https://www.atsdr.cdc.gov/pfc/index.html).

Region 10

Eielson Air Force Base, Fairbanks AK

In March 2015, Eielson Air Force Base tested the base drinking water wells and found that some were contaminated with per- and polyfluoroalkyl substances (PFAS). The Air Force has taken the contaminated wells offline. The Air Force continues to monitor the remaining wells to ensure that PFAS levels in the water system are not above the HA.

Air Force investigations conducted in late spring and summer of 2015 determined that the PFAS moved into private drinking water wells in the Moose Creek community (north of the Eielson Air Force Base). The Air Force is providing alternative drinking water to the impacted homes. The Alaska Division of Public Health (ADPH), under the ATSDR Cooperative Agreement Program (https://www.atsdr.cdc.gov/states/index.html), will evaluate the test results to see if the past exposure may harm people's health. For more information about PFAS, visit the ATSDR PFAS website at https://www.atsdr.cdc.gov/pfc/index.html (https://www.atsdr.cdc.gov/pfc/index.html).

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File Formats Help:

How do I view different file formats (PDF, DOC, PPT, MPEG) on this site? (https://www.cdc.gov/Other/plugins/)

(https://www.cdc.gov/Other/plugins/#pdf)

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An Overview of Perfluoroalkyl and Polyfluoroalkyl Substances and Interim Guidance for Clinicians Responding to Patient Exposure Concerns

Interim Guidance

Revised on 6/7/2017

Introduction

The purpose of this fact sheet is to provide interim guidance to aid physicians and other clinicians with patient consultations on perfluoroalkyl and polyfluoroalkyl substances (PFAS). It highlights what PFAS are, which chemicals fall into this category of substances, identifies health effects associated with exposure to various PFAS, and suggests answers to specific patient questions about potential PFAS exposure.

Background

What are PFAS?

PFAS, sometimes known as PFCs, are synthetic chemicals that do not occur naturally in the environment. There are many different types of PFAS such as perfluorocarboxylic acids (e.g., PFOA, sometimes called C8, and PFNA) and perfluorosulfonates (e.g., PFOS and PFHxS). PFAS may be used to keep food from sticking to cookware, to make sofas and carpets resistant to stains, to make clothes and mattresses more waterproof, and to make some food packaging resistant to grease absorption, as well as use in some firefighting materials. Because PFAS help reduce friction, they are also used in a variety of other industries, including aerospace, automotive, building and construction, and electronics.

Why are PFAS a possible health concern?

According to the U.S. Environmental Protection Agency (EPA), PFAS are considered emerging contaminants. An "emerging contaminant" is a chemical or material that is characterized by a perceived, potential, or real threat to human health or the environment or by a lack of published health standards.

PFAS are extremely persistent in the environment and resistant to typical environmental degradation processes. The pathway for dispersion of these chemicals appears to be long-range atmospheric and oceanic currents transport. Several PFAS and their potential precursors are ubiquitous in a variety of environments. Some long-chain PFAS bioaccumulate in animals and can enter the human food chain.

PFOS and PFOA are two of the most studied PFAS. Exposure to PFOA and PFOS is widespread and global. PFOS and PFOA also persist in the human body and are eliminated slowly. Both PFOS and PFOA can be found in blood, and at much lower levels in urine, breast milk and in umbilical cord blood.

PFOS and PFOA may pose potential adverse effects for human health given their potential toxicity, mobility, and bioaccumulation potential. The likelihood of adverse effects depends on several factors such as amount and concentration of PFAS ingested as well as the time span of exposure.

Routes of Exposure and Health Effects

What are the main sources of exposure to PFAS?

For the general population, ingestion of PFAS is considered the major human exposure pathway. The major types of human exposure sources for PFAS include:

- Drinking contaminated water.
- Ingesting food contaminated with PFAS, such as certain types of fish and shellfish.
- Until recently, eating food packaged in materials containing PFAS (e.g., popcorn bags, fast food containers, and pizza boxes). Using PFAS compounds has been largely phased out of food packaging materials.
- Hand-to-mouth transfer from surfaces treated with PFAS-containing stain protectants, such as carpets, which is thought to be most significant for infants and toddlers.

- Workers in industries or activities that manufacture, manipulate or use products containing PFAS may be exposed to higher levels than the general population.

What are other low level exposure sources?

Individuals can also be exposed by breathing air that contains dust contaminated with PFAS (from soil, carpets, upholstery, clothing, etc.), or from certain fabric sprays containing this substance.

Dermal exposure is a minor exposure pathway. Dermal absorption is slow and does not result in significant absorption.

What are the potential PFAS exposure risks to fetuses and children?

Recent research evaluating possible health effects to fetuses from PFAS exposures have shown that developing fetuses can be exposed to PFAS when umbilical cord blood from their mothers crosses the placenta during pregnancy. It is important to note that different PFAS have varying levels of permeability to the placental barrier.

Newborns can be exposed to PFAS through breast milk. The level of neonatal exposure depends on the duration of breastfeeding. Older children may be exposed to PFAS through food and water, similar to adults. In addition, young children have a higher risk of exposure to PFAS from carpet cleaners and similar products, largely due to time spent lying and crawling on floors in their early years.

How long do PFAS remain in the body?

PFAS with long carbon chains have estimated half-lives ranging from 2-9 years such as:

- PFOA 2 to 4 years
- PFOS 5 to 6 years
- PFHxS 8 to 9 years

What are exposure limits for PFAS in drinking water?

The Environmental Protection Agency (EPA) has published a Lifetime Health Advisory (LTHA) recommending that the concentration of PFOA and PFOS in drinking water, either individually or combined, should not be greater than 70 parts per trillion (0.07 parts per billion). The LTHA concentrations do not represent definitive cut-offs between safe or unsafe conditions, but rather provide a margin of protection for individuals throughout their life from possible adverse health effects. EPA health advisories are non-regulatory recommendations and are not enforceable.

What are PFAS levels in the U.S. population?

Most people in the United States and in other industrialized countries have measurable amounts of PFAS in their blood.

The National Health and Nutrition Examination Survey (NHANES) is a program conducted by the Centers for Disease Control and Prevention (CDC) to assess the health and nutritional status of adults and children in the United States. NHANES (2011–2012) measured the concentration of PFAS in the blood of a representative sample of the U.S. population (12 years of age and older). The average blood levels found were as follows:

- PFOA: 2.1 parts per billion, with 95% of the general population at or below 5.7 parts per billion
- PFOS: 6.3 parts per billion, with 95% of the general population at or below 21.7 parts per billion
- PFHxS: 1.3 parts per billion, with 95% of the general population at or below 5.4 parts per billion

In the last decade, major manufacturers of PFOA and PFOS related products joined EPA in a global stewardship program to phase out production of these agents by 2015. Based on data collected from previous NHANES

cycle years, levels of PFOA and PFOS are generally decreasing in the blood of the general population as a result of this important initiative.

Health Studies

How can PFAS potentially affect human health?

Studies in humans and animals are inconsistent and inconclusive but suggest that certain PFAS may affect a variety of possible endpoints. Confirmatory research is needed.

Below are summaries of studies in animals and humans.

Animal Studies:

Adverse health effects have been demonstrated in animal studies, but these occurred at exposure levels higher than those found in most people. The main health effects observed were: enlargement and changes in the function of the liver, changes in hormone levels (e.g., reduced testosterone synthesis, potential to affect T_4 and TSH levels) and adverse developmental outcomes. Developmental and reproductive effects, including reduced birth weight, decreased gestational length, structural defects, delays in postnatal growth and development, increased neonatal mortality, and pregnancy loss have all been associated with prenatal rodent exposure to PFOS and PFOA.

Human Studies:

C8 Health Project

The C8 Health Project was a large epidemiological study conducted because drinking water in six water districts across two states near Parkersburg, West Virginia were contaminated by release of PFOA (also called C8) from the 1950s until 2002 (when the contamination was discovered). These releases migrated and contaminated the air, parts of the Ohio River, and ground water. The study included 69,030 persons ≥18 years of age. The C8 Science Panel analyzed study data and found probable links (as defined by litigation) between elevated PFOA blood levels and high cholesterol (hypercholesteremia), ulcerative colitis, thyroid function, testicular cancer, kidney cancer, preeclampsia, as well as elevated blood pressure during pregnancy. Residents in the area of these releases showed 500 percent higher PFOA-concentrations in blood compared to a representative U.S. population (i.e., NHANES).

Table 1: Overview of C8 and Other Human Studies

Cholesterol	Some epidemiological studies demonstrated statistically significant associations between serum PFOA and PFOS levels and total cholesterol in: - workers exposed to PFAS, and - residents of communities with high levels of PFOA in the drinking water compared to NHANES data that is representative of the U.S. population. Other studies have found no association between PFAS exposures and the total cholesterol levels.
Uric acid	Several studies have evaluated the possible association between serum PFOA and serum PFOS levels and uric acid. Significant associations were found between serum PFOA and uric acid levels at all evaluated exposure levels.
Liver effects	A number of human studies have used liver enzymes as biomarkers of possible liver effects. In occupational studies, no associations between liver enzymes and serum PFOA or PFOS levels were consistently found. A study of highly

	exposed residents demonstrated significant associations but the increase in liver enzymes was small and not considered to be biologically significant.
Cancer	The International Agency for Research on Cancer (IARC) has classified PFOA as possibly carcinogenic and EPA has concluded that both PFOA and PFOS are possibly carcinogenic to humans. Some studies have found increases in prostate, kidney, and testicular cancers in workers exposed to PFAS and people living near a PFOA facility. Findings from other studies report otherwise and most did not control for other potential factors including heavy smoking. Additional research is needed to clarify if there is an association.

Note: Additional studies have identified possible associations between ulcerative colitis, thyroid disease and pregnancy induced hypertension and higher exposure to PFAS.

What health screenings were used in the C8 study?

The C8 Medical Panel suggested health screening to evaluate the C8 study population that included blood tests for cholesterol, uric acid, thyroid hormones and liver function as well as other age or situationally appropriate screenings like blood pressure and urine protein measures. For individual patients exposed to PFAS who are not among the C8 study screening population, there are no official guidelines supporting health screening. However the tests listed above are well established in clinical medicine and may be a consideration to discuss with your patient based on the patient history, concerns and symptoms.

What are potential health effects from prenatal PFAS exposure to fetuses?

Multiple studies have reported an association between elevated maternal blood and cord blood concentrations of PFAS (primarily PFOS and PFOA) and decreased birth weight. Specifically, one meta-analysis suggests that each 1 ng/mL increase in prenatal PFOA levels is associated with up to 18.9 g reductions in birth weight (Johnson, 2014). Studies have also observed decreased birth weight with prenatal exposures to PFOS. The association between maternal PFAS level and decreased birth weight is not statistically significant across all studies. Further, the observed reduction in birth weight does not consistently equate with increased risk of a low birth weight (LBW) infant. Only one study revealed a statistically significant association between LBW risk and PFOS (Stein 2009); no studies have found a statistically significant association between LBW risk and PFOA.

Additional studies are needed to conclusively link the relationships between fetal PFAS exposure and health effects.

Patient Questions and Key Message Answers

As a clinician, you know careful listening and patient engagement is critical for ensuring quality patient care, especially when health concerns are raised. Perhaps the most difficult challenge in speaking with patients about their health concerns is addressing uncertainty. If your patient has concerns about an exposure to PFAS, you may face the challenge of helping your patient cope with the uncertainty of potential health effects from a PFAS exposure.

Based on feedback from clinicians and from individuals who have spoken to their health care provider about their PFAS exposure concerns, a set of patient questions have been identified. To assist you in speaking with your patients about their concerns, key messages and supporting facts needed to answer the anticipated patient questions are provided in the table below for your information and potential use.

Table 2: Patient Questions and Key Message

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
There are high levels of PFAS in my water. What should I do?	If the water you use is above the EPA health advisory level for PFOA and PFOS, you can reduce exposure by using an alternative water source for drinking, food preparation, cooking, brushing teeth or any activity that might result in ingestion of water.	Potential health effects are associated with exposure to PFAS. EPA has established a lifetime health advisory for PFOA and PFOS in drinking water. This advisory states that the concentration of PFOA and PFOS in drinking water, either individually or combined, should not be greater than 70 parts per trillion. There needs to be additional research to establish levels of health risk, but patients may want to reduce exposures below the EPA health advisory level to be on the safe side. A home water filtration system can reduce the contaminant levels in drinking water. Researchers are still clarifying how to best use home filtration for PFAS contamination. Installing a home filtration system or using a pitcher-type filter may reduce PFAS levels. However, these filters may not reduce PFAS enough to meet the EPA Lifetime Health Advisory (LTHA) level. Three factors determine how much PFAS are removed by filtration. These factors are the PFAS contaminant levels, the type of filter, and how well the filter is maintained. Manufacturers of the filtration system may be able to make recommendations to optimize removal of PFAS. This may include more sophisticated media cartridges or increasing the frequency of exchanging filter media. For bottled water questions (how it is treated and if it is safe) contact the CFSAN Information Center at

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
		1-888-SAFEFOOD (1-888-723-3366).
Could my health problems be caused by PFAS exposure? **(Based on the health problems the patient has, there are two possible responses to this question.)** **(a)** If the patient's health problem is in the list below, it may potentially be associated with PFAS exposure, based on limited evidence from human studies. The potential health effects include: - Thyroid function (potential to affect T4 and TSH levels) - High cholesterol - Ulcerative colitis - Testicular cancer - Kidney cancer - Pregnancy-induced hypertension - Elevated liver enzymes - High uric acid **(b)** If the patient's health problem is not in the bulleted list above, then there is no current evidence that it is related to PFAS exposure. (However, research is ongoing and not all health outcomes have been adequately studied.)	(a) Although the evidence is not conclusive, your health problem could potentially be associated with exposure to PFAS. However, health effects can be caused by many different factors, and there is no way to know if PFAS exposure has caused your health problem or made it worse. (b) Based on what we know at this time, there is no reason to think your health problem is associated with exposure to PFAS.	For supporting facts on the listed health effects in this question (a), see **"How can PFAS potentially affect human health."** The information on potential illnesses and health effects will be briefly reviewed for each of these illnesses or health effects. This information can be found in this fact sheet on page 3 and 4. If your patient presents with health concerns that might be associated with PFAS exposure, it is appropriate to discuss the patient's concerns and perform a thorough health and exposure history and also a physical exam relative to any symptoms reported.
Are there future health problems that might occur because of PFAS exposure?	We know PFAS can cause health issues but there is no conclusive evidence that predicts PFAS exposure will result in future health problems. We can watch for symptoms related to PFAS associated health problems and investigate any that you notice, especially those that reoccur.	Studies in humans and animals are inconsistent and inconclusive but suggest that certain PFAS can cause possible health effects. Additional research is needed to better understand health risks associated with PFAS exposure.

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
Should I get a blood test for PFAS?	If you are concerned and choose to have your blood tested, test results will tell you how much of each PFAS is in your blood but it is unclear what the results mean in terms of possible health effects. The blood test will not provide information to pinpoint a health problem nor will it provide information for treatment. The blood test results will not predict or rule-out the development of future health problems related to a PFAS exposure.	There currently is no established PFAS blood level at which a health effect is known nor is there a level that predicts health problems. Most people in the US will have measureable amounts of PFAS in their blood. There are no health-based screening levels for specific PFAS that clinicians can compare to concentrations measured in blood samples. As a result, interpretation of measured PFAS concentrations in individuals is limited in its use. The patient may be aware of blood and urine test for PFAS being taken at other locations. These tests are used by public health officials to investigate community-wide exposure in order to understand the kinds and amounts of PFAS exposures in a community and how those exposures compare to those in other populations. Serum PFAS measurements are most helpful when they are part of a carefully designed research study.
What do my PFAS blood tests results mean?	The blood test for PFAS can only tell us the levels of specific PFAS in your body at the time you were tested. The blood tests results cannot be interpreted and used in patient care. The blood test results cannot predict or rule-out the development of future problems related to a suspected exposure.	There is currently no established PFAS blood level at which a health effect is known nor is there a level that is clearly associated with past or future health problems. The individual patient's blood concentration of PFAS can only be compared to the average background blood concentration levels for different PFAS that are nationally identified through the representative sampling of the NHANES studies conducted by CDC. A patient's PFAS concentrations can only show the patient if his or her blood levels are within range of the national norms or if the

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
		individual's levels are high or low compared to the national background averages.
An adult patient asks: **"Should I be tested for any of the potential health effects associated with PFAS exposure (like cholesterol and uric acid levels, or liver and thyroid function, etc.)?"**	Let's look at your health history and past lab results and discuss what steps we may want to consider moving forward. One way we can address cholesterol is through your annual physical. For others PFAS associated conditions, we need to watch for symptoms and investigate any that you notice, especially those that reoccur. If any unusual symptoms occur, we will investigate those and treat as needed. Laboratory tests will not tell us if PFAS are the cause of any of your health symptoms or abnormal lab results, but conducting these routine health screenings and watching for any related symptoms do offer us a way to better understand your current health status.	Health effects associated with PFAS are not specific and can be caused by many other factors. There are no guidelines to support laboratory testing to monitor PFAS health concerns. However, if your patient is concerned about PFAS exposure, discussing routine cholesterol screening can reassure the patient that his or her PFAS exposure concerns are being addressed. Some of the other possible health effects can be screened for based on symptoms.
A parent asks: **"Should I have my child tested for any of the potential health effects associated with PFAS exposure (like cholesterol and uric acid levels, or liver, thyroid function, etc.)?"**	The American Academy of Pediatrics has endorsed cholesterol testing for children starting at 9 years of age. Following this guidance cholesterol level testing can be done for older children. If cholesterol level measures are outside the normal range, we can discuss options for bringing cholesterol levels within the normal range for your child. For very young children, keeping well child visits is the best plan of action to monitor your child's	According to NHLBI guidelines endorsed by the American Academy of Pediatrics, all children should be screened for cholesterol levels between ages 9 and 11 years, and again between ages 17 and 21 years, even those who are not at an increased risk of high cholesterol and heart disease. Health effects associated with PFAS are not specific and can be caused by many other factors. There are no guidelines to support use of laboratory testing to monitor PFAS health concerns.

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
	health and watch for symptoms of illness. We can discuss any symptoms you notice, especially those that reoccur. If any unusual symptoms occur, we will investigate those and treat as needed. Laboratory tests will not tell us if PFAS are the cause of any of your child's health symptoms and are not recommended. Conducting routine well child visits and watching for any related symptoms do offer us a way to better understand your child's current health status.	However, if your patient presents with health concerns that have been associated with PFAS exposures, discussing recommended cholesterol screening, can reassure the patient's parents that their concerns are being addressed. Some of the other possible health effects can be screened for based on symptoms.
How will exposure to PFAS affect my pregnancy?	Exposure to PFAS before pregnancy has been associated with pregnancy-induced hypertension and pre-eclampsia. We will monitor your blood pressure closely, as we do for all pregnant women; however, there is no need for additional blood pressure measurements as a result of your exposure.	Health effects associated with PFAS are not specific and can be caused by many other factors. Pregnancy induced hypertension occurs in many pregnancies and the specific etiology is often unknown.
Is it safe for me to breastfeed my baby?	Breastfeeding is associated with numerous health benefits for infants and mothers. At this time, it is recommended that you as a nursing mother continue to breastfeed your baby. The science on the health effects of PFAS for mothers and babies is evolving. However, given the scientific understanding at this time, the benefits of breastfeeding your baby outweighs those of not breastfeeding.	Extensive research has documented the broad and compelling advantages of breastfeeding for infants, mothers, families, and society. Some of the many benefits include immunologic advantages, lower obesity rates, and greater cognitive development for the infant as well as a variety of health advantages for the lactating mother. Even though a number of environmental pollutants readily pass to the infant through human milk, the advantages of

Questions Patients May Ask	Key Patient Messages	Key Message Supporting Facts
		breastfeeding continue to greatly outweigh the potential risks in nearly every circumstance.
How will exposure to PFAS affect my child's immunizations?	Although few studies have reported that PFOS and PFOA might slightly lower the immune response to some immunizations, these studies have not suggested a need to re-evaluate the normal immunization schedule.	A study with 656 children has reported that elevated levels of PFOA and PFOS in serum are associated with reduced humoral immune response to some routine childhood immunizations (rubella, tetanus and diphtheria) among children aged five to seven years.
Will I need to get my child vaccinated again?	There is no recommendation for repeating any vaccinations.	Studies have not suggested a need to re-evaluate the normal immunization schedule nor the use of an immunize booster for impacted children.
I have been very anxious about health risks from PFAS exposure. How can I deal with this uncertainty?	It is normal to be anxious about uncertain risks. I am here to listen to your questions and will do my best to provide honest answers. First let's identify ways to reduce ongoing exposures to PFAS so that overtime we can lower your health risks. Let's set up appointment for (X date) and we can discuss any new questions you have and check to see if there are any changes in how you feel. In the meantime, I have more information that may answer questions that you may have later about PFAS.	Listen sympathetically and explore the concerns of the patient Check for serious stress issues such as ongoing depression and treat accordingly. Review resources/references at the end of this fact sheet.

Resources

Below is a list of resources that can be helpful to clinicians. These include the Pediatric Environmental Health Specialty Units (PEHSU). The PEHSU are a national network of experts available to provide consultation and education to clinicians and communities wishing to learn more about PFAS and other hazardous substances. These units are staffed by clinicians with environmental health expertise in pediatrics, reproductive health, occupational and environmental medicine, medical toxicology, and other related areas of medicine.

Resource	Link
ATSDR: PFAS Overview Toxic Substance Portal ToxFAQs	 http://www.atsdr.cdc.gov/pfc/index.html http://www.atsdr.cdc.gov/substances/index.asp http://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=1116&tid=237
CDC: PFCs	http://www.cdc.gov/biomonitoring/PFCs_FactSheet.html
C8 Science Panel C8 Medical Panel	http://www.c8sciencepanel.org/prob_link.html http://www.c8sciencepanel.org/publications.html http://www.c-8medicalmonitoringprogram.com/ http://www.c-8medicalmonitoringprogram.com/docs/med_panel_education_doc.pdf
EPA: PFAS	https://www.epa.gov/chemical-research/research-perfluorooctanoic-acid-pfoa-and-other-perfluorinated-chemicals-pfcs
IARC	http://www.iarc.fr/
NIEHS: PFAS	https://www.niehs.nih.gov/health/materials/perflourinated_chemicals_508.pdf
NHLBI Lipid Screening in Children & Adolescents	https://www.nhlbi.nih.gov/health-pro/guidelines/current/cardiovascular-health-pediatric-guidelines/full-report-chapter-9
PEHSU	http://www.pehsu.net/
Uncertainty and Stress in the Clinical Setting	Helping Patients and Clinicians Manage Uncertainty During Clinical Care - https://publichealth.wustl.edu/helping-patients-and-clinicians-manage-uncertainty-during-clinical-care/ Navigating the Unknown: Shared Decision-Making in the Face of Uncertainty J Gen Intern Med. 2015 May; 30(5): 675–678. http://tinyurl.com/zrd587f Patient Health Questionnaire to determine if patient is suffering from depression. http://tinyurl.com/gv6h3wk Uncertainty Toolbox: Principles in the Approach to Uncertainty in the Clinical Encounter-J Gen Intern Med. 2015 May; 30(5): 675–678. http://tinyurl.com/gtlf2mk

Per- and Polyfluoroalkyl Substances (PFAS)
Frequently Asked Questions

What are PFAS?

PFAS are a large group of man-made chemicals that have been used since the 1950s. Use of some of these chemicals has decreased in the United States over the last 10 years. People can still be exposed to PFAS because they are still present in the environment. PFAS do not break down easily in the environment. They also build up in the bodies of exposed humans and animals. Over the last decade, interest in PFAS has grown.

How can I be exposed to PFAS?

ATSDR and our state health partners are studying exposure to PFAS at a number of sites. PFAS are found near areas where they are manufactured or used. Listed below are places where they can be found.

- Public water systems and drinking water wells, soil, and outdoor air near industrial areas with frequent PFAS use
- Indoor air in spaces that contain carpets, textiles, and other consumer products treated with PFAS to resist stains
- Surface water (lakes, ponds, etc.) and run-off from areas where aqueous (water-based) film-forming fire fighting foam (AFFF) was often used (like military or civilian airfields)
- Locally caught fish from contaminated bodies of water
- Food items sold in the marketplace

Consumer products can be source of exposures to PFAS. These products include

- Some grease-resistant paper, fast food wrappers, microwave popcorn bags, pizza boxes, and candy wrappers
- Nonstick cookware
- Stain resistant coatings used on carpets, upholstery, and other fabrics
- Water resistant clothing
- Cleaning products
- Personal care products (shampoo, dental floss) and cosmetics (nail polish, eye makeup)
- Paints, varnishes, and sealants

Recent efforts to stop using some PFAS in consumer products appear to have lowered exposure in the U.S. population. CDC surveys have shown that blood levels of PFAS have dropped over time. People who work with PFAS are more likely to be exposed than the general population. Workers may be exposed to PFAS by inhaling them, getting them on their skin, and swallowing them, but inhaling them is the most likely route for exposure.

How can I reduce my exposure to PFAS?

PFAS are found in people and animals all over the world. They are found in some food products and in the environment (air, water, soil, etc.). Completely stopping exposure to PFAS is unlikely. But, if you live near sources of PFAS contamination you can take steps to reduce your risk of exposure to PFAS:

- Some states have warnings about eating fish from bodies of water with high PFAS levels. Check with your state public health and environmental quality departments to learn the types and local sources of fish that are safe to eat.
- If your water contains PFAS, you can reduce exposure by using an alternative or treated water source for drinking, food preparation, cooking, brushing teeth, and any activity that might result in ingestion of water.
- It is safe to shower and bathe in PFAS-contaminated water. Neither routine showering or bathing are a significant source of exposure. Studies have shown very limited absorption of PFAS through the skin.

How can PFAS affect people's health?

Scientists are not sure about the health effects of human exposure to PFAS. Some studies in humans have shown that certain PFAS may affect the developing fetus and child, including possible changes in growth, learning, and behavior. In addition, they may decrease fertility and interfere with the body's natural hormones, increase cholesterol, affect the immune system, and even increase cancer risk.

- PFAS build up and stay in the human body and the amount goes down very slowly over time. So scientists and doctors are concerned about their effects on human health.
- Some studies show that animals given PFAS have changes in the liver, thyroid, pancreas, and hormone levels. Scientists are not sure what animal data means about human health. PFAS act differently in humans than they do in animals and may be harmful in different ways.

How can I learn more?

Contact 1-800-CDC-INFO for updated information on this topic.

Contact the Consumer Product Safety Commission at (800) 638-2772 if you have questions about the products you use in your home.

Visit the following websites for more information:

ATSDR Websites

http://www.atsdr.cdc.gov/pfc/index.html

Environmental Protection Agency

http://www2.epa.gov/chemical-research/perfluorinated-chemical-pfc-research

List of Common PFAS and Their Abbreviations

Compound	Abbreviation
Perfluorobutane sulfonate	PFBS
Perfluorohexane sulfonate	PFHxS
Perfluorooctane sulfonate	PFOS
Perfluoroheptanoic acid	PFHpA
Perfluorooctanoic acid	PFOA
Perfluorononanoic acid	PFNA
Perfluorodecanoic acid	PFDA
Perfluoroundecanoic acid	PFUnA
Perfluorododecanoic acid	PFDoA
Perfluorooctane sulfonamide	PFOSA
2-(N-Methyl-perfluorooctane sulfonamido) acetate	Me-PFOSA-AcOH
2-(N-Ethyl-perfluorooctane sulfonamido) acetate	Et-PFOSA-AcOH

Notes

[1]Use of trade names is for identification only and does not imply endorsement by the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry, the Public Health Service, or the U.S. Department of Health and Human Services

The family tree of perfluoroalkyl and polyfluoroalkyl substances (PFAS)

Names and abbreviations

6/9/17

This fact sheet tells you about chemical names within the family of perfluoroalkyl and polyfluoroalkyl substances (PFAS) and their basic chemical structure. It also spells out abbreviations for common PFAS.

PFAS are a family of man-made chemicals that contain carbon, fluorine, and other elements.

The family tree image below, Figure 1, shows some of the different families of PFAS. For simplicity, it does not include all PFAS subfamilies. Follow along – starting at the "fallen apple" of PFC and then continuing up the tree trunk into the branches.

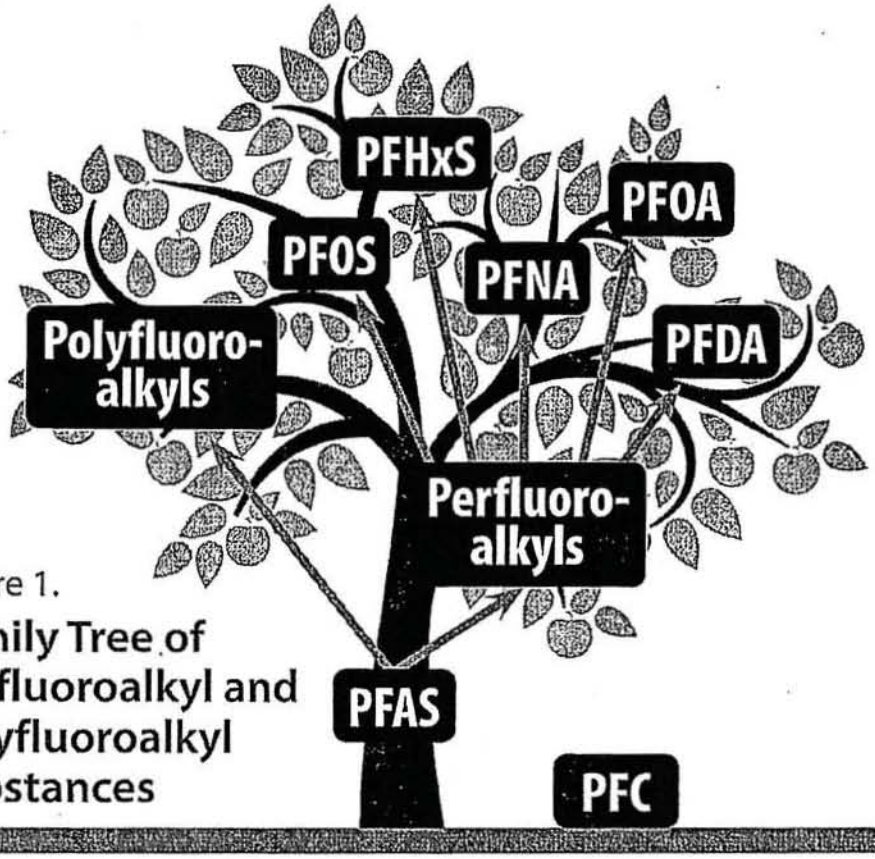

Figure 1.
Family Tree of perfluoroalkyl and polyfluoroalkyl Substances

PFC

In the past, scientists used the abbreviation PFC to stand for perfluorinated chemicals.

However, using the abbreviation PFC can be confusing because it is also an abbreviation for perfluorocarbons. Perfluorocarbons are an entirely different family of chemicals, also known as greenhouse gases.

The term PFC has fallen off the family tree, but it remains in the diagram as a reminder of past use. You may still see informational materials using the term "PFC" instead of PFAS.

PFAS

Perfluoroalkyl substances and polyfluoroalkyl substances are called PFAS for short. The PFAS family includes hundreds of chemicals. The different structures of the PFAS molecules are the basis for different chemical properties and different chemical names. See Table 1 for abbreviations and chemical names.

Table 1. **Common PFAS: Abbreviations and Names**

Abbreviation	Chemical name
PFOS	Perfluorooctane sulfonic acid
PFOA (aka C8)	Perfluorooctanoic acid
PFNA	Perfluorononanoic acid
PFDA	Perfluorodecanoic acid
PFOSA (aka FOSA)	Perfluorooctane sulfonaminde
MeFOSAA (aka Me-PFOSA-AcOH)	2-(N-Methyl-perfluorooctane sulfonamido) acetic acid
Et-FOSAA (aka Et-PFOSA-AcOH)	2-(N-Ethyl-perfluorooctane sulfonamido acetic acid
PFHxS	Perfluorohexane sulfonic acid

PUBLIC HEALTH STATEMENT
Perfluoroalkyls

Division of Toxicology and Human Health Sciences **August 2015**

This Public Health Statement summarizes the Division of Toxicology and Human Health Science's findings on perfluoroalkyls, tells you about them, the effects of exposure, and describes what you can do to limit that exposure.

The U.S. Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are sites targeted for long-term federal clean-up activities. Perfluoroalkyls have not been reported at EPA NPL sites; however, it is unknown how many of the 1,699 current or former NPL sites have been evaluated for the presence of perfluoroalkyls. As more sites are evaluated, the sites at which perfluoroalkyls is found may increase. This information is important because these future sites may be sources of exposure, and exposure to perfluoroalkyls may be harmful.

If you are exposed to perfluoroalkyls, many factors determine whether you'll be harmed. These include how much you are exposed to (dose), how long you are exposed to it (duration), and how you are exposed (route of exposure). You must also consider the other chemicals you are exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

WHAT ARE PERFLUOROALKYLS?

Perfluoroalkyls are a family of human-made chemicals that do not occur naturally in the environment. Thirteen perfluoroalkyl compounds are discussed in this profile. The names of these perfluoroalkyls are as follows: perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorododecanoic acid (PFDoA), perfluorodecanoic acid (PFDeA), perfluorobutyric acid (PFBA), perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), perfluoroundecanoic acid (PFUA), perfluorohexane sulfonic acid (PFHxS), perfluorobutane sulfonic acid (PFBuS), perfluorooctane sulfonamide (PFOSA), 2-(N-methyl-perfluorooctane sulfonamide) acetic acid (Me-PFOSA-AcOH), and 2-(N-ethyl-perfluorooctane sulfonamide) acetic acid (Et-PFOSA-AcOH).

PUBLIC HEALTH STATEMENT
Perfluoroalkyls

Division of Toxicology and Human Health Sciences **August 2015**

Perfluoroalkyls are unique because they repel oil, grease, and water. They have been used in surface protection products such as carpet and clothing treatments and coatings for paper and cardboard packaging. Some perfluoroalkyls have also been used in fire-fighting foams.

WHERE ARE PERFLUOROALKYLS FOUND?

