Health Consultation

Evaluation of per-and polyfluoroalkyl substances (PFAS) detected in private residential drinking water wells located within 1 mile of the Pease International Tradeport

PEASE AIR FORCE BASE
PORTSMOUTH, NEWINGTON, AND GREENLAND, NEW HAMPSHIRE

EPA FACILITY ID: NH7570024847

February 24, 2022

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Toxic Substances and Disease Registry
Division of Community Health Investigations
Atlanta, Georgia 30333

Health Consultation: A Note of Explanation

An ATSDR health consultation is a verbal or written response from ATSDR to a specific request for information about health risks related to a specific site, a chemical release, or the presence of hazardous material. In order to prevent or mitigate exposures, a consultation may lead to specific actions, such as restricting use of or replacing water supplies; intensifying environmental sampling; restricting site access; or removing the contaminated material.

In addition, consultations may recommend additional public health actions, such as conducting health surveillance activities to evaluate exposure or trends in adverse health outcomes; conducting biological indicators of exposure studies to assess exposure; and providing health education for health care providers and community members. This concludes the health consultation process for this site, unless additional information is obtained by ATSDR which, in the Agency's opinion, indicates a need to revise or append the conclusions previously issued.

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Prepared By:

U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry
Office of Community Health and Hazard Assessment
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Summary

Introduction

In April 2015, the U.S. Air Force (USAF) asked the Agency for Toxic Substances and Disease Registry (ATSDR) to evaluate per- and polyfluoroalkyl substances (PFAS) exposure in the private drinking water wells near Pease International Tradeport in Portsmouth, New Hampshire (NH). The source of PFAS is believed to be firefighting foam (aqueous film-forming foam: AFFF) used on the former Pease Air Force Base (AFB). Chemicals from the foam likely traveled from Pease AFB, now Pease International Tradeport, through soil and water to nearby private wells supplying residential drinking water.

Perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), and perfluoro-hexanesulfonic acid (PFHxS) are three forms of PFAS that were detected in several of the private wells tested. Scientific information suggests an association between PFOA, PFOS, and PFHxS exposures and various health endpoints, including effects on cholesterol (not PFHxS), immune responses, fetal growth and development, endocrine systems (e.g., thyroid), and the liver. Several other PFAS were detected in the water, some of which have may have similar health effects as PFOA and PFOS.

This report reviews data from June 2014 through June 2020 for 42 private wells near the Pease International Tradeport. If any other private drinking water wells are identified in the PFAS exposure area, the USAF will include them in future sampling and assessment efforts. The USAF used "RES" followed by the well number to identify the wells sampled around Pease. ATSDR used the same designations in the health consultation to avoid confusion.

On April 30, 2020, ATSDR released this health consultation report for public comment. The comment period ended on July 30, 2020. ATSDR received 65 comments from individuals, government agencies, and a corporation during the public comment period. Appendix C provides responses to the comments received.

Conclusions

ATSDR evaluated the public health implications of past and current PFAS exposure to the users of private wells near the Pease International Tradeport and reached four conclusions. These conclusions are limited by several uncertainties. The specific PFAS formulation in the AFFF used at the former Pease AFB is not known. ATSDR used a health-protective approach to evaluate concentrations of 23 PFAS in drinking water wells. ATSDR's conclusions are based on

evaluation of the PFAS that were measured in the water. However, there might be other PFAS in the water that were not measured.

Conclusion 1—Wells with Possible PFAS Hazard/Risk

Past PFAS exposures may have increased the risk of harmful non-cancer health effects, especially to young children, who drank water from RES17, RES19, RES21, RES23, and RES37 or were born to mothers who did. The cancer risk from past exposures to all PFAS in these wells is uncertain. No current or future harmful exposures are expected for residents using these five water supply wells because actions have been taken to reduce or eliminate their exposures.

Basis for conclusion

The combined past exposures to PFOA, PFOS, and PFHxS to users of RES17, RES19, RES21, RES23, and RES37 approached health effect levels from animal studies. Thus, these exposures may have increased the risk of harmful non-cancer health effects, especially for developmental, endocrine (e.g., thyroid), and immune effects, in young children. Harmful effects for other health outcomes shown to be associated with PFOA, PFOS, or PFHxS may also occur, such as effects on cholesterol and the liver. Harmful non-cancer health effects for adults are only a concern for users of RES17. The risk of harmful effects to adult users of the other wells (RES19, RES21, RES23, and RES37) is uncertain because of the limited scientific information to evaluate the public health implications of the combined exposures to all PFAS in these wells.

Human studies provide some evidence that PFOA is associated with kidney, testicular, and prostate cancers. Animals given PFOA orally have shown high rates of various cancers (liver, testicular, kidney, stomach, thyroid, and pancreatic). However, it is not known if the way these cancers occur in animals is relevant to humans. Human and animal studies have shown an association with both kidney and testicular cancers. Suggestive evidence that PFOS causes cancer is based on limited evidence of liver cancer in rats. However, the evidence is too limited to support a quantitative cancer assessment for PFOS. Therefore, although there is suggestive evidence that both PFOA and PFOS are carcinogenic, the science on PFOA, PFOS, and other PFAS is too limited at this time to quantify risk.

Limited data exist on the potential of other PFAS to cause cancer. ATSDR cannot calculate the estimated cancer risk for other past PFAS exposures or a total cancer risk from all potentially cancer-causing PFAS exposures. Therefore, the total cancer risk from past PFAS exposures from these private wells is uncertain.

Exposure to PFAS from food (including some shellfish from Great Bay and deer liver from the area) and consumer products, and to other PFAS in the water, likely contribute to the overall amount of PFAS in a person's body. Some pre-existing risk factors might increase the risk for harmful health effects (e.g., persons with compromised immune systems or liver function).