Perfluoroalkyls can be released into the air, water, and soil at places where they are produced or used. Perfluoroalkyls were made in large amounts in the United States. PFOA and PFOS are the two perfluoroalkyl compounds made in the largest amounts. Companies have stopped production or have begun changing manufacturing practices to reduce releases and the amounts of these chemicals in their products. Some facilities are replacing many of the perfluoroalkyls with other substances.

Perfluoroalkyls have been found in both air and dust; surface water and groundwater; and soil and sediment. The highest levels of perfluoroalkyls in the environment are typically found near facilities that have made or used these substances. However, they have also been found at remote locations such as the Arctic and the open ocean. They may be subject to long-range transport. Perfluoroalkyls are very stable compounds and are resistant to being broken down in the environment. Perfluoroalkyls in the air are expected to settle to the ground within days to weeks. Perfluoroalkyls may be carried through soil by groundwater and flooding and become airborne during windy conditions.

HOW MIGHT I BE EXPOSED TO PERFLUOROALKYLS?

Exposure to perfluoroalkyl compounds is widespread. PFOA, PFOS, PFNA, and PFHxS were detected in 95–100% of samples of people's blood in 1999–2000 and 2003–2004. More recent monitoring data still show widespread exposure; however, the levels of these substances in people's blood appear to be declining. You may be exposed to perfluoroalkyls from the air, indoor dust, food, water, and various consumer products. Food is expected to be the primary source of exposure to perfluoroalkyls such as PFOA and PFOS for most people. Some communities near facilities where PFOA and PFOS were previously manufactured had high levels of these substances in drinking water supplies, and this is the primary route of exposure for these populations. Limited information has been located regarding

pathways of human exposure to most of the other perfluoroalkyls discussed in this toxicological profile. Human breast milk may contribute to the exposure of infants to perfluoroalkyls since these substances have been detected in human breast milk. You may also be exposed to perfluoroalkyls from treated carpets and upholstery; this is especially true for children. The greatest source of exposure to PFOA and PFOS for toddlers and children is hand-to-mouth activities from treated carpets.

People who work where perfluoroalkyls are made or used are exposed to higher levels of these substances than the general population. Levels of PFOS and PFOA measured in the blood of some people who have worked at these locations were higher than levels in people from the same communities who did not work at these locations. Workplace exposure also occurred for people with jobs that required frequent handling or use of perfluoroalkyl-treated substances, such as carpet installers. At sites where aqueous film-forming foam (AFFF) that contained perfluoroalkyl substances was used in firefighting, workers could be exposed to these substances and possibly transport them home from contaminated clothing.

HOW CAN PERFLUOROALKYLS ENTER AND LEAVE MY BODY?

Perfluoroalkyls can enter your body if you breathe air, eat food, or drink water containing them. We do not know how much will enter your body through your lungs or your digestive tract. If your skin comes into contact with dusts or aerosols of perfluoroalkyl or with liquids containing perfluoroalkyls, it is possible that a small amount may enter the body through your skin.

Once in your body, perfluoroalkyls tend to remain unchanged for long periods of time. The most commonly used perfluoroalkyls (PFOA and PFOS) stay in the body for many years. It takes approximately 4 years for the level in the body to go down by half, even if no more is taken in. It appears that, in general, the shorter the carbon-chain length, the faster the perfluoroalkyl leaves the body. Perfluoroalkyls leave the body primarily in the urine.

PUBLIC HEALTH STATEMENT
Perfluoroalkyls

Division of Toxicology and Human Health Sciences **August 2015**

HOW PERFLUOROALKYLS CAN AFFECT YOUR HEALTH?

A large number of studies have examined the possible health effects of PFOA and PFOS in humans. The effect of inhalation exposure to PFOA and PFOS has been examined in workers exposed to high concentrations of these compounds. Studies have also examined a large community exposed to high levels of PFOA in the drinking water and compared this community to the general population; ingestion was the primary route of exposure for these two groups. Most human studies have looked for a relationship between levels of perfluoroalkyls in the blood and a health effect. It is difficult to interpret the results of these studies because they are not consistent; some studies have found associations, but others looking at the same health effect have not found these associations. Even though some studies have found significant associations between serum perfluoroalkyl levels and adverse health effects, it does not mean that perfluoroalkyls caused these effects. The effects may have been due to other factors that were not considered by the researchers. The available studies suggest that increases in blood cholesterol levels are associated with higher PFOA or PFOS blood levels in workers inhaling PFOA and/or PFOS as well as in people ingesting these compounds. There are data to suggest an association between serum PFOA and PFOS levels and increased uric acid levels, which may be associated with an increased risk for high blood pressure. There is also some evidence that PFOA and PFOS exposure may cause liver damage.

Humans and rodents react differently to PFOA and PFOS, and not all of the effects observed in rats and mice may occur in humans. The liver appears to be the most sensitive target in animals ingesting perfluoroalkyls. The effects include increases in liver weight, changes in the liver cells, and changes in blood cholesterol and triglyceride levels. Studies in mice also found that the immune system is a sensitive target of PFOA and PFOS; effects include decreases in the size of the spleen and thymus and impaired immune function.

A short exposure of rats to very high levels of PFOA in the air caused irritation of the eyes and nose. Damage to the liver and weight loss were observed in rats exposed to lower levels of PFOA in the air.

Short-term application of large amounts of PFOA to the skin of animals has caused skin irritation and changes in the liver. These liver effects indicate that PFOA can be absorbed into the body through the skin and affect other parts of the body.

There is limited information on whether perfluoroalkyls can cause cancer in humans. Some increases in prostate, kidney, and testicular cancers have been found in workers or in community members living near a PFOA facility. These results should be interpreted cautiously because the effects were not consistently found and most studies did not control for other potential factors such as smoking. Feeding PFOA and PFOS to rats caused them to develop tumors. Some scientists believe that, based on the way this happens in rats and the differences between rats and humans, humans would not be expected to get cancer. Others believe that it is possible for perfluoroalkyls to cause cancer in humans, and the studies in rats should not be dismissed. More research is needed to clarify this issue. The International Agency for Research on Cancer and the Department of Health and Human Services have not yet evaluated the carcinogenicity of perfluoroalkyls. The EPA has begun an evaluation.

HOW CAN PERFLUOROALKYLS AFFECT CHILDREN?

This section discusses potential health effects of perfluoroalkyls exposure in humans from when they're first conceived to 18 years of age, and how you might protect against such effects.

No associations between serum PFOA and birth defects were observed in children of mothers living in an area with high PFOA levels in the water. Some studies of the general population and people living near a PFOA manufacturing facility have found that higher levels of serum PFOA or PFOS are associated with lower infant birth weights. However, the decrease in birth weight is small and may not affect the infant's health. A study in children exposed to high levels of PFOA in drinking water found increases in blood cholesterol, which was similar to the findings in adults.

Birth defects were seen in mice born to females that ingested relatively high amounts of PFOS during pregnancy. The blood PFOS levels associated with these effects were at least 10 times higher than the highest PFOS levels measured in workers. Oral exposure to PFOA and PFOS has resulted in early death

and delayed development of mouse and rat pups, but this did not occur in animals exposed to PFBA or PFHxS. Alterations in motor activity have also been observed in mouse pups exposed to PFOA, PFOS, or PFHxS, but not PFDeA. Scientists believe that some of the effects observed in rats and mice exposed to PFOA or PFOS may not be relevant to humans.

HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO PERFLUOROALKYLS?

If your doctor finds that you have been exposed to significant amounts of perfluoroalkyls, ask whether your children might also be exposed. Your doctor might need to ask your state health department to investigate.

In the past, some perfluoroalkyls such as PFOA and PFOS were used in the manufacture of many consumer products, and low levels of these substances were detected in things such as treated carpeting, treated apparel, and paper food packaging. Companies are no longer using PFOA in the manufacture of non-stick coatings or PFOS in the manufacture of stain resistant carpet treatments; however, older products and imported materials may still contain these substances. Families may choose to use products that do not contain pre-treated stain repellent products or grease resistant food packaging. Families that have been told that their tap or well water contains high levels of perfluoroalkyls may choose to drink or cook with bottled water or to install activated carbon water filters in their drinking water system. Consuming bottled water and the use of activated carbon water filters have been shown to lead to lower PFOA levels in the blood over time by decreasing exposure to perfluoroalkyl compounds.

ARE THERE MEDICAL TESTS TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO PERFLUOROALKYLS?

Perfluoroalkyl compounds can be measured in blood, but this is not a routine test that can be performed in a doctor's office. You should, however, see a physician if you believe that you have been exposed to high levels of perfluoroalkyls. Perfluoroalkyls have been measured in blood samples in 2009–2010 from a representative sample of the U.S. general population; the geometric mean serum PFOA and PFOS concentrations were 3.07 and 9.32 µg/L, respectively. Elevated serum PFOA levels were reported in

Mid-Ohio Valley residents who had environmental exposure to PFOA from drinking water contaminated by a nearby industrial facility. The range of median serum PFOA levels across several communities was 12.1–224.1 ng/mL and the mean serum PFOA concentration across all of the communities was 83.6 µg/L in 2005. Higher serum perfluoroalkyl concentrations have been reported in fluorochemical product workers. Mean serum PFOA and PFOS levels for at one facility were 1,780 and 1,320 µg/L, respectively. Workers at another facility had serum PFOA levels of 1,000 µg/L.

WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA). Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH).

Regulations and recommendations can be expressed as "not-to-exceed" levels; that is, levels of a toxic substance in air, water, soil, or food that do not exceed a critical value usually based on levels that affect animals; levels are then adjusted to help protect humans. Sometimes these not-to-exceed levels differ among federal organizations. Different organizations use different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or emphasize some factors over others, depending on their mission.

Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that issued the regulation or recommendation.

PUBLIC HEALTH STATEMENT
Perfluoroalkyls

Division of Toxicology and Human Health Sciences **August 2015**

The EPA has recommended provisional drinking water health advisories of 0.4 µg/L for PFOA and 0.2 µg/L for PFOS. OSHA has not set any legal limits for perfluoroalkyl compounds in air. NIOSH has not set any recommended limits for perfluoroalkyl compounds in air.

WHERE CAN I GET MORE INFORMATION?

If you have any questions or concerns, please contact your community or state health or environmental quality department, or contact ATSDR at the address and phone number below. ATSDR can also provide publically available information regarding medical specialists with expertise and experience recognizing, evaluating, treating, and managing patients exposed to hazardous substances.

- Call the toll-free information and technical assistance number at 1-800-CDCINFO (1-800-232-4636) or
- Write to:

  Agency for Toxic Substances and Disease Registry
  Division of Toxicology and Human Health Sciences
  1600 Clifton Road NE
  Mailstop F-57
  Atlanta, GA 30329-4027

Toxicological profiles and other information are available on ATSDR's web site: http://www.atsdr.cdc.gov.

EXHIBIT D

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

REGION III
1650 ARCH STREET
PHILADELPHIA, PA 19103

REGION V
77 WEST JACKSON BOULEVARD
CHICAGO, IL 60604

IN THE MATTER OF:

E. I. du Pont de Nemours
and Company, Incorporated

Washington Works Facility
Route 892
Washington, WV 26181

ORDER ON CONSENT

Proceeding under section 1431(a)(1)
of the Safe Drinking Water Act,
42 U.S.C. § 300i(a)(1)

Docket Nos. SDWA-03-2002-0019,
SDWA-05-2002-0008

I. STATUTORY AUTHORITY

1. This Order on Consent ("Order") is issued pursuant to the authority vested in the Administrator of the United States Environmental Protection Agency ("EPA") by Section 1431(a)(1) of the Safe Drinking Water Act ("SDWA"), 42 U.S.C. § 300i(a)(1).

2. The authority to issue this Order was delegated to the Regional Administrators by Delegation No. 9-17, dated May 11, 1994.

3. Under the SDWA, Congress has delegated to EPA broad authority for the protection of public water supplies and drinking water sources.

II. DEFINITIONS

4. The term "Underground Source of Drinking Water" ("USDW") means an "aquifer" or its portion which supplies a public water system ("PWS") or which contains a sufficient quantity of ground water to supply a PWS and which currently supplies drinking water for human consumption, or contains fewer than 10,000 milligrams per liter (mg/l) total dissolved solids, and is not an exempted aquifer. See 40 C.F.R. § 144.3.

III. FINDINGS OF FACT AND CONCLUSIONS OF LAW

5. E. I. du Pont de Nemours and Company, Incorporated ("DuPont"), is a corporation and is therefore a "person" within the meaning of Section 1401(12) of the SDWA, 42 U.S.C. § 300f(12).

6. DuPont owns and operates a manufacturing facility, known as the Washington Works ("Facility"), located in Washington, Wood County, West Virginia.

7. Ammonium perfluorooctanoate, CAS Number 3825-26-1 (hereafter "C-8"), is a perfluorinated surfactant that DuPont has used in its fluoropolymer-related manufacturing processes at the Facility since the early 1950s.

8. Residues containing C-8 generated by the Facility are or have been released to the air, discharged to the Ohio River, disposed of at the Facility, Dry Run and Letart landfills in West Virginia ("disposal sites") and otherwise shipped off-site for destruction and/or disposal including into unlined landfills.

9. Studies performed by DuPont and Minnesota Manufacturing and Mining Corporation (a manufacturer of C-8) ("3M") have determined that C-8 in sufficient doses, i.e., considering both amount and duration of exposure, is toxic to animals through ingestion, inhalation and dermal contact. Studies have also found that C-8 is persistent in humans and the environment. EPA is conducting a preliminary hazard assessment of C-8 under the Toxic Substances Control Act ("TSCA").

10. Recently, C-8 has been detected in the underground source of drinking water used to supply the following locations, at the following levels :

Lubeck, WV, PSD:	0.8 micrograms/liter (ug/l) (1st quarter 2000)
Facility Production Wells:	1.99 ug/l (Well 336, 1998) 1.45 ug/l (Well 332, 1999)
Facility Drinking Water Taps:	0.213 ug/l (Building 5, 1999) 0.496 ug/l (Building 293, 1999) 0.306 ug/l (Building 231, 1999) 0.135 ug/l (Building 368, 2000)
Little Hocking, OH, PWS:	1.840 ug/l (Well 1, 12/01) 8.780 ug/l (Well 2, 12/01) 0.855 ug/l (Well 3, 12/01) 7.690 ug/l (Well 5, 12/01) 1.720 ug/l (Well 1, 1/02) 2.970 ug/l (Well 2, 1/02) 0.744 ug/l (Well 3, 1/02)

6.220 ug/l (Well 5, 1/02)

11. Although recent sampling shows lower levels, groundwater data from Letart landfill has shown C-8 concentrations as high as:

On-site monitoring well MW1	24,000 ug/l (1998)
On-site monitoring well MW-2A	990 ug/l (1998)

Private wells near the Letart landfill when tested for C-8 in 2001 showed levels of 0.42 ug/l, 0.296 ug/l, and 0.085 ug/l; tap samples from the only well in the area of Letart landfill which is currently known to supply drinking water showed levels of 0.031 ug/l, 0.046 ug/l and 0.053 ug/l (duplicate sample).

12. The C-8 discharged by the Facility is a contaminant present in or is likely to enter a PWS or an USDW through the migration from air emissions, surface water discharges or from unlined landfills, and may present an imminent and substantial endangerment at levels exceeding 14 ug/l in water used for human consumption based on "A Hazard Narrative for Perfluorooctanoate (PFOA)" a final report prepared by ENVIRON International Corporation, January 24, 2002 (hereafter "ENVIRON report") for DuPont.

13. DuPont, the West Virginia Department of Environmental Protection ("WVDEP"), and the West Virginia Department of Health and Human Resources ("WVDHHR") have entered in an agreement on consent ("WV Order"), dated November 15, 2001, attached hereto, which provides for, *inter alia*, a toxicological and human health risk assessment of C-8 to be conducted under the supervision of a C-8 Assessment of Toxicity ("CAT") Team pursuant to the WV Order, as well as ground and surface water monitoring and plume identification. DuPont, in a letter dated February 11, 2002, attached hereto, also agreed to perform sampling of private and public ground water wells within a 1-mile radius of the Little Hocking, Ohio PWS well field, following the protocol established in the WV Order. (Hereafter, the sampling required by the WV Order and the additional sampling agreed to by DuPont will be referred to as "sampling in WV/OH.")

14. C-8 is currently not a contaminant for which a national primary drinking water regulation has been established pursuant to the SDWA, however, for the purpose of this Order, DuPont and EPA agree to use the level of 14 ug/l C-8, as set forth in the ENVIRON report, as the temporary threshold level for provision of alternate water as required by paragraph 17 of this Order.

15. DuPont and EPA further agree to use the screening level for C-8 to be established by the WV Order as the threshold level for the provision of alternate water required by paragraphs 18 through 23 of this Order, in lieu of the level set forth in paragraphs 12 and 14 of this Order.

16. EPA has consulted with the WVDEP, WVDHHR, the Ohio Environmental Protection Agency ("OEPA") and the Ohio Department of Health ("ODH") to confirm that the information on which this Order is based is correct and to ascertain the action that the state and local authorities are or will be taking. WVDHHR, OEPA, and ODH have requested that EPA take this action. EPA has concluded that all requisite conditions have been satisfied for EPA action under Section 1431(a)(1) of the SDWA, 42 U.S.C. § 300i(a)(1).

IV. ORDER ON CONSENT

Pursuant to the authority issued to the EPA Administrator by Section 1431(a)(1) of the SDWA, 42 U.S.C. § 300i(a)(1), and delegated to the Regional Administrators, DuPont is ORDERED and hereby consents to the following:

Provision of Alternate Drinking Water

17. As soon as practicable, but not later than fifteen (15) days following receipt of validated sampling results performed in accordance with the WV Order for sampling in WV/ OH, DuPont shall provide a temporary alternate drinking water supply for users of any private drinking water well and PWS in West Virginia or Ohio where such results show the level of C-8 exceeds 14 ug/L. A "temporary alternate drinking water supply" shall mean connection to a PWS, connection to a new water well, adequately treated water or water from some other source, including bottled water or bulk water from a tank truck that meets the water quality requirements of 40 C.F.R. § 141 and has a level of C-8 no greater than 14 ug/l; is in sufficient quantity for all reasonable domestic uses including drinking and cooking; and is provided in a manner convenient to the users. DuPont shall continue to provide this temporary alternate drinking water supply until DuPont fully implements the Alternate Drinking Water Plan pursuant to paragraphs 18 through 23 of this Order. DuPont shall be responsible for all operation and maintenance costs of the alternate drinking water supply.

18. As soon as practicable but not later than thirty (30) days after a determination by the Groundwater Investigation Steering Team ("GIST") established pursuant to the WV Order that a private drinking water well or PWS in West Virginia or Ohio contains C-8 at levels greater than the screening level developed pursuant to the WV Order, DuPont shall submit to EPA for approval, and to WVDHHR, WVDEP and OEPA, as appropriate, for review, an Alternate Drinking Water Plan which identifies all actions necessary to enable DuPont to fully comply with the requirements of paragraph19 through 23 of this Order. The Alternate Drinking Water Plan shall include a schedule of implementation for such actions.

19. The Alternate Drinking Water Plan shall provide that:

a. DuPont shall assure the provision of an alternate supply of drinking water to all users of any PWS and any private drinking water well in West Virginia or Ohio, identified pursuant to sampling in WV/OH, where, and for so long as, the level of C-8 exceeds the screening level developed pursuant to the WV Order.

b. Such levels shall be determined by monitoring performed using a test procedure established by the GIST pursuant to the WV Order. Such alternate supply of drinking water is to be provided at no cost to the users of such PWS or private drinking water wells, except for usual service fees incurred by users of a PWS.

c. DuPont will provide notice to all users of such PWS and private drinking water wells of the availability of the alternate supply of drinking water.

d. An "alternate supply of drinking water" shall mean connection to a PWS, connection to new water well, adequately treated water or water from some other source, acceptable to EPA, that meets the water quality requirements of 40 C.F.R. § 141 and has a level of C-8 no greater than the screening level established pursuant to the WV Order; is in sufficient quantity for all reasonable domestic uses including drinking and cooking; and is provided in a manner convenient to the users. DuPont shall be responsible for all operation and maintenance costs of the alternate supply of drinking water for the duration of operation pursuant to this Order, unless the alternate supply of drinking water is provided by connection to a PWS.

20. Following the initial submittal of the Alternate Drinking Water Plan by DuPont, if EPA, in consultation with WVDHHR, WVDEP, and OEPA, as appropriate, determines that modifications are necessary to DuPont's Alternate Drinking Water Plan, DuPont shall make such modifications as EPA may specify to satisfy the requirements of this Order and submit a revised Alternate Drinking Water Plan within forty-five (45) calendar days of notification by EPA.

21. Upon EPA's approval of the Alternate Drinking Water Plan (or revised Alternate Drinking Water Plan, as the case may be), DuPont shall implement, in accordance with the approved schedule, any and all actions necessary to comply with the requirements of paragraphs 18-20.

22. Within thirty (30) calendar days of EPA's approval of the Alternate Drinking Water Plan (or revised Alternate Drinking Water Plan, as the case may be), and quarterly thereafter, DuPont shall submit to EPA, WVDHHR, WVDEP, and OEPA, written reports summarizing all actions taken in accordance with this Order ("progress reports"). DuPont shall continue to submit progress reports until such time as EPA provides written notice that the reports are no longer necessary, or this Order is terminated.

All progress reports required by this paragraph shall contain the following certification, which shall be signed by a responsible corporate officer:

> I certify under penalty of law that this document and all attachments were prepared under my direction or supervision in accordance with a system designed to assure that qualified personnel properly gathered and evaluated the information submitted. Based on my inquiry of the person or persons who manage the system, or those persons directly responsible for gathering the information, the information submitted is, to the best of my knowledge and belief, true, accurate, and complete. I am aware that there are significant penalties for submitting false information, including the possibility of fines and imprisonment for knowing violations.

For purposes of this Order, a responsible corporate officer shall be (i) a president, secretary, treasurer, or vice-president of DuPont in charge of a principal business function, or any other person who performs similar policy- or decision-making functions for DuPont, or (ii) the manager of the Facility, if the Facility employs more than 250 persons or has gross annual sales or

expenditures exceeding $25 million (in second quarter 1980 dollars), if authority to sign documents has been delegated to the manager in accordance with corporate procedures.

28. All submittals, including reports, required under this Order shall be submitted to the following addressees:

As to EPA:

Roger Reinhart (3WP32)
U.S. EPA Region III
1650 Arch Street
Philadelphia, PA 19103-2029

Kelley Moore (WG-15J)
U.S. EPA Region V
77 West Jackson Boulevard
Chicago, IL 60604

As to WVDHHR:

Victor Wilford
Division of Environmental Engineering
Office of Environmental Health Services
Department of Health and Human Resources
815 Quarrier Street, Suite 418
Charleston, WV 25301

As to WVDEP:

David Watkins
Ground Water Protection Section
Division of Water Resources
West Virginia Department of Environmental Protection
1201 Greenbrier Street
Charleston WV 25301

As to OEPA:

Michael Baker
Division of Drinking & Ground Waters
Ohio Environmental Protection Agency
122 South Front Street
Columbus, OH 43215

V. GENERAL PROVISIONS

24. DuPont admits the jurisdictional allegations set forth herein and waives any defenses it might have as to jurisdiction and venue and agrees not to contest any of the findings of fact or conclusions of law herein in any action to enforce this Order. Except as to any proceeding brought by EPA to enforce this Order, in agreeing to this Order DuPont makes no admission of fact or law and reserves all rights and defenses available regarding liability or responsibility in any other legal proceeding related to the subject matter of this Order.

25. This Order shall apply to and be binding upon DuPont and its agents, successors, and assigns.

26. This Order may be modified only upon written consent of all parties.

27. Nothing in this Order shall be construed as prohibiting, altering or in any way eliminating the ability of EPA to seek any other remedies or sanctions available by virtue of DuPont's violations of this Order or of the statutes and regulations upon which this Order is based or for DuPont's violation of any applicable provision of law.

28. This Order shall not relieve DuPont of its obligation to comply with all applicable provisions of federal, state or local law, nor shall it be construed to be a ruling on, or determination of, any issue related to any federal, state or local permit.

29. Nothing in this Order is intended to nor shall be construed to operate in any way to resolve any criminal liability of DuPont. Compliance with this Order shall not be a defense to any actions subsequently commenced for any violation of federal laws and regulations administered by EPA, and it is the responsibility of DuPont to comply with such laws and regulations. EPA reserves the right to undertake action against any person, including DuPont, in response to any condition which EPA determines may present an imminent and substantial endangerment to the public health, public welfare or the environment.

30. The undersigned representative of DuPont certifies that he is fully authorized by DuPont to enter into the terms and conditions of this Order and to execute and legally bind that party to it.

31. Pursuant to Section 1431(b) of the SDWA, 42 U.S.C. § 300i(b), violation of any term of this Order, or failure or refusal to comply with this Order, may subject DuPont to a civil penalty of up to $15,000 per day per violation for each such day in which a violation occurs or failure to comply continues, as assessed by an appropriate United States District Court.

32. When DuPont knows or should have known, by the exercise of due diligence, of an event that might delay completion of any requirement of this Order, DuPont shall provide notice to EPA, in writing, within ten (10) business days after DuPont first knew, or in the exercise of due diligence, should have known, of such event. The notice shall describe in detail the basis for the delay, including whether it is a Force Majeure event, and describe the length of, precise cause(s) of, and measures to be taken to prevent or minimize such delay. If EPA agrees that such event constitutes Force Majeure, EPA shall extend the time for performance of such requirement, in

writing, to compensate for the delay caused by the Force Majeure event. DuPont's failure to notify EPA in accordance with this paragraph shall render this paragraph void and of no effect. For purposes of this Order, Force Majeure is defined as an event arising from the causes beyond the control of DuPont, and any entity controlled by DuPont, which delays or prevents the performance of any obligation under this Order. Unanticipated or increased costs or expenses associated with the implementation of this Order and changed financial circumstances, failure to apply for a required permit or approval or to provide in a timely manner all information to obtain a permit or approval or to obtain or approve contracts, shall not, in any event, constitute Force Majeure events. DuPont reserves what ever rights it may have to dispute EPA's determination that a particular event does not constitute Force Majeure in any action to enforce this Order.

33. This Order shall be effective upon execution by all parties. This Order shall remain in effect until DuPont fulfills its obligations pursuant to paragraphs 17 through 28 herein, submits a written request to EPA to terminate this Order, and EPA approves such termination request.

34. This Consent Order may be executed in any number of counterpart originals, each of which shall be deemed to constitute an original agreement, and all of which shall constitute one agreement. The execution of one counterpart by any party shall have the same force and effect as if that party had signed all other counterparts.

35. All of the terms and conditions of this Order together comprise one agreement, and each of the terms and conditions is in consideration of all of the other terms and conditions. In the event that this Order, or one or more of its terms and conditions, is held invalid, or is not executed by all of the signatories in identical form, or is not approved in such identical form by the Regional Administrators, then the entire Order shall be null and void.

SO ORDERED:

_____ Date: _____
Donald S. Welsh
Regional Administrator
U.S. Environmental Protection Agency, Region III

_____ Date: 3-7-02
Thomas V. Skinner
Regional Administrator
U.S. Environmental Protection Agency, Region V

writing, to compensate for the delay caused by the Force Majeure event. DuPont's failure to notify EPA in accordance with this paragraph shall render this paragraph void and of no effect. For purposes of this Order, Force Majeure is defined as an event arising from the causes beyond the control of DuPont, and any entity controlled by DuPont, which delays or prevents the performance of any obligation under this Order. Unanticipated or increased costs or expenses associated with the implementation of this Order and changed financial circumstances, failure to apply for a required permit or approval or to provide in a timely manner all information to obtain a permit or approval or to obtain or approve contracts, shall not, in any event, constitute Force Majeure events. DuPont reserves what ever rights it may have to dispute EPA's determination that a particular event does not constitute Force Majeure in any action to enforce this Order.

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34. This Consent Order may be executed in any number of counterpart originals, each of which shall be deemed to constitute an original agreement, and all of which shall constitute one agreement. The execution of one counterpart by any party shall have the same force and effect as if that party had signed all other counterparts.

35. All of the terms and conditions of this Order together comprise one agreement, and each of the terms and conditions is in consideration of all of the other terms and conditions. In the event that this Order, or one or more of its terms and conditions, is held invalid, or is not executed by all of the signatories in identical form, or is not approved in such identical form by the Regional Administrators, then the entire Order shall be null and void.

SO ORDERED:

Donald S. Welsh — Date: MAR 1 2002

Donald S. Welsh
Regional Administrator
U.S. Environmental Protection Agency, Region III

Date: _____

Thomas V. Skinner
Regional Administrator
U.S. Environmental Protection Agency, Region V

AGREED TO:

Paul J. Bossert Jr Date: March 4, 2002

Paul Bossert
Plant Manager, Washington Works Facility
E. I. du Pont de Nemours and Company, Incorporated

CERTIFICATE OF SERVICE

I certify that on the date noted below, I delivered by hand two copies of this Order on Consent to the Regional Hearing Clerk, U.S. EPA Region III, and one copy to the addressees below as indicated:

VIA CERTIFIED MAIL
RETURN RECEIPT
REQUESTED

Bernard J. Reilly, Esq.
DuPont Legal, Room D 7082
1007 Market Street
Wilmington, DE 19898

Paul Bossert, Plant Manager
DuPont Washington Works Facility
Route 892
Washington, WV 26181

Dated: 3/11/02

Janet E. Sharke (3EC00)
Senior Asst. Regional Counsel
Office of Enforcement, Compliance,
and Environmental Justice
EPA, Region III
1650 Arch Street
Philadelphia, PA 19103-2029

EXHIBIT E

EPA
United States
Environmental Protection
Agency

DuPont Agrees to Lower Limit Of PFOA in Drinking Water

DuPont Washington Works
Parkersburg, West Virginia March 2009

A new legal agreement between U.S. Environmental Protection Agency and E.I. du Pont de Nemours & Co. will lower the limit of PFOA in drinking water for people who live near DuPont's Washington Works facility in Parkersburg, W.Va. Under terms of the agreement – known as a "consent order" – DuPont will offer water treatment or bottled water to people on public or private water systems when the level of a chemical called PFOA – also known as perfluorooctanoic acid or C-8 -- in water supplies reaches 0.40 parts per billion (ppb).

EPA's Office of Water issued a Provisional Health Advisory (PHA) in January for PFOA that establishes a reasonable, health-based value above which action should be taken to reduce exposure to PFOA in drinking water. The time frame for action is short-term – meaning weeks to months. This PHA prompted the new agreement to lower the allowable concentration of PFOA in drinking water from 0.50 ppb to 0.40 ppb in communities near the Washington Works facility. If affected homes cannot be connected to a public water system or a treatment system within 30 days, DuPont must offer bottled water. People who live in the PFOA-contaminated water areas affected by the new action level may reduce their exposure by not drinking the water until treatment systems are installed, or they are connected to a public water system.

EPA expects a limited number of residents will be affected by the new action level. Current data identifies about 14 private residences that may need a treatment system installed or connection to a public water system. If these residences cannot be connected to a public water system or treatment system within 14 days after the order is signed, then DuPont must offer alternative water. In addition, there may be a small number of private drinking water wells, installed after 2006, that need to be tested for PFOA. EPA is also assessing monitoring data and other information to determine if there are any previously untested areas that need to be surveyed.

Under a 2006 consent order, all public and private water systems that had PFOA levels above 0.50 ppb were offered alternative water or treatment, and DuPont is maintaining the alternative water or treatment at those systems today.

EPA issued the 2006 order in response to a study available at the time that evaluated about 340 residents living in the most heavily affected communities in Ohio near DuPont's Washington Works plant. That study showed residents had an average PFOA level of 298 to 369 ppb in their bloodstreams. More recent data gathered under a PFOA health study involving some 64,000 people, indicates the average PFOA levels in the bloodstreams of everyone in the affected communities to be about 28 ppb. These values are still much higher than the average 5 ppb level found in the national population.

If you want to know more

For general information about this order:
EPA hot line -- 866-575-8543

The 2009 consent order is available at:
www.epa.gov/region5/water/gwdw/dupont/index.htm

The 2006 consent order is available at:
www.epa.gov/regio03/enforcement/dupot_order.pdf

For information on the PFOA Stewardship Program and on the risk assessment activity see:
www.epa.gov/oppt/pfoa.

For reference materials and information on the C-8 Health Project, residents and physicians can refer to the documents available on these Web sites:
www.odh.ohio.gov/odhPrograms/eh/hlth_as/chemfs1.aspx and
www.c8healthproject.org

The 2006 order also relied on other studies that demonstrated various kinds of toxic effects on experimental animals. EPA believed the results were a concern for public health. EPA's Office of Water used new information, an advanced risk assessment technique and a different principal study from the one used in 2006 to establish the new national limit for PFOA of 0.4 ppb.

Boiling does not remove PFOA from water. That is done by treatment with granular activated carbon. Where this treatment has been installed in a water system, consumers are receiving water with either undetectable PFOA levels or very low concentrations of .003 ppb, well below the 0.40 ppb action level. All of the area's large public water systems, including Belpre, Little Hocking, Lubeck, Mason County, Tupper Plains/Chester and Pomeroy, are already treating water for PFOA.

As for private water systems – primarily water wells for private homes – since 2006 DuPont tested a large number of systems and either connected them to a public water system or installed treatment equipment on 50 systems that had PFOA levels of 0.50 ppb or above.

Order requires expanded survey

DuPont is required under the terms of the new consent order to survey geographical areas defined by EPA to determine if additional public or private water systems contain water that exceeds the new 0.40 ppb PFOA action level. These areas will be further evaluated and refined in consultation with Ohio and West Virginia officials as analytical data become available. Residents with newly drilled drinking water wells or wells not previously tested for PFOA may be eligible for sampling. They should contact EPA at 866-575-8543.

EPA does not certify labs for analysis of PFOA. Due to the complex nature of analytical procedures for this substance, EPA strongly encourages residents to allow DuPont to sample their water.

There is no consensus on how PFOA may affect people. However, concerns have been raised because of data from animal experiments and data from blood samples from people who live near the Washington Works facility. More studies are in progress but results may not be available for several more years. In the meantime, the new action level will reduce local exposure to PFOA from drinking water and reduce the possibility of adverse health effects.

Technical background: What is PFOA?

PFOA, or C-8, is a man-made chemical that resists heat, water, oil, grease and stains. It has been used in making common household and industrial items such as non-stick pots and pans, flame resistant and water-proof clothing, wire coatings, and chemical resistant tubing. PFOA can also be formed by the breakdown of other highly fluorinated chemicals used in stain-resistant carpets and fabrics, stain-resistant paints, fire fighting foam, and oil- and grease-resistant food cartons and wrappers. PFOA does not occur naturally in the environment and is highly persistent, with little or no degradation occurring in air, water or soil.

History of legal orders

This order supersedes the Emergency Administrative Order on Consent that was issued in 2006 under the authority of the Safe Drinking Water Act. Section 1431 of the Act requires a finding that "a contaminant is present in or is likely to enter a public water system or underground source of drinking water ... which may present an imminent and substantial endangerment to the health of persons." It does not require a conclusive finding that a contaminant has, or definitely will, cause harm.

The 2006 order contained a temporary threshold value of 0.50 ppb PFOA based on information available at the time about blood serum levels of the chemical in the local population and scientific studies. The 2006 order was a revision to a 2002 order, which established an action level of 150 ppb. The new order's revised action level of 0.40 ppb PFOA is based on new and different information than what was used to calculate the 2006 action level. The former 0.50 ppb site-specific action level for PFOA was a threshold for DuPont to provide treatment or alternate water to public and private water users in the vicinity of the facility, and the new action level of 0.40 ppb is an updated threshold. The Agency continues to conduct its risk assessment under the authority of the federal Toxic Substances Control Act. Until that process is complete there will not be a reference dose or an official maximum contaminant level for drinking water.

West Virginia and Ohio authorities have relied on EPA to review the existing 2006 order and have requested EPA's assistance with this matter.

PFOA levels in drinking water and human blood

The average human blood serum PFOA concentration in the United States is around 5 ppb. PFOA can be absorbed though swallowing, breathing and skin exposure. We do not know which exposure routes account for the background levels of PFOA in the general population.

Some residents in the vicinity of the Washington Works plant had median blood serum levels ranging from around 298 to 369 ppb PFOA. Data from a more recent study indicate the average has dropped to about 28 ppb. The high blood serum levels in residents are attributed to accumulation of PFOA in the bloodstream and its slow elimination from the human body. The half-life of PFOA in humans is approximately 3.8 years. Half-life is the time required to reduce the chemical to one-half the initial concentration. For example, with no additional PFOA input it will take approximately four years for blood values of 100 ppb to be reduced to 50 ppb. Ingestion of PFOA through drinking water is considered a major source of the chemical found in the blood of residents in the vicinity of the DuPont facility. Reducing exposure to PFOA in drinking water will reduce the accumulation of the chemical in residents.

The drinking water levels in nearby water systems have historically averaged from 1 to 20 ppb PFOA. For the six public water systems in the area and for private residences that accepted treatment, PFOA levels in drinking water have been significantly reduced to undetectable concentrations and most often less than .003 ppb. While much is known about the occurrence of PFOA in the vicinity of this DuPont facility, the substance is not a regulated drinking water contaminant. Therefore, public water systems are not required to monitor for PFOA.

Recent scientific information

EPA's Office of Water used new scientific information, an advanced risk assessment technique, and a different principal study from the one used in 2006 to develop the PHA. The principal study the Office of Water used involves peer-reviewed research in mice that looked at developmental effects of PFOA as the toxicological endpoint. The 2006 calculation used an earlier study of monkeys that looked at mortality rates as the toxicological endpoint. Additionally, since the 2006 order was issued new information and data has become available on PFOA half-lives in some animal species that the Office of Water used in its calculation. The Office of Water also applied a more advanced risk assessment technique that resulted in an update to some of the values used to calculate the new Provisional Health Advisory from those used in 2006. EPA continues to monitor emerging scientific information regarding PFOA in the interest of public health. EPA and DuPont agreed to revise the existing order.

Other legal actions

In 2001 DuPont, the West Virginia Department of Environmental Protection and the West Virginia Department of Health and Human Resources entered into a consent agreement. The legal order required a toxicological and human health risk assessment of C-8 be conducted under the supervision of a C-8 assessment of toxicity team. Ground-water and surface-water monitoring and plume identification in West Virginia and Ohio were conducted under the supervision of a ground-water investigation team.

An order issued in 2005 in response to a 2001 civil suit in Wood County, W.Va., (*Leach, et al v. E.I. DuPont de Nemours & Company)* required collection of blood serum and health data from about 70,000 people who live near DuPont's Washington Works facility. The collection of blood serum and health data is known as the Brookmar Study. It also provided for the installation of carbon filters for six public water service districts in West Virginia and Ohio. EPA was not a party to the civil action or the settlement. EPA will, however, evaluate data produced by these studies as well as other information generated as part of its ongoing review in the risk assessment process.

Major human health studies in progress

PFOA Health Project: In 2006 about 64,000 people completed questionnaires and had blood drawn. Brookmar Inc. has been hired to collect and compile the health data and blood serum levels. Then a three-member science panel will assess whether there are adverse health effects to humans associated with elevated levels of PFOA in the blood serum. Although the full results of the study are not expected until about 2011, the blood serum concentrations are available to the people who participated. Ohio Department of Health, the federal Agency for Toxic Substances and Disease Registry, Ohio Environmental Protection Agency, West Virginia Department of Environmental Protection and West Virginia Department of Health Human Resources wanted to have reference materials available to local physicians as their patients received data. Information is available at: www.odh.ohio.gov/odhPrograms/eh/hlth_as/chemfs1.aspx

Status of EPA risk assessment

Under the Toxic Substances Control Act, EPA is evaluating PFOA and related perfluorochemicals. A formal risk assessment process is under way. EPA's Science Advisory Board completed a review of a draft risk assessment of PFOA in 2006, and the board made recommendations for the further development of the assessment. A final risk assessment may not be completed for several years. Once a final risk assessment is completed, or if further information about the health effects of PFOA indicates it is necessary , the action level of 0.40 ppb PFOA established in the latest legal order with DuPont will be re-evaluated. The Agency is funding additional research regarding the toxicity of PFOA and other perfluorochemicals, as well as research to help identify where these chemicals are coming from and how people may be exposed to them.

Other EPA actions on PFOA

The EPA risk assessment activity on PFOA and its salts will take time to complete, but the Agency has already taken action to reduce the amount of PFOA getting into the environment. In 2006 EPA invited major companies in the industry to commit to a voluntary, global PFOA Stewardship Program. All invited companies, including DuPont, have committed to the goals of the program, which include reducing facility emissions and product content of PFOA and related chemicals by 95 percent by 2010 and working toward elimination of releases and product content of these chemicals by 2015. As of the end of 2006, DuPont had reduced annual air discharges of the chemical from the Washington Works facility by 99.1 percent and had reduced annual water discharges by 99.2 percent since 2000. DuPont and the other companies are submitting reports to EPA on their past activities and on their progress toward the Stewardship Program goals.

UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY

REGION III
1650 Arch Street
Philadelphia, PA 19103-2029

REGION V
77 West Jackson Boulevard
Chicago, IL 60604

IN THE MATTER OF:

E.I. du Pont de Nemours and Company
1007 Market Street
Wilmington, DE 19898

Respondent.

Washington Works Facility
Route 892 South
Washington, WV 26181

ORDER ON CONSENT

Proceeding under Section 1431(a)(1) of the Safe Drinking Water Act, 42 U.S.C. § 300i(a)(1)

Docket Nos. SDWA-03-2009-0127 DS
SDWA-05-2009-0001

I. STATUTORY AUTHORITY

1. This Order on Consent ("Order") is issued pursuant to the authority vested in the Administrator of the United States Environmental Protection Agency ("EPA") by Section 1431(a)(1) of the Safe Drinking Water Act ("SDWA" or "the Act"), 42 U.S.C. § 300i(a)(1), and supersedes the Order on Consent (Docket Nos. SDWA-03-2007-0039-DS and SDWA-05-2007-001) issued on November 20, 2006.

2. The authority to issue this Order was delegated to the Regional Administrators by Delegation No. 9-17, dated May 11, 1994.

3. Under the SDWA, Congress has authorized EPA to exercise broad authority for the protection of public health from contaminants entering a public water system or an underground source of drinking water.

II. STIPULATIONS

4. E.I. du Pont de Nemours and Company ("DuPont") consents to EPA's jurisdiction to issue this Order. DuPont does not admit to the EPA Findings in this Order.

5. DuPont waives any defenses it might have as to jurisdiction and venue and agrees not to contest any of the findings of fact or conclusions of law herein in any action to enforce this Order. Except as to any proceeding brought by EPA to enforce this Order, in agreeing to this Order, DuPont makes no admission of fact or law and reserves all rights and defenses available regarding liability or responsibility in any other legal proceeding related to the subject matter of this Order. DuPont further waives any rights to appeal this Order that would be otherwise applicable under the SDWA.

III. DEFINITIONS AND BACKGROUND

6. "Contaminant" means "any physical, chemical, biological, or radiological substance or matter in water." See 42 U.S.C. § 300f(6).

7. The term "underground source of drinking water" ("USDW") means an aquifer or a portion thereof which supplies a public water system ("PWS"), or which contains a sufficient quantity of ground water to supply a PWS and which currently supplies drinking water for human consumption, or contains fewer than 10,000 milligrams per liter total dissolved solids, and is not an exempted aquifer. See 40 C.F.R. § 144.3.

8. C-8, for purposes of this Order, is perfluorooctanoic acid, CAS # 335-67-1 (PFOA) and its salts, including ammonium perfluorooctanoate, CAS # 3825-26-1 (APFO). These are man-made perfluorinated compounds that do not occur naturally in the environment.

9. The term "day" means calendar day. When a stated time expires on a Saturday, Sunday or Federal Holiday, the stated time period shall be extended to include the next business day.

10. Micrograms per liter (µg/l) is the same as parts per billion (ppb).

11. The term "source water" shall mean water prior to any kind of treatment.

12. A "public water system," hereafter "PWS," provides piped drinking water for human consumption to persons within the meaning of Section 1401 (4) of the Act, 42 U.S.C. §300f(4) and 40 CFR §141.2.

13. A private water system is used by individual residents, or serves less than 25 persons per year from a well or other surface or ground water source and is otherwise not a "PWS."

14. The term "finished water" shall mean water that has passed through all the processes in a system's water treatment plant and is ready to be delivered to consumers.

IV. EPA FINDINGS

15. DuPont is a corporation and is therefore a "person" within the meaning of Section 1401(12) of the SDWA, 42 U.S.C. § 300f(12).

16. DuPont owns and operates a manufacturing facility known as the Washington Works ("Facility"), located in Washington, Wood County, West Virginia.

17. DuPont has used C-8, in the form of APFO, in its manufacturing processes at the Facility since the early 1950s.

18. On November 15, 2001, DuPont, the West Virginia Department of Environmental Protection ("WVDEP") and the West Virginia Department of Health and Human Resources ("WVDHHR") entered into an agreement on consent ("WV Order"), which provided for, *inter alia*, a toxicological and human health risk assessment of C-8 to be conducted under the supervision of a C-8 Assessment of Toxicity ("CAT") Team. Ground water and surface water monitoring and plume identification in West Virginia and Ohio was conducted under the supervision of a Ground Water Investigation Steering ("GIS") Team.

19. In April 2002, the CAT Team conducted a toxicological and human health risk assessment of C-8 and developed a screening level of 150 ppb for C-8 in drinking water.

20. From 2000 to 2006 DuPont implemented recycling and abatement technologies that reduced both air emissions and water discharges of C-8 from the Facility. Annual emissions to air in 2005 were reported to be approximately 12,600 kilograms lower than annual air emissions in 2000. Annual discharges to water in 2005 were reported to be approximately 20,400 kilograms lower than annual water discharges in 2000. As of year-end 2006, DuPont had reduced annual air discharges by 99.1% and had reduced annual water discharges by 99.2% since 2000.[1]

21. On November 20, 2006, DuPont and EPA entered into an Order on Consent ("2006 Order"), which required DuPont to offer, *inter alia*, alternative drinking water or treatment to public water systems or owners of residences using private water systems living in the vicinity of the Facility where levels of C-8 detected in the finished water of public and private drinking water systems were equal to or greater than 0.50 ppb.

22. The 0.50 ppb action level established in the 2006 Order was a precautionary level to reduce exposure from C-8 to the population living in the vicinity of the Facility.

23. On January 8, 2009, the EPA Office of Water issued a Provisional Health Advisory which established a national value of 0.4 ppb for PFOA.[2]

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1 DuPont. "Data Assessment DuPont Washington Works (OPPT-2004-0113 PFOA Site-related Environmental Assessment Program)," (October 2, 2008).

2 United States Environmental Protection Agency's Office of Water, "Provisional Health Advisories for Perfluorooctanioic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS)" (2009). (including Administrative Record thereto). Available: www.epa.gov/waterscience/criteria/drinking/pha-PFOA_PFOS.pdf

24. Provisional Health Advisory values reflect reasonable, health-based hazard concentrations above which action should be taken to reduce exposure to PFOA in drinking water.[3]

25. Sampling conducted through the GIS Team effort since 2001, and by DuPont, has detected C-8 in private and public drinking water sources in Ohio and West Virginia at concentrations ranging from below the limits of quantitation up to 21.1 ppb.[4] As set forth in more detail in paragraphs 26, 27 & 28, DuPont has already taken measures to address PFOA in drinking water at or above 0.50 ppb.

26. The 2006 Order achieved comprehensive identification of private and public water systems in the vicinity of the Facility and ensured alternate water and/or treatment was offered, installed, and maintained at all public and private water systems that exceeded 0.50 ppb of C-8 in their finished water.

27. Prior to the 2006 Order, DuPont had offered a granular activated carbon water treatment ("GAC Treatment") at two public water systems that contained levels of C-8 that exceeded 0.50 ppb in their finished water. Those public water systems are the Little Hocking Water Association ("Little Hocking"), located in Ohio, and the Lubeck Public Service District ("Lubeck"), located in West Virginia. Upon acceptance of the offer and completion of construction, DuPont has provided for operation and maintainence of GAC Treatment at Little Hocking and Lubeck pursuant to the 2006 Order.

28. Initiating prior to and continuing pursuant to the 2006 Order, DuPont has offered to either connect to a public water system or install GAC Treatment to owners of residences using private water systems for which data have demonstrated levels of C-8 at or above 0.50 ppb in their finished water. DuPont has either connected to a public water system or has installed and is operating GAC Treatment at approximately 50 private water systems with finished water that exceeded 0.50 ppb of C-8 and whose owners have accepted DuPont's offer.

29. To date, approximately four owners of private water systems in the vicinity of the Facility with finished water that exceeds 0.50 ppb of C-8 have declined or not responded to DuPont's offer for installation of treatment or connection to a public water system.

30. With the issuance of the Provisional Health Advisory for PFOA, EPA has identified additional geographic areas in the vicinity of the Facility where USDWs may contain C-8 at concentrations at or above 0.40 ppb.

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3 Id.

4 Hartten, Andrew S., Project Director, DuPont, "Amended 3Q05, and 4Q05 and 1Q06 Residential Sampling Results, West Virginia and Ohio DuPont Washington Works, Washington, WV (EPA Docket ID Number OPPT 2004-0113 PFOA Site-Related Environmental Assessment Program," submitted to Chad Board, West Virginia Department of Environmental Protection (April 5, 2006).

31. C-8 is currently not a contaminant for which a national primary drinking water regulation, including a maximum contaminant level ("MCL"), has been established pursuant to the SDWA.

32. EPA is conducting a risk assessment of C-8 under the Toxic Substances Control Act ("TSCA"), 15 U.S.C. §§ 2601 *et seq*.

33. DuPont has released C-8 to the air, discharged C-8 to surface waters, and disposed of residues containing C-8 at the Facility. DuPont has also disposed of residues containing C-8 to its Dry Run, Local, and Letart Landfills in West Virginia and has otherwise shipped residues containing C-8 off-site for destruction and/or disposal.

34. The releases, discharges, and/or disposal referred to in Paragraph 33 have resulted in releases of C-8 to air, ground water, surface water, and soil.

35. The releases referred to in Paragraph 33 have entered USDWs and surface waters and resulted in levels of C-8 at concentrations at or above 0.40 ppb in some of the receiving waters.

36. Public and private water systems in the vicinity of the Facility are using water sources contaminated with C-8 at levels that may be at or above 0.40 ppb; and therefore further investigation is warranted.

37. Based on existing data, there are approximately 10-15 private water systems in the vicinity of the Facility that contain levels of C-8 at or above 0.40 ppb in their finished water.[5]

38. Although EPA has not yet completed its risk assessment for C-8, EPA has determined that the 0.50 ppb Site-Specific Action Level requires modification.

39. Section 1431 of the SDWA requires a finding that "a contaminant which is present in or is likely to enter a public water system or an underground source of drinking water...may present an imminent and substantial endangerment to the health of persons...." It does not require a conclusive finding that a contaminant has, or definitely will, cause harm. As required by Section 1431 of the SDWA and for purposes of this Order, EPA has determined that C-8 is a contaminant present in or likely to enter a PWS or a USDW which may present an imminent and substantial endangerment to human health at concentrations at or above 0.40 ppb in drinking water.[6] The 0.40 ppb action level is a precautionary Site-Specific Action Level to reduce exposure to the population living in the vicinity of the Facility.

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5 Hartten A., Project Director, DuPont, "PFOA concentration at or above 0.40 ug/L" (Tables 1 and 2). (dated 2/16/2009).

6 United States Environmental Protection Agency's Office of Water, "Provisional Health Advisories for Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS)" (2009). (including Administrative Record thereto). Available: www.epa.gov/waterscience/criteria/drinking/pha-PFOA_PFOS.pdf

40. State and local authorities rely on the expertise and resources of EPA to review and evaluate unregulated contaminants. The WVDEP, WVDHHR, OEPA, the Ohio Department of Health ("ODH"), and local authorities are relying on the EPA to establish a Site-Specific Action Level for C-8 in drinking water that reduces exposure to C-8 for residents in the vicinity of the Facility. State agency actions taken to date, including actions taken by WVDEP, WVDHHR, OEPA, and ODH, have been based on the Site-Specific Action Level of 0.50 ppb established in the 2006 Order.

41. EPA has consulted with WVDEP, WVDHHR, OEPA, and ODH to confirm that the information upon which this Order is based is correct. The WVDEP, WVDHHR, OEPA, and ODH have requested that EPA take this action. Therefore, all requisite conditions have been satisfied for EPA action under Section 1431(a)(1) of the SDWA, 42 U.S.C. § 300i(a)(1).

V. ORDER ON CONSENT

42. Pursuant to the authority given to the EPA Administrator by Section 1431(a)(1) of the SDWA, 42 U.S.C. § 300i(a)(1), and delegated to the Regional Administrators, DuPont is ORDERED and hereby consents to the following:

a) Temporary Provision of Alternate Drinking Water. For those private water systems where existing validated data demonstrates levels of C-8 at or above 0.40 ppb in their finished water, DuPont shall provide an alternate drinking water supply as soon as practicable, but in any event no later than fourteen (14) days after the execution of this Order. Where DuPont conducts a water system survey pursuant to Paragraphs 42(e) or (f) and identifies private and public water systems where the level of C-8 in the finished water is at or above 0.40 ppb, DuPont shall provide an alternate drinking water supply as soon as practicable, but in any event no later than thirty (30) days, from the receipt of validated data. An "alternate drinking water supply" shall mean: water from some other source, acceptable to EPA, that meets the water quality requirements of 40 C.F.R. Part 141 and has a level of C-8 less than 0.40 ppb in finished water where applicable; is in sufficient quantity for drinking and cooking; and is provided in a manner convenient to the users. DuPont shall continue to provide an alternate drinking water supply until it can fully implement the permanent remedies described *infra* pursuant to Paragraph 42 of this Order or the resident declines the offer or is non-responsive to the offer of treatment (as determined by EPA). DuPont shall be responsible for all costs of the provision of alternate drinking water.

b) Private Water Systems Receiving Treatment. For private water systems at which DuPont has already installed GAC Treatment, DuPont shall provide for operation and maintenance of each GAC Treatment system in good working order, including but not limited to timely replacement of carbon filters, until it demonstrates to the satisfaction of EPA that the source prior to GAC Treatment

contains less than 0.40 ppb of C-8 for four consecutive quarters, or the conditions of Paragraph 46 have been met. DuPont may also elect to satisfy any ongoing obligation under this Paragraph by connecting a particular location to a public water system that contains less than 0.40 ppb of C-8 in finished water.

c) Public Water Systems Receiving Treatment. For public water systems, at which DuPont has already installed GAC Treatment, DuPont shall provide for operation and maintenance of each GAC Treatment system in good working order, including but not limited to timely carbon bed changes, until it demonstrates to the satisfaction of EPA that the source water in the system prior to GAC Treatment contains less than 0.40 ppb of C-8 for four consecutive quarters, or the conditions of Paragraph 46 have been met.

d) Action at Private Water Systems Based On Existing Data. For those private water systems where existing validated data demonstrates levels of C-8 at or above 0.40 ppb in their finished water, DuPont shall, within fourteen (14) days of execution of this Order, submit to EPA for approval, and to WVDHHR, WVDEP, OEPA, and ODH for review, a written Water Treatment Plan for each of these water systems in accordance with the provisions of Paragraph 42(g).

e) Survey and Identification of Additional Private and Public Water Systems. For geographical areas defined by EPA (upon consultation with West Virginia and Ohio), DuPont shall conduct a water system survey and where any private or public water system (not already sampled) is identified, monitor the finished and source waters for the presence of C-8. DuPont shall notify EPA of monitoring results immediately, but in any event no later than 7 days, after the data are finalized through DuPont's internal data quality control/quality assurance procedures. DuPont shall also notify owners or operators of private and public water systems of monitoring results within 7-10 days after the data are finalized through DuPont's internal data quality control/quality assurance procedures.

f) Newly Activated or Permitted Water Systems. Upon notification by EPA of any newly activated public water system or any newly constructed/permitted/put into use private water system that conforms to state and local code and is located in the geographical areas defined by EPA (upon consultation with West Virginia and Ohio), DuPont shall monitor the finished and source waters for the presence of C-8 in accordance with the provisions of Paragraph 42(e). On the anniversary date of the effective date of this Order and annually thereafter, DuPont shall survey the geographical areas defined by EPA for any new private or public water systems until DuPont demonstrates to the satisfaction of EPA that the USDWs in these geographical areas (or a subset of those areas) contain less than 0.40 ppb of C-8 for four consecutive quarters, or the conditions of Paragraph 46 have been met. DuPont shall monitor the finished and source

waters of any new systems for the presence of C-8 in accordance with the provisions of Paragraph 42(e).

g) Water Treatment Plan. If any additional private or public water systems covered by this Order contain C-8 at or above 0.40 ppb in their finished water, DuPont shall, within 30 days of receipt of validated data, submit to EPA for approval, and to WVDHHR, WVDEP, OEPA, and ODH for review, a written Water Treatment Plan for each of these water systems. DuPont shall perform all monitoring using a reliable procedure published in the scientific literature by Moody,[7] MPI (formerly known as Exygen Research),[8] other equivalent publication or an EPA approved analytical method. The Water Treatment Plan shall include:

   i. a written offer to install and provide for operation and maintenance of GAC Treatment (including a draft operation and maintenance agreement);

   ii. identification of anticipated necessary permits;

   iii. a schedule for design and implementation of the GAC Treatment system; and

   iv. identification of technical and other information needed from the owner or operator of the water source in order for DuPont to design and install the system.

h) Implementation of Water Treatment Plan. Following approval from EPA, DuPont shall implement the Water Treatment Plan for any additional water system whose owner or operator accepts DuPont's offer. DuPont shall act with all deliberate speed to design treatment, seek necessary regulatory permits, and install GAC Treatment or an alternative approved by EPA. If an owner or operator of a water system rejects DuPont's offer, either through express rejection or silence, DuPont shall inform EPA of this rejection and provide documentation.

i) DuPont's Operation and Maintenance Obligations. DuPont has or will execute operation and maintenance agreements ("O&M Agreements") with each water system owner or operator who has accepted the offer for treatment. DuPont will provide for operation and maintenance of the GAC Treatment or an alternative

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7 Moody, C.A.; Kwan, W.C.; Martin, J.; Muir, D.C.G. & Mabury, S.A., "Determination of Perfluorinated Surfactants in Surface Water Samples by Two Independent Analytical Techniques: Liquid Chromatography/Tandem Mass Spectrometry 19F NMR," *Anal. Chem.* vol. 73, pp. 2200-2206 (2001).

8 Risha, K.; Flaherty, J.; Wille, R.; Buck, W.; Morandi, F. & Isemura, T., "Method for Trace Level Analysis of C-8, C-9, C-10, C-11, and C-13 Perfluorocarbon Carboxylic Acids in Water," *Anal. Chem.*, vol. 77, pp. 1503-1508 (2005).

approved by EPA consistent with the specific terms of these O&M Agreements until it demonstrates to the satisfaction of EPA that the water system's source water prior to treatment is less than 0.40 ppb of C-8 for four consecutive quarters, or the conditions of Paragraph 46 have been met.

j) Follow-up Monitoring. After GAC Treatment is terminated, DuPont shall monitor annually the source water at EPA-specified public and private water systems for a period of five (5) years.

43. Progress Reports. DuPont shall submit Progress Reports as follows:

a) Beginning April 1, 2009, and quarterly thereafter, DuPont shall submit to EPA, WVDHHR, WVDEP, OEPA and ODH written reports summarizing all actions taken in response to Paragraph 42 herein ("Progress Reports"). This reporting requirement shall remain in effect until DuPont submits a written request to EPA to submit Progress Reports on an annual basis and EPA approves such a request. DuPont shall continue to submit Progress Reports until such time as EPA provides written notice that the reports are no longer necessary, or this Order is terminated.

b) All Progress Reports required by this Paragraph shall contain the following certification, which shall be signed by a responsible corporate officer:

> "I certify under penalty of law that this document and all attachments were prepared under my direction or supervision in accordance with a system designed to assure that qualified personnel properly gather and evaluate the information submitted. Based on my inquiry of the person or persons who manage the system, or those persons directly responsible for gathering the information, the information submitted is, to the best of my knowledge and belief, true, accurate, and complete. I am aware that there are significant penalties for submitting false information, including the possibility of fine and imprisonment for knowing violations."

c) For purposes of this Order, a responsible corporate official shall be:

> (A) a president, secretary, treasurer, or vice-president of DuPont in charge of a principal business function, or any other person who performs similar policy or decision-making functions for DuPont; or
>
> (B) the manager of DuPont's Washington Works, West Virginia Facility, so long as authority to sign documents has been delegated in writing to the manager in accordance with corporate procedures.

VI. GENERAL PROVISIONS

44. The Administrative Record to this Order is incorporated herein by reference.

45. Nothing in this Order is intended to supersede, impede, interfere with or otherwise affect the development of an MCL or other regulatory limit for C-8 that may be established by EPA through its regulatory processes in the future.

46. The Site-Specific Action Level identified in this Order for C-8 in drinking water is a temporary value that will be re-evaluated when EPA determines a reference dose under TSCA or establishes a drinking water standard for C-8, whichever comes first.

47. Notwithstanding any other provision of this Order, the EPA reserves the right to modify the Site-Specific Action Level identified in this Order if information previously unknown to EPA is received and EPA determines that this previously unknown information, together with any other relevant information, indicates that the Site-Specific Action Level may not be protective of human health, and DuPont reserves all rights and defenses should EPA take action under this Paragraph.

48. All submissions, including Progress Reports, required under this Order shall be submitted to the following addressees:

As to EPA:

Roger Reinhart
Groundwater and Enforcement Branch
U.S. EPA Region III
1650 Arch Street (3WP22)
Philadelphia, PA 19103-2029
Ryan Bahr
Ground Water and Drinking Water Branch
U.S. EPA Region V
77 West Jackson Boulevard (WG-15J)
Chicago, IL 60604

As to WVDHHR:

Walter Ivey, Director
Division of Environmental Engineering
Office of Environmental Health Services
Dept. of Health and Human Resources
Capital and Washington Streets
One Davis Square, Suite 200
Charleston, WV 25301-1798

As to WVDEP:

William Timmermeyer
Groundwater Protection Section
Division of Water and Waste Management
W.Va. Dept. of Environmental Protection
601 57th Street, SE
Charleston, WV 25304

As to OEPA:

Mike Baker, Chief
Division of Drinking and Ground Waters
Ohio EPA
122 South Front Street
Columbus, OH 43214

As to ODH:

W. Gene Phillips, RS, Bureau Chief
Bureau of Environmental Health
Ohio Department of Health
246 North High Street
P.O. Box 118
Columbus, OH 43216

49. This Order shall apply to and be binding upon DuPont and its agents, successors and assigns.

50. Nothing in this Order shall be construed as prohibiting, altering or in any way eliminating the ability of EPA to seek any other remedies or sanctions available by virtue of DuPont's violations of this Order or of the statutes and regulations upon which this Order is based or for DuPont's violation of any applicable provision of law.

51. This Order shall not relieve DuPont of its obligation to comply with all applicable provisions of federal, state or local law, nor shall it be construed to be a ruling on, or determination of, any issue related to any federal, state or local permit.

52. Nothing in this Order is intended to nor shall be construed to operate in any way to resolve any criminal liability of DuPont. Compliance with this Order shall not be a defense to any actions subsequently commenced for any violation of federal laws and regulations administered by EPA, and it is the responsibility of DuPont to comply with such laws and regulations. EPA reserves the right to undertake action against any person, including DuPont,

in response to any condition which EPA determines may present an imminent and substantial endangerment to the public health, public welfare or the environment.

53. The undersigned representative of DuPont certifies that he or she is fully authorized by DuPont to enter into the terms and conditions of this Order and to execute and legally bind DuPont to it.

54. Pursuant to Section 1431(b) of the SDWA, 42 U.S.C. § 300i(b), and the Adjustment of Civil Monetary Penalties for Inflation, 40 C.F.R. Part 19, as revised (74 Fed. Reg. 626 (Jan.7, 2009)), the violation of any term of this Order, or failure or refusal to comply with this Order, may subject DuPont to a civil penalty not to exceed $16,500 for each day in which such violation occurs or failure to comply continues.

55. When DuPont knows or should have known, by the exercise of due diligence, of an event that might delay completion of any requirement of this Order, DuPont shall provide notice to EPA, in writing, within two (2) business days after DuPont first knew, or in the exercise of due diligence, should have known, of such event. The notice shall describe in detail the basis for the delay, including whether it is a *force majeure* event, and describe the length of, precise cause(s) of, and measures taken or to be taken to prevent or minimize such delay. If EPA agrees that such event constitutes *force majeure*, EPA shall extend the time for performance of such requirement, in writing, to compensate for the delay caused by the *force majeure* event. DuPont's failure to notify in writing in accordance with this Paragraph shall render this Paragraph void and of no effect concerning such event. For purposes of this Order, *force majeure* is defined as an event arising from causes beyond the control of DuPont, and any entity controlled by DuPont, which delays or prevents the performance of any obligation under this Order. Unanticipated or increased costs or expenses associated with implementation of this Order and changed financial circumstances shall not, in any event, be considered *force majeure* events. In addition, failure to apply for a required permit or approval or to provide in a timely manner all information required to obtain a permit or approval that is necessary to meet the requirements of this Order, or to obtain or approve contracts, shall not, in any event, constitute *force majeure* events.

56. This Consent Order may be executed in any number of counterpart originals, each of which shall be deemed to constitute an original agreement, and all of which shall constitute one agreement. The execution of one counterpart by any party shall have the same force and effect as if that party had signed all other counterparts.

57. All of the terms and conditions of this Order together comprise one agreement, and each of the terms and conditions is in consideration of all of the other terms and conditions. In the event that this Order is not executed by all of the signatories in identical form, or is not approved in such identical form by the Regional Administrators, then the entire Order shall be null and void.

58. The effective date of this Order is the date on which, after approval by the Regional Administrators, this Order is filed with the Regional Hearing Clerks of both Region III and Region V, if not, then on the same day.

59. This Order shall remain in effect until DuPont fulfills its obligations pursuant to Paragraphs 42 and 43 herein, submits a written request to EPA to terminate this Order, and EPA approves such termination request.

60. This Order constitutes final agency action.

SO ORDERED:

William Wisniewski

Date: MAR 10 2009

William T. Wisniewski
Acting Regional Administrator
U.S. Environmental Protection Agency,
Region III

Walter W. Kovalick for

Bharat Mathur
Acting Regional Administrator
U.S. Environmental Protection Agency,
Region V

Date: 3/10/09

AGREED TO:

William H. Hopkins

Date: 3/5/2009

William H. Hopkins
Plant Manager, Washington Works Facility
E.I. du Pont de Nemours and Company, Incorporated

EXHIBIT F

Bilott, Robert A.

From:	U.S. Environmental Protection Agency <noreply-subscriptions@epa.gov>
Sent:	Monday, January 09, 2017 1:51 PM
To:	Bilott, Robert A.
Subject:	EPA Amends Drinking Water Order to DuPont

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION III - OFFICE OF COMMUNICATIONS & GOVERNMENT RELATIONS
1650 Arch Street Philadelphia, Pennsylvania 19103-2029
Phone - 215/814-5100 Fax - 215/814-5102

EPA Environmental News

Contact: David Sternberg 215-814-5615 dandrea.michael@epa.gov

EPA Amends Drinking Water Order to DuPont

PHILADELPHIA (January 9, 2017) - The U.S. Environmental Protection Agency today announced an amendment to the 2009 Safe Drinking Water Act consent order between EPA and E.I. du Pont de Nemours and Company (DuPont). The amendment adds The Chemours Company (Chemours) to the 2009 order, and requires both DuPont and Chemours to take additional actions to reduce exposure to perfluorooctanoic acid (PFOA) in drinking water for residents in Ohio and West Virginia living near the Washington Works facility in Parkersburg, WV.

The amendment contains a new action level of .07 parts per billion (ppb) of PFOA which triggers the temporary provision of an alternate source of drinking water by DuPont and Chemours. The temporary provision of drinking water will continue until a permanent alternate drinking water supply is provided. The amendment also expands the geographic areas to be investigated and requires appropriate action if levels of PFOA in drinking water of .07 ppb or more are discovered.