Protective measures

Between October 2014 and August 2016, the USAF installed whole-house water treatment systems for wells RES17, RES19, RES21, and RES23. The USAF has monitored the treated water quarterly for contaminants. ATSDR considers the USAF installation of the treatment systems, quarterly monitoring, and provision of bottled water to the seasonal users at RES37/GBNWR in Great Bay National Wildlife Refuge to be protective public health actions. As a long-term remedy, the USAF prefers to connect the four residences with water treatment systems to the Pease Tradeport public water supply (identified as ID NH1951020). Users of RES19 and RES21 were connected to public water in November 2019, whereas RES17 and RES23 still have whole-house treatment systems maintained and monitored by the USAF.

Next steps—Inform and study

- ATSDR will work with the USAF and Town of Newington to make every effort to provide the findings of this report to the prior owners/residents of the affected properties**.**
- ATSDR and the Centers for Disease Control and Prevention (CDC) are conducting a health study of children and adults exposed to PFAS-contaminated drinking water at the Pease International Tradeport and from nearby private wells. The study will evaluate associations between PFAS blood levels and signs of changes in the body (e.g., cholesterol levels, kidney and thyroid function, and the development of specific diseases), and will serve as the first site in CDC/ATSDR's Multi-site Health Study looking at the relationship between PFAS drinking water exposures and health outcomes. ATSDR has funded seven cooperative agreement partners as primary investigators for the Multi-site Health Study.
- ATSDR and CDC are conducting analyses that use previously collected data to look at rates of certain health outcomes, including many adult and pediatric cancers, in communities that have been exposed to PFAS through drinking water and those that have not. These are exploratory analyses (hypothesis-generating and ecologic design) and any observed associations will require further study. ATSDR and CDC are also developing plans for a study of PFAS and selected adult cancers using data from an existing study population (cohort).
- ATSDR and CDC have conducted exposure assessments in communities near current and former military bases and that are known to have had PFAS in their drinking water. The exposure assessments will provide information to communities about the levels of PFAS

in their bodies. Using this information, public health professionals provide guidance to help people reduce or stop exposure.

- ATSDR is providing technical assistance to tribal, state, local, and territorial health departments nationwide so they can effectively evaluate PFAS exposure in contaminated communities. ATSDR is also providing educational materials to the public to better understand PFAS and the health implications of PFAS exposures (see https://www.atsdr.cdc.gov/pfas/health-effects/index.html).

Conclusion 2—Wells Where PFAS Hazard/Risk Cannot be Determined

The risk of harmful health effects (non-cancer and cancer) from past and current exposures to mixtures of all PFAS in drinking water from 30 wells without treatment systems (see Table 5 for list of wells), now or in the past, cannot be determined.

Basis for conclusion

The public health implications of past or current exposures to users of these 30 wells cannot be determined because we lack health information onthe entire mixture of PFAS in these wells and the cancer risk from past and current exposure to all PFAS in these wells is uncertain because of the limited data on the potential for these PFAS to cause cancer.

Exposure to PFOS, PFOA, and PFHxS individually or combined in drinking water from these 30 wells were evaluated and determined to not likely result in an increased risk of harmful non-cancer health effects. However, other PFAS were detected in wells which could not be evaluated because of the lack of scientific information on the health effects. Moreover, for all 30 wells, the number of PFAS detected in these wells ranged from one (RES34 and RES54) up to 13 to 16 in a few wells (RES01, RES03, RES23, RES41, and RES49). Table A-1 shows that RES01, RES03, RES15, RES20, RES22, RES25, and RES41 had the highest total PFAS concentrations and number of different PFAS detected (based on at least nine PFAS detected and a total PFAS concentration greater than 0.1 micrograms per liter (µg/L) or 100 parts per trillion (ppt). In addition to PFAS exposures from drinking water, PFAS exposure from food (including some shellfish from the Great Bay and deer liver from the area) and consumer products likely contribute to the overall amount of PFAS in a person's body. See Section 2.3 (Surface Water and Biota Issues) for links to the NH DES reports on shellfish and deer sampling.

Next steps

ATSDR recommends that the U.S. Environmental Protection Agency (EPA), NH Department of Environmental Services (NHDES), and the USAF implement the following steps:

- continue investigations to characterize PFAS groundwater contamination at the site. This is especially important since PFAS drinking water regulatory standards are continuing to evolve.
- continue monitoring the private drinking water supply wells.
- identify and sample any affected private drinking water wells that were not part of the original inventory plan.

These steps will allow the agencies to stop exposures to contaminated private drinking water sources containing PFAS above the most current NH drinking water standards.

Investigations by applicable agencies will proceed under the Comprehensive Environmental Response, Compensation, and Liability Act, or CERCLA, and the signed Federal Facility Agreement; further decisions will be based on risk as determined by a Human Health Risk Assessment using accepted toxicity values.

- The USAF preferred long-term remedy for the four residences currently with water treatment systems is to connect them to the Pease Tradeport public water supply. ATSDR recommends that the USAF with EPA and NHDES regulators continue their efforts to implement a long-term remedy, which will permanently stop exposure to contaminated private drinking water sources that have PFAS above EPA or other applicable health-based drinking water guidelines and reduce exposures to PFAS compounds that have no health-based comparison values (HBCVs).
- ATSDR recommends affected residents reduce their exposure to PFAS in their water by using an alternative or treated water source for drinking, food preparation, cooking, brushing teeth, and other uses by which they might consume well water. Using PFAS-contaminated water for bathing or showering, washing dishes, and doing laundry is not expected to result in significant PFAS exposure.
- ATSDR recommends that residents using wells where ATSDR has determined a hazard exists for past exposures (Conclusion 1) or where current exposures cannot be determined (Conclusion 2) should consider not consuming shellfish from certain areas of Great Bay and not consume liver from deer harvested in the Great Bay area.

Conclusion 3—Wells Where PFAS Hazard/Risk Unlikely or No Hazard

Past and current exposure to PFAS in drinking water from 7 wells without treatment systems is unlikely to result in an increased risk of harmful health effects.

Basis for conclusion

For these 7 wells, harmful effects are not expected because either no PFAS have been detected above an HBCVs or, if detected, were below or near ATSDR's lowest HBCV.