This amendment to the 2009 Order, which had included a temporary action level of .40 ppb, is supported by site-specific data, as well as the Lifetime Health Advisory issued by EPA on May 19, 2016, that established .07 ppb, of PFOA in drinking water as protective of human health.

EXHIBIT G

EPA United States Environmental Protection Agency

FACT SHEET
PFOA & PFOS Drinking Water Health Advisories

Overview

EPA has established health advisories for PFOA and PFOS based on the agency's assessment of the latest peer-reviewed science to provide drinking water system operators, and state, tribal and local officials who have the primary responsibility for overseeing these systems, with information on the health risks of these chemicals, so they can take the appropriate actions to protect their residents. EPA is committed to supporting states and public water systems as they determine the appropriate steps to reduce exposure to PFOA and PFOS in drinking water. As science on health effects of these chemicals evolves, EPA will continue to evaluate new evidence.

Background on PFOA and PFOS

PFOA and PFOS are fluorinated organic chemicals that are part of a larger group of chemicals referred to as perfluoroalkyl substances (PFASs). PFOA and PFOS have been the most extensively produced and studied of these chemicals. They have been used to make carpets, clothing, fabrics for furniture, paper packaging for food and other materials (e.g., cookware) that are resistant to water, grease or stains. They are also used for firefighting at airfields and in a number of industrial processes.

Because these chemicals have been used in an array of consumer products, most people have been exposed to them. Between 2000 and 2002, PFOS was voluntarily phased out of production in the U.S. by its primary manufacturer. In 2006, eight major companies voluntarily agreed to phase out their global production of PFOA and PFOA-related chemicals, although there are a limited number of ongoing uses. Scientists have found PFOA and PFOS in the blood of nearly all the people they tested, but these studies show that the levels of PFOA and PFOS in blood have been decreasing. While consumer products and food are a large source of exposure to these chemicals for most people, drinking water can be an additional source in the small percentage of communities where these chemicals have contaminated water supplies. Such contamination is typically localized and associated with a specific facility, for example, an industrial facility where these chemicals were produced or used to manufacture other products or an airfield at which they were used for firefighting.

EPA's 2016 Lifetime Health Advisories

EPA develops health advisories to provide information on contaminants that can cause human health effects and are known or anticipated to occur in drinking water. EPA's health advisories are non-enforceable and non-regulatory and provide technical information to states agencies and other public health officials on health effects, analytical methodologies, and treatment technologies associated with drinking water contamination. In 2009, EPA published provisional health advisories for PFOA and PFOS based on the evidence available at that time. The science has evolved since then and EPA is now replacing the 2009 provisional advisories with new, lifetime health advisories.

FACT SHEET
PFOA & PFOS Drinking Water Health Advisories

EPA's 2016 Lifetime Health Advisories, continued

To provide Americans, including the most sensitive populations, with a margin of protection from a lifetime of exposure to PFOA and PFOS from drinking water, EPA established the health advisory levels at 70 parts per trillion. When both PFOA and PFOS are found in drinking water, the combined concentrations of PFOA and PFOS should be compared with the 70 parts per trillion health advisory level. This health advisory level offers a margin of protection for all Americans throughout their life from adverse health effects resulting from exposure to PFOA and PFOS in drinking water.

How the Health Advisories were developed

EPA's health advisories are based on the best available peer-reviewed studies of the effects of PFOA and PFOS on laboratory animals (rats and mice) and were also informed by epidemiological studies of human populations that have been exposed to PFASs. These studies indicate that exposure to PFOA and PFOS over certain levels may result in adverse health effects, including developmental effects to fetuses during pregnancy or to breastfed infants (e.g., low birth weight, accelerated puberty, skeletal variations), cancer (e.g., testicular, kidney), liver effects (e.g., tissue damage), immune effects (e.g., antibody production and immunity), thyroid effects and other effects (e.g., cholesterol changes).

EPA's health advisory levels were calculated to offer a margin of protection against adverse health effects to the most sensitive populations: fetuses during pregnancy and breastfed infants. The health advisory levels are calculated based on the drinking water intake of lactating women, who drink more water than other people and can pass these chemicals along to nursing infants through breastmilk.

Recommended Actions for Drinking Water Systems

Steps to Assess Contamination

If water sampling results confirm that drinking water contains PFOA and PFOS at individual or combined concentrations greater than 70 parts per trillion, water systems should quickly undertake additional sampling to assess the level, scope and localized source of contamination to inform next steps

Steps to Inform

If water sampling results confirm that drinking water contains PFOA and PFOS at individual or combined concentrations greater than 70 parts per trillion, water systems should promptly notify their State drinking water safety agency (or with EPA in jurisdictions for which EPA is the primary drinking water safety agency) and consult with the relevant agency on the best approach to conduct additional sampling.

Drinking water systems and public health officials should also promptly provide consumers with information about the levels of PFOA and PFOS in their drinking water. This notice should include specific information on the risks to fetuses during pregnancy and breastfed and formula-fed infants from exposure to drinking water with an individual or combined concentration of PFOA and PFOS above EPA's health advisory level of 70 parts per trillion. In addition, the notification should include actions they are taking and identify options that consumers may consider to reduce risk such as seeking an alternative drinking water source, or in the case of parents of formula-fed infants, using formula that does not require adding water.

FACT SHEET
PFOA & PFOS Drinking Water Health Advisories

Recommended Actions for Drinking Water Systems, continued

Steps to Limit Exposure

A number of options are available to drinking water systems to lower concentrations of PFOA and PFOS in their drinking water supply. In some cases, drinking water systems can reduce concentrations of perfluoroalkyl substances, including PFOA and PFOS, by closing contaminated wells or changing rates of blending of water sources. Alternatively, public water systems can treat source water with activated carbon or high pressure membrane systems (e.g., reverse osmosis) to remove PFOA and PFOS from drinking water. These treatment systems are used by some public water systems today, but should be carefully designed and maintained to ensure that they are effective for treating PFOA and PFOS. In some communities, entities have provided bottled water to consumers while steps to reduce or remove PFOA or PFOS from drinking water or to establish a new water supply are completed.

Many home drinking water treatment units are certified by independent accredited third party organizations against American National Standards Institute (ANSI) standards to verify their contaminant removal claims. NSF International (NSF®) has developed a protocol for NSF/ANSI Standards 53 and 58 that establishes minimum requirements for materials, design and construction, and performance of point-of-use (POU) activated carbon drinking water treatment systems and reverse osmosis systems that are designed to reduce PFOA and PFOS in public water supplies. The protocol has been established to certify systems (e.g., home treatment systems) that meet the minimum requirements. The systems are evaluated for contaminant reduction by challenging them with an influent of 1.5±30% µg/L (total of both PFOA and PFOS) and must reduce this concentration by more than 95% to 0.07 µg/L or less (total of both PFOA and PFOS) throughout the manufacturer's stated life of the treatment system. Product certification to this protocol for testing home treatment systems verifies that devices effectively reduces PFOA and PFOS to acceptable levels.

Other Actions Relating to PFOA and PFOS

Between 2000 and 2002, PFOS was voluntarily phased out of production in the U.S. by its primary manufacturer, 3M. EPA also issued regulations to limit future manufacturing, including importation, of PFOS and its precursors, without first having EPA review the new use. A limited set of existing uses for PFOS (fire resistant aviation hydraulic fluids, photography and film products, photomicrolithography process to produce semiconductors, metal finishing and plating baths, component of an etchant) was excluded from these regulations because these uses were ongoing and alternatives were not available.

In 2006, EPA asked eight major companies to commit to working toward the elimination of their production and use of PFOA, and chemicals that degrade to PFOA, from emissions and products by the end of 2015. All eight companies have indicated that they have phased out PFOA, and chemicals that degrade to PFOA, from emissions and products by the end of 2015. Additionally, PFOA is included in EPA's proposed Toxic Substance Control Act's Significant New Use Rule (SNUR) issued in January 2015 which will ensure that EPA has an opportunity to review any efforts to reintroduce the chemical into the marketplace and take action, as necessary, to address potential concerns.

FACT SHEET
PFOA & PFOS Drinking Water Health Advisories

Other Actions Relating to PFOA and PFOS, continued

EPA has not established national primary drinking water regulations for PFOA and PFOS. EPA is evaluating PFOA and PFOS as drinking water contaminants in accordance with the process required by the Safe Drinking Water Act (SDWA). To regulate a contaminant under SDWA, EPA must find that it: (1) may have adverse health effects; (2) occurs frequently (or there is a substantial likelihood that it occurs frequently) at levels of public health concern; and (3) there is a meaningful opportunity for health risk reduction for people served by public water systems.

EPA included PFOA and PFOS among the list of contaminants that water systems are required to monitor under the third Unregulated Contaminant Monitoring Rule (UCMR 3) in 2012. Results of this monitoring effort are updated regularly and can be found on the publicly-available National Contaminant Occurrence Database (NCOD) (https://www.epa.gov/dwucmr/occurrence-data-unregulated-contaminant-monitoring-rule#3). In accordance with SDWA, EPA will consider the occurrence data from UCMR 3, along with the peer reviewed health effects assessments supporting the PFOA and PFOS Health Advisories, to make a regulatory determination on whether to initiate the process to develop a national primary drinking water regulation.

In addition, EPA plans to begin a separate effort to determine the range of PFAS for which an Integrated Risk Information System (IRIS) assessment is needed. The IRIS Program identifies and characterizes the health hazards of chemicals found in the environment. IRIS assessments inform the first two steps of the risk assessment process: hazard identification, and dose-response. As indicated in the 2015 IRIS Multi-Year Agenda, the IRIS Program will be working with other EPA offices to determine the range of PFAS compounds and the scope of assessment required to best meet Agency needs. More about this effort can be found at https://www.epa.gov/iris/iris-agenda.

Non-Drinking Water Exposure to PFOA and PFOS

These health advisories only apply to exposure scenarios involving drinking water. They are not appropriate for use, in identifying risk levels for ingestion of food sources, including: fish, meat produced from livestock that consumes contaminated water, or crops irrigated with contaminated water.

The health advisories are based on exposure from drinking water ingestion, not from skin contact or breathing. The advisory values are calculated based on drinking water consumption and household use of drinking water during food preparation (e.g., cooking or to prepare coffee, tea or soup). To develop the advisories, EPA considered non-drinking water sources of exposure to PFOA and PFOS, including: air, food, dust, and consumer products. In January 2016 the Food and Drug Administration amended its regulations to no longer allow PFOA and PFOS to be added in food packaging, which will likely decrease one source of non-drinking water exposure.

Where Can I Learn More?

- EPA's Drinking Water Health Advisories for PFOA and PFOS can be found at: https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos
- PFOA and PFOS data collected under EPA's Unregulated Contaminant Monitoring Rule are available: https://www.epa.gov/dwucmr/occurrence-data-unregulated-con taminant-monitoring-rule
- EPA's stewardship program for PFAS related to TSCA: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/and -polyfluoroalkyl-substances-pfass-under-tsca
- EPA's research activities on PFASs can be found at: http://www.epa.gov/chemical-research/perfluorinated-chemical-pfc-research
- The Agency for Toxic Substances and Disease Registry's Perflourinated Chemicals and Your Health webpage at: http://www.atsdr.cdc.gov/PFC/

EPA
United States Environmental Protection Agency

EXHIBIT H

Brief Overview of the Feasibility Assessment for Epidemiological Studies at Pease International Tradeport

May 23, 2017

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.

<u>Health-related endpoints feasible to study at Pease</u>:

- 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

<u>Health-related endpoints that may be possible to study at Pease</u> (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.

DRAFT for Review Purposes

Feasibility Assessment for Epidemiological Studies at Pease International Tradeport, Portsmouth, New Hampshire

May 23, 2017

The findings and conclusions in this report/presentation have not been formally disseminated by the Agency for Toxic Substances and Disease Registry and should not be construed to represent any agency determination or policy.

Contents

Summary

This report describes the activities and the conclusions of ATSDR's feasibility assessment of possible future drinking water epidemiological studies at the Pease International Tradeport, Portsmouth, New Hampshire ("Pease"). The drinking water at Pease was contaminated with perfluoroalkyl substances (PFAS), in particular perfluorooctane sulfonate (PFOS) and perfluorohexane sulfonate (PFHxS), from the use of aqueous film-forming foam (AFFF) at the former Pease Air Force Base. The base used AFFF for firefighting training and to extinguish flammable liquid fires. In 2015, the New Hampshire Department of Health and Human Services (NH DHHS) established a PFAS blood testing program at Pease. A total of 1,578 persons submitted a blood sample for analysis. The results from the blood testing program indicated that the exposed population had higher serum levels of PFOS and PFHxS than did the U.S. population.

In March 2016, ATSDR established a community assistance panel (CAP) as a mechanism for the community to voice its concerns and provide input on decisions concerning potential health activities at Pease. A key concern expressed by the community was the lack of information on the possible short-term and long-term health effects to children and adults exposed to the PFAS contaminants in the drinking water at Pease. Specifically, the community was concerned about cancers, elevated lipids, effects on thyroid and immune function, and developmental delays in children.

ATSDR then assessed whether epidemiological studies focusing on populations at Pease were feasible and whether such studies could answer the concerns of the community. When evaluating whether an epidemiological study would be scientifically feasible, ATSDR used three main criteria:

1. Meaningful and credible results — a study should have sufficient validity and precision, be capable of detecting health-related effects, and be as responsive as possible to the community's questions and concerns. Ideally, a study should also be capable of detecting health-related effects, for example a 20% to 100% increase in risk with sufficient statistical power (i.e., statistical power ≥80%).

2. 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.

3. Public health significance — a study should provide a basis for determining if PFAS exposures increase the risks for 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.

The feasibility assessment is guided by these three criteria and does not address considerations of financial or operational feasibility. Feasibility was also assessed in terms of whether sufficient participation (sample size) could be obtained from within the Pease community to achieve sufficient statistical power for the health-related endpoints being considered, or whether the study would need to be expanded to other communities beyond the Pease population.

ATSDR reviewed the epidemiological literature on PFAS exposures to identify the health-related endpoints that have been studied and current data gaps, in particular, for the effects of PFHxS. The literature review also was used to identify adverse effect sizes observed in the PFAS studies for PFAS serum levels similar to those found in the Pease population.

The literature review found that most information on potential health effects concerned exposures to perfluorooctanoic acid (PFOA). In particular, numerous studies have been conducted of West Virginia and Ohio residents and workers exposed to PFOA from a chemical plant (the "C8" studies) [Frisbee 2009]. Studies of other workforces also were primarily focused on PFOA exposures. 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.

The literature review identified many health-related endpoints evaluated in previous epidemiological studies of PFAS exposures. These included cancers, lipids, effects on thyroid and immune function, and developmental delays. They also included effects on kidney and liver function and sex hormones, and diseases such as endometriosis, ulcerative colitis and osteoporosis. Many of these health-related endpoints were also previously raised by the community and the Pease CAP.

In considering possible study designs, ATSDR focused on the methods used in previous epidemiological research of PFAS exposures. Adopting study design methods consistent with previous research would facilitate the interpretation and synthesis of findings across studies. The literature review found that most of the epidemiological studies of PFAS exposures were cross-sectional and evaluated serum PFAS measurements. Some studies also evaluated cumulative PFAS serum levels that were estimated from modeling methods. ATSDR concluded that any study of populations exposed to the PFAS-contaminated drinking water at the Pease Tradeport should be cross-sectional and evaluate measured serum PFAS measurements as well as estimated cumulative PFAS serum levels. ATSDR also concluded that methods used to evaluate health-related endpoints in the Pease Tradeport populations should be consistent with methods used in previous epidemiological research of PFAS exposures.

Potential Study Designs

A. Cross-sectional study of children

The first design is a cross-sectional study of children who were exposed to the PFAS-contaminated drinking water while attending the two day-care centers at Pease. Inclusion would be limited to children who attended the day-care centers any time before June 2014, and who would be in the age range of 4–16 years at the time the study begins. During the 2015 blood testing program at Pease, 370 children aged 1–13 years contributed blood samples. If a study were to begin in 2018, these children would be ages 4–16 years. The study would involve re-contacting these participants and obtaining new blood samples. To increase the sample size, the study would also recruit and obtain blood samples from children who attended the day-care centers at Pease, but who did not participate in the New Hampshire blood testing program. 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...

A comparison group of children, who did not attend day care at the Pease Tradeport and whose parents did not work at the Pease Tradeport or have occupational exposures to PFAS, would be recruited and blood samples collected. The comparison group would be sampled from the Portsmouth public schools and selected to have similar demographics as the Pease children.

Based on the health-related endpoints included in the final study, blood samples could be used to evaluate PFAS serum levels and several biomarkers of effect, including lipids, thyroid function, kidney function, immune function, and sex hormones. The children could also be assessed for neurological endpoints such as intelligence quotient (IQ), learning problems, and attention-deficit/hyperactivity disorder (ADHD) behaviors.

Calculations were conducted assuming a sample size of 350 exposed children who attended day care at the Pease Tradeport and 175 unexposed children from the Portsmouth area who did not attend day care at the Pease Tradeport. Additional sample size calculations assumed a sample size of 500 exposed children and 250 unexposed children. The sample size calculations also assumed a simple comparison of exposed versus unexposed children. A second approach was to determine the sample sizes needed to detect effects found in other PFAS studies of children with serum PFAS levels similar to those observed in the Pease children population. For some health-related endpoints, there was insufficient information to conduct any sample size calculations.

Based on sample size considerations, health-related endpoints were grouped into three categories: 1) feasible to study, 2) possible to study (but would require a larger sample size than 350 exposed children and 175 unexposed children), and 3) not feasible to study using the Pease children population unless additional populations exposed to PFAS-contaminated drinking water from other affected communities 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, a measure of kidney function
- 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 responses 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

To evaluate exposure-response trends, the study participants would need to be split into tertiles or quartiles based on their serum PFAS levels. This might require a larger sample size for some of the health-related endpoints listed as feasible to study.

B. Cross-sectional study of adults

The second cross-sectional study design would involve obtaining blood samples from adults aged ≥18 years who worked anytime at the Pease Tradeport during January 2008–May 2014. This study would evaluate PFAS serum levels, lipids, thyroid function, liver function, kidney function, and immune function. The study would also evaluate diseases such as kidney disease, liver disease, cardiovascular disease, thyroid disease, ulcerative colitis, rheumatoid arthritis, osteoporosis, osteoarthritis, and endometriosis. In the 2015 blood testing program at Pease, 1,182 adults aged ≥18 years participated, and 1,083 (91.6%) adults reported that they last worked at Pease during 2008–2014.

Calculations were conducted assuming a sample size of 1,500 adults exposed while employed at the Pease Tradeport and 1,500 unexposed adults from the Portsmouth area who never worked at the Pease Tradeport. The sample size calculations also assumed a simple comparison of exposed versus unexposed adults. A second approach was to determine the sample sizes needed to detect effects found in other PFAS studies of adults with serum PFAS levels similar to those observed in the Pease adult population.

Based on sample size considerations, health-related endpoints were grouped into three categories: 1) feasible to study, 2) possible to study (but would require a larger sample size than 1,500 exposed and 1,500 unexposed adults), and 3) not feasible to study using the Pease adult population unless additional populations exposed to PFAS-contaminated drinking water are included in the study.

Health-related endpoints feasible to study in adults at Pease

- Mean difference in lipids (total cholesterol, LDL, HDL, triglycerides)
- Elevated total cholesterol (hypercholesterolemia)
- Mean difference in uric acid, a measure of kidney function
- 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 in adults 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 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 evaluate these health-related endpoints)

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

To evaluate exposure-response trends, the study participants would need to be split into tertiles or quartiles based on their serum PFAS levels. This might require a larger sample size for some of the health endpoints listed as feasible to study.

C. Mortality study of former military service and civilian worker personnel

A third study design that was considered would evaluate mortality and cancer incidence among former military service and civilian worker personnel at the former Pease Air Force Base and other military bases where drinking water was contaminated with PFOS and PFHxS from the use of AFFF. Comparison military bases would also need to be identified that had no PFAS-contaminated drinking water or drinking water contamination from other chemicals above the U.S. Environmental Protection Agency's maximum contaminant levels (MCLs). Personal identifier information (e.g., Social Security number, name, date of birth, sex) necessary for data linkage with the national death index and state and federal cancer registries could be obtained from the Defense Manpower Data Center.

However, 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 a study 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.

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 definitive 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.

Introduction

This draft report describes the approach and the conclusions of the Agency for Toxic Substance and Disease Registry's (ATSDR's) feasibility assessment of possible drinking water epidemiological studies at the Pease International Tradeport ("Pease"), Portsmouth, New Hampshire. The purpose of the feasibility assessment was to determine whether epidemiological studies are reasonable to conduct at Pease and whether data exist to conduct scientifically credible epidemiological studies. This draft feasibility assessment report for possible future studies at Pease International Tradeport is being distributed to the Pease Community Assistance Panel (CAP) for members' review and input. Input from the CAP is intended to help ATSDR ensure the proposed research is relevant to community concerns. The report is a DRAFT document that may be edited based on CAP input; it is not intended to be a protocol or systematic literature review. The final study design, including sample size, the health endpoints that can be considered and the development of the study protocol itself, including the statistical analysis approach have yet to be determined. The Pease CAP will have an opportunity to review and provide input on a draft of the study design before it is finalized. The draft feasibility assessment does not represent a commitment by ATSDR to conduct research at Pease International Tradeport, given that funding and staffing to conduct the described research are not available at this time.

Three criteria were used to determine whether epidemiological studies are warranted at Pease:

1. **Meaningful and credible results** —a study should have sufficient validity and precision, be capable of detecting health-related effects, and be as responsive as possible to the community's questions and concerns. Ideally, a study should also be capable of detecting health-related effects, for example a 20% to 100% increase in risk with sufficient statistical power (i.e., statistical power ≥80%). To achieve sufficient validity, a study should minimize biases such as selection bias and confounding bias. Sufficient precision can be achieved by a sample size that has at least 80% statistical power to detect health-related effect sizes observed in other studies for PFAS serum levels similar to those in the Pease population.

2. **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 and fill important data gaps. Evidence for the biological plausibility of a health-related endpoint can come from animal studies of PFAS exposures, information on how PFAS exposures cause adverse effects (i.e., mechanistic information), and epidemiological studies. Since PFHxS and PFOS serum levels were elevated in the Pease population compared to national data, a Pease study should focus on data gaps concerning the health effects of exposures to these chemicals. The feasibility assessment included a literature search of epidemiological studies of PFAS exposures to identify the health-related endpoints evaluated in these studies and the data gaps that exist on the health effects of PFHxS and PFOS.

3. **Public health significance** — a study should provide a basis for determining if PFAS exposures increase the risks for specific adverse health effects, and if so, what public health actions are necessary to reduce the risks. In particular, the study should provide a basis for early medical intervention for health outcomes that are not routinely evaluated in physical exams. The study should also be relevant to other populations with similar exposures.

In addition to the above criteria, a feasibility assessment must address specific questions:

1. Can the study population be enumerated and selected to minimize selection bias? (Selection bias occurs when the probability of selection is related both to exposure status and to disease status.)
2. Is there an appropriate comparison population?
3. Is there a complete exposure pathway, well-defined exposed population, and ability to assign levels of exposure with adequate accuracy?
4. Is there justification for studying the specific health outcome(s) being considered? (e.g., is there suggestive biological evidence? A finding in a previous study?)
5. Can the health effect(s) be validly ascertained or measured?
6. Is the exposed population sufficiently large so that risks can be estimated with precision?
7. Can information be obtained on other risk factors that need to be taken into account?
8. Can a study answer the questions of concern to the Pease community?

Site history

The Pease International Tradeport is located in Portsmouth, New Hampshire. It contains over 250 companies employing more than 9,525 people. In 1993, companies began to operate at the Pease Tradeport. Two day-care centers are located at the Tradeport. One of the day-care centers estimated that about 695 children attended the center during 1996–2016. The other day-care center could not easily compile total enrollment statistics, but its capacity is 220 children, they usually enroll about 180–195 children at a time, and they have been operating for almost 7 years. As of July 2015, the estimated population of Portsmouth was 21,530 (**http://www.census.gov/quickfacts/table/PST045215/3362900**). According to the 2010 census, 4.7% were children younger than 5 years, 11.9% were children ages 6–17 years, 67.5% were adults ages 18–64 years, and 15.9% were adults ages 65 years and older. Additionally, 51.5% of the population were female, 91.5% were white, and 95.6% of persons ages 25 years and older were high school graduates.

The area on which the Tradeport is located was originally built in 1951 as part of the Pease Air Force Base. In October 1989, 3,465 military personnel were assigned to the base, accompanied by 4,746 dependents. The Air Force estimated that 537 civilian employees worked on-base at that time (ATSDR 1999). During 1970–1990, an average of 3,000 personnel and their families were assigned to the base at any one time. Before 1970, the base supported a maximum of 5,000 personnel (ATSDR 1999).

Three major supply wells provided drinking water to the base: the Haven, Smith, and Harrison wells. Before 1981, the wells fed directly into the distribution system so that a particular area of base would primarily receive water from the nearest well. After 1981, the water from the three wells were mixed together and treated before entering the distribution system. These same three supply wells provided drinking water to the Pease Tradeport after it opened.

In 1977, water from the base wells was found to contain trichloroethylene (TCE). Two of the three wells serving the base were contaminated. The maximum concentrations of TCE measured in the Haven and Harrison supply wells were 391 micrograms per liter (µg/L) and 28.5 µg/L, respectively. After the discovery of the contamination, those wells were shut down and the city of Portsmouth supplied drinking water to the base during 1977–1978. In the fall of 1978, the wells were back in operation. TCE levels in the Haven well fluctuated between 50 µg/L and 115 µg/L from the fall of 1978 through January

1980, then fell below 50 µg/L, with an occasional spike above 50 µg/L through October 1980. From November 1980 through July 1981, TCE levels averaged about 30 µg/L, then fell to around 10 µg/L from August 1981 through May 1983. Levels continued to decline, but did not remain consistently below the current U.S. Environmental Protection Agency (EPA) maximum contaminant level (MCL) in drinking water of 5 µg/L until January 1986 (ATSDR 1999).

The base officially closed in October 1991, and most of the property was transferred to the Pease Development Authority (PDA). During 1993, the business and aviation industrial park began operation. The City of Portsmouth entered into a long-term lease and operation agreement with the PDA to operate and maintain the public water system serving the Tradeport.

From approximately 1970 until the base closed, aqueous film-forming foam (AFFF) was used to extinguish and prevent flammable liquid fires. AFFF was also used during firefighting training at the base. Through 2001, perfluoroalkyl substances (PFAS) were used in the manufacturing of AFFF, including perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), and perfluorohexane sulfonate (PFHxS). AFFF containing PFAS likely leached into the soil and groundwater and migrated to the three supply wells serving the Pease Tradeport. It is not known when these wells were contaminated with PFAS, but it is possible that the contamination began before the opening of the Tradeport, when the Air Force base was still in operation.

The Haven, Smith and Harrison wells have also served the Tradeport. In addition, the City of Portsmouth has the capability to supply water to the Tradeport via its main distribution system. Monthly pumping records for the three wells were provided by the City of Portsmouth, Department of Public Works. Up through 1999, the Haven well on average provided about 56% of the total water supply at the Tradeport, with the Smith well providing 44% and the Harrison well out of service. In 2000-2001, the Haven well supplied 88% of the supply and the Smith well supplied 12%. From 2003 until it was taken out of service in May 2014, the Haven well on average supplied about half the water supply. By 2006, the Harrison well was back in service and the Smith and Harrison wells together supplied on average about half of the water supply at the Tradeport. After May 2014, the Smith and Harrison wells supplied 56% of the Tradeport water supply and the City of Portsmouth provided the other 44%.

In 2009, EPA established provisional health advisory levels for PFOS and PFOA of 0.2 µg/L and 0.4 µg/L, respectively [US EPA 2009]. In 2013, sampling of monitoring wells at the former Pease Air Force Base fire training areas detected PFOS and PFOA above these EPA provisional health advisory levels. In May 2016, EPA established a new lifetime health advisory for PFOS and PFOA that said the combined concentrations of PFOS and PFOA in drinking water should not exceed 0.07 µg/L [US EPA 2016a]. No drinking water health advisory level has been established for PFHxS or other PFAS chemicals. While the EPA has a lifetime health advisory for PFOS and PFOA, no federal regulatory standards for these contaminants have been issued.

In April and May 2014, the three supply wells serving the Tradeport were sampled for PFAS. In the April sampling, the Haven well had PFOS, PFOA, and PFHxS levels of 2.5 µg/L, 0.35 µg/L, and 0.83 µg/L, respectively. In the May sampling, the Haven well had PFOS, PFOA, and PFHxS levels of 2.4 µg/L, 0.32 µg/L, and 0.96 µg/L. Other PFASs were also detected in the Haven well. The Harrison well had much lower levels of these contaminants with maximum PFOS, PFOA, and PFHxS levels of 0.048 µg/L, 0.009 µg/L, and 0.036 µg/L, respectively. The Smith well had maximum levels of PFOS and PFHxS of 0.018 µg/L and 0.013 µg/L, respectively, with an estimated level of PFOA of about 0.004 µg/L.

No samples of the Pease Tradeport distribution system for PFAS are available from the period when the Haven well was in operation. We can use a simple mixing model to estimate the PFAS levels in the distribution system, assuming that contamination concentrations are approximately uniform throughout the system. The model takes into account the pumping rates for each of the three wells, the total water demand, and the concentrations of PFAS in the wells during the April and May 2014 sampling. Using this simple approach, the estimated levels of PFOS, PFOA, and PFHxS in the Pease Tradeport distribution system in April 2014 would be approximately 1.4 µg/L, 0.2 µg/L, and 0.5 µg/L, respectively.

In April 2015, the City of Portsmouth created a community advisory board (CAB) to address the PFAS contamination in the Tradeport drinking water. The CAB was established to act as a liaison between the affected community and the New Hampshire Department of Health and Human Services (NH DHHS), to represent the diverse views of the affected community, to review the blood testing conducted by NH DHHS, and to provide input into future direction of the blood testing program (CAB 2015). The CAB held 14 public meetings during May through December 1, 2015, and disbanded after issuing its final report of its activities on December 21, 2015. Among the recommendations of the CAB in its final report were the following:

1. Establish a community body to coordinate ongoing issues with ATSDR, NH DHHS, and the U.S. Air Force's Restoration Advisory Board at Pease and to provide an effective mechanism for communication with all persons working or cared for at the Pease Tradeport.

2. A new community body should, along with its partner agencies, provide health education to the public regarding environmental chemical exposures and how exposures and risks can be reduced.

In February 2016, ATSDR began recruiting community volunteers to serve as members of a Pease community assistance panel (CAP). Technical advisors who could help CAP members in reviewing the scientific information on PFAS and proposed health activities were also recruited. The purpose of the CAP was to provide a mechanism for the community to participate directly in ATSDR's health activities related to the exposures to the contaminated drinking water at the Tradeport. The CAP would provide input concerning possible health activities proposed by ATSDR. CAP members would also work with ATSDR to gather and review community health concerns, provide information on how people might have been exposed to hazardous substances, and inform ATSDR about ways to involve the community. The first public meeting of the CAP was held in May 2016 in Portsmouth. The second public meeting was held in September 2016. ATSDR has also convened monthly calls with the CAP.

Community concerns

The final report of the CAB, issued on December 21, 2015, noted that "...the lack of any definitive information regarding the possible health effects of PFC [perfluorinated compound] exposure remains a source of frustration and concern." [CAB 2015] The report concluded, "There is a great need to better understand what if any health effects might result for PFC exposure, and at what levels of exposure these risks might be manifested."

In an email sent to ATSDR in November 2015, the CAB asked that ATSDR consider the following question: "What, if any, long-term health effects, such as specific cancers, elevated blood lipids, thyroid

function, immune function and developmental delays, are associated with the PFC exposure at Pease? This question should be broken down with regard to specific populations including children, nursing/pregnant women, firefighters, and adult exposed workers." This question was reiterated at the first in-person CAP meeting in May 2016. Some CAP members, as parents, were very concerned about the health of their children who were exposed at a critical, early age of development while attending the two day-care centers at the Pease Tradeport. They noted the lack of pediatric studies associated with PFAS exposure and wanted ATSDR to consider testing the exposed children for health endpoints such as lipids. CAP members also voiced concern about the exposed adult population, especially former military service personnel and civilian workers at the former Pease Air Force Base. Concern was also expressed for firefighters who were exposed to contaminated drinking water at Pease and also directly to AFFF as part of their firefighting duties. CAP members expressed their desire for a longitudinal approach (compared to a cross-sectional approach) to evaluate short-term and long-term health conditions, including cancers.

Exposure assessment

Using the information currently available on PFAS concentrations in the supply wells during April and May 2014, supply well pumping data, the total demand in the system, and assuming that PFAS concentrations in the supply wells during the April–May 2014 sampling reflect historical concentrations (given the persistence of these chemicals in the environment), a simple but crude assessment of PFAS drinking water exposures could be conducted. However, to accurately estimate historical PFAS concentrations in the Haven, Harrison, and Smith supply wells and the distribution system they served, both during the operation of the Air Force base and the Tradeport, would require the following steps:

1. Obtain information on the locations and use of AFFF at the Air Force base, including accidental releases.

2. Model the migration of contaminants from the soil where AFFF was used or released to the groundwater and then to the supply wells.

3. Model the PFAS concentrations throughout the distribution system.

Historical reconstruction of PFAS concentrations in the drinking water distribution system would be needed to assess exposures to service personnel and civilian employees who were at the Air Force base during its operations, and to workers and day-care attendees at the Tradeport.

Another important source of information on exposures at the Pease Tradeport was the NH DHHS PFAS blood testing program conducted during April–October 2015. A person was eligible for this program if he or she had worked at, lived on, or attended childcare at the Pease Tradeport or Pease Air Force Base, or lived in a home near the Pease Tradeport that was served by a PFAS-contaminated private well. A total of 1,578 persons volunteered to submit a blood sample for PFASs testing [NH DHHS 2016]. This was a convenience (or volunteer) sample, not a statistically based sample. Nevertheless, the testing program provided important information on the extent and magnitude of exposures to the PFAS-contaminated drinking water at the Pease Tradeport.