No PFAS without HBCVs were detected in RES30 and RES42; therefore, no harmful effects are expected. For wells with only a few detections of PFAS (e.g., RES07, RES10, RES12, RES13, and RES27), the risk of harmful health effects is likely low as they were detected at concentrations below or near ATSDR's lowest HBCV.

Conclusion 4—Breastfeeding remains a healthy option

Current scientific information suggests that the health and nutritional benefits of breastfeeding outweigh the potential risks associated with PFAS in breastmilk.

Basis for conclusion

Community members, particularly mothers who have been exposed to PFAS from the Pease International Tradeport site, have expressed concern about the health implications of PFAS exposures to breastfed infants. Studies have shown that infants can be exposed to PFAS during pregnancy by transfer through the mother to the fetus and through breastfeeding. However, breastfeeding provides clear health and nutritional benefits. Some of the many benefits for infants include a reduced risk for ear and respiratory infections, asthma, obesity, and sudden infant death syndrome. Breastfeeding can also help lower a mother's risk for high blood pressure, type 2 diabetes, and ovarian and breast cancer. In general, the Center for Disease Control and Prevention (CDC) and the American Academy of Pediatrics recommend breastfeeding despite the potential presence of chemical contaminants in breast milk. (see https://www.atsdr.cdc.gov/pfas/health-effects/index.html).

Next steps

ATSDR recommends nursing mothers continue to breastfeed and contact their healthcare providers with specific concerns. ATSDR is available to consult with healthcare providers as needed. To help protect formula-fed infants from potential exposure, caregivers are encouraged to use pre-mixed formula or reconstitute dry formula with water sources not containing PFAS.

Abbreviations used in this report

µg/L..... micrograms per liter
6:2 FTS ..... 6:2 fluorotelomer sulfonate
8:2 FTS ..... 8:2 fluorotelomer sulfonate
AFB..... Air Force Base
AFFF ..... aqueous film-forming foam
ATSDR ..... Agency for Toxic Substances and Disease Registry
CDC ..... Centers for Disease Control and Prevention
CTE ..... central tendency exposure
DHHS..... NH Department of Health and Human Services
EPA..... US Environmental Protection Agency
EtFOSA ..... N-ethyl perfluorooctane sulfonamide
EtFOSE..... N-ethyl perfluorooctane sulfonamidoethanol
GBNWR ..... Great Bay National Wildlife Refuge
HBCVs ..... health-based comparison values
HI ..... hazard index
HQ..... hazard quotient
kg ..... kilogram
L ..... liter
LOAEL..... lowest observed adverse effect level
LOAEL HED ... Human Equivalent Dose for LOAEL
MeFOSA ..... N-methyl perfluorooctane sulfonamide
MeFOSE ..... N-methyl perfluorooctane sulfonomidoethanol
mg ..... milligram
MDH..... Minnesota Department of Health
MOE ..... margin of exposure
NH ..... New Hampshire
NHANES ..... National Health and Nutrition Examination Survey
NHDES..... NH Department of Environmental Services
NOAEL..... no observed adverse effect level
NOAEL HED.... Human Equivalent Dose for NOAEL
nc..... not calculated
ND ..... not detected
PFAS ..... per and polyfluoroalkyl substances
PFBS..... perfluorobutanesulfonic acid
PFBA ..... perfluorobutanoic acid
PFCA ..... perfluoroalkyl carboxylic acids
PFCs..... perfluorochemicals
PFDS ..... perfluorodecanesulfonic acid
PFDA..... perfluorodecanoic acid
PFDoA..... perfluorododecanoic acid
PFHpS ..... perfluoroheptane sulfonate
PFHpA..... perfluoroheptanoic acid
PFHxS..... perfluorohexanesulfonic acid
PFHxA ..... perfluorohexanoic acid
PFNA..... perfluorononanoic acid
PFOSA..... perfluorooctane sulfonamide (aka FOSA)
PFOS ..... perfluorooctanesulfonic acid
PFOA..... perfluorooctanoic acid
PFPeA ..... perfluoropentanoic acid
PFSAs..... perfluoroalkane sulfonates
PFTeDA..... perfluorotetradecanoic acid
PFTrDA..... perfluorotridecanoic acid
PFUnA..... perfluoroundecanoic acid
POE..... point of entry
ppt..... parts per trillion
RME..... reasonable maximum exposure
USAF..... United States Air Force

Table of Contents

1. Background and Statement of Issues

The Pease International Tradeport encompasses almost 4,300 acres in Greenland, Portsmouth, and Newington, NH (see Appendix A, Figure A-1). The Tradeport is on land formerly occupied by the Pease AFB. The Pease AFB began operations in 1956 and closed in 1991 [ATSDR 1999]. The USAF transferred the Pease AFB to the Pease Development Authority in October 1991. In February 1992, the facility was named the Pease International Tradeport. The Pease Development Authority welcomed its first tenant in 1993 [Pease Development Authority 2017]. EPA added the site to the National Priorities List[1] on February 21, 1990, because of groundwater and soil contamination by chlorinated volatile organic compounds, including trichloroethylene, petroleum-related volatile organic compounds[2], and metals [ATSDR 1999]. Under the National Priorities List, the USAF signed a federal facility agreement with the EPA and State of NH in 1991. The federal facility agreement identified the Installation Restoration Program sites and the Comprehensive Environmental Response, Compensation, and Liability Act or CERCLA process. Sites included the former Fire Department Area 2 and the Installation Restoration Program sites within the Haven well vicinity. ATSDR evaluated past contamination issues in a 1999 public health assessment [ATSDR 1999].