Table 1 shows the serum concentrations of PFOS, PFOA, PFHxS, and perfluorononanoic acid (PFNA) for the 366 children younger than 12 years at the time of testing and comparison values from studies conducted in Texas [Schecter 2012] and California (Wu 2015). Data from the National Health and

Nutrition Examination Survey (NHANES) are not available for children younger than 12 years. NHANES testing for serum PFAS was restricted to those ages 12 years and older. The California study [Wu 2015] conducted a random sample of households in northern California and obtained blood samples from 68 children ages 2–8 years for PFAS analyses during December 2007–November 2009. The parents of the children had higher education levels than the general population. The Texas study [Schecter 2012] analyzed serum samples collected from 300 children ages ≤12 years at a children's hospital during 2009. Whether the children in the Texas study were healthy or receiving treatment for illness was not reported. None of the California and Texas children were known to be exposed to PFAS-contaminated drinking water. The children in both studies were considered to be representative of general population exposures to PFAS via diet and consumer products.

Table 1 shows that the median and geometric mean serum PFHxS and PFOS levels in the Pease children (ages <12 years) are considerably higher than background median and geometric mean levels seen in the Texas and California studies. For PFOA, the Pease children have slightly higher levels than the reference group in the Texas study, but lower than in the California study. However, the comparisons with Texas and California results might not be appropriate given the difference in sampling years. Nationally, serum levels of PFOS and PFOA have been declining sharply over time. For example, in the 1999–2000 NHANES cycle, the geometric mean serum PFOA level for persons aged ≥12 years was 5.2 µg/L. By the 2013–2014 cycle, it had declined to 1.9 µg/L. Serum PFOS declined even more sharply, from 30.4 µg/L during the 1999–2000 cycle to 5.0 µg/L in the 2013–2014 cycle. PFHxS also declined, but more gradually, from 2.1 µg/L during the 1999–2000 cycle to 1.3 µg/L in the 2013–2014 cycle. In the NHANES 2013–2014 cycle, children ages 12–19 years had geometric mean PFOA, PFOS, and PFHxS serum levels of 1.66 µg/L, 3.54 µg/L, and 1.27 µg/L, respectively. Therefore, the most appropriate PFAS comparison values for the Pease blood testing program would be serum levels obtained near in time to the Pease sampling (i.e., 2015). Such comparison values are not currently available.

Table 2 shows the serum concentrations of PFOS, PFOA, PFHxS, and PFNA for the 1,212 participants ages 12 years and older at the time of testing and comparison values from NHANES for 2013–2014 (the most recent years data are currently available). Table 2 indicates that, similar to the children at Pease, the median and geometric mean serum levels of PFHxS and PFOS among those ages ≥12 years are considerably higher than those in the NHANES 2013–2014 cycle. The median and geometric mean serum PFOA among those at Pease were also slightly elevated compared with NHANES results.

In analyses conducted by NH DHHS, geometric mean PFHxS serum levels were higher for persons who drank ≥4 cups of water per day compared to those who drank <4 cups per day. Of all the PFAS serum levels measured, water consumption had the strongest effect on PFHxS serum levels. In particular, water consumption had the highest effect on PFHxS serum levels among persons aged ≤19 years ($\beta = 0.31$, SE = 0.15, marginal effect = 36.4%). Geometric mean PFOS and PFOA serum levels were also higher among persons who drank ≥4 cups of water per day compared with those who drank <4 cups per day [NH DHHS 2016]. Linear trends were observed for geometric mean serum levels of PFOS, PFOA, and PFHxS and increasing time spent at the Pease Tradeport. The trend was strongest for PFOS and PFHxS [NH DHHS 2016].

Summary of literature review

ATSDR reviewed published health studies to identify health-related endpoints that have been studied and the data gaps that exist, in particular, for the effects of PFHxS and PFOS. The literature review also was used to identify adverse effect sizes observed in the PFAS studies for PFAS serum levels similar to those found in the Pease population.

The Appendix has a listing of the epidemiological literature on PFAS exposures and adult cancers, other adult diseases, and adverse outcomes in children. Tables 3 and 4 provide a summary. In these tables, a "+" indicates that at least one study had a finding for a specific PFAS chemical that suggests an increased risk of an adverse outcome (e.g., an odds ratio [OR] or risk ratio [RR] of ≥1.20), and a "*" indicates that no study has been conducted for that PFAS chemical. In these tables, an "I" indicates that the findings from studies have not suggested an increased risk for an adverse outcome (e.g., all odds ratios or risk ratios are <1.20) but the information is too limited to conclude that there is no association between the PFAS exposure and the adverse outcome.

These tables are for illustrative purposes, to indicate where data gaps exist and therefore additional research may be needed. Tables 3 and 4, and the tables and descriptions of the studies in the appendix, should not be interpreted as implying causation or as an assessment of the weight of evidence for an association. Currently, epidemiological research on the health effects of PFAS exposures is at an early stage. This is particularly true for PFHxS in addition to PFAS chemicals other than PFOA and PFOS. However, even for PFOA and PFOS, additional research on all the health-related endpoints mentioned in these tables will be needed to provide sufficient evidence for causal assessments and to address community health concerns.

Adult cancers and other adult diseases

Based on its assessment of the epidemiological literature, ATSDR concluded that there was limited or no information concerning associations with PFAS exposures and most cancers and other adult diseases (Table 3). In particular, very few studies have evaluated PFHxS exposures and cancers and other adult diseases. Although more information is available for PFOS exposures and cancers and other adult diseases than for PFHxS exposures, the information is still very limited and therefore inadequate to determine whether PFOS exposures increase the risk for most of the adult diseases evaluated. Although more information is available on PFOA exposure, the information is still too limited to determine whether a causal association exists between PFOA and specific cancers and other adult disease. Therefore, additional research on the effects of PFHxS, PFOS, and PFOA would be needed to determine whether exposures increase the risk for many adult cancers and non-cancer diseases.

Health effects in children

There is some evidence that PFAS exposures are associated with decreased birth weight, small fetus size for gestational age, measures of intrauterine growth retardation, and preterm birth. In particular, two meta-analyses have found an overall decrease in birthweight associated with PFOA and PFOS [Verner 2015; Bach 2015]. However, the findings across studies are inconsistent for these outcomes and for other adverse birth outcomes, and few studies have evaluated PFHxS. Several studies of infants have

found that prenatal PFAS exposures affect thyroid function, but only two studies have evaluated thyroid function in older children. A few studies have found elevated uric acid with PFAS exposures, but the possibility of reverse causation cannot be ruled out. Four studies of PFAS exposures and testosterone and other sex hormones have been conducted. However, the findings have not been consistent across studies and further research is needed. Three of the studies did find that PFAS exposures decreased testosterone in boys or girls. There is some evidence from four studies that PFAS exposures might be associated with ADHD, but findings have not been consistent across studies. Evaluating the evidence for PFAS exposures and neurobehavioral outcomes is difficult for several reasons: 1) the studies used different methods to measure the outcomes, 2) studies are inconsistent in the outcomes evaluated, and 3) too few studies have been conducted. A few studies have found associations between PFAS exposures and a decline in antibody response to specific vaccines, but only two studies evaluated the same vaccine (i.e., rubella). In summary, there are considerable data gaps concerning the health effects in children of PFAS exposures. This is because of the small number of studies conducted, inconsistencies in methods and findings across studies, and limited sample sizes in some studies. As for other adverse outcomes, few studies have evaluated the effects on children of PFHxS exposures.

Sources of adverse outcome data for the Pease population

The adverse outcomes of interest for PFAS exposure that can be ascertained from the birth certificate are pregnancy-induced hypertension, diabetes, small for gestational age (SGA), low birth weight, birth weight, preterm birth, and gestational age. Although the birth certificate has a checklist for congenital anomalies, the most reliable data on birth defects are provided by population-based birth defect registries. Birth defects registries exist in 41 states, including New Hampshire. The New Hampshire Birth Conditions Program (NHBCP), based at the Geisel School of Medicine at Dartmouth College, began collecting data on births occurring in-state to New Hampshire residents in 2003 (http://www.cdc.gov/ncbddd/birthdefects/states/newhampshire.html). Data reported on 46 different birth defects are ascertained for infants aged ≤1 year are collected through active surveillance methods. Congenital hypothyroidism data can be obtained from the newborn screening program. Newborn screening for congenital hypothyroidism is conducted in every state, including New Hampshire.

The birth certificate has information on sex of the child, plurality, gestational and pre-pregnancy diabetes, previous preterm birth, parity and gravidity, cigarette smoking before and during pregnancy, principal source of payment for the delivery (a measure of socio-economic status), date of last pregnancy, date of last normal menses, date of first and last prenatal care visit and total number of prenatal care visits, race/ethnicity of the mother and father, education of the mother and father, parents' names and address, mother's marital status, labor and delivery complications, and whether the infant is being breastfed at discharge. The New Hampshire Division of Vital Records Administration collects information on births in New Hampshire from hospitals and midwives, birth certificates, and interstate exchange agreements for births occurring out-of-state to New Hampshire residents (http://www.dhhs.nh.gov/dphs/hsdm/birth/).

Mortality information is available from the National Death Index (NDI) operated by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention. Currently, 2014 data are complete and available for searches. "Early release data" for 2015 are ≥90% complete (98% complete for New Hampshire) and also available for searches. NDI "plus" provides information on cause of death (underlying, contributing and all other causes of death listed on the death certificate) and date and state of death based on death certificate data provided by the states. The NDI has data starting from 1979.

New Hampshire death certificate data are available from the New Hampshire Division of Vital Records Administration, which collects information on deaths of New Hampshire residents and deaths occurring in New Hampshire (http://www.dhhs.nh.gov/dphs/hsdm/death/index.htm). Information on deaths of New Hampshire residents that occur out-of-state is captured through interstate exchange agreements. Information on underlying cause of death and up to 14 contributing causes of death is collected. Complete data are available approximately 24–48 months after the close of a calendar year.

Population-based cancer registries exist in all 50 states and Washington, DC. The New Hampshire State Cancer Registry (NHSCR) is a statewide, population-based cancer surveillance program that has collected incidence data on all cancer cases diagnosed or treated in the state since 1985 (http://geiselmed.dartmouth.edu/nhscr/). NHSCR, which is contracted to the Geisel School of Medicine at Dartmouth College, currently collects data from the larger hospitals in the state. NHSCR also receives case reports from physician practices, free standing radiation oncology centers, pathology laboratories and other sources. NHSCR staff assist hospitals with fewer than 100 cases per year with reporting. Through interstate data exchange agreements, NHSCR also receives case reports for New Hampshire residents who are diagnosed outside the state.

The New Hampshire Uniform Hospital Discharge Data Set (UHDDS) collects discharge data from all health care facilities in the state (acute care hospitals, specialty hospitals, freestanding hospital emergency facilities, and walk-in urgent care centers), as required by law (http://www.dhhs.nh.gov/dphs/hsdm/hospital/index.htm). Discharge data from Maine, Massachusetts, and Vermont hospitals for New Hampshire residents are included in the UHDDS via interstate data exchange agreements. The dataset includes transfers of NH residents. Chronic diseases such as asthma, chronic obstructive pulmonary disease, angina, hypertension, congestive heart failure, hypoglycemia, and diabetes are included in the UHDDS. Limitations of this dataset are that discharges are not de-duplicated and one person with multiple admissions might falsely increase the number of persons hospitalized. Additionally, state law requires health care professionals to report information on chronic health conditions relating to children, infectious diseases, immunizations, and autism to NH DHHS (http://www.healthinfolaw.org/state-topics/30,67/f_topics).

To ascertain autism or ADHD reliably, a review of school special education records and medical records from providers that conduct developmental evaluations of children or provide treatment is necessary. In Portsmouth, records are available from three elementary schools (serving grades K–5), one middle school (serving grades 6–8), and one high school (serving grades 9–12). Projected enrollment for the 2016–17 school year was 988 students in the elementary schools, 516 students in the middle school, and 1,183 students in the high school (http://cityofportsmouth.com/school/FY16BudgetBooklet.pdf). In school year 2015–2016, the Portsmouth Public Schools provided special education services to 416 students. Among those students, 121 (29.1%) had an orthopedic impairment, 36 (8.7%) had a speech/language impairment, 32 (7.7%) had a developmental delay, 25 (6.0%) had autism, 17 (4.1%) had an emotional disturbance, 11 (2.6%) had some other disability, and 174 (41.8%) were classified as having a "specific learning disability."

Various studies have focused on West Virginia and Ohio residents and workers exposed to PFOA from a chemical plant (the "C8" studies) [Frisbee 2009]. In a C8 study that evaluated ADHD, affected persons were identified via questionnaire, which included a question requesting information on medications used [Stein 2011]. For chronic diseases, the C8 studies relied primarily on self-reported information from questionnaires with attempted confirmation of self-reports by obtaining medical records.

Sources of exposure data

An important source of exposure information is PFAS biomonitoring. Measuring serum levels of PFAS chemicals provides information on the amount of these chemicals that has entered the body from all sources. At Pease, 1,578 persons volunteered to submit blood samples for PFAS analyses during the NH DHHS biomonitoring program in 2015. In the C8 study, blood samples for PFAS analyses were obtained from 66,899 persons during the 13-month baseline period, 2005–2006 [Frisbee 2009]. Biomonitoring for PFAS is useful in estimating past exposures, given the long half-lives of PFOS (approximately 5.4 years) and PFHxS (approximately 8.5 years). Although biomonitoring integrates PFAS exposures from all sources, including diet and consumer products, PFAS levels in serum from populations exposed to PFAS-contaminated drinking water will mostly reflect the drinking water exposures, unless the person is or was also exposed occupationally (e.g., firefighters, PFAS manufacturing workers).

The use of PFAS biomonitoring in epidemiological studies has some limitations. A key limitation is the issue of "reverse causation," in which the disease under investigation (e.g., kidney disease or kidney function) affects the elimination of PFAS in the body, causing higher serum levels of PFAS. Other problems include potential confounding by a factor that is both a risk factor for the disease of interest and a factor influencing serum PFAS levels (e.g., parity in the evaluation of adverse birth outcomes). Another limitation is that biomonitoring results, by themselves, might not provide sufficient information to estimate historical exposures. Estimating historical exposures is necessary to assess cumulative exposure and to characterize periods of special vulnerability to PFAS exposures, such as prenatal or early childhood exposures.

Modeling methods are used to reconstruct historical PFAS serum levels. The results of PFAS biomonitoring can be used to validate estimates of PFAS serum levels obtained from modeling. C8 researchers have successfully used physiologically based pharmacokinetic modeling of absorption, distribution, metabolism, and excretion of PFOA in the body in conjunction with drinking water contaminant levels, estimates of water intake, and residential history to predict historical and current PFOA serum levels [Shin 2011]. Researchers have also been able to simulate PFOS serum levels using information on drinking water levels and PBPK modeling [Loccisano 2011]. Therefore, reconstruction of historical PFOS serum levels is also feasible. However, reconstruction of PFOA and PFOS serum levels is limited by various uncertainties. These include lack of accurate information on individual consumption of drinking water and length of time exposed and limited information on factors that produce inter-individual variability (e.g., gender, age) and pre-existing medical conditions (e.g., compromised renal function) [Loccisano 2011]. Nevertheless, the ability to predict serum PFOS and PFOA levels based on drinking water contamination levels can substitute for, and enhance, the information provided by PFAS biomonitoring.

Issues concerning cross-sectional study designs

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]. However, if the cross-sectional study concurrently measures the exposure and the outcome (i.e., the disease or effect biomarker), then it might be difficult to determine whether the exposure caused the outcome or whether the outcome influenced the measured exposure level [Flanders 1992, 2016]. For example, as discussed above, the concurrent measurement of serum PFAS levels and kidney function biomarkers might raise

the question of "reverse causation" because kidney function can affect the levels of PFAS in serum. This issue can be addressed by estimating exposures based on the historical reconstruction modeling of serum PFAS levels. In addition, it might be possible to estimate exposures during critical vulnerable periods (e.g., in utero exposure) through the modeling of historical serum PFAS levels. However, the modeling of historical PFAS serum levels is subject to uncertainties and data limitations, as discussed above, and published methods are available only to model serum levels of PFOA and PFOS.

Other issues concerning cross-sectional study designs are similar to those that confront other observational study designs, such as cohort studies. These issues include: 1) the ability to clearly define, enumerate and recruit (without introducing selection bias) the exposed and comparison populations, 2) the comparability of the exposed and comparison populations on risk factors other than the PFAS exposures, 3) accurate exposure assessment, and 4) accurate measurement of effect biomarkers and ascertainment of diseases.

Based on its review of the literature, ATSDR concludes that several health-related endpoints could be considered for studies of the Pease population. It is also clear that exposures to the PFAS-contaminated drinking water have occurred in the Pease population, as documented by the observed serum PFAS levels in the NH DHHS PFAS blood testing program. Therefore, it is reasonable to conduct epidemiological 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. The usual approach to determine the necessary size of the study population for each health-related endpoint is to conduct sample size calculations.

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. No single study of the Pease population will provide definitive answers to the community about whether their exposures to the PFAS-contaminated drinking water caused their health problems. The ability of a study of the Pease population to provide useful information will depend to a great extent on the success of recruiting a sufficient number of study participants.

Feasibility of an epidemiological study of children at the Pease Tradeport

The first population that ATSDR considered for an epidemiological study was the children who attended the two day-care centers at the Pease Tradeport. One reason to focus on children is that they are more vulnerable to environmental exposures, in particular exposures to potential endocrine-disrupting chemicals. In addition, there is serious concern in the community about the possible health effects to children from the drinking water exposures, which was conveyed to ATSDR by the Pease CAP. Finally, a study of children who attended daycare at the Pease Tradeport is the most feasible epidemiological study to conduct. The population is less transient than an adult population and the adverse health endpoints of interest do not require as large a sample size as adult chronic conditions.

The public health significance of conducting a study of these children consists of 1) the possibility of early intervention if early signs of adverse health effects, including developmental delays, are observed and 2) the relevance of a study at Pease for other populations exposed to drinking water primarily

contaminated with PFOS and PFHxS. A study of children at Pease would have scientific importance because of key data gaps concerning PFAS exposure effects on sex hormones and on neurobehavioral, immunological, and thyroid function. Animal studies support the biological plausibility of immune effects. Animal data also suggest that PFAS might be developmental neurotoxicants that can alter cognitive function and reduce learning ability. PFAS also have endocrine-disruptive properties and could interfere with thyroid function and sex hormones. A study of children at Pease would be responsive to the community's concerns and has the potential (from the perspective of statistical power) to provide meaningful and credible results for some of the adverse outcomes of interest. However, a study limited to the population of children who attended the Pease Tradeport day-care centers would likely not be sufficiently large for some of the possible adverse outcomes of interest (e.g., higher prevalences of rare diseases or very subtle changes in biomarkers of effect that have been observed in research conducted elsewhere).

A. Study population

The population of interest could be persons who attended day care at the Pease Tradeport before June 2014 and are in the age range of 4–16 years at the start of the study. The end of the period was selected because the Haven well was taken out of service in May 2014. 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 age range for the Pease children study was determined by taking into account the age ranges in previous PFAS studies and the age range appropriate for the candidate endpoints. Previous epidemiological studies of children exposed to PFAS included varying age ranges. Because of data limitations (i.e., no PFAS serum data for those aged <12 years), the studies that used NHANES data evaluated those aged 12–18 years or 12–19 years. Some of the C8 studies limited participant ages to those <12 years; other C8 studies included persons up to 18 years of age. The upper age limit for many of the Taiwan children studies of PFAS was 15 years. An age range of 4–16 years would overlap the age ranges in these studies.

The chosen age range also reflected the focus of the study (i.e., children exposed to the PFAS-contaminated drinking water while attending daycare at the Pease Tradeport). The younger age limit of 4 years was chosen because intelligence quotient (IQ) testing is available for those aged 4 years and older. (For example, the Wechsler Preschool and Primary Scale of Intelligence test has an age band of 4 years to 7 years, 7 months that overlaps the Wechsler test for those aged 6–16 years.) The Strengths and Difficulties Questionnaire (SDQ), a behavioral screening questionnaire used in a Faroes study [Oulhote 2016], a Taiwan study [Lien 2016] and a Danish study [Fei 2011] has an age range of 4 – 16 years. The upper age limit of 16 years was chosen for three reasons:

1. Age at puberty was a candidate endpoint and virtually all of the children in a C8 study achieved puberty by age 16 years.

2. The IQ and SDQ testing instruments for children have an upper age limit of 16 years.

3. Children aged >16 years would have been last exposed (i.e., last attended daycare) more than 10 years ago.

Table 5 provides the data on serum PFOS, PFOA, and PFHxS for the 370 children who participated in the 2015 NH DHHs testing program at Pease and who were aged 1–13 years at the time of blood draw. These children would be aged 4–16 years in 2018. The geometric mean serum PFHxS in these children was 3.80 μg/L, approximately three times higher than the serum levels reported in the Texas [Schecter 2012] and California [Wu 2015] studies and in the NHANES data for 2013–2014.

We currently do not know how many children attended daycare at the Pease Tradeport before June 2014 and who would be in the 4–16 years age range in 2018. The Discovery Child Enrichment Center is located at the Pease Tradeport and began operation in 1994. Its yearly enrollment is approximately 149 children ages 6 weeks to 5 years. Computerized records at this day-care center start in 1996. A preliminary records search by the director of the Discovery Child Enrichment Center identified 695 children who attended the daycare during 1996–2015 and who would be aged of 6–18 years in 2018. Based on the results of this search, the number of children who attended this day care prior to June 2014 and would be between the ages of 4 and 16 years in 2018 could be within the range of 250 – 450 individuals.

The Great Bay Kids' Company is also located at the Pease Tradeport and began operation in 2010. Its annual enrollment is approximately 270 children aged ≤12 years. Assuming that most of the children enrolled would be ≤5 years of age, and that most of the children attend daycare for 4 years, about 300 children might have attended this daycare during the period of interest and would be aged 4–16 years in 2018.

Assuming that a minimum of about 500 children attended the two day-care centers at Pease before June 2014 and would be aged 4–16 years in 2018, and assuming a reasonable participation rate of 70%, it would be possible to recruit 350 Pease children into the study. It would also be feasible to recruit at least 175 children in the same age range from the public 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. It is reasonable to assume that participation rates would be high because of strong interest in the community concerning the Pease Tradeport situation. Moreover, the Pease CAP members have pledged to support recruitment efforts if and when a study is to be conducted. Pease CAP members have strong ties and are active in the Portsmouth community. If the actual number of children who attended the two day-care centers prior to June 2014 and would be aged 4 – 16 years in 2018 is in the range of 650 – 750, then as many as 500 children could be recruited from the Pease population. It should also be possible to recruit at least 250 children in the same age range from the Portsmouth public schools for the unexposed group.

A sample size of 350 exposed children and 175 unexposed children would be similar to the sample sizes used in the Faroes study [Grandjean 2012, 2016] and in a C8 study of 320 exposed children [Stein 2013, 2014b]. However, the sample size of 350 exposed and 175 unexposed would be considerably smaller than most of the C8 children studies and some of the other epidemiological studies of children exposed to PFAS. Therefore, a total of 525 children, 350 exposed and 175 unexposed, should be considered a minimum sample size, and attempts should be made to recruit a higher number of exposed and unexposed children to improve the statistical power of the study.

B. Study Hypotheses

As indicated in the literature review summary, the scientific literature has little information on the health effects of exposures to PFHxS. PFHxS is a key contaminant associated with the use of AFFF for firefighting training and extinguishing flammable liquid fires. The study would be an important contribution in filling this data gap and would generate knowledge relevant to other populations exposed to drinking water contaminated by PFHxS from the use of AFFF. In addition, few studies have been conducted to evaluate possible associations between childhood exposures to PFASs and effects on thyroid function, uric acid and sex hormone levels, delays in reaching puberty, IQ, and immune function. Inconsistent findings have been observed for most of these endpoints, likely in part because of differences in exposures (e.g., drinking water and other sources, such as diet) and PFAS levels of exposure, study population differences (e.g., age differences), and differences in methods. Moreover, few studies have evaluated the same neurobehavioral or immune endpoint. The study would address these issues by using methods and evaluating health effects similar to those used in previous studies of PFAS exposures in children, in particular, methods used in the C8 studies.

Based on the literature review, the following hypotheses could be evaluated:

1. Higher serum levels of PFOA, PFOS, or PFHxS are associated with higher total cholesterol, low-density lipoprotein, and triglycerides, and higher prevalence of hypercholesterolemia.

2. Higher serum levels of PFOA, PFOS, or PFHxS are associated with differences in thyroid stimulating hormone (TSH), TT4, and TT3, and a higher prevalence of hypothyroidism.

3. Higher serum levels of PFOA, PFOS, or PFHxS are associated with a higher level of uric acid and a higher prevalence of hyperuricemia.

4. Higher serum levels of PFOA, PFOS, or PFHxS are associated with differences in testosterone, estradiol, and sex hormone-binding globulin (SHBG).

5. Higher serum levels of PFOA, PFOS, or PFHxS are associated with delayed puberty.

6. Higher serum levels of PFOA, PFOS, or PFHxS are associated with lower IQ.

7. Higher serum levels of PFOA, PFOS, or PFHxS are associated with ADHD behaviors and learning problems.

8. Higher serum levels of PFOA, PFOS, or PFHxS are associated with a higher prevalences of hypersensitivity-related outcomes (e.g., asthma, rhinitis infectious diseases).

9. Higher serum levels of PFOA, PFOS, or PFHxS are associated with lower antibody responses to rubella, mumps, and diphtheria vaccines.

C. Recruitment and Consent

Based on sample size calculations (see Appendix), a minimum of 350 exposed children aged 4–16 years who attended the day-care centers at Pease before June 2014 would need to be recruited. To recruit the children who participated in the blood testing program, NH DHHS would have to send letters to the

parents to ask that their child participate in the study. Additional children who were exposed to the contaminated drinking water while attending the two day-care centers could be recruited via outreach to the two day-care centers at Pease, the Portsmouth public schools, media, and community organizations in the Portsmouth area. The Pease CAP has also offered to assist in recruitment, and CAP involvement will be crucial in achieving high participation rates.

A minimum of 175 children aged 4–16 years, who were unexposed to the PFAS-contaminated drinking water at the Pease Tradeport and whose mother did not work at the Pease Tradeport (or in an occupation that involved PFAS exposure) during the pregnancy and breastfeeding of the child would be recruited from the Portsmouth, NH, public schools. Before enrollment in the study, the child's mother would be interviewed to determine whether the child is eligible for the study. Recruitment would involve outreach to the eight day-care centers in Portsmouth that were located outside the Pease Tradeport, the Portsmouth public schools, media, and community organizations. The Pease CAP has offered to help with the recruitment effort. The total enrollment of Portsmouth's elementary, middle, and high schools is projected to be 2,687 in 2016–17. To encourage participation of exposed and unexposed children, an appropriate incentive would be provided.

The Pease blood testing program's consent form was strictly limited to the use of the participant's blood sample for PFAS analyses only. The participant also consented to complete a brief questionnaire at the time of blood draw concerning demographic information, time at Pease Tradeport, and consumption of drinking water. The consent form did not mention the use of the blood sample for research purposes or the possibility of re-contacting the participant for future studies. Moreover, the amount of blood drawn from the children was only sufficient for the PFAS analyses. Therefore, ATSDR cannot directly contact the participants in the Pease blood testing program to recruit them for a children's study. In addition, these participants must sign a new consent form to participate in a research study.

A parent of each child would be asked to sign a parental permission form requesting a blood sample (about 4 teaspoons or 20 mL) from the child for the analyses of PFASs and the effect biomarkers (i.e., lipids, TSH, uric acid, sex hormones, and immune function parameters). The consent form would also ask that the child be administered the Wechsler Abbreviated Scale of Intelligence (IQ) tests if aged 6 years or older or the Wechsler Preschool and Primary Scale of Intelligence for children younger than 6 years. The consent form would ask permission to access the child's school records, including special education records. The parent would be asked to sign a consent form to complete a questionnaire. Children ages 7 years and older would be asked to give their assent to participate in the study.

D. Questionnaire

The parents of the child participant could be asked to complete the questionnaire. The questionnaire could obtain demographic information, medical history of the parents and child, the child's medications, the dates the child's mother worked at the Pease Tradeport (or in other occupations involving PFAS exposures) and her reproductive history, the dates the child attended daycare at the Pease Tradeport, water consumption of the mother and child while at Pease Tradeport (including use of water for formula, juices, etc.) if applicable, bottled water consumption by the mother and child, length of time the child was breastfed, parental information (e.g., education, primary occupation, maternal age at birth of the participating child), the child's height and weight, and whether the child regularly exercises, currently smokes (and the number of cigarettes/day), or consumes alcohol (and the number of drinks/week).

Specific questions could be included in the questionnaire that address health outcomes of interest based on the final study design. For example, for ADHD, the questionnaire could ask, "Has a doctor or health professional ever told your child that your child has/had ADD or ADHD?" If the answer is "yes," a second question could ask for a list of medications being used for the condition. Parents would also be asked if the child had learning or behavioral problems, and if so, the type of problem and the treatment being used. Questions would be included for the hypersensitivity-related outcomes, asthma, atopic dermatitis (or atopic eczema), and allergies. Information on the child's vaccination history would also be requested from the parents. The parents would also be asked when the female child first began to menstruate.

E. Biomarkers of exposure and effect

The following biomarkers of lipids, thyroid function, kidney function, sex hormones, and immune function could be analyzed in the serum:

- Total cholesterol, low density lipoprotein, high density lipoprotein, total triglycerides
- Thyroxine (T4), T3, thyroid stimulating hormone (TSH)
- Uric acid, creatinine
- Testosterone, estradiol, sex hormone-binding globulin (SHBG), follicle stimulating hormone, insulin-like growth factor
- Immunoglobulin G (IgG), IgA, and IgM; antibodies to measles, mumps, rubella, tetanus, and diphtheria

Approximately 4 teaspoons of blood (20 mL) could be drawn from each participant to be analyzed for the standard panel of PFAS compounds and the effect biomarkers. An attempt would be made to obtain an 8-hour fasting blood sample. The parents could be asked how long the child fasted before the blood draw. The cut points of 50 ng/dL of total testosterone and 20 pg/mL of estradiol would be used to identify sexual maturation in boys and girls, respectively. IgG antibodies for measles, rubella, and diphtheria would be analyzed to determine vaccine responses. Allergen-specific IgE (mold, dust mites, dog, cat, cow's milk, peanut, hen's egg, and birch) could be analyzed. Serum levels of thyroid stimulating hormone (TSH) and total T4 could be analyzed separately and also used to determine clinical and subclinical hypothyroidism. Uric acid, total cholesterol, low-density and high-density lipoprotein, and triglycerides could be analyzed.

For children older than 6 years, the Wechsler Abbreviated Scale of Intelligence could be administered to the child to assess verbal IQ, performance IQ, and full-scale IQ. For children aged 4–6 years, the Wechsler Preschool and Primary Scale of Intelligence would be administered. For each child, school records, including special education records could be reviewed to identify learning problems and behavioral problems. The SDQ could be administered to parents to assess emotional, conduct, and peer relationship problems as well as problems with hyperactivity and inattention.

F. Exposure Assessment

As stated earlier, the analyses by NH DHHS of the data from the blood testing program at Pease indicated that geometric mean PFHxS serum levels were higher for persons who drank ≥4 cups of water per day than for those who drank <4 cups per day. The strongest finding was for serum PFHxS in participants aged 0–19 years and water consumption ($\beta = 0.31$, SE=0.15, marginal effect=36.4%).

Geometric mean PFOS and PFOA serum levels were also higher among those who, while at the Tradeport, drank ≥4 cups of water per day than for those who drank <4 cups per day [NH DHHS 2016]. Although these findings are based on a "convenience sample" (or a "volunteer sample," i.e., not a statistically-based sample), it is clear from these results that consumption of PFAS-contaminated drinking water at the Pease Tradeport was a complete exposure pathway.

Study participants could submit blood samples for PFAS and biomarker analyses during 2018. For those who participated in the 2015 blood testing program, these measurements would be used to assess their exposures. For those who did not participate in the 2015 blood testing program but who attended daycare at the Pease Tradeport during January 2008–May 2014, the PFAS serum levels obtained in 2018 could be used to estimate serum levels during 2015 by adjusting for PFAS elimination rates and taking into account background PFAS exposures. For those who consumed drinking water from the Pease Tradeport after the Haven well was taken out of service, the adjustment could also take into account the PFAS levels in the drinking water after May 2014. The 2015 (estimated or measured) PFAS serum levels and 2018 measured PFAS serum levels would be used in the analyses.

No water samples from the Pease Tradeport distribution system for PFAS testing are available before 2014. Using a simple mixing model that takes into account the pumping rates for each of the three wells, the total water demand, and the concentrations of PFAS in the wells during the April and May 2014 sampling, we can estimate historical PFAS levels in the distribution system, assuming that contamination concentrations are approximately uniform throughout the distribution system and assuming that the contamination was present at least from 2008 through May 2014.

To estimate serum levels of PFOA and PFOS over the child's life, the historical estimates of the drinking water contamination could be combined using PBPK modeling with information from the questionnaires on 1) the dates and length of time the child attended daycare at the Tradeport and the child's consumption of drinking water at the daycare and 2) whether the child's mother worked at the Pease Tradeport during pregnancy and during the period of breastfeeding and the length of the period when the child was breastfed. PBPK modeling estimates would also incorporate information from NHANES and from the PFAS serum levels of the unexposed comparison group to estimate background levels of PFAS in serum. For those children whose mothers worked at the Pease Tradeport, estimates of the mother's serum levels during the pregnancy and breastfeeding of the child would be needed. If the mother participated in the 2015 blood testing program at Pease, her measured PFAS serum levels could be used in the modeling. Children's serum levels from the 2015 NH DHHS Pease blood testing program and serum levels obtained for this study would be used to calibrate the PBPK models.

No human PBPK model for PFHxS is currently available. However, correlation coefficients for serum PFHxS and serum PFOS and PFOA were quite high among persons ages 2–14 years who participated in the 2015 testing (Pearson correlation for PFHxS was 0.75, and for PFOS and PFOA was 0.73). Therefore, it might be possible to predict historical serum levels of PFHxS based on historical estimates for serum PFOA and PFOS.

G. Sample Size

The sample size for the Pease children study should include at a minimum 350 exposed children. It should also include a minimum of 175 unexposed children randomly sampled from the Portsmouth public schools with frequency matching to the exposed children on age, sex, and race. This minimum sample size is based on several considerations. First, 370 children ages 1–13 years participated in the

2015 blood testing at Pease. That would be a 75% participation rate, assuming that a minimum of 500 children attended daycare at Pease and would be in that age range in 2015. It should be possible to recruit a similar percentage of the children who attended daycare at Pease. However, children who did not participate in the 2015 blood testing would have to be recruited, as well as a high percentage of those who did participate. Second, some studies conducted of PFAS exposure and children had similar or smaller sample sizes than the 350 exposed and 175 unexposed children at Pease (e.g., Zeng [2015] and Qin [2016] in Taiwan, Grandjean [2012] in the Faroes, Stein [2013] in a C8 study of neurobehavioral effects, Hoffman [2010] in a NHANES study), but had sufficient statistical power to observed findings to achieve statistical significance. Finally, sample size calculations conducted for this feasibility assessment indicated that at least some of the health-related endpoints of interest could be evaluated, with sufficient statistical power (i.e., statistical power ≥80%) to detect effects of exposure that are equal to or greater than those listed in Tables 6a and 6b as well as effects observed in other PFAS studies that occurred at PFAS serum levels similar to those in the Pease children population.

Sample size calculations were conducted using four different combinations for type 1 error (α error or false positive error) and type 2 error (β error, false negative error, or 1 – statistical power):

1. Type 1 error = 0.05 (corresponds to a two-tail hypothesis test using a p-value cutoff of 0.05, or a 95% confidence interval, to determine statistical significance) and a type 2 error = 0.05 (corresponding to statistical power of 95%).

2. Type 1 error = 0.05 and type 2 error = 0.20 (80% power).

3. Type 1 error = 0.10 (corresponds to a one-tail hypothesis test using a p-value cutoff of 0.05, or a 90% confidence interval, to determine statistical significance) and a type 2 error = 0.10 (90% power).

4. Type 1 error = 0.10 and type 2 error = 0.20 (80% power).

(Note: Setting the type 1 and type 2 errors to be equal indicates an equal concern for false negatives and false positives and could be justified from a public health perspective.)

Table 6a indicates the minimum effect sizes that can be detected with a sample size of 350 Pease children and 175 unexposed children from the Portsmouth area using the four combinations of type 1 and type 2 errors. Table 6b also includes the minimum effect sizes that can be detected with a sample size of 500 exposed and 250 unexposed. These minimum effect sizes assume a simple comparison between the exposed and unexposed children that is not adjusted for possible confounding risk factors or stratified into smaller exposure groupings (e.g., low, medium, and high exposure).

Another approach to sample size calculations that might be informative was to fix the minimum detectable effects to the effect sizes observed in previous studies for PFAS serum levels similar to those observed in the Pease population, select the type 1 and type 2 error rates, and allow the sample size to "float" instead of the minimum detectable effect. However, this approach is problematic because there are few studies of PFAS exposures and the childhood outcomes being considered for the Pease children study. In some instances, studies evaluating similar PFAS serum levels obtained very different effect sizes for the same outcome. In other instances, a study with a lower PFAS serum level obtained a higher effect size for an outcome than a study with a higher PFAS serum level. Moreover, there are no studies of children exposed to PFAS drinking water contamination as a result of AFFF use. Therefore, there is

much uncertainty about the effect size for each health-related endpoint that would be expected for PFAS serum levels observed among the Pease children.

With these caveats, the following sample size per stratum calculations use the findings from studies of PFAS-exposed children. (Note: a sample size of 500 per stratum means that the study would need 500 exposed and 500 unexposed children. If the goal is to compare an outcome by exposure quartiles, then each quartile would need 500 children. Also, a 2:1 ratio of exposed to unexposed requires a larger total sample size than a 1:1 ratio of exposed to unexposed.) Table 6c provides a summary of the sample size considerations for each health-related endpoint.

Lipids

Mean Total Cholesterol, LDL, HDL, triglycerides: In the Taiwan study of lipids (Zeng 2015), the sample size of 225 children aged 12-15 was sufficient to detect total cholesterol and LDL differences of 11-12 mg/dL for PFOA serum levels similar to Pease. Table 6 indicates that with a sample size of 350 exposed and 175 unexposed, much lower mean differences in total cholesterol could be detected with sufficient statistical power. However, the observed PFOA OR of 1.2 for hypercholesterolemia would have required a sample size of over 1,700 per stratum with a type 1 error of 0.10 and 80% power (using the prevalence of hypercholesterolemia in this study of 28.4%). Using a lower type 1 error and/or higher statistical power would require even larger sample sizes to detect an OR of 1.2 for hypercholesterolemia.

The serum levels of PFOA and PFOS among the children at Pease would put them in the first quartile (i.e., the reference level) if they had been in the C8 study (Frisbee 2010). In the lower PFOA and PFOS quartiles, the ORs for hypercholesterolemia were between 1.2 and 1.3, requiring sample sizes of 800 – 1660 per stratum with type 1 error of 0.10 and 80% power (using the prevalence of hypercholesterolemia in this study of 34.2%). The strongest findings in this study for total cholesterol were observed for the top quintile of PFOS serum levels. When the top quintile PFOS serum level was compared with the reference level, the mean difference in total cholesterol was 8.5 mg/dL and the OR for hypercholesterolemia was 1.6. Both of these findings are within the range that could be detected with sufficient statistical power in a Pease study with 350 exposed and 175 unexposed children. However, the top quintile for PFOS in the C8 study contained serum levels several times higher than serum levels in the top quintile of the Pease children.

A study using NHANES data for 1999–2008 [Geiger 2014] observed a mean difference in total cholesterol of 4.7 mg/dL for the 2nd tertile serum levels of PFOA compared with the reference level. The 2nd tertile serum levels of PFOA in this study correspond to the PFOA serum levels among children at Pease. To calculate a sample size to detect this mean difference, a standard deviation of 28 mg/dL (similar to the standard deviations for total cholesterol in the Taiwan and C8 study) was used. With type 1 error of 0.10 and 80% power, the sample size required to detect a mean difference of 4.7 mg/dL would be 439 per stratum (or with an exposed to unexposed ratio of 2, as suggested for the Pease children study, 660 exposed and 330 unexposed would be required). In the NHANES study, the 2nd tertile PFOS serum levels corresponded to the PFOS serum levels among Pease children. The mean difference in total cholesterol for this tertile was 3.4 mg/dL, which would require 630 per stratum with type 1 error of 0.10 and 80% power.

In the NHANES study, the ORs for hypercholesterolemia corresponding to serum PFOA and PFOS levels among children at Pease were 1.49 and 1.35, respectively. To detect an OR of 1.49 with type 1

error of 0.10 and 80% power would require 358 per stratum (or with an exposed to unexposed ratio of 2, 540 exposed and 270 unexposed).

Kidney function and uric acid

In a study of adolescents (aged 12–19 years) and kidney function using NHANES data for 2003–2010 [Kataria 2015], the top quartile for serum PFOA would correspond to the top quartile for serum PFOA among the Pease children. The mean difference in the estimated glomerular filtration (eGFR) for the top quartile of PFOA compared with the 1st quartile reference level was -6.6 mL/min/1.73 m^2, which would be in the range detectable, with sufficient statistical power, by the Pease study sample size of 350 exposed and 175 unexposed children.

In this study, the serum uric acid mean difference of 0.21 mg/dL was observed, comparing the top quartile PFOA to the reference level. To detect this difference with a type 1 error of 0.10 and 80% power would require a sample size larger than that projected for the Pease children study, i.e., 398 per stratum (or for an exposed to unexposed ratio of two, 596 exposed and 298 unexposed children).

The serum PFOS levels in the 3rd quartile of the NHANES study would correspond to the top quartile for serum PFOS among the Pease children. The mean difference in eGFR for the 3rd quartile PFOS level compared to the reference level was -7.2 mL/min/1.73 m^2, which would be in the range detectable with sufficient statistical power by the Pease study sample size of 350 exposed and 175 unexposed children. However, the mean difference in uric acid was 0.05 mg/dL which would require a sample size of more than 5,000 per stratum.

In a Taiwan study of uric acid [Qin 2016], the sample size of 225 children aged 12–15 years was sufficient to obtain a statistically significant OR for hyperuricemia of 1.65 for PFHxS at serum levels much lower than among the Pease children. For PFOA, the OR for hyperuricemia was 2.2 at serum levels much lower than observed among the Pease children. A sample size of 350 exposed and 175 unexposed children would be sufficient to detect this OR with sufficient statistical power.

Attention Deficit/Hyperactivity Disorder (ADHD) and other neurobehavioral endpoints

In a C8 study of ADHD (Stein 2011), the first quartile or reference level for PFOA and PFOS would correspond to the serum PFOA and PFOS levels among the children at Pease. For PFHxS, the serum levels among the children at Pease would correspond to the 3rd quartile level in the C8 study. For the 3rd quartile of PFHxS, the OR for ADHD was 1.43, and with current medications, the OR was 1.55. The prevalence of ADHD was 12.4%, and with current medications, 5.1%. To detect an OR of 1.43 with a prevalence of 12.4 %, the required sample size for a type 1 error of 0.10 and 80% power would be 829 per stratum. To detect an OR of 1.55 with a prevalence of 5.1%, the required sample size for a type 1 error of 0.10 and 80% power would be 1,179 per stratum.

In a study that used NHANES data for 1999–2004 [Hoffman 2010], the serum PFHxS levels were about half the levels among the children at Pease. For serum levels corresponding to the top quintile level among the Pease children, the OR for ADHD was 1.67 (using the regression coefficient in the logistic model). To detect this OR, a sample size of 540 per stratum would be required for type 1 error of 0.10 and 80% power. For PFOA, the serum levels corresponding to the top quintile level among the children

at Pease in the NHANES population would have an OR of 1.82 for ADHD. For this OR, the required sample size would be 390 per stratum (or 596 exposed and 298 unexposed children) for a type 1 error of 0.10 and 80% power.

For neurobehavioral outcomes other than ADHD, some of the neurobehavioral outcome studies (e.g., Stein [2013, 2014b]; Wang [2015], Lien [2016]) were also in the range of the minimum sample size suggested for the Pease children study. IQ differences in the range of 3 to 4 points could be detected with reasonable statistical power with a sample size of 350 exposed and 175 unexposed children.

One study [Liew 2015] evaluated autism spectrum disorder and obtained an OR of 1.3 for serum PFHxS. With a prevalence of about 1.5%, a sample size of several thousand children would be necessary to detect this OR. To detect an OR of 2.0 with sufficient statistical power would require sample sizes of over 1,600 exposed and 1,600 unexposed.

Sex hormones and delayed puberty

In the C8 study of sex hormones [Lopez-Espinosa 2016], the serum levels of PFOA, PFOS, and PFHxS were considerably higher than among the children at Pease. For PFOS, the natural log estradiol percent difference in boys of -4% (per interquartile range of the natural log of PFOS) would require at least 1,154 per stratum for type 1 error of 0.10 and 80% power. The strongest finding in this study was the decrease in testosterone among girls associated with PFOS. The natural log testosterone percent difference in girls was -6.6% per interquartile range of the natural log of PFOS. To detect a percent difference this large with type 1 error of 0.10 and 80% power would require at least 290 per stratum, or 434 exposed and 217 unexposed children.

There was insufficient information to make sample size calculations for the endpoint, delayed puberty. The C8 study that evaluated this endpoint in included thousands of boys and girls [Lopez-Espinosa 2011].

Growth hormone

In the C8 study that evaluated sex hormones, insulin-like growth factor-1 (IGF-1) was also evaluated [Lopez-Espinosa 2016]. The difference in the natural log IGF-1 among boys and girls was -2.5% and -2.1% per interquartile range of the natural log of PFHxS, respectively. To detect these differences with sufficient statistical power, a sample size of 350 exposed and 175 unexposed children would be sufficient.

Thyroid disease and function

A C8 study [Lopez-Espinosa 2012] evaluated thyroid disease among children. The prevalence of participant-reported thyroid disease among children in this study was very low, about 0.6% and an OR of 1.44 was obtained for PFOA serum levels considerably higher than those in the Pease population. To detect this OR with 80% statistical power would require a sample size of over 10,000 exposed children.

In the C8 study of thyroid function [Lopez-Espinosa 2012], the largest percent difference for natural log TSH was 3.1%, and 2.3% for TT_4. These percent changes were for PFOA and PFOS serum levels considerably higher than the serum levels among the children at Pease. To detect a 2.3% change in TT_4 would require a sample size of at least 850 per stratum (type 1 error = 0.10 and 80% power). To detect a 3.1% change in natural log TSH would require a sample size of at least 8,545 per stratum (type 1 error = 0.10 and 80% power).

In the Taiwan study of thyroid function [Lin 2013], the sample size for those aged 12–19 years was 212. The geometric means for serum PFOA and PFOS were lower than the geometric mean serum levels among the children at Pease. For males and females, the natural log TSH declined by 0.5 mIU/L and 0.35 mIU/L respectively, for the >90th percentile serum PFOA compared with the reference level. To detect either of these differences with sufficient statistical power, a sample size of 350 exposed and 175 unexposed children would be sufficient.

Immune function and diseases related to immune function

For immune function, one study [Grandjean 2012] had a similar sample size (N = 532) as the minimum proposed for the Pease children study (i.e., 350 exposed and 175 unexposed children), and two studies had somewhat larger sample sizes that might be achievable at Pease (Stein [2016a], N = 640; and Buser [2016], N = 637). The data reported in these studies were insufficient to conduct sample size calculations.

For asthma, the ORs observed in the NHANES studies [Humblet 2014, Stein 2016a] were in the range of 1.2 – 1.3 and would require much larger sample sizes than can be recruited at Pease to achieve sufficient statistical power. However, a Taiwan study [Dong 2013] obtained ORs for asthma between 3.8 and 4.0 for PFHxS and PFOA serum levels lower than those observed in the Pease children population. A sample size of 350 exposed and 175 unexposed would be sufficient to detect these ORs with sufficient statistical power.

Only one study [Stein 2016a] evaluated rhinitis and observed an OR of 1.35 for serum PFOA. To detect an OR this low with sufficient statistical power would require a sample size larger than could be recruited from the Pease population. However, with sufficient statistical power, ORs in the range of 1.5 – 1.6 could be detected in a study of the Pease population with a sample size of 500 exposed and 250 unexposed children. These ORs would fall within the 95% CI for the finding in this study.

Other health-related endpoints

A NHANES study [Geiger 2014b] evaluated PFOS and PFOA serum levels and hypertension and obtained ORs < 1.0. Since there is no evidence so far of an association between PFAS serum levels and hypertension in children, this endpoint is not considered further.

A study conducted in the Faroes [Karlsen 2016] evaluated serum levels of PFOA, PFOS and PFHxS and overweight/obesity in children. At age 5 years, the ORs for overweight/obesity and the third tertile serum levels of PFOA, PFOS and PFHxS were 1.88, 0.94, and 1.22. The serum levels of the PFAS chemicals were considerably lower than at Pease. An OR of 1.62 could be detected with 80% statistical power with a sample size of 350 exposed and 175 unexposed children.

Childhood cancers

For childhood cancers such as leukemias, the incidence and prevalence is very low, requiring large sample sizes. For example, the probability of getting a leukemia at ≤15 years is 0.08% or 8 per 10,000. For ages ≤20 years, the probability is 0.09% or 9 per 10,000. At ages ≤14 years, the incidence rate for leukemias is 5.5 per 100,000 person-years. A study that attempted to evaluate leukemias or other childhood cancers would have to be multi-site or national.

H. Conclusion

Very little is known about the health effects from exposure to PFHxS, a PFAS that was considerably elevated in the serum of children tested at Pease. More information is available on the health effects of PFOS exposure, which was also elevated in the serum of children at Pease. However, there are still major data gaps and inconsistencies in the findings concerning the health effects of PFOS exposure, particularly effects on immune, thyroid and kidney function, neurobehavioral endpoints, sex hormones, and age at puberty. Based on sample size calculations, a study of children at Pease could have sufficient statistical power to evaluate several health-related endpoints. The study could also meet the criteria of public health significance and scientific importance, and could address some of the health concerns voiced by the Pease CAP and the previous CAB.

The study population can be enumerated and selection bias can be minimized if recruitment is carefully done to avoid selection bias (i.e., selection that is associated with exposure and disease status). A sample of Portsmouth public school students would be an appropriate comparison group for the Pease children. There is a complete exposure pathway and a well-defined exposed population. The health-related endpoints under consideration have been evaluated in at least one epidemiological study of PFAS exposures to children, and these endpoints can be measured accurately. Information on potential confounding factors can be obtained via questionnaire. The issue of reverse causation and confounding from the use of measured serum PFAS levels can be avoided by predicting serum levels using PBPK modeling. Therefore, a children's study at Pease could provide meaningful and credible results.

A key issue is whether a study limited to the children exposed at the Pease Tradeport would have sufficient statistical power and precision for some of the endpoints under consideration. A minimum sample size of 350 exposed Pease children and 175 unexposed children from the Portsmouth area would be sufficient for several outcomes of interest. For example, Table 6 indicates that a sample size of 350 exposed and 175 unexposed children is sufficient to detect effects of reasonable size for most of the endpoints listed in the table. In addition, some of the immune and neurobehavioral studies that had sufficient statistical power to obtain effect estimates that achieved statistical significance had sample sizes within the range suggested as a minimum for the Pease children study.

When the effect sizes seen in previous PFAS studies are considered, the suggested minimum sample size for the Pease children study could be sufficient for several endpoints, such as mean differences in lipids, eGFR, and IGF-1. For other outcomes, such as uric acid mean difference, the sex hormones testosterone and estradiol, and thyroid function, the sample size of a study limited to the Pease children population might not be sufficient. Based on sample size calculations assuming 350 Pease children and 175 unexposed children, and assuming a simple comparison of exposed versus unexposed, health endpoints are grouped below into three categories: 1) feasible to study, 2) possible to study (but might require a

larger sample size, e.g. 500 exposed and 250 unexposed), and 3) not feasible to study using the Pease children population, unless additional populations exposed to PFAS-contaminated drinking water are included in the study.

Health 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 (IGF-1, a measure of growth hormone deficiency)
- Overweight/Obesity

Health endpoints that might be possible to study in children at Pease (although a larger sample size may be needed)

- Mean difference in uric acid, a measure of kidney function
- 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 responses to rubella, mumps, and diphtheria vaccines

Health endpoints not feasible to study using the Pease children population (to address these health endpoints, populations from other sites 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

To evaluate exposure response relationships, more than two strata are necessary. For some of the candidate outcomes that are listed above as feasible to study or possible to study, the Pease children population that can be recruited to participate will not be large enough to be split into exposure tertiles or quartiles and still have sufficient statistical power for comparisons between each of the exposure strata and a reference (unexposed) stratum.

Data analyses similar to those used in the C8 studies could be used. The methods include linear regression of continuous (untransformed and natural log transformed) effect biomarkers on continuous (untransformed and natural log transformed) PFAS serum levels and categorized PFAS serum levels, and logistic regression of categorized effect biomarkers (e.g., hypercholesterolemia) or disease prevalence on continuous (untransformed and natural log transformed) and categorical PFAS serum

levels. Restricted cubic splines for linear and logistic regression would be conducted to obtain flexible, smoothed exposure-response curves. Measured PFAS serum levels would be evaluated. In addition, for PFOS and PFOA (and possibly PFHxS, if an historical reconstruction modeling method becomes available), estimated cumulative serum levels and estimated serum levels during critical vulnerability periods (e.g., in utero exposure) could be evaluated.

In summary, a study limited to the Pease children population will likely have a sufficient sample size for some of the candidate endpoints if the comparisons are simply between an exposed and unexposed group. For some of the candidate endpoints, the sample size will be insufficient for even a simple comparison between an exposed an unexposed group. Moreover, for many of the candidate endpoints, the Pease children population will be of insufficient size to split into tertiles or quartiles to evaluate exposure–response trends. Therefore, the inclusion of other sites with PFAS-contaminated drinking water could be considered.

Feasibility of an epidemiological study of adults at the Pease Tradeport

Compared with NHANES data, PFHxS serum levels were elevated among adults who participated in the 2015 NH DHHS blood testing program. However, the literature review indicated that very few studies have been conducted that evaluated PFHxS exposures and adult health effects. PFOS serum levels were also elevated among the adults who participated in the NH DHHS blood testing program. Although considerably more studies found evaluated PFOS exposures and adult health effects, there remain data gaps and inconsistencies in the findings for liver function, kidney function and kidney disease, thyroid disease and thyroid function, autoimmune diseases and immune function, osteoporosis/osteoarthritis, endometriosis, and most cancers.

The public health significance of conducting a study of adults at Pease is that the study will be relevant to other adult populations exposed to drinking water primarily contaminated with PFOS and PFHxS. A study might also provide an opportunity for early medical intervention for certain health endpoints that might be associated with PFAS exposure but not evaluated in routine physical exams, such as alterations in thyroid, liver, and kidney function. A study of adults at Pease would have scientific importance because it potentially could help to fill critical data gaps mentioned above concerning the health effects of PFHxS and PFOS exposures. Based on animal studies, there is biological plausibility that PFAS exposures could result in alterations of immune function and might have endocrine-disruptive properties that could lead to alterations in thyroid function. However, few epidemiological studies have evaluated PFHxS or PFOS exposures and these health endpoints. Finally, a study of adults at Pease has the potential to provide meaningful and credible results (from the perspective of statistical power) for some of the adverse outcomes of interest and would be responsive to community concerns. However, a study limited to Pease adults would likely not be sufficiently large to associate exposures and some adverse health outcomes (e.g., rare diseases such as specific cancers and specific chronic diseases).

A. Study hypotheses

Based on the literature review, the following hypotheses could be evaluated:

1. Higher serum levels of PFOA, PFOS, or PFHxS are associated with higher total cholesterol, low-density lipoprotein and triglycerides, and a higher prevalence of hypercholesterolemia.

2. Higher serum levels of PFOA, PFOS, or PFHxS are associated with higher prevalences of coronary artery disease and hypertension.

3. Higher serum levels of PFOA, PFOS, or PFHxS are associated with differences in thyroid stimulating hormone (TSH), TT4, and TT3, and a higher prevalence of hypothyroidism.

4. Higher serum levels of PFOA, PFOS, or PFHxS are associated with a higher level of uric acid and a higher prevalence of hyperuricemia.

5. Higher serum levels of PFOA, PFOS, or PFHxS are associated with a lower estimated glomerular filtration rate (eGFR) and a higher prevalence of kidney disease.

6. Higher serum levels of PFOA, PFOS, or PFHxS are associated with higher levels of liver function biomarkers alanine transaminase (ALT), γ-glutamyltransferase (GGT), and direct bilirubin and a higher prevalence of liver disease.

7. Higher serum levels of PFOA, PFOS, or PFHxS are associated with higher prevalences of osteoarthritis and osteoporosis.

8. Higher serum levels of PFOA, PFOS, or PFHxS are associated with a higher prevalence of endometriosis.

9. Higher serum levels of PFOA, PFOS, or PFHxS are associated with higher prevalences of autoimmune diseases such as ulcerative colitis, rheumatoid arthritis, lupus, and multiple sclerosis.

10. Higher serum levels of PFOA, PFOS, or PFHxS are associated with differences in serum levels of IgA, IgE, IgG, IgM, C reactive protein (CRP), and antinuclear antibodies (ANA) and alterations in specific cytokines.

A study of adults could include the collection of new blood samples to analyze PFAS serum levels. The blood samples would also be analyzed for lipids and biomarkers of kidney, liver, thyroid, and immune function. A questionnaire could be used to ascertain kidney disease, liver disease, cardiovascular disease, hypertension, thyroid disease, autoimmune diseases, osteoporosis, osteoarthritis, pregnancy-induced hypertension, and endometriosis. Diseases ascertained via questionnaire would be confirmed using medical records

B. Study population

According to the census, Portsmouth has 21,530 residents. About 67.5 % are adults aged 19–64 years and another 15.9% are aged 65 years and older. This would mean that there are about 14,500 adults aged 18–64 years and about 3,400 aged 65 years and over. Although the actual number is unknown, some of the workers at the Pease Tradeport live in New Hampshire towns other than Portsmouth or in the bordering states of Massachusetts and Maine. The Pease Tradeport has a workforce of >9,000 persons. In the 2015 blood testing program at Pease, 1,182 adults aged ≥18 years participated. Table 5 provides PFAS serum data for the 1,190 participants in the 2015 Pease blood testing program who will be age ≥18 years in 2018.

C. Recruitment and consent

As stated previously, the NH DHHS Pease blood testing program's consent form was strictly limited to use of the participant's blood sample for PFAS analyses only. The participant also consented to complete a brief questionnaire at the time of blood draw concerning demographics, time at Pease Tradeport, whether the worker was a firefighter, and consumption of drinking water. The consent form did not mention the use of the blood sample for research purposes or the possibility of re-contacting the participant for future studies. Therefore, the blood samples were not stored for future use, and ATSDR cannot directly contact the participants in the Pease blood testing program to recruit them for a study. Adults would need to sign a new consent form to participate.

The consent form would request a blood sample (about 35 mL or 1.2 ounces) from the adult for the analyses of PFASs and the effect biomarkers. (Note: 35 mL was the maximum amount of blood obtained from adults in the C8 studies.) The consent form could also ask the participant to complete a questionnaire covering demographics, water consumption, dates and length of time working at Pease, occupational history, lifestyle and health behaviors, diseases diagnosed by a physician or other health provider, and provider contact information.

To recruit adult study participants, NH DHHS would have to contact those who participated in the 2015 blood testing program. Another approach is to work with the Tenants Association at Pease (TAP) and the Pease International Development Authority (PDA) to contact firms on their mailing lists. TAP sends newsletters and email notices to subscribing firms at the Tradeport. The PDA list, with mailing addresses and email addresses of all firms at the Pease Tradeport, was provided to ATSDR to help recruit members to the Pease CAP. This list could be used to conduct outreach to recruit adult study participants. Other methods of outreach include contacting community groups and the media.

D. Biomarkers of effect

The following biomarkers would be analyzed in the serum:

- Total cholesterol, low density lipoprotein, high density lipoprotein, total triglycerides
- Thyroxine (T4), T3, thyroid stimulating hormone (TSH)
- Uric acid, creatinine
- Alanine transaminase (ALT), γ-glutamyltransferase (GGT) and direct bilirubin
- Immunoglobulin G (IgG), IgA, IgE and IgM; C reactive protein, and antinuclear antibodies (ANA), and alterations in specific cytokines.

E. Exposure assessment

Exposure assessment could be based on the serum PFAS levels obtained in the study supplemented by the serum PFAS levels for those who participated in the 2015 NH DHHS Pease blood testing program. Using historical estimates of the PFAS contaminant levels in the drinking water at the Pease Tradeport (based on water modeling methods), PBPK modeling can be used to estimate historical serum levels of PFOA and PFOS, combining information from the questionnaire on water consumption and dates and length of time employed at Pease Tradeport, and information on background PFAS serum levels from NHANES and from a comparison group unexposed to PFAS-contaminated drinking water or occupationally exposed to PFAS or AFFF. Serum levels from the 2015 NH DHHS Pease blood testing

program and serum levels obtained for this study would be used to calibrate the PBPK models. If feasible, historical estimates of serum PFHxS can be based on historical estimates for serum PFOA and PFOS, because serum levels of PFHxS and PFOS were highly correlated among the Pease adults who participated in the 2015 blood testing program (Pearson correlation coefficient = 0.73).

F. Sample size considerations

A key problem for an adult study at Pease will be identifying an appropriate comparison population of workers from the Portsmouth area with similar occupations as the Pease workforce and who were not exposed to PFAS-contaminated drinking water or occupationally exposed to PFAS or AFFF. Another key problem will be recruiting a sufficient number of participants to achieve reasonable statistical power and precision of effect estimates.

Studies conducted of the adult C8 population included tens of thousands of participants. For example, studies of thyroid disease [Winquist 2014a], cardiovascular disease and lipids [Winquist 2014b], kidney disease [Dhingra 2016], and liver function [Darrow 2016] included 28,541 community members and 3,713 workers at the DuPont plant. Smaller studies using NHANES data (e.g., Wen [2013], Webster [2016], Shankar [2011], Gleason [2015], and Lin [2010]) had sample sizes of 1,181–4,333 adults.

Table 7a indicates the minimum detectable effects for a study that included 1,500 participants per stratum. For a simple comparison between exposed and unexposed, this would require a total of 3,000 participants, i.e., 1,500 exposed and 1,500 unexposed. If the study population were divided into quartiles of PFAS serum levels, with the first quartile being the reference exposure level, then this would result in a total sample size of 6,000 persons (i.e., 4,500 exposed and 1,500 unexposed). Four combinations of type 1 error (α error) and type 2 error (β error) are used in the table. A type 1 error of 0.05 corresponds to a two-tailed hypothesis test using a p-value cutoff of 0.05 to determine statistical significance, or using a 95% confidence interval. A type 1 error of 0.10 corresponds to a one-tail hypothesis test using a p-value cutoff of 0.05 to determine statistical significance, or using a 90% confidence interval. A type 2 errors of 0.05, 0.10, and 0.20 correspond to statistical power of 95%, 90% and 80%, respectively.

Another possible approach to sample size calculations that might be informative would be to fix the minimum detectable effects to the effect sizes observed in previous studies for similar levels of exposure, select the type 1 and type 2 error rates, and allow the sample size to "float" instead of the minimum detectable effect. However, this approach is problematic because there are few studies of PFAS exposures and the adult outcomes being considered for the Pease adult study. In some instances, studies evaluating similar PFAS serum levels obtained very different effect sizes for the same outcome. In other instances, a study with a lower PFAS serum level obtained a higher effect size for an outcome than a study with a higher PFAS serum level. Moreover, there are no studies of adults exposed to PFAS drinking water contamination as a result of AFFF use. Therefore, there is much uncertainty about the effect size for each health-related endpoint that would be expected for PFAS serum levels observed among the Pease adults. With these caveats, the following sample size per stratum calculations use the findings from studies of PFAS-exposed adults. Table 7b provides a summary of the sample size considerations for each health-related endpoint.

Lipids

In the lipid study conducted of the C8 adult population [Steenland 2009], PFOS serum levels corresponding to the PFOS serum levels among adults who participated in the Pease blood testing program would result in a 3–4 mg/dL change in total cholesterol and in LDL. Table 7a indicates that detecting a difference of about 4 mg/dL in total cholesterol would require a sample size of about 1,500 per stratum. To detect a difference of 3 mg/dL would require a larger sample size. For LDL, a sample size of 1,500 per stratum would be sufficient for mean differences in the 3–4 mg/dL range.

The predicted increase in total cholesterol at the highest decile for PFOA and PFOS in the C8 study was 11–12 mg/dL. To detect a difference of 11 mg/dL, a sample size in the range of 200–300 per stratum would probably be sufficient. However, the highest decile for PFOA and PFOS in the C8 population is considerably higher than the serum levels observed for the adult participants in the Pease 2015 blood testing.

In a C8 study [Steenland 2009] and a Canadian study [Fisher 2013], ORs in the range of 1.35 – 1.6 were observed for hypercholesterolemia. Although PFAS serum levels were higher in the C8 population than the Pease population, the PFAS serum levels in the Canadian study were lower than in the Pease population. Table 7a indicates that ORs in this range for hypercholesterolemia can be detected with sufficient statistical power with a sample size of 1,500 per stratum.

Kidney disease/function, and uric acid

In the C8 study of chronic kidney disease [Dhingra 2016], the highest hazard ratio (HR) was observed for the lowest quintile of exposure (compared with the reference level) and was equal to 1.36. To detect this HR, given the low prevalence of the disease (approximately 1.4%). would require a sample size of at least 8,600 per stratum.

In the C8 study of uric acid [Steenland 2010], serum PFOS levels that correspond to those observed among the adult participants in the Pease blood testing program resulted in a difference of 0.14 mg/dL. To detect this difference would require a sample size in the range of 1,600–2,100 per stratum.

The largest differences in uric acid observed in this study was 0.28 mg/dL for PFOA serum levels ≥188.7 ng/mL and 0.22 mg/dL for PFOS serum levels ≥40.5 ng/mL. These serum levels are considerably higher than those observed for the adults at Pease. Based on sample size calculations, a uric acid difference of 0.28 mg/dL could be detected with reasonable statistical power and a sample size in the range of 500–600 per stratum. Table 7a indicates that much lower differences in uric acid could be detected with reasonable statistical power using a sample size of 1,500 per stratum.

In the C8 study, the OR for hyperuricemia for PFOA serum levels similar to those at Pease equaled 1.02. For the top quintile of serum PFOA in the C8 population, the OR was 1.47. Based on sample size calculations, a sample size in the range of 450–600 would be sufficient to detect an OR of 1.47 with reasonable statistical power. However, the top quintile serum PFOA level in the C8 study was considerably higher than observed in the Pease population.

In a study using NHANES data [Shankar 2011], a change in uric acid of 0.40 mg/dL was observed for serum PFOA levels similar to those observed for Pease. Based on sample size calculations, this difference could be detected with reasonable statistical power using a sample size of about 300 per

stratum. For hyperuricemia, an OR of 1.90 was observed for serum PFOA levels similar to Pease. Based on sample size calculations, an OR of 1.90 can be detected with reasonable statistical power using a sample size of about 240 per stratum.

Liver function

For liver function, to detect the very subtle changes observed in the C8 studies [Gallo 2012; Darrow 2016] would require a sample size as large as the C8 study itself. The same is true for liver disease. In the Darrow 2016 study, the highest OR observed was 1.19 for the 2nd quintile of serum PFOA. The 2nd quintile of serum PFOA in the C8 study is higher than the serum levels at Pease. To detect an OR of 1.19 would require a sample size of at least 20,000 per stratum.