In 2013, 22 monitoring wells located at the Former) Fire Department Area 2 (Site 8), known as AT008, on the Pease International Tradeport were sampled[3] for PFOA and PFOS (see Appendix A, Figure A-2). Fifteen monitoring wells had detections of PFOA exceeding the former EPA provisional health advisory of 0.4 µg/L. Eighteen monitoring wells had detections of PFOS exceeding the former EPA provisional health advisory of 0.2 µg/L. When those concentrations are compared to the current EPA health advisory of 0.070 µg/L, the exceedances increased to 17 wells for PFOA, and 20 wells for PFOS [CB&I 2014]. Sampling was initiated because PFAS-containing aqueous film-forming foam

[1] The National Priorities List is the list of sites of national priority among the known releases or threatened releases of hazardous substances, pollutants, or contaminants throughout the United States and its territories. The EPA lists sites on the National Priorities List upon completion of Hazard Ranking System screening, public solicitation of comments about the proposed site, and after all comments have been addressed. More details are available from: https://www.epa.gov/superfund/superfund-national-priorities-list-npl.

[2] Volatile organic compounds are defined as any carbon compound, excluding carbon monoxide, carbon dioxide, carbonic acid, metallic carbides, or carbonates and ammonium carbonate, which participates in atmospheric photochemical reactions, except those designated by EPA as having negligible photochemical reactivity. Volatile organic compounds are organic chemical compounds whose composition makes it possible for them to evaporate under normal indoor atmospheric conditions of temperature and pressure. More details are available from: https://www.epa.gov/indoor-air-quality-iaq/technical-overview-volatile-organic-compounds.

[3] Sample collection parameters: 1-liter polycarbonate bottles and stored at 4 degrees Celsius (±2 degrees C). Samples extracted within 14 days of sample collection. Equipment rinsate blanks collected at a frequency of 10 percent using PFC-free water supplied from the laboratory [CB&I 2014]. Detection limits for PFAS typically range from 0.0026 µg/L for PFOS to 0.0046 µg/L for PFOA [Walton R. (Air Force Civil Engineer Center-BRAC Program Management Division) email to Gary Perlman (ATSDR), 2018 February 22.

(AFFF) was used at former Pease AFB to respond to airplane fuel leaks, fires, and training exercises conducted at Site 8 [CB&I 2014]. AFFF leached into the soil and groundwater and migrated into the water supply wells that serve the Pease International Tradeport.

AFFF was first used at Pease AFB about 1970 [NH DHHS 2015; Prevedouros et al. 2006; NRL 2015]. In addition to Site 8, there are 21 other potentially PFAS contaminated areas that have been investigated (see Appendix A, Figure A-3). AFFF was reported to be stored, handled, used, or released in these areas [AMECFW 2016]. Eleven AFFF areas are subject to further evaluation. Ten sites currently are not the focus of additional investigations [AMECFW 2017].

In 2014, private drinking water wells located within one mile of the former Pease AFB have been under investigation to determine if PFAS has migrated to the wells [AMEC 2014]. These wells are in the towns of Newington and Greenland, NH. Figure 1 depicts the areas where the private wells are located.

PFAS are a class of manufactured chemicals not currently regulated by the EPA in public drinking water supplies. PFAS have been used since the 1950s to make products resistant to heat, oil, stains, grease, and water. They are found in some fire-fighting foams and consumer products such as nonstick cookware, stain-resistant carpets, fabric coatings, food packaging, cosmetics, and personal care products [EPA 2017]. People can be exposed to PFAS in the air, indoor dust, food, water, and consumer products. Because of their extensive use, most people in the United States have been exposed to PFAS [NIEHS 2016; EPA 2016a; CDC 2018].

PFAS persist in the environment, are water soluble, and may be detected in the soil, sediment, water, or biota. Studies indicate that some PFAS move through the soil and easily enter groundwater where they may travel long distances [MDH 2017a].

In April 2015, the USAF asked ATSDR to evaluate past and current exposures to PFAS found in private wells near the former base [AMEC 2014]. The PFAS contamination in groundwater likely came from AFFF used when Pease was an Air Force base [AMEC 2014]. It is important to note that the type of AFFF used at the former Pease AFB and the specific PFAS formulation is not known. The water sampling results for PFAS may not capture the full spectrum of exposures.

2. History of PFAS Groundwater Contamination

2.1 Private Drinking Water Well Monitoring

To determine whether PFAS in groundwater migrated beyond the former Pease AFB at concentrations that would be a public health concern, the USAF initiated an off-base private well sampling program in 2014. That program located and sampled private drinking water wells within one mile of the former Pease AFB boundaries.[4] The PFAS monitored are identified in Table A-2 (see Appendix A). Figure 1 depicts the off-site well inventory zone boundaries. Figure 2 depicts the boundary of the Great Bay National Wildlife Refuge where RES37 is located. The private wells within one mile of the former Pease AFB boundaries are in the Towns of Newington and Greenland, NH.

2.2 Fate and Transport of PFAS

Ongoing investigations by the USAF are designed to determine whether groundwater information may provide details on the depth of contamination, groundwater flow direction, and why some wells are more contaminated than others. The USAF is evaluating contaminant concentrations over time to learn more about how and when the contaminants are migrating [Walton R (USAF), personal communication to Gary Perlman (ATSDR), 2018 December 6].

2.3 Surface Water and Biota Issues

Some community members noticed foam floating on the surface waterways where they used to play. ATSDR cannot confirm that the foam observed by the community was AFFF. If AFFF impacted the surface water bodies, residents in the area may have been exposed to PFAS while playing in the nearby waterways. The USAF is coordinating an investigation regarding potential effects on surface water from springs and brooks that lead to the Great Bay. Great Bay surface water sampling was planned for inclusion in the investigation [Walton R (USAF), email to Gary Perlman (ATSDR), 2018 December 6].

The NH DES evaluated PFAS exposures in shellfish and deer in and near Great Bay. Based on NHDES' evaluation, it appears that

- any exposures that might have occurred to PFAS (primarily PFOS) in shellfish from the Great Bay are not likely to result in harmful health effects;
- the existing restrictions in place would further reduce the potential for any exposures; and
- evaluation of all PFAS present in shellfish could not be done because of the lack of toxicity data.

[4] The plan included the identification and inventory of private wells in Newington and Greenland, NH within one mile of the former Pease AFB boundary. The contractor conducted a door-to-door survey in the neighborhoods within the survey areas. Property owners were interviewed, and well water usage data were collected. Follow-up visits were conducted if the contractor was unable to contact a property owner during outreach. In some cases, as many as six attempts were made. There is no indication that property owners refused to participate in the well inventory and sampling.

Moreover, the NHDES indicated that PFOS detections occurred in shellfish collected from the Broad Cove at the mouth of Knights Brook, Great Bay at the Mouth of McIntyre Brook, and Trickys Cove at the mouth of Pickering Brook. The NHDES report is available from: http://www4.des.state.nh.us/IISProxy/IISProxy.dll?ContentId=4824416.

In addition to the shellfish sampling from the Great Bay, in 2019, the NH Department of Fish and Game sampled muscle and liver of deer in the Great Bay area. Their report is available from: https://www.wildlife.state.nh.us/hunting/deer-pfas.html. The following is their overall findings:

> *No PFAS chemicals were detected in any of the muscle tissue samples tested, suggesting venison consumption likely represents a low risk for PFAS exposure. While PFAS levels detected in deer livers were considered moderately low, the Department still recommends hunters do not consume deer liver. The liver is a filtering organ and therefore has potential to have high levels of a number of contaminants.*

If any residents with contaminated wells in Newington consume shellfish or deer liver from these areas, this would add to the PFAS exposures they have received from the private wells and from other sources. The focus of this health consultation is the evaluation of PFAS drinking water exposures through private wells. Because the health evaluations of shellfish and deer meat exposures have been performed by the NHDES, these exposures are not quantitatively evaluated in this health consultation.

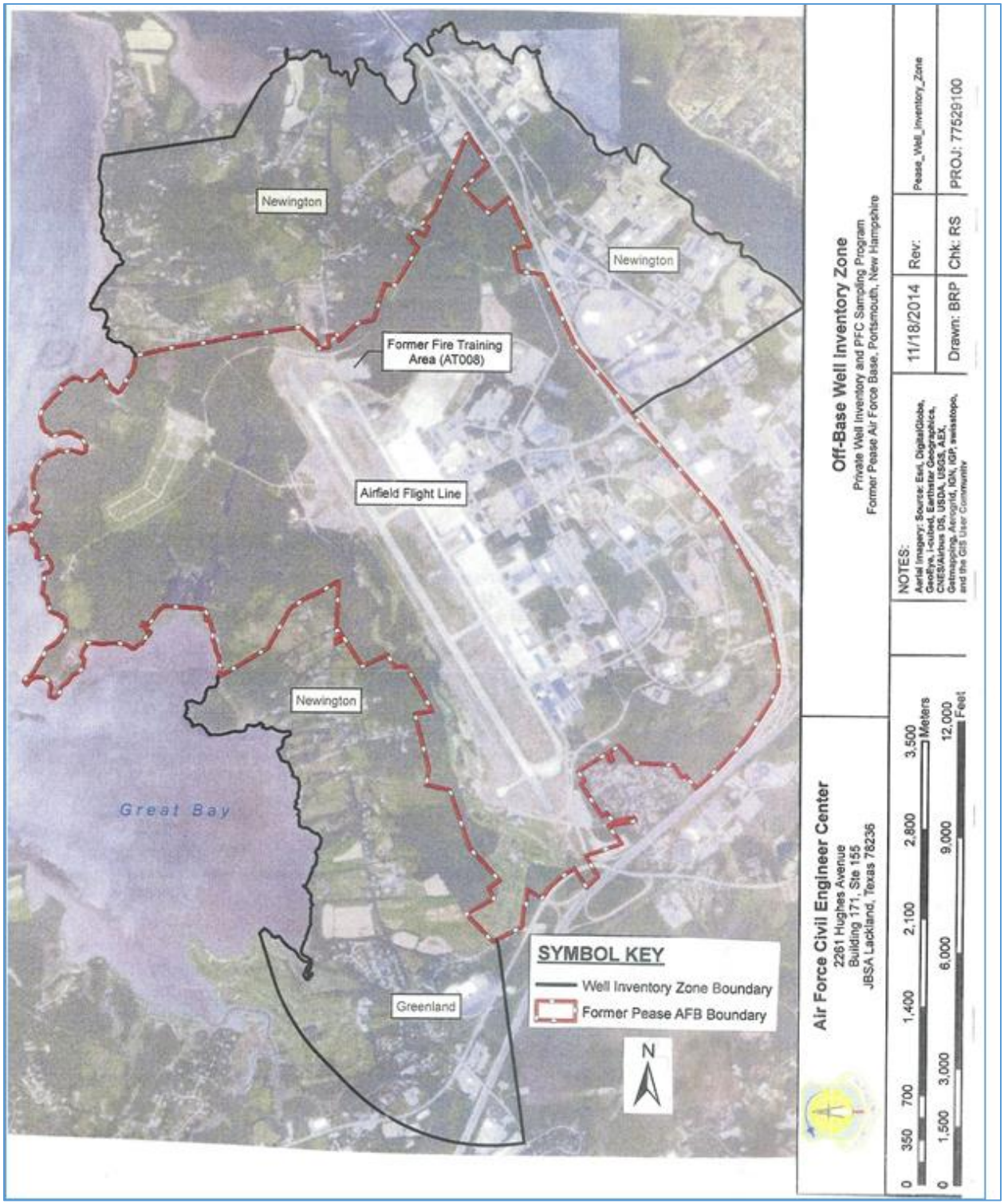

Figure 1 Off-site well inventory zone (adapted from AMEC 2014)