A study using NHANES data [Gleason 2015] was able to detect associations with uric acid and liver function biomarkers at serum PFAS levels similar to those observed at Pease and with a total sample size of 4,333 persons. This study evaluated quartiles of serum PFAS, so each stratum had a sample size of about 1,083 persons. Another study that used NHANES data [Lin 2010] also was able to detect associations with liver function biomarkers with a total sample size of 2,216 persons. This study also evaluated quartiles, so each stratum had a sample size of about 554 persons.

Cardiovascular disease

The C8 study that evaluated coronary artery disease did not find an elevation in risk [Winquist 2014b]. However, a study that used NHANES data [Shankar 2012] obtained an OR of 2.01 for cardiovascular disease for the 4th quartile PFOA serum levels. These PFOA serum levels, ≥6 ng/mL, would correspond to the 5th quintile of PFOA serum levels among Pease adults. The prevalence of cardiovascular disease in this study was 13%. To detect an OR of 2.01, a sample size of about 250/stratum would probably be sufficient.

Hypertension

One study evaluated hypertension in a community population and observed an OR <1.0 [Winquist 2014b]. The prevalence of hypertension in this study was about 38%. With a sample size of 1,500 per stratum and a prevalence of 38%, ORs between 1.21 and 1.31 could be detected with sufficient statistical power.

Thyroid disease/function

For thyroid disease, the C8 study evaluated self-reported disease and self-reported disease that was confirmed by medical records [Winquist 2014a]. For serum PFOA levels similar to those at Pease, the hazard ratios were in the range of 1.2–1.3. For all self-reported thyroid disease (prevalence = 11.3%), a sample size of about 2,100 per stratum would probably be sufficient to detect a hazard ratio of 1.3. The prevalence for confirmed disease was 6.5%, so that a sample size of about 3,500 per stratum would probably be necessary to detect an HR of 1.3.

A study that used NHANES data evaluated thyroid disease [Melzer 2010]. For confirmed thyroid disease (prevalence = 2.4% in this study), the ORs were slightly above 1.1 for PFOS and PFOA serum levels similar to those at Pease. To detect this OR would require a sample size equivalent to the C8

population. The highest OR observed was 1.89 among men in the top quartile of PFOS and PFOA. To detect this odds ratio, a sample size of about 1,400 per stratum would probably be sufficient.

The C8 study that evaluated thyroid function biomarkers [Knox 2011] observed very subtle changes that would require a study of equivalent size (52,296) to detect associations with sufficient statistical power. On the other hand, a study that used NHANES data [Wen 2013] to evaluate thyroid function observed larger changes that could be detected with a total sample size of <1,200 (or <300 per quartile stratum).

Immune function and autoimmune diseases

Only one published study [Stein 2016b] evaluated serum immune biomarkers at baseline (i.e., cross-sectionally) and PFAS serum levels. The study evaluated de-identified archived blood samples from 75 adults aged 21-49. Given the very small sample size, this should be considered a pilot study. The PFHxS serum levels in this study were considerably lower than in the Pease adult population and a few positive findings were observed but the confidence intervals for these findings were extremely wide indicating little precision and a high degree of uncertainty in the effect estimates. Given the strong animal evidence of effects on the immune system from PFAS exposures [NTP 2016], a cross-sectional evaluation of PFAS serum levels and immune biomarkers in a Pease adult study could provide important information on the effects of PFAS exposures on immune function in humans.

The prevalences of ulcerative colitis, rheumatoid arthritis, lupus, and multiple sclerosis in a C8 study [Steenland 2013] were ≤ 1.2%. As indicated in Table 7a, ORs ≤2.0 cannot be detected with sufficient statistical power for these endpoints with a sample size of 1,500 per stratum. For lupus and multiple sclerosis, ORs <3.5 cannot be detected with sufficient statistical power with a sample size of 1,500 per stratum.

Osteoarthritis and Osteoporosis

Two studies evaluated osteoarthritis. In a C8 study [Innes 2011], an OR of about 1.4 was observed for serum PFOA levels considerably higher than those at Pease. However, in an NHANES study [Uhl 2013], an OR of 1.5 was observed for serum PFOA levels similar to those at Pease. Table 7a indicates that ORs in the range of 1.4 – 1.6 can be detected with sufficient statistical power with a sample size of 1,500 per stratum.

An NHANES study evaluated osteoporosis in women [Khalil 2016] and obtained an OR > 10 for serum PFHxS levels lower than those at Pease. With 750 women per stratum, an OR of 1.58 can be detected with sufficient statistical power.

Endometriosis

An NHANES study [Campbell 2016] obtained ORs of 1.47 and 2.86 for serum PFHxS and PFOA, respectively. The serum levels for these two PFAS were similar to those in the Pease population. Table 7a indicates that with a sample size of 750 per stratum, ORs in the range of 1.55 – 1.85 can be detected with sufficient statistical power.

Pregnancy-induced hypertension

Several C8 studies evaluated pregnancy-induced hypertension. One study observed an OR of 1.6 for serum PFOS. However, the PFOS serum levels in the C8 study were higher than those at Pease. Table 7a indicates that ORs in the range of 1.6 – 1.9 can be detected with sufficient statistical power for a sample size of 750 pregnancies per stratum.

Cancer incidence

For kidney cancer, Table 7a indicates that ORs <3.8 cannot be detected with sufficient statistical power with a sample size of 1,500 per stratum. Even for a cancer with a much higher prevalence than kidney cancer, e.g., prostate cancer, ORs < 2.0 cannot be detected with sufficient statistical power with a sample size of 750 men per stratum.

F. Conclusion

A sample size of about 1,500 per stratum (or a total sample size of 6,000 if quartiles are evaluated) would have sufficient statistical power to detect several of the health-related endpoints, as indicated by Tables 7a and 7b. For some endpoints, such as mean difference in uric acid, hyperuricemia, and cardiovascular disease, smaller sample sizes of about 500 per stratum might be sufficient. For other endpoints, such as ulcerative colitis, rheumatoid arthritis, and chronic kidney and liver disease, sample sizes larger than 1,500 per stratum would be necessary. Based on the sample size calculations that assume a sample size of 1,500 adults employed at the Pease Tradeport and 1,500 adults from the Portsmouth area who were never employed at the Pease Tradeport, and assuming a simple comparison of exposed versus unexposed, health endpoints are grouped below into three categories: 1) feasible to study, 2) possible to study (but might require a larger sample size from the Pease population), and 3) not feasible to study using the Pease adult population unless additional populations exposed to PFAS-contaminated drinking water are included in the study.

Health endpoints feasible to study in adults at Pease

- Mean difference in lipids (total cholesterol, LDL, HDL, triglycerides)
- Elevated total cholesterol (hypercholesterolemia)
- Mean difference in uric acid, a measure of kidney function
- 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 endpoints that may be possible to study in adults at Pease (although a larger sample size may be needed)

- Liver function
- Thyroid disease (confirmed)
- Thyroid function
- Endometriosis
- Pregnancy-induced hypertension

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

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

To evaluate exposure–response trends, the study participants would need to be split into tertiles or quartiles based on their serum PFAS levels. For some of the candidate health endpoints that are listed above as feasible to study or possible to study, the Pease adult population that can be recruited to participate will not be large enough to be split into exposure tertiles or quartiles and still have sufficient statistical power for comparisons between each of the exposure strata and a reference (unexposed) stratum. For example, if the study population is to be divided into quartiles, and assuming that a sample size of 1,500 per stratum would be sufficient for many of the endpoints of interest, then it would be necessary to recruit 4,500 adults (aged ≥18 years at the start of the study) from the Pease workforce and a representative group (i.e., employed in similar occupations as the Pease workforce) of 1,500 adults from the Portsmouth area who were not exposed at Pease.

Data analyses similar to those used in the C8 studies would be used. The methods include linear regression of continuous (untransformed and natural log-transformed) effect biomarkers on continuous (untransformed and natural log-transformed) PFAS serum levels and categorized PFAS serum levels; and logistic regression of categorized effect biomarkers (e.g., hypercholesterolemia) or disease prevalence on continuous (untransformed and natural log-transformed) and categorical PFAS serum levels. Restricted cubic splines for linear and logistic regression would be conducted to obtain flexible, smoothed exposure-response curves. Measured PFAS serum levels would be evaluated. In addition, for PFOS and PFOA (and possibly PFHxS if an historical reconstruction modeling method becomes available), estimated cumulative serum levels would be evaluated.

In summary, a study limited to the Pease adult population could likely have a sufficient sample size for some of the candidate endpoints **if** the comparisons are simply between an exposed and unexposed group. Recruitment of at least 1,500 adults from Pease should be feasible, given that the 2015 blood testing program at Pease was able to recruit at least 1,182 adults aged >18 years who worked at Pease.

However, a study limited to the Pease adult population might not have a sufficient sample size to evaluate exposure–response relationships. Moreover, a study limited to the Pease worker population might not have sufficient variability in serum PFAS levels to evaluate exposure–response trends effectively. Sufficient variability in PFAS serum levels might be achieved by including other populations with residential exposures to PFAS-contaminated drinking water.

Feasibility of an epidemiological study of former military service and civilian workers at the former Pease Air Force base

Drinking water contamination at a military base involves potential residential exposures to those living and training at the base and potential exposures to those working at the base. At the former Pease Air Force Base, starting in the 1970s, AFFF foam was used for fire training and to extinguish flammable liquid fires. The PFAS contamination in the Haven well water supply likely occurred sometime during the period from the start of AFFF usage and the closing of the base and would have resulted in exposures to those living and working at the base.

To evaluate the incidence and mortality of specific cancers, a large population of adults would need to be followed for a sufficient number of years to account for the long induction periods of most cancers and to have sufficient statistical power. For example, the Camp Lejeune mortality study of U.S. Marines and Navy personnel followed a cohort of 154,932 from 1979 to 2008 for a total of over 4 million person-years [Bove 2014]. To evaluate cancer incidence for the Camp Lejeune cohort, ATSDR will conduct follow-up using state and federal cancer registries for the period 1996–2016 (1996 is the earliest date that >90% of the state registries were in operation), for a total of over 3 million person-years. For the civilian worker cohort at Camp Lejeune, 8,085 workers will be followed over the period 1996–2016 for cancer incidence, for a total of 121,875 person-years. This is similar in size to a study of cancer incidence among workers at a PFAS manufacturing plant [Raleigh 2014]. A recent study of firefighters followed a pooled cohort of 29,993 from San Francisco, Chicago, or Philadelphia from 1985 through 2009, for a total of 403,152 person-years [Daniels 2014]. A C8 study of cancer incidence that relied on self-reported cancers that were confirmed by medical records and cancer registry review included 32,254 who contributed over 1 million person-years of follow-up [Barry 2013].

In October 1989, 3,465 military personnel were assigned to Pease Air Force Base, accompanied by 4,746 dependents. The Air Force estimates that 537 civilian employees were employed on base at that time [USAF 1990]. From 1970 to 1990, an average of 3,000 personnel and their families were assigned to the base at any one time. Before 1970, the base supported a maximum of 5,000 personnel [USAF 1994]. One important consideration about including Pease service personnel and civilian workers in a cancer incidence and mortality study is that drinking water at the base was also contaminated by TCE from the Haven well during some of the years the base operated. Service personnel and civilian workers stationed at the base before 1986 should not be included because of this contamination. Because the base closed by 1991, the number of service personnel and civilian workers at Pease AFB that could be included in a study would be insufficient to evaluate cancers with sufficient statistical power.

Because of the relatively small numbers of personnel assigned to Pease Air Force Base, we conclude that it is not feasible to conduct a study of cancer incidence and mortality that is limited to the Pease military service personnel and civilian worker cohorts stationed at the base from 1986

onward. For a study to be feasible, it would require a larger population size, for example, by including service personnel and civilian workers from other military bases with PFAS-contaminated drinking water as a result of the use of AFFF. Exposures to other drinking water contaminants, such as TCE, other chlorinated organic chemicals, and benzene, must also be taken into account when considering candidate military bases and defining the cohorts.

Cohorts of service personnel and civilian workers can be identified at military bases from personnel data maintained at the Defense Manpower Data Center. Personnel data are available from 1971, although information on military unit, which is needed to determine the base where the individual was stationed, does not begin until the second quarter of 1975. For civilian workers, data are available starting in the last quarter of 1972, with data missing for the first quarter of 1973. The data contain the location of the workplace (codes for state, city, and ZIP code). The Defense Manpower Data Center data contain Social Security number, name, date of birth, and sex to facilitate follow-up.

Military service personnel constitute a highly mobile population after their tours of duty are completed. For a mortality study, this is not a problem, because the NDI is available to obtain information on causes of death. However, there is no national cancer registry to ascertain cancer incidence. Therefore, a study of military service personnel and civilian workers would require gaining the participation of all or most of the state cancer registries and the Department of Veterans Affairs Central Cancer Registry (VACCR). The Camp Lejeune Cancer Incidence Study is one model for such a study. This study is attempting to recruit at least two-thirds of the state cancer registries and VACCR to cover >90% of the Camp Lejeune and Camp Pendleton cohorts. The study will send the personal identifiers for each cohort member to each registry for matching with the registry's data. For any matches that occur, the registry will send to ATSDR the cancer information that is linked to personal identifier (e.g., Social Security number or a unique identification number linked to the Social Security number). This will allow assessment of exposures and other covariates and cancers at the individual level.

The most appropriate military sites for inclusion would be those with water systems that are not complex so that simple mixing models can be used to estimate PFAS-contaminant levels throughout the distribution system. In addition, candidate sites should have information on the history of AFFF use at the base including major incidents such as spills, fires, etc.

Other study designs and health-related endpoints

1. Adverse birth outcomes

To evaluate adverse birth outcomes such as SGA, preterm birth, and specific congenital malformations with sufficient statistical power, several thousand births should be studied. For example, to detect an OR of 1.5 for SGA (5th percentile) with 80% power would require 1,775 births per stratum. For SGA (10th percentile) and preterm birth, with 80% power, an OR of 1.5 can be detected with a sample size of about 960–990 births per stratum. For rare birth defects, such as neural tube defects, to detect an OR of 2.5 with 80% power would require a sample size of about 22,000 births per stratum. For oral clefts, to detect an OR of 2.0 would require about 15,000 births per stratum.

Birth weight, SGA and preterm birth can be evaluated using birth certificate data. For birth defects, a population-based registry must be used to identify cases.

An adverse birth outcome study is not feasible at Pease because there were too few births to mothers who worked at the Tradeport during their pregnancy. The most appropriate candidate populations for a study of adverse birth outcomes would be one or more large municipalities with residential exposures to PFAS-contaminated drinking water where a simple mixing model could be used to estimate contaminant levels throughout the distribution system, i.e., a system that is not complex but instead has relatively uniform contaminant levels throughout the distribution system.

2. Registry

Creating a registry of exposed children and adults at the Pease Tradeport involves following the health status over a period of time and is similar to an epidemiological, longitudinal study of an exposed cohort. The difference is that an epidemiological study would usually include a comparison, unexposed cohort. A registry, like a longitudinal epidemiological study, can be resource-intensive. A decision would also have to be made concerning the length of the follow-up. As in any longitudinal effort, individuals will drop out over time, resulting in interpretation difficulties (e.g., selection bias resulting from loss to follow-up). In any event, before a registry or longitudinal study can be contemplated, an initial cross-sectional study must first be conducted, similar to the children's study and adult study discussed above.

3. Multi-site studies

The results of sample size calculations indicated that the exposed populations at the Pease Tradeport and the former Pease Air Force Base were of insufficient size for some of the health-related endpoints of interest to the community. Moreover, Pease CAP members have expressed interest in linking the Pease communities with other communities that have been exposed to PFAS-contaminated drinking water. A national database exists that can be used to identify other communities with PFAS-contaminated drinking water. Data on PFAS contamination of public drinking water supplies are available for large systems (serving >10,000 retail customers) and a small sample of small systems (n = 800 or 0.5% of a total of 144,165 systems serving <10,000 retail customers) via the Third Unregulated Contaminant Monitoring Rule (UCMR-3) database maintained by the EPA [US EPA 2016b].

UCMR-3 monitoring for PFAS is required at the entry point to the distribution system for each well and at any interconnection that is in operation. Water utilities had to sample twice during a 12-month period from 2013–2015 with sampling events occurring 5–7 months apart. The UCMR dataset contains sampling data from January 2, 2013 through March 1, 2016. Table A1 in the Appendix lists the utilities ranked by the maximum level of combined PFOS and PFHxS detected in the system. The highest level was detected in the system serving the Mariana Islands. Among the U.S. water systems, the top 10 systems for combined PFOS and PFHxS were Artesian Water Company in Delaware; Security Water System in Colorado Springs, CO; Horsham and Warminster systems in Pennsylvania; Oatman Water Company in Arizona; Issaquah Water System in Washington; Hyannis Water System in Massachusetts; Suffolk County Water Authority in New York; Warrington Township Water in Pennsylvania; and United Water in Pennsylvania, which serves various municipalities.

Although the UCMR database can be used to identify potential sites for further consideration for health studies, it has several limitations. First, most small systems are not included in the database. Second, the data represent levels of contamination at the entry points to the distribution system of the water utility

(e.g., contaminant levels in a supply well) and generally do not represent the levels of contamination reaching particular residences served by the utility. To estimate the population receiving contaminated drinking water and the levels of PFAS in their drinking water, the UCMR data must be supplemented with information on the configuration and operation of the utility's system. For a system that mixes all its sources of water before to entering the distribution system, a simple mixing model can be used to estimate the contaminant levels in the drinking water serving the residences by taking into account the contaminant levels in each source and the contribution of each source to the total supply. This is the situation at the Pease Tradeport, where water from each of the supply wells is mixed at the treatment plant before entering the distribution system. However, many utilities have more complex systems in which each of the supply wells (or surface water sources) primarily serve particular areas of the distribution system. For these systems, additional information is needed (for example, on the operation of the supply wells, tank levels, and the water demand in each area of the distribution system), and complex modeling methods must be used.

Conclusions

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 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.

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.

Table 3. Summary of the PFAS literature on adults.

	PFOS	PFHxS	PFOA
Cancer			
Prostate	+	+	+
Bladder	+	*	+
Colorectal	+	*	I
Breast	I	I	+
Pancreatic	I	*	+
Testicular	*	*	+
Kidney	*	*	+
Thyroid	*	*	+
Liver	*	*	+
Leukemia	*	*	+
non-Hodgkin lymphoma	*	*	+
Multiple myeloma	*	*	*
Ovarian	*	*	+
Other diseases			
Kidney disease/kidney function	*	*	+
Hyperuricemia	+	I	+
Liver disease/liver function	+	+	+
Cardiovascular Disease, hypertension, hypercholesterolemia	+	+	+
Thyroid disease/function	+	+	+
Autoimmune diseases	*	*	+
Osteoarthritis, osteoporosis and bone mineral density	+	+	+
Immune response	+	+	+
Reproductive outcomes	+	+	+

"+" One or more studies suggesting increased risk of an adverse outcome (e.g., OR or RR $\geq$ 1.20)
"*" no studies were conducted (for liver cancer and PFOS, and multiple myeloma and PFOA, there were too few deaths ($\leq$2) to evaluate).
"I" inconclusive – the findings have not suggested an increased risk (e.g., an OR or RR <1.20)

Table 4. Summary of the PFAS literature on children.

	PFOS	PFHxS	PFOA
Adverse birth outcomes	+	+	+
Lipids	+	I	+
Thyroid function	+	*	+
Thyroid disease	I	*	+
Uric acid	+	+	+
Sex hormones	+	+	+
Delay in reaching puberty	+	I	+
Neurobehavioral outcomes	+	+	+
Immune function	+	+	+
Hypertension	I	*	I
Adiposity/BMI/Overweight	+	+	+

"+" One or more studies suggesting increased risk of an adverse outcome (e.g., OR or RR ≥ 1.20)
"*" no studies were conducted.
"I" inconclusive – the findings have not suggested an increased risk (e.g., an OR or RR <1.20)

Note: adverse birth outcomes are not included in this table because these outcomes are not feasible to study at Pease. Although the number of children potentially exposed to the PFAS-contaminated drinking water while attending daycare at the Pease Tradeport can be estimated, there is a lack of information on the number of children potentially exposed in utero to the PFAS-contaminated drinking water because their mothers were employed at the Pease Tradeport during the pregnancy. To evaluate adverse birth outcomes with sufficient statistical power would require the inclusion of several hundreds of exposed births.

Table 6a. Minimum detectable effects for a Pease children study with 350 exposed and 175 unexposed.*

Endpoint	α and β = .05	α = .05, β=.20	α and β = .10	α = .10, β=.20
Total cholesterol (mean difference)	9.8 mg/dL	7.6 mg/dL	8.0 mg/dL	6.8 mg/dL
Hypercholesterolemia	OR = 2.00	OR = 1.73	OR = 1.77	OR =1 .63
Hyperuricemia	OR = 2.30	OR = 1.96	OR = 2.00	OR = 1.83
Uric acid (mean difference)	0.40 mg/dL	0.31 mg/dL	0.33 mg/dL	0.28 mg/dL
eGFR (mean difference)#	8.0	6.2	6.5	5.5
ADHD¶	OR = 2.47	OR = 2.09	OR = 2.13	OR = 1.94
ADHD + meds¶	OR = 3.50	OR = 2.80	OR = 2.89	OR = 2.52
Atopic dermatitis	OR = 2.49	OR = 2.10	OR = 2.15	OR = 1.95
Asthma	OR = 2.56	OR = 2.16	OR = 2.21	OR = 2.00
Rhinitis	OR = 2.08	OR = 1.79	OR = 1.83	OR = 1.69
Hypertension	OR = 2.12	OR = 1.80	OR = 1.85	OR = 1.69
Overweight/Obese	OR = 2.00	OR = 1.72	OR = 1.76	OR = 1.62

Table 6b. Minimum detectable effects for a Pease children study with 500 exposed and 250 unexposed.*

Endpoint	α and β = .05	α = .05, β=.20	α and β = .10	α = .10, β=.20
Total cholesterol (mean difference)	8.2 mg/dL	6.4 mg/dL	6.7 mg/dL	5.7 mg/dL
Hypercholesterolemia	OR = 1.78	OR = 1.57	OR = 1.60	OR =1 .50
Hyperuricemia	OR = 2.04	OR = 1.75	OR = 1.79	OR = 1.65
Uric acid (mean difference)	0.34 mg/dL	0.26 mg/dL	0.27 mg/dL	0.23 mg/dL
eGFR (mean difference)#	6.7	5.2	5.4	4.6
ADHD¶	OR = 2.18	OR = 1.85	OR = 1.90	OR = 1.73
ADHD + meds¶	OR = 2.98	OR = 2.40	OR = 2.48	OR = 2.19
Atopic dermatitis	OR = 2.20	OR = 1.86	OR = 1.91	OR = 1.74
Asthma	OR = 2.26	OR = 1.91	OR = 1.96	OR = 1.78
Rhinitis	OR = 1.85	OR = 1.62	OR = 1.65	OR = 1.54
Hypertension	OR = 1.88	OR = 1.64	OR = 1.68	OR = 1.56
Overweight/Obese	OR = 1.79	OR = 1.58	OR = 1.61	OR = 1.50

* Some health-related endpoints are not included in the table because there was insufficient information to calculate minimum detectable effects. For sex hormones, insulin-like growth factor – 1, and thyroid function, see the appendix for a description of the assumptions used in the sample size calculations and the resulting calculations.

mL/min/1.73 m^2

¶ The prevalence of an ADHD diagnosis reported by a study participant in the C8 study (Stein 2011) was 12.4%. In this study, the prevalence of an ADHD diagnosis reported by a study participant who also reported currently using a medication commonly used to treat ADHD was 5.1%.

Table 6c. Summary of information used to categorize the feasibility of studying health-related endpoints for a Pease children study.

Health-related Endpoint	**Minimum Detectable Effect Size: 350 exposed, 175 unexposed**	**Other Sample Size Considerations**	**Conclusion**
Lipids (total cholesterol)	6.8 mg/dL	A Taiwan study (Zeng 2015) obtained mean differences of 11-12 mg/dL for total cholesterol and low density lipoprotein at PFOA serum levels similar to Pease.	Feasible to study at Pease
Estimated glomerular filtration rate (eGFR)	5.5 mL/min/1.73 m^2	A NHANES study (Kataria 2015) observed a mean difference of 6.6 mL/min/1.73 m^2 for PFOA serum levels similar to those at Pease. For PFOS, the mean difference was 7.2 mL/min/1.73 m^2	Feasible to study at Pease
Insulin-like growth hormone-1 (IGF-1)	See appendix for sample size calculations and assumptions required for the calculations.	A C8 study (Lopez-Espinosa 2016) observed a reduction of IGF-1 for PFHxS serum levels similar to those at Pease that could be detected with sufficient power by a sample size of 350 exposed and 175 unexposed.	Feasible to study at Pease.
Overweight/Obesity	OR=1.62	A Faroes study (Karlsen 2016) observed and OR of 1.88 for PFOA serum levels below those at Pease. This OR could be detected with a sample size of 350 exposed and 175 unexposed children.	Feasible to study at Pease.
Hypercholesterolemia	OR=1.63	A NHANES study (Geiger 2014) obtained ORs of 1.49 and 1.35 for serum PFOA and PFOS levels similar to those at Pease. To detect an OR of 1.49 with 80% power requires a minimum of 540 exposed and 270 unexposed	Possible to study at Pease although a sample size of at least 500 exposed and 250 unexposed would be necessary (see table 6b).
Uric acid	0.28 mg/dL	A NHANES study (Kataria 2015) obtained a mean difference of 0.21 mg/dL for PFOA serum levels similar to Pease. However, for PFOS, the mean difference was 0.05 mg/dL.	Possible to study at Pease although a larger sample size than 500 exposed and 250 unexposed would be necessary.

Health-related Endpoint	Minimum Detectable Effect Size	Other Sample Size Considerations	Conclusion
Hyperuricemia	OR=1.83	A Taiwan study (Qin 2016) obtained an OR of 1.65 for PFHxS serum levels much lower than at Pease. For PFOA serum levels lower than at Pease, an OR of 2.2 was obtained.	Possible to study at Pease although a sample size of at least 500 exposed and 250 exposed may be necessary to evaluate the effect of serum PFHxS. (For serum PFOA, the Pease sample size of 350 exposed and 175 unexposed may be sufficient)
IQ	3 point mean difference	A Taiwan study (Wang 2015) obtained IQ mean differences of ≤2 points for PFOS serum levels higher than at Pease. A C8 study (Stein 2013) did not find a decrease in IQ with PFOA exposure and did not evaluate PFOS or PFHxS.	Possible to study at Pease although a sample size larger than 500 exposed and 250 unexposed would be necessary.
Neurobehavioral	Could not be calculated due to insufficient information	Some studies had sample sizes achievable at Pease while others had much larger sample sizes. The effects observed were not large (e.g., an OR for learning problems was 1.2 for PFHxS and lower for the other PFAS, and ORs for hyperactivity and coordination problems were <1.5 for each of the PFAS). The few studies that have been conducted evaluated different neurobehavioral tests.	Similar conclusion as for IQ: Possible to study at Pease although a sample size larger than 500 exposed and 250 unexposed would be necessary.
Sex hormones	See appendix for sample size calculations and assumptions required for the calculations.	At PFOS serum levels much higher than at Pease, a C8 study (Lopez-Espinosa 2016) observed reductions in estradiol that would require a sample size of over a thousand of exposed to achieve sufficient statistical power. However, the observed reductions in testosterone would require a sample size of between 500 and 1,000 exposed.	Possible to study at Pease although a sample size larger than 500 exposed and 250 unexposed would be necessary.

Health-related Endpoint	Minimum Detectable Effect Size	Other Sample Size Considerations	Conclusion
Thyroid function	See appendix for sample size calculations and assumptions required for the calculations.	A C8 study (Lopez-Espinosa 2012) observed small differences for PFOS and PFOA serum levels considerably higher than at Pease. To detect these differences would require a sample size of over a thousand exposed. On the other hand, a Taiwan study (Lin 2013) observed differences that could be detected with sufficient power with a sample size of 350 exposed and 175 unexposed.	Possible to study at Pease.
Atopic dermatitis	OR=1.95	A Taiwan study (Wang 2011) obtained an OR of 2.19 for PFOS serum levels similar to Pease. However, the study evaluated children aged 2 years. No other PFAS study evaluated atopic dermatitis	Possible to study at Pease.
Asthma	OR=2.00	Two NHANES studies (Humblet 2014, Stein 2016) observed ORs between 1.2 and 1.3 which would require a sample size of over 2,000 exposed. However, a Taiwan study (Dong 2013) obtained ORs between 3.8 and 4.0 for PFHxS and PFOA serum levels lower than at Pease.	Possible to study at Pease.
Rhinitis	OR=1.69	A NHANES study (Stein 2016a) evaluated rhinitis and obtained an OR of 1.35 for serum PFOA similar to those at Pease. To detect this OR would require over a thousand exposed. However, ORs between 1.5 and 1.6 could be detected with sufficient statistical power with a sample size of 500 exposed and 250 unexposed. These are ORs that are reasonable to detect and fall within the 95% CI for the finding in the NHANES study.	Possible to study at Pease
Antibody response to childhood vaccines	Could not be calculated due to insufficient information	Three studies that have been conducted of these endpoints had sample sizes that could be achievable at Pease. Only two studies (Granum 2013, Stein 2016) have evaluated the same endpoint – rubella.	Possible to study at Pease although a sample size larger than 500 exposed and 250 exposed may be necessary.

Health-related Endpoint	Minimum Detectable Effect Size	Other Sample Size Considerations	Conclusion
Attention deficit/hyperactivity disorder (ADHD)	ORs: 1.9 – 2.5	A C8 study (Stein 2011) obtained an OR of 1.55 (ADHD + meds) for PFHxS serum levels similar to Pease. A NHANES study (Hoffman 2010) observed an OR of 1.67 for PFHxS serum levels similar to Pease.	Not feasible to study using the Pease population alone (for ADHD confirmed by current medications)
Autism spectrum disorder (ASD)	ORs > 4.0	One study (Liew 2015) obtained an OR of 1.3 for serum PFHxS levels lower than at Pease. To detect this OR would require >10,000 exposed.	Not feasible to study using the Pease population alone.
Delayed puberty	Could not be calculated due to insufficient information	Only one study evaluated delayed puberty among children. This was a C8 study (Lopez-Espinosa 2011) that evaluated several thousand children. It is likely that sample sizes much larger than at Pease would be necessary.	Not feasible to study using the Pease population alone.
Thyroid disease	OR > 8.0	A C8 study (Lopez-Espinosa 2012) obtained an OR of 1.44 for PFOA serum levels considerably higher than those in the Pease population. To detect this OR with 80% statistical power would require a sample size of over 10,000 exposed children.	Not feasible to study using the Pease population alone.
Childhood cancers		No PFAS study has evaluated childhood cancers. Given the incidence and prevalence of cancers such as leukemia, a sample size of many thousands of exposed would be necessary.	Not feasible to study using the Pease population alone.

The minimum detectable effect size is based on a sample size of 350 children exposed and 175 children unexposed, and specifying statistical power of 80% (or a type 2 or "β" error of .20) and a type 1 ("α") error of .10 (see table 6a). This minimum detectable effect size is compared to the adverse effect sizes observed in other PFAS studies. Where possible, the focus is on adverse effect sizes in the PFAS studies observed for PFAS serum levels similar to those among the Pease children. An endpoint is considered feasible to study at Pease if an adverse effect size observed in PFAS study can be detected with sufficient statistical power (i.e., statistical power of ≥80%) by a sample size achievable at Pease, i.e., a sample size of 350 exposed children at Pease and 175 children unexposed to the PFAS-contaminated drinking water at Pease. If only one PFAS study has been conducted on a health-related endpoint, then the endpoint was considered feasible to study at Pease if an odds ratio of <2.0 could be detected with statistical power of 80%.

Note: The studies mentioned in the column of the table labeled "Other Sample Size Considerations" are included only to give a sense of the adverse effect sizes that might occur in a Pease study. Due to the paucity of studies for each health-related endpoint, there is considerable uncertainty concerning the effect sizes that might be expected to occur in a Pease study.

OR: Odds ratio. The odds ratio roughly approximates the risk ratio. The risk ratio is the proportion of the exposed population with a disease divided by the proportion of the unexposed population with a disease.

Note: Hypertension is not included in this table because there is no evidence so far of an association between PFAS serum levels and hypertension in children. Adverse birth outcomes are not included in this table because these outcomes are not feasible to study at Pease. Although the number of children potentially exposed to the PFAS-contaminated drinking water while attending daycare at the Pease Tradeport can be estimated, there is a lack of information on the number of children potentially exposed in utero to the PFAS-contaminated drinking water because their mothers were employed at the Pease Tradeport during the pregnancy. To evaluate adverse birth outcomes with sufficient statistical power would require the inclusion of several hundreds of exposed births.

Note: The health-related endpoints listed in this table satisfy the criteria of scientific importance and public health significance as discussed on page 8 of the text.