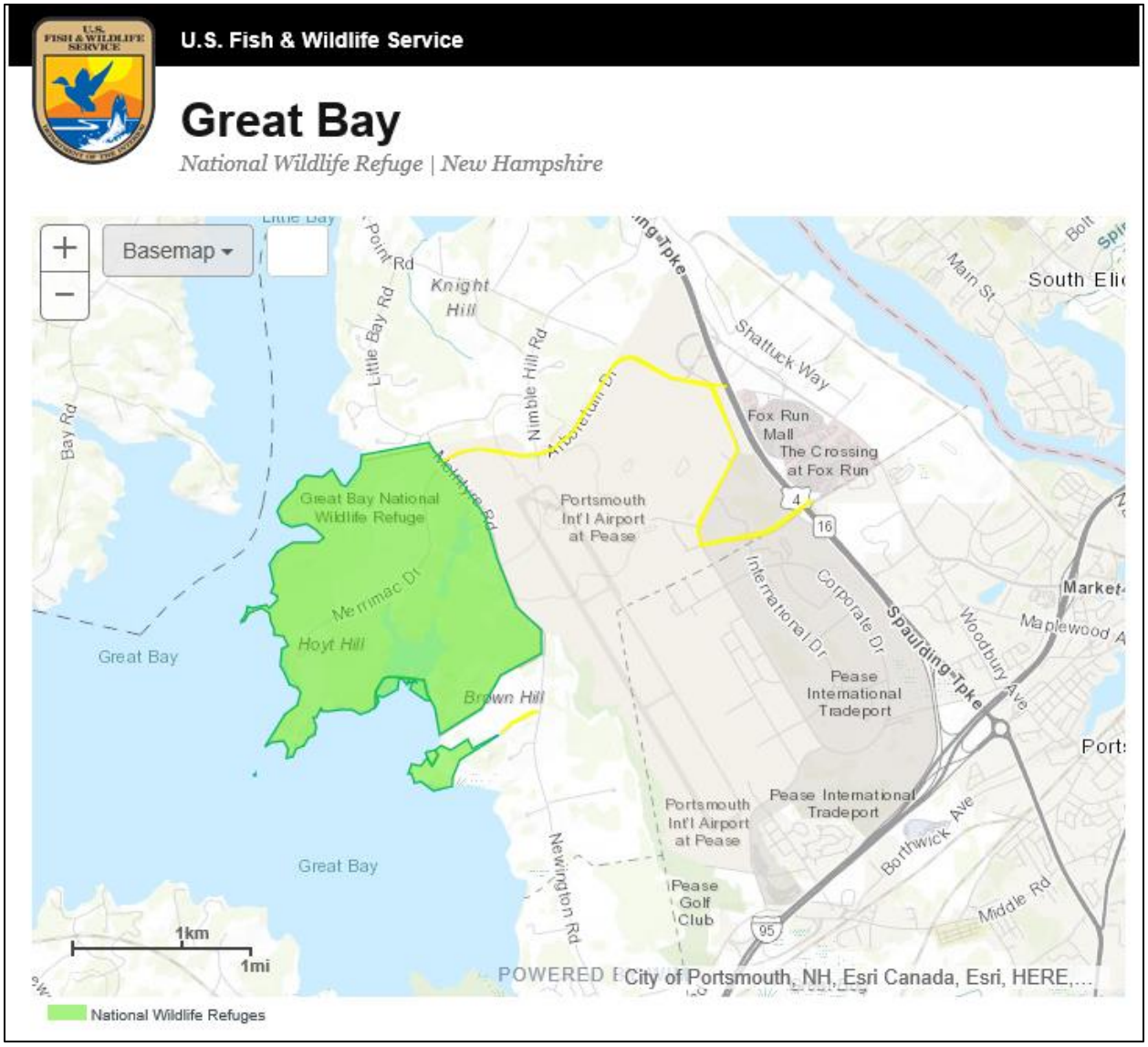

Figure 2 Great Bay National Wildlife Refuge (adapted from U. S. Fish & Wildlife Service, Base map of Great Bay National Wildlife Refuge, NH, available from: https://www.fws.gov/refuge/Great_Bay/map.html)

2.4 Private Well Monitoring Results

Between June 2014 and June 2020, 42 residential wells in Newington and Greenland, NH were sampled for 23 PFAS, including PFBA, PFBS, PFHxS, PFNA, PFOS and PFOA. Table A-3 (Appendix A) lists the maximum detected PFAS concentrations in these wells. PFAS were detected in 40 private wells [AMEC 2014, AMECFW 2016, Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 16. Includes one file attachment with private well PFAS data from 2014 to 2017, and Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2020 September 9. Includes one file attachment with private well PFAS data through June 2020.]. Twenty-five wells had PFOA, PFOS, or both. Depicted below (Figure 3) is a summary of the wells with various

numbers of PFAS detections. The range of the number of PFAS detected was from none to a maximum of 16 (out of a possible 23 PFAS analyzed). Two wells had no PFAS detections. One well had a maximum of 16 PFAS.

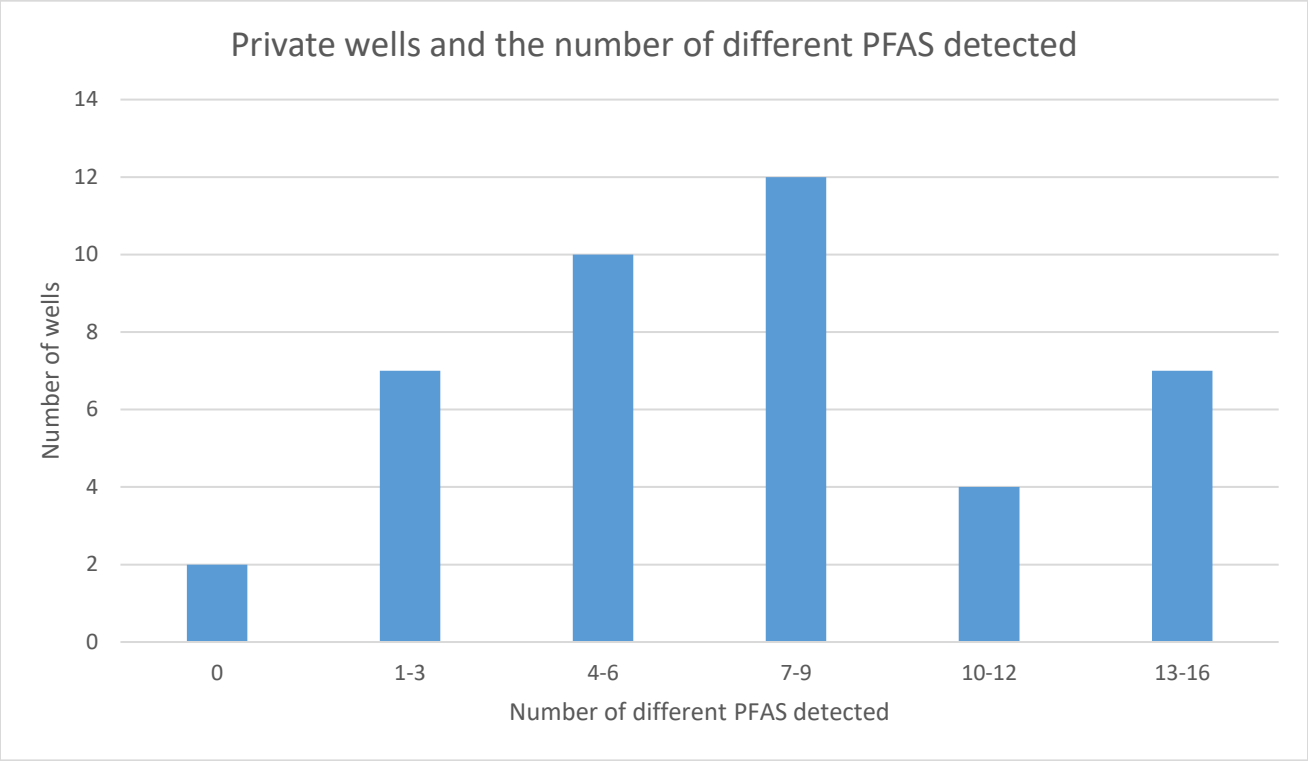

Figure 3. Private wells with various number of PFAS detections

In September 2014, one private residential drinking water well—designated as RES17 and located in Newington, NH—exceeded the former EPA provisional health advisory for PFOS of 0.2 µg/L. On October 18, 2014, in response, the USAF installed an activated carbon whole-home water treatment system [AMEC 2014]. The USAF has monitored the treated water from RES17 quarterly for breakthrough. The USAF maintains the activated carbon whole-home water treatment system [Hilton S (NHDES), email to Dave Gordon (NHDES), 2015 September 28].

EPA announced the health advisory for PFOA and PFOS (0.07 µg/L; individually or combined) in May 2016. Four private wells exceeded (RES19 and RES21) or nearly exceeded (RES23 and RES37) this level. In response, the USAF immediately provided bottled water to the users of these drinking water wells as a prudent public health action.

Between July and August 2016, the USAF installed whole-home water treatment systems in, RES19, RES21, and RES23. In November 2019, RES19 and RES21 were connected to public water.

In June 2016, the USAF and the State of NH first learned that a well located at the Great Bay National Wildlife Refuge (GBNWR; also referred to as RES37/GBNWR) was used seasonally by two volunteer workers who connected to it from their recreational vehicle [Sandin P (NHDES), email to Dave Gordon (NHDES), 2016 June 8]. The summed PFOS and PFOA concentrations for that well exceeded the EPA health advisory. The seasonal users were provided bottled water from June through October 2016 when they moved off the property [Forbes P (USAF), email to Dave Gordon (NHDES), 2016 June 24; Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 22]. The well has remained unused since 2016. The USAF will reevaluate if it is used again. Since the well at the Great Bay National Wildlife Refuge has been inactive, the USAF has checked with staff each spring to determine whether they expect the well will be used. They have confirmed each spring (2017, 2018, and 2019) that they do not expect the well to be used by seasonal employees. The well is in a portion of the site that is behind a locked gate and is not accessible to the public [Libby Bowen (John Wood Group PLC), email to Gary Perlman (ATSDR), 2019 June 6].

3. ATSDR's Evaluation Process

3.1 Identifying Exposure

People near an environmental release are exposed to a contaminant only if they come into contact with the contaminant. A release does not always result in exposure. Exposure might occur by ingestion (eating or drinking), breathing air, or skin contact with a substance.

ATSDR evaluates site conditions to determine if people could have been (a past scenario), are (a current scenario), or could be (a future scenario) exposed to site-related contaminants. ATSDR also considers the route a substance takes from its source (where it began) to its end point (where it ends), and how people can come into contact (or get exposed) to it. This is an exposure pathway. An exposure pathway has five elements:

1) a source of contamination (for example spill or release)
2) an environmental media and transport mechanism (groundwater)
3) a point of exposure (tap water)
4) a route of exposure (drinking)
5) a receptor population (people potentially or actually exposed)

When evaluating exposure pathways, ATSDR identifies whether exposure to contaminated media (such as drinking water) has occurred, is occurring, or might occur. ATSDR also identifies an exposure pathway as completed or potential or eliminates the pathway from further evaluation.

Exposure pathways are complete if all five elements of a human exposure pathway are present. A potential pathway occurs when information on one or more pathway elements is missing but could exist. A pathway is eliminated if at least one element is missing. (See Appendix A, Table A-4 for a description of the exposure pathways.)

For evaluating PFAS exposures from private wells, ATSDR considered only the drinking (ingestion) exposure route and did not include breathing (inhalation) or skin contact (dermal) contributions to exposure. PFAS do not easily evaporate from water during bathing and showering, and absorption of PFAS through skin is slow or limited [ATSDR, 2021]. Therefore, inhalation or skin exposures from private well water will be negligible compared to ingestion exposures.