Table 7a. Minimum detectable effects for an adult epidemiological study, 1,500 per stratum.*

Endpoint	α and $\beta = .05$	$\alpha = .05$, $\beta = .20$	α and $\beta = .10$	$\alpha = .10$, $\beta = .20$
Chronic kidney disease	OR=2.54	OR=2.14	OR=2.20	OR=2.00
Thyroid disease, unconfirmed	OR=1.48	OR=1.36	OR=1.38	OR=1.32
Thyroid disease, confirmed	OR=1.63	OR=1.48	OR=1.50	OR=1.42
Total cholesterol (mean difference)	5.5 mg/dL	4.3 mg/dL	4.5 mg/dL	3.8 mg/dL
LDL (mean difference)	4.5 mg/dL	3.5 mg/dL	3.7 mg/dL	3.1 mg/dL
Hypercholesterolemia	OR=1.42	OR=1.32	OR=1.34	OR=1.28
Uric acid (mean difference)	0.21 mg/dL	0.17 mg/dL	0.18 mg/dL	0.15 mg/dL
Hyperuricemia	OR=1.35	OR=1.27	OR=1.28	OR=1.24
Elevated ALT (>45 IU/L, men; >34 IU/L, women)	OR=1.49	OR=1.37	OR=1.39	OR=1.33
Elevated GGT (>55 IU/L, men; >38 IU/L, women)	OR=1.44	OR=1.33	OR=1.35	OR=1.29
Elevated direct bilirubin (>0.03 mg/dL)	OR=2.80	OR=2.34	OR=2.40	OR=2.16
ALT (mean difference)	2.65 IU/L	2.06 IU/L	2.15 IU/L	1.83 IU/L
GGT (mean difference)	5.92 IU/L	4.60 IU/L	4.80 IU/L	4.09 IU/L
Direct bilirubin (mean difference)	0.079 mg/dL	0.060 mg/dL	0.064 mg/dL	0.055 mg/dL
Liver disease	OR=2.24	OR=1.92	OR=1.97	OR=1.80
Cardiovascular disease	OR=1.45	OR=1.34	OR=1.36	OR=1.30
Hypertension	OR=1.31	OR=1.24	OR=1.25	OR=1.21
Ulcerative colitis	OR=4.13	OR=3.24	OR=3.38	OR=2.94
Rheumatoid arthritis	OR=2.70	OR=2.25	OR=2.32	OR=2.10
Lupus	OR=6.87	OR=4.97	OR=5.24	OR=4.33
Multiple Sclerosis	OR=5.30	OR=3.97	OR=4.15	OR=3.50
Osteoporosis	OR=1.73	OR=1.55	OR=1.58	OR=1.48
Osteoarthritis	OR=1.58	OR=1.44	OR=1.46	OR=1.39
Endometriosis (750 per stratum)	OR=1.92	OR=1.69	OR=1.73	OR=1.61
Pregnancy-induced hypertension (750 per stratum)	OR=1.84	OR=1.63	OR=1.66	OR=1.55
Kidney cancer	OR=5.60	OR=4.27	OR=4.45	OR=3.80

* Some health-related endpoints are not included in the table because there was insufficient information to calculate minimum detectable effects. For thyroid function, see the appendix for a description of the assumptions used in the sample size calculations and the resulting calculations.

Table 7b. Summary of information used to categorize the feasibility of studying health-related endpoints for a Pease adult study.

Health-related Endpoint	**Minimum Detectable Effect Size: 1,500 exposed and 1,500 unexposed**	**Other Sample Size Considerations**	**Conclusion**
Lipids (total cholesterol)	3.8 mg/dL	A C8 study (Steenland 2009) observed a 3 – 4 mg/dL change in total cholesterol and LDL for PFOS serum levels similar to those at Pease.	Feasible to study at Pease
Hypercholesterolemia	OR=1.28	A Canadian study (Fisher 2013) obtained an OR of 1.57 for PFHxS serum levels similar to those at Pease.	Feasible to study at Pease
Uric acid	0.15 mg/dL	A NHANES study (Shankar 2011) observed a mean difference of 0.40 mg/dL for serum PFOA levels similar to those at Pease.	Feasible to study at Pease
Hyperuricemia	OR=1.24	A NHANES study (Shankar 2011) obtained an OR of 1.90 for serum PFOA levels similar to those at Pease.	Feasible to study at Pease
Thyroid disease (unconfirmed)	OR=1.32	A C8 study (Winquist 2014a), hazard ratios ≤1.3 were obtained for PFOA serum levels similar to those at Pease. (Only PFOA was evaluated in this study.)	Feasible to study at Pease
Cardiovascular disease	OR=1.30	A NHANES study (Shankar 2012) obtained an OR of 2.01 for PFOA serum levels similar to those at Pease.	Feasible to study at Pease
Hypertension	OR=1.21	Only one community study (a C8 study, Winquist 2014b), evaluated hypertension and obtained an OR < 1.0 for serum PFOA (the only PFAS evaluated). However, the sample size achievable at Pease is capable of detecting very low ORs with sufficient statistical power.	Feasible to study at Pease
Osteoarthritis	OR=1.39	A NHANES study (Uhl 2013) obtained an OR of 1.5 for serum PFOA levels similar to those at Pease.	Feasible to study at Pease
Osteoporosis	OR=1.48	A NHANES study (Khalil 2016) obtained an OR > 10 among women, for serum PFHxS levels lower than those at Pease.	Feasible to study at Pease

Health-related Endpoint	Minimum Detectable Effect Size	Other Sample Size Considerations	Conclusion
Serum Immune Biomarkers	Could not be calculated due to insufficient information	Only one published study (Stein 2016b) has been conducted that evaluated serum immune biomarkers at baseline (i.e., cross-sectionally). This study had a sample size of 75 adults. A cross-sectional evaluation of PFAS serum levels and immune biomarkers in a Pease adult study could provide important information on the effects of PFAS exposures on immune function in humans.	Feasible to study at Pease
Liver function: Elevated ALT Elevated GGT Elevated direct bilirubin	 OR=1.33 OR=1.29 OR=2.16	A NHANES study (Gleason 2015) evaluated PFAS serum levels similar to those at Pease. For elevated ALT, ORs between1.2 and 1.5 were obtained. For elevated GGT, ORs between 1.0 and 1.3 were obtained. For elevated direct bilirubin, ORs between 1.1 and 1.7 were obtained.	Possible to study at Pease, but may require a larger sample size than 1,500 exposed and 1,500 unexposed to evaluate PFOS and PFHxS serum levels and ALT and GGT. Direct bilirubin is probably not feasible to study using the Pease population alone.
Thyroid disease (confirmed)	OR=1.42	A C8 study (Winquist 2014a), hazard ratios ≤1.3 were obtained for PFOA serum levels similar to those at Pease. (Only PFOA was evaluated in this study.)	Possible to study at Pease, but will require a larger sample size than 1,500 exposed and 1,500 unexposed.
Thyroid function	See appendix for sample size calculations and assumptions required for the calculations.	A C8 study (Knox 2011) observed very subtle changes that would require a study of equivalent size (52,296) to detect associations with sufficient statistical power. On the other hand, a NHANES study (Wen 2013) observed larger changes (at PFAS serum levels similar to those at Pease) that could be detected with a sample size achievable at Pease.	Possible to study at Pease.

Health-related Endpoint	Minimum Detectable Effect Size	Other Sample Size Considerations	Conclusion
Endometriosis	OR=1.61 (750 exposed & 750 unexposed)	A NHANES study (Campbell 2016) obtained ORs of 1.47 and 2.86 for serum PFHxS and PFOA, respectively. The serum levels for these two PFAS were similar to those in the Pease population.	Possible to study at Pease if sufficient numbers of women can be recruited.
Pregnancy-induced hypertension	OR=1.55 (750 exposed pregnancies and 750 unexposed pregnancies	A C8 study (Stein 2009, Darrow 2013) obtained an OR of 1.6 for serum PFOS levels higher than at Pease.	Possible to study at Pease but may require a larger sample size than 1,500 exposed and 1,500 unexposed in order to achieve a sufficient number of pregnancies.
Liver disease	OR=1.80	A C8 study (Darrow 2016) and a NHANES study (Melzer 2010) observed no elevation in liver disease. However, the C8 study evaluated only PFOA and the NHANES study evaluated PFOA and PFOS but not PFHxS.	Not feasible to study using the Pease population alone.
Kidney disease	OR=2.00	A C8 study (Dhingra 2016a) evaluated only PFOA and obtained ORs of 1.26 and 1.36 for the retrospective and prospective analyses, respectively, at the second quintile PFOA serum level. (Smaller ORs were observed at higher PFOA serum levels.)	Not feasible to study using the Pease population alone.
Ulcerative colitis	OR=2.94	A C8 study (Steenland 2013) observed RRs between 2.8 and 3.1 at the highest serum PFOA levels, considerably higher than those at Pease. At lower PFOA serum levels, the RRs were <2.2	Not feasible to study using the Pease population alone.
Rheumatoid arthritis	OR=2.10	A C8 study (Steenland 2013) observed RRs between 1.3 and 1.7 for serum PFOA.	Not feasible to study using the Pease population alone.
Lupus	OR=4.33	A C8 study (Steenland 2013) observed RRs <1.3 for serum PFOA.	Not feasible to study using the Pease population alone.
Multiple sclerosis	OR=3.50	A C8 study (Steenland 2013) observed RRs between 1.1 and 1.6 for serum PFOA	Not feasible to study using the Pease population alone.

Health-related Endpoint	Minimum Detectable Effect Size	Other Sample Size Considerations	Conclusion
Kidney cancer	OR=3.80 for kidney cancer	A C8 study of a community population (Vieira 2013) observed an RR of 1.70 for those served by the Little Hocking water system.	Not feasible to study using the Pease population alone. (Due to the very low background prevalences of other adult cancers, it is not feasible to study cancers using the Pease population alone.)

The minimum detectable effect size is based on a sample size of 1,500 adults exposed and 1,500 adults unexposed, and specifying statistical power of 80% (or a type 2 or "β" error of .20) and a type 1 ("α") error of .10 (see table 6a). This minimum detectable effect size is compared to the adverse effect sizes observed in other PFAS studies. Where possible, the focus is on adverse effect sizes in the PFAS studies observed for PFAS serum levels similar to those among the Pease adults. An endpoint is considered feasible to study at Pease if an adverse effect size observed in PFAS study can be detected with sufficient statistical power (i.e., statistical power of ≥80%) by a sample size of 1,500 exposed and 1,500 unexposed. If only one PFAS study has been conducted on a health-related endpoint, then the endpoint was considered feasible to study at Pease if an odds ratio of <2.0 could be detected with statistical power of 80%.

Note: the studies mentioned in the column of the table labeled "Other Sample Size Considerations" are included only to give a sense of the adverse effect sizes that might occur in a Pease study. Due to the paucity of studies for each health-related endpoint, there is considerable uncertainty concerning the effect sizes that might be expected to occur in a Pease study.

OR: odds ratio. The odds ratio roughly approximates the risk ratio (RR). The risk ratio is the proportion of the exposed population with a disease divided by the proportion of the unexposed population with a disease.
A hazard ratio can be interpreted in the same way as a risk ratio.

Note: The health-related endpoints listed in this table satisfy the criteria of scientific importance and public health significance as discussed on page 8 of the text.

Other sites with PFAS-contaminated drinking water from the UCMR-3

Table A1 shows the maximum combined levels of PFHxS and PFOS in any sample taken from each utility. Only utilities with detectable levels of either PFHxS or PFOS are listed. The data are from the UCMR-3 database as of July 2016 (US EPA 2016b). The ten utilities with the highest PFOS/PFHxS levels in a sample are the Commonwealth Utilities Corporation serving the Mariana Islands, the Artesian Water Company serving portions of the state of Delaware, the Security Water and Sanitation Districts serving Colorado Springs, the Horsham Water & Sewer (PA), the Warminster Municipal Authority (PA), the Oatman Water Company (AZ), the Issaquah Water System (WA), the Hyannis Water System (MA), the Suffolk County Water Authority (NY) and the Warrington Township Water & Sewer (PA). Three of the top 10 utilities are located near each other in the vicinity of Philadelphia, PA: Horsham, Warminster, and Warrington. ATSDR is currently considering whether it is feasible to include children and adults from these towns in studies that would also evaluate the Pease populations.

Willow Grove Naval Air Station/Air Reserve Station (a.k.a. Naval Air Station Joint Reserve Base and Air Force Reserve Station), Montgomery County, Pennsylvania

The Naval Air Station Joint Reserve Base (NASJRB) and Air Reserve Station (ARS) at Willow Grove ("Willow Grove") are two separate, but co-located military facilities in Montgomery County, Pennsylvania. The Navy acquired site in 1942 and began jet training there in 1949; the air force base began operations in 1958. In 2001, the Willow Grove bases employed 1,571 active-duty individuals, 993 members of the National Guard, 3,500 members of the Reserves, and 778 civilians with approximately 1,700 staff on-station daily. About 230 people resided on the bases year-round: less than 30 people resided in single family dwellings and less than 200 resided in barracks. Additionally, there were five officer family units, 200 enlisted family units, and 250 unaccompanied enlisted units as well as a daycare center on base for 96 children. The Willow Grove Branch Medical Clinic was also located there and provided primary care, medical support, preventive medicine, and occupational health services to 20,000 active duty, reserve, retired personnel, and their family members (ATSDR 2002a). Willow Gove became an Air National Guard Base in September 2011. The surplus land with the runways was turned over to Horsham Township for redevelopment.

AFFF used on the Willow Grove bases resulted in PFAS contamination of two nearby water systems – the Warrington Township Water and Sewer Department (WTWSD) which served the eastern portion of Warrington and the Horsham Water and Sewer Authority (HWSA).

In late October 2014, three of eight wells in the southern portion of the WTWSD were above the EPA Provisional Health Advisory Level (PHAL) for PFOS and were taken out of service. PFOS levels were the following: Well 1 (0.21 µg/L), Well 2 (1.6 µg/L), and Well 6 (1.3 µg/L). Although the wells pump directly into the distribution system, wells 1, 2, and 6 are blended together at a tank and enter the distribution system at one point. These wells constituted about 30% of the WTWSD supply. Well 3, in the northeast area of the eastern section, and well 9, which is centrally located in the eastern section, had very low levels of contamination.

Using currently available water distribution system information, ATSDR determined that for "present-day" conditions, the northern part of the eastern section of the WTWDS system generally received water that did not contain PFOA and PFOS. If any customers in the northern part of the system received water containing PFOA and PFOS, it was at levels below the EPA Lifetime Health Advisory (LTHA). The central part of the eastern section of the system may have received water containing PFOA

and PFOS concentrations above the EPA LTHA. The southeastern part of the eastern section of the system received water containing PFOA and PFOS concentrations up to 10 times the EPA LTHA. More detailed analyses of the water-distribution system need to be conducted to estimate historical PFAS concentrations at specific housing areas. These analyses would involve looking at the water-distribution system operating conditions, historical monthly well pumping records, and customer consumption information in more detail.

The western section of the Warrington system is supplied by water purchased from North Wales Water Authority and is not contaminated with PFAS. However, there is an interconnection between the eastern and western sections of the system which is used when there is a need in the eastern section.

Warrington Township Water and Sewer Department (WTWSD) UCMR 2014-2015 data*

Well	PFOS (µg/L)	PFHxS (µg/L)	PFOA (µg/L)	PFNA (µg/L)
Wells 1, 2, 6	0.67	0.24	0.12	-
Well 3	0.06	0.04	0.02	-
Well 9	0.09	0.06	0.03	-

*Wells 1, 2, 3, and 6 were sample 11/11/2014; Well 9 was sampled 5/11/2015

The HWSA is served by 15 wells as well as interconnections with other nearby water utilities. The water system is separated into two pressure zones, "high" and "low," with the wells in each zone pumping to fill storage tanks. The high zone has two storage tanks supplied by three wells and two interconnections. The low zone has three storage tanks served by 11 wells and an interconnection with Aqua Pennsylvania Southeastern Division. (Note: the Aqua system had 0.009 µg/L of PFOS and .005 µg/L PFOA during UCMR-3 sampling in 4/16. There are now samples from 7/16 which measured 0.0068 µg/L for PFOS and 0.0065 µg/L for PFOA.). June 2014 drinking water sample results indicated that PFAS contamination was solely in the low pressure zone which serves the majority of the service area. Prior to 1996 the system did not have pressure zones which means customers located in the current high pressure zone may have received water from wells in the low pressure zone. Generally, demand is met using water from the storage tanks. There are three elevated tanks, and each tank generally supplies a certain area of the system. Each tank will have different PFAS concentrations depending on which wells are supplying water to them. However, it is possible that a property in close proximity to a well which has a demand at the same time the well is pumping will have a higher percentage of water from the nearby well than other areas.

In June 2014, HWSA wells were tested for PFAS as part of the UCMR-3. Two wells, well #26 and well #40, had levels of PFOS greater than the EPA PHAL of 0.2 µg/l, and well #26 also exceeded the EPA HAL of 0.4 µg/l for PFOA. The PFAS contamination levels from the UCMR-3 for the Horsham supply wells are shown in the table below. Both wells #26 and #40 were removed from service in July 2014. According to the 2014 consumer confidence report for the HWSA, the average level of PFOS reported was 0.06 ppb, the average level of PFH_xS was 0.037 ppb, and PFOA was not detected. The two contaminated wells generally supplied about 25% of the water for the system; however, there were times that the two contaminated wells supplied as much as 35% of the water for the system.

In May 2016 subsequent to the EPA announcement of its lifetime health advisory for PFOA/PFOS, wells 10, 17, and 21 were immediately taken out of service. One of these three wells was shut down to comply with the EPA's new LTHA. The other two wells, which tested below the LTHA,

were shut down as a precaution. The other nine wells that now supply public drinking water across the township have tested below the EPA lifetime health advisory levels.

ATSDR used currently available water-distribution system information to determine that for "present-day" conditions, some areas in the southern and southeastern part of the low pressure zone received water containing PFOA and PFOS concentrations up to 9 times the EPA LTHA. The northeastern part of the low pressure zone received water containing PFOA and PFOS concentrations less than the EPA LTHA. More detailed analyses of the system need to be conducted to estimate historical PFAS concentrations at specific housing areas. These analyses would involve looking at the water-distribution system operating conditions, historical monthly well pumping records, and customer consumption information in more detail.

In addition to the five total public wells that HWSA shut down, the Navy and the EPA identified approximately 40 additional private wells in Horsham that are at or above the EPA guidance of 70 parts per trillion (ppt). The Navy is providing bottle water to these private well owners.

Horsham Water and Sewer Authority (HWSA) UCMR 2014 data*

Well	PFOS (µg/L)	PFHxS (µg/L)	PFOA (µg/L)	PFNA (µg/L)
Well 10	0.05	0.04	0.03	-
Well 17	0.10	0.05	0.03	-
Well 21	0.14	0.08	-	-
Well 26	0.70	0.39	0.29	-
Well 40	1.00	0.59	0.06	-

*Wells 10 and 17 were sampled 12/9/2014; Wells 21, 26, and 40 were sampled 6/24/2014

Other drinking water contaminants

Supply wells on base contained volatile organic compounds (VOC) and metals. Maximum detected levels in supply wells from sampling conducted in 1979-1984 were 91 ppb for PCE and 300 ppb for TCE. After contamination was detected, the well with the highest levels of contamination was used mainly for fire protection. Additionally, the Navy installed an air stripper to treat groundwater prior to distribution, and monitoring of treated water between 1996 and 1998 found no contaminants above EPA's Maximum Contaminant Levels (MCLs) (ATSDR 2002a). According to the EPA, over 800 employees at the two facilities may have drank or come into contact with treated water from the Navy supply wells (https://cumulis.epa.gov/supercpad/cursites/csitinfo.cfm?id=0303820). VOC contamination in off-site wells has not been attributed to the base, and the local water authorities (HWSA and WTWSD) treat the water for VOCs before distribution (ATSDR 2002a).

Naval Air Warfare Center (a/k/a Naval Air Development Center), Warminster Township, Bucks County, Pennsylvania

The former Naval Air Warfare Center (NAWC) is located in Warminster Township. The base operated from 1944 until its closure in September 1996. In 1994, approximately 1,850 civilians and 1,000 military personnel were stationed or employed on base. At its peak, the base employed 2,800 civilians, 200 military personnel, and up to 300 daily contractors (ATSDR 2002b).

Approximately 800 to 1,000 military personnel and their families stationed at nearby Willow Grove Naval Air Station lived in two on-base housing areas at NAWC while as many as six families may have resided in officer housing. Between 450-550 enlisted personnel and their families lived at the Shenandoah Woods housing complex. Site 5, a former landfill, was located in Shenandoah Woods. Quarters A and B, located within Area C, provided housing for the base's commanding officer and second-in-command (ATSDR 2002b).

Four out of eighteen of the Warminster Municipal Authority (WMA) public water supply wells are in close proximity to the former NAWC site. The WMA provides water to approximately 40,000 people. The water supplied to the customers is from water supply wells in the WMA system and may be purchased from the North Wales Water Authority (NWWA) as well as the Upper Southampton Municipal Authority on an emergency basis. WMA's water supply wells are connected individually to the distribution network and are subsequently blended within the distribution system in tanks and standpipes. Therefore, customers located geographically closest to a given water supply well will likely receive more water from that well than users located further away (ATSDR 2016).

AFFF was used for decades at the base for firefighting training activities. PFAS were first tested for in groundwater as emerging contaminants in preparation for the CERCLA 2012 Five Year Review for this site. In summer 2013, PFOS levels above the EPA PHAL were first discovered in groundwater on the former Navy property. As part of the EPA's UCMR-3, sampling for six PFAS in the WMA first occurred in November 2013. UCMR-3 monitoring for PFAS is required at the entry point to the distribution system for each well and at any interconnection in operation. Accordingly, WMA conducted sampling in November 2013 and May 2014 for all wells and conducted sampling in November 2013 and February, May, and August 2014 for the interconnection with NWWA (ATSDR 2016).

Samples taken in the WMA system detected levels of PFOS, PFOA, PFHxS and/or PFHpA. The source of the contamination was the use of AFFF at NAWC. In November 2013, three WMA public water wells had levels at or above EPA's PHAL for PFOS. In this sampling event, 17 samples covering 17 wells in the WMA and one sample of the NWWA interconnection were taken and analyzed for PFAS. One of the 17 WMA samples represents the combined water extracted from WMA Wells 43 and 44. Water from these two wells is combined for treatment and samples are taken after treatment at the entry point to the distribution system. PFOS was detected in 6 public wells and PFOA was detected in 8 public wells. PFOS was detected in Well 26 at 0.791 µg/L, more than three times the 0.2 µg/L PFOS PHAL value. Wells 10 and 13 had PFOS concentrations of 0.193 and 0.16 µg/L that can be rounded to 0.2 µg/L. None of the PFOA detections exceeded the PFOA PHAL in the WMA wells. Well 26 had the highest detections for PFOA and PFOS. In summer 2014, PFOS was detected in four public wells. The highest concentrations were in Well 26 at 1.09 µg/L, more than five times the 0.2 µg/L PFOS PHAL value, and in Well 10 at 0.176 µg/L. PFOA was detected in four wells, including Well 26 at 0.349 µg/L, close to the 0.4 µg/L PHAL for PFOA. Wells 13 and 26 were shut down in June 2014. Well 10 was shut down in September 2014. On May 19, 2016, wells 2, 14 and 15 were removed from service due to the EPA new lifetime health advisory level for PFOA/FPOS (ATSDR 2016).

PFOS levels above the PHAL were also detected in private drinking water samples. As of September 2015, 100 private wells (94 residential and 6 non-residential) were identified and sampled within an approximate 1-3 mile radius of the site. At least one PFAS was detected in the majority (93 out of 100) of these private water wells. Of the 94 residential private water wells, five were non-detect for PFOA and PFOS, 18 had detections of PFOA only, and 71 had both PFOA and PFOS. Eleven exceeded the PFOS PHAL, ranging from 0.152 µg/L to 0.729 µg/L. The PFOS PHAL exceedances are

in two general locations: one location is south of the Jacksonville Road and East Bristol Road intersection and the other location is in the area of York Road and W Street. Six residential wells with PFOS levels that range from 0.102 to 0.109 µg/L (50% of the PHAL) are located at the Jacksonville/East Bristol Roads intersection (ATSDR 2016).

The Navy and EPA provided a limited number of residents whose private well water was at or above EPA's PHAL (with rounding up to one significant digit) with bottled water to use for drinking and cooking water, and is currently working to connect these locations to public water (ATSDR 2016).

Using currently available water-distribution system information, ATSDR determined that for "present day" conditions, the southwestern part of the Warminster system typically received water that did not contain PFOA and PFOS concentrations. If any customers in this part of the system received water containing PFOA and PFOS concentrations, it was at levels below the EPA LTHA. The northwestern part of the Warminster system typically received water containing PFOA and PFOS concentrations at or below the EPA LTHA. Some areas in the eastern parts of the Warminster system received water containing PFOA and PFOS concentrations at levels up to three times the EPA LTHA, and areas in the central part received water containing concentrations at level up to 15 times the EPA LTHA. More detailed analyses of the system need to be conducted to estimate historical PFAS concentrations at specific housing areas. These analyses would involve looking at the water-distribution system operating conditions, historical monthly well pumping records, and customer consumption information in more detail.

Although some WMA customers received the majority of their water from one of the contaminated wells, the majority of water customers likely received water that either did not contain PFAS or had levels less than the PHALs (but levels may be higher than the EPA LTHA for PFOS/PFOA). If one assumes that all the wells supply a similar amount of water to the system (each well typically supplied 5-10% of the water to the system), then the number of customers potentially exposed to elevated PFAS in their drinking water could be approximately 7,000.

Warminster Municipal Authority (WMA) UCMR 2013-2014 data*

Well	PFOS (µg/L)	PFHxS (µg/L)	PFOA (µg/L)	PFNA (µg/L)
Well 2	0.06	0.03	0.03	
Well 10	0.19	0.10	0.09	-
Well 13	0.16	0.09	0.12	-
Well 14	0.06	0.03	0.02	-
Well 15	0.06	0.04	0.02	-
Well 26	1.09	0.39	0.35	-

*Wells 2, 10, 13, 14, and 15 were sampled 11/19/2013; Well 26 was sampled 6/9/2014

Other drinking water contaminants

Samples taken in 1979 showed maximum levels of contamination in on-site supply wells of 36 ppb for PCE and 293 ppb for TCE. These wells were closed in 1979. Contamination levels in samples taken from off-site municipal supply wells found 17 ppb for PCE and 67.8 ppb for TCE; past off-base residents may have been exposed to these VOCs between 1974, when the well first began supplying water, until it was closed in 1979. Sampling of VOCs in off-site private wells detected PCE at 31 ppb; as

a result, affected homes were connected to municipal water supplies or groundwater treatment systems were installed (ATSDR 2002b).

Because the TCE- and PCE-contaminated wells were shut down in 1979, military service personnel and DOD civilian workers who began service/employment at NAWC after 1979 might be eligible for a PFAS study. More information is needed to determine when the water supply may have been contaminated with PFAS.

More detailed analyses will help determine which specific housing areas received water containing PFOA and PFOS from the NASJRB and ARS at Willow Grove and the NAWC in Warminster. To conduct more detailed analyses, including modeling, additional information and specific data pertinent to each water system's operations needs to be obtained from site visits to the water utilities.

Appendix tables

Table A1. Maximum levels (parts per billion) of combined PFHxS and PFOS from the US EPA's Third Unregulated Contaminant Monitoring Rule (UCMR-3)

Water Utility Name	State	Size	PFHxS & PFOS sum
Commonwealth Utilities Corp. (Saipan)	MP	L	8.60
Artesian Water Company	DE	L	2.48
Security WSD	CO	L	1.89
Horsham Water & Sewer Authority	PA	L	1.59
Warminster Municipal Authority	PA	L	1.479
Oatman Water Company	AZ	S	1.03
Warrington Township Water & Sewer Department	PA	L	0.91047
Issaquah Water System	WA	L	0.841
Hyannis Water System	MA	L	0.7
Suffolk County Water Authority	NY	L	0.67
United Water PA	PA	L	0.572
Emerald Coast Utilities Authority	FL	L	0.56
GU Waterworks Authority - Northern System	GU	L	0.55
Widefield WSD	CO	L	0.54
Oakdale	MN	L	0.4913
City of Tucson	AZ	L	0.476
City of Cleveland Heights	OH	L	0.4
Sanford Water District	ME	L	0.4
Wright-Patterson AFB Area A/C	OH	L	0.36
Liberty Water LPSCO	AZ	L	0.33
Westfield Water Department	MA	L	0.33
City of Zephyrhills	FL	L	0.32
Bemidji	MN	L	0.32
City of Fountain	CO	L	0.29
City of Stuart Water Plant	FL	L	0.259

Water Utility Name	State	Size	PFHxS & PFOS sum
City of Tempe	AZ	L	0.245
CA American Water Co. - Suburban	CA	L	0.241
City of Newburgh	NY	L	0.24
CA Water Service - Visalia	CA	L	0.212
Eastern Municipal Water District	CA	L	0.202
New Windsor Consolidated Water District	NY	L	0.1936
VAW Water System, Inc.	AL	L	0.18
Freeport	IL	L	0.18
La Crosse Waterworks	WI	L	0.172
Salt River Public Works	09*	L	0.166
City of Martinsburg	WV	L	0.157
Dyer Water Department	IN	L	0.1437
Atlantic City MUA	NJ	L	0.142
West Morgan - East Lawrence Water Authority	AL	L	0.13
City of Greensboro	NC	L	0.124
Rome	GA	L	0.12
Dover Water Department	NH	L	0.12
CA Water Service - Chico	CA	L	0.118
Moore County Public Utilities - Pinehurst	NC	L	0.118
Rhinelander Water & Wastewater	WI	S	0.1173
Bayleaf Master	NC	L	0.11
City of Ocala	FL	L	0.104
NJ American Water Co. - Raritan	NJ	L	0.103
Mahwah Water Department	NJ	L	0.098
City of Abilene	TX	L	0.09781
West Lawrence Water Co-op	AL	L	0.09
Hampton Bays Water District	NY	L	0.082
Fort Drum	NY	L	0.08

Water Utility Name	State	Size	PFHxS & PFOS sum
City of Lathrop	CA	L	0.076
Northeast Alabama Water System	AL	L	0.07
City of Anaheim	CA	L	0.07
Fair Lawn Water Department	NJ	L	0.06603
City of Orange	CA	L	0.0659
Montebello Land & Water Company	CA	L	0.065
Vienna	WV	L	0.0641
Chatsworth	GA	L	0.06303
Bethany	OK	L	0.063
City of Pico Rivera Water Department	CA	L	0.062
Camp Pendleton (South)	CA	L	0.062
Montgomery County Water Services #2	OH	L	0.061
Rainbow City Utilities Board	AL	L	0.06
Florence Water-Wastewater Department	AL	L	0.06
Plainfield Township	MI	L	0.06
Pendleton County Water District #1/South	KY	S	0.05853
City of Miami Beach	FL	L	0.058
Ridgewood Water	NJ	L	0.058
Woodbury	MN	L	0.0577
Montgomery County Water Services #1	OH	L	0.0542
CA Water Service - East Los Angeles	CA	L	0.054
Town of Nashville	NC	S	0.05312
Metropolitan DWID	AZ	L	0.053
City of Downey Water Department	CA	L	0.053
Pierre	SD	L	0.053
Park Water Company - Bellflower/Norwalk	CA	L	0.051
Washington Township MUA	NJ	L	0.0503

Water Utility Name	State	Size	PFHxS & PFOS sum
Colbert County Rural Water System	AL	L	0.05
Gadsden Waterworks & Sewer Board	AL	L	0.05
Southside Waterworks	AL	L	0.05
City of North Miami	FL	L	0.05
Kennebunk, Kennebunkport & Wells WD	ME	L	0.05
Bell Arthur Water Corp.	NC	S	0.05
City of Garden Grove	CA	L	0.0496
City of Lauderhill	FL	L	0.049
FKAA	FL	L	0.049
Yorba Linda Water District	CA	L	0.0474
City of Miramar	FL	L	0.047
Miami International Airport	FL	L	0.047
City of Corona	CA	L	0.046
Orchard Dale Water District	CA	L	0.045
Lima City Water	OH	L	0.045
Pico Water District	CA	L	0.044
Golden State Water Co. - Norwalk	CA	L	0.043
MDWASA - Main System	FL	L	0.043
Ann Arbor	MI	L	0.043
City of Fullerton	CA	L	0.0412
Cliffdale West	NC	L	0.041
Central ASG	AS	L	0.04
City of DeFuniak Springs Water System	FL	L	0.04
Cottage Grove	MN	L	0.0381
City of Great Bend	KS	L	0.037
City of Pleasanton	CA	L	0.036
Sacramento Suburban Water District	CA	L	0.036

Water Utility Name	State	Size	PFHxS & PFOS sum
Mashpee Water District	MA	L	0.033
Belvidere	IL	L	0.03167

L=large system (serves >10,000); S=small system (serves <10,000)

* Tribal nation located in Arizona

EXHIBIT I

NEW YORK STATE OF OPPORTUNITY. | Department of Health

ANDREW M. CUOMO
Governor

HOWARD A. ZUCKER, M.D., J.D.
Commissioner

SALLY DRESLIN, M.S., R.N.
Executive Deputy Commissioner

August 24, 2017

Brenda Fitzgerald, M.D.
Director
Center for Disease Control and Prevention
Administrator, Agency for Toxic Substances and Disease Registry
US Department of Health & Human Services
1600 Clifton Road
Atlanta, Georgia 30329-4027

Dear Dr. Fitzgerald:

The presence of perfluoroalkyl substances (PFAS) in drinking water is a growing national issue, with the number of affected water systems identified throughout the U.S. increasing rapidly. As Health Commissioners and Directors in states that have identified PFAS, including perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), in local water systems, we request that ATSDR undertakes a longitudinal, national health effects study of communities impacted by PFAS across the country.

Our state health departments, along with other states in the northeastern United States, have been working to address PFAS contamination since 2015, by minimizing exposure to PFAS in drinking water and some states are offering blood testing for affected residents. These efforts are supported by fact sheets, online tools and resources, and assistance with blood testing from the Centers for Disease Control and Prevention's (CDC) National Center for Environmental Health (NCEH) and Agency for Toxic Substances and Disease Registry (ATSDR).

ATSDR recently released a draft document, "Feasibility Assessment for Epidemiological Studies at Pease International Tradeport in Portsmouth, New Hampshire," documenting an approach to appropriate follow-up health studies for children and adults as well as highlighting population-size related issues that our states would be confronted with if we conducted these studies individually.

Our communities are familiar to your staff – Hoosick Falls, Petersburgh, and Newburgh in New York; Portsmouth, New Hampshire; North Bennington, Vermont; Warminster and Willow Grove, Pennsylvania; Oscoda and Graying, Michigan. We welcome the opportunity to share additional information about our affected populations as part of a national effort to develop a plan to study health outcomes in multiple PFAS-affected communities.

Through prior communication between the CDC, our departments, and Senators Gillibrand and Schumer, we understand that ATSDR and NCEH are determining if a long-term community health study would answer some questions about the health effects of exposure to PFAS. This letter is our official request for ATSDR to move quickly to launch a longitudinal study of health outcomes in communities affected by PFAS from legacy industrial sources and from firefighting foams used by the military and others.

Sincerely

Howard Zucker M.D.

Howard A. Zucker, MD, JD
Commissioner of Health

Jay Butler, MD
Director of Public Health
Alaska

Nick Lyon
Director, Department of Health and Human Services
Michigan

Lisa Morris, MSSW
Director, Division of Public Health Service
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