3.2 Exposure and Health Effects

At sufficient exposure levels, chemicals in the environment can cause harmful health effects. The type and severity of effects are influenced by complex factors such as

- concentration (how much)
- the frequency or duration of exposure (how often and how long)
- the way the chemical enters the body
- combined exposure to other chemicals

Age, gender, nutritional status, genetics, health status, and other characteristics can affect how a person's body responds to an exposure and whether the exposure harms their health. When a completed exposure pathway is identified, ATSDR evaluates chemicals in that pathway by comparing exposure levels to screening values. Screening values are developed from available scientific findings about exposure levels and health effects. They reflect an estimated contaminant concentration that is not expected to cause adverse health effects for a given chemical, assuming a standard daily contact rate (such as amount of water consumed) and body weight. To be protective of public health, screening values are generally based on contaminant concentrations many times lower than levels at which no effects were observed in experimental animals or human studies. ATSDR does not use screening values to predict the occurrence of adverse health effects, but rather to serve as a health protective first step in the evaluation process.

3.3 Identifying Chemicals of Concern

As a first step in the evaluation process, ATSDR uses health-based comparison values[5] (HBCVs) as screening values. HBCVs are developed based on data from the epidemiologic and toxicological literature. Uncertainty factors[6], sometimes known as safety factors, are applied to ensure that the health-based comparison values amply protect human health. Estimated doses that are below health guidelines are not expected to cause adverse health effects. When no federal HBCVs are available, ATSDR considers applicable state values. Data on contaminants for which there were no federal or state HBCVs are retained for further evaluation.

ATSDR used six HBCVs in the evaluations of PFAS exposures. Four of the ATSDR-derived HBCVs (PFHxS, PFNA, PFOA, and PFOS) were used. The remaining two HBCVs were derived by the Minnesota Department of Health (PFBA and PFBS). Table A-5 shows the HBCVs used in this evaluation. Please see Appendix B for details on the Minnesota evaluation process.

3.4 Summary of Screening Analysis

Table 1 summarizes the PFAS exceeding HBCVs in private water supply wells within 1 mile of the former Pease AFB. Three PFAS (PFHxS, PFOA, and PFOS) were identified as chemicals of concern for past and current exposures. Of the 42 sampled wells

- 9 had detectable levels of PFAS that exceeded at least one HBCV
- 31 had detectable levels of PFAS, but none above a HCBV
- 2 had no detectable levels of PFAS

Some PFAS lacking an HBCV (i.e., 6:2 FTS, EtFOSE, PFHpA, PFHpS, PFHxA, PFOSA, and PFPeA) were also retained for further qualitative evaluation. For some of the PFAS without HBCVs, concentrations in the water were very low, and adequate toxicological data were unavailable. These PFAS were included in the evaluation of exposure to PFAS mixtures. Several private wells will not be further evaluated as water from these wells either did not contain any PFAS (RES30 and RES42) or had only a few detections of PFAS (i.e., RES07, RES10, RES12, RES13, and RES27) indicating that the risk of harmful health effects is likely low because they were detected at concentrations below or near ATSDR's lowest HBCV.

[5] Not all comparison values used to screen data were from ATSDR or other federal agency sources, because there were no federal comparison values available. As the state of science on these compounds progresses, more values may become available. Some values might be revised from their current values.

[6] Uncertainty factors are used to account for uncertainties associated with extrapolations from animal to human data as well as adjustments for intraspecies variability

ATSDR evaluated post-treatment residential drinking water data from private wells up to June 2020. During this period, there were very low concentrations detected for a few PFAS in samples from the faucet of all four wells with treatment systems. For RES17, the PFAS detected in 2015 occurred shortly after the GAC treatment was installed in March 2015, with only one detection after that in 2018. The PFAS detected were below ATSDR's most conservative HBCV. For the other wells that have had a treatment system, there have been only a few instances of PFAS detections in treated water at the faucet, and the detections have been below ATSDR's most conservative HBCV. No current exposures are occurring to water from the seasonal well RES37 as it is no longer in use.

Only four wells (RES01, RES03, RES17, and RES23) had detectable levels of PFNA, and none were above the HBCV indicating that no further evaluation is needed for PFNA. However, PFNA was included as part of the mixture evaluation for RES03 and RES23 (see Public Health Implications of Exposure to PFAS in Private Drinking Water Section below).

Other PFAS that lacked HBCVs (6:2 FTS, EtFOSE, PFHpA, PFHpS, PFHxA, PFOSA, and PFPeA) were further evaluated to the extent possible based on available toxicological data. Other PFAS with no HBCVs, detected at low concentrations and with limited toxicological data, were included as part of the overall public health evaluation of the PFAS mixture. These are summarized in Table 3 in Public Health Implications of Exposure to PFAS in Private Drinking Water Section.

Table 1. Summary of maximum PFAS detections (µg/L) exceeding HBCVs in private drinking water wells near the former Pease Air Force Base, Portsmouth, NH

Well ID	PFAS ==> HBCV† ==>	PFOS 0.014	PFOA 0.021	PFHxS 0.14
RES03		0.015 J	0.024	0.011 J
RES17‡		0.57	0.11	0.53
RES19‡		0.089	0.02	0.1
RES20		0.038	0.021 J	0.075
RES21‡		0.043	0.021	0.1
RES22		0.029	0.0088 J	0.056
RES23‡		0.055	0.016	0.014
RES25		0.014 J	0.017 J	0.012 J
RES37/GBNWR inactive*		0.13	0.014 J	0.099

Notes:
Shading indicates concentration is equal to or exceeds an HBCV.
PFAS = per and polyfluoroalkyl substances, HBCV = health-based comparison value
J - Analyte was identified, but the concentration was estimated.
† ATSDR health-based comparison values [ATSDR 2021].
‡ These wells have activated carbon whole house treatment systems. However, samples were collected at the faucet before treatment.
* The RES37/GBNWR well is for a seasonal trailer on the Great Bay National Wildlife Refuge. Users were provided bottled water, but no treatment was installed. The well is no longer active.

Sources: AMEC 2014, AMECFW 2016, Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 16. Includes one file attachment with private well PFAS data from 2014 to 2017, and Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2020 September 9. Includes one file attachment with private well PFAS data through June 2020.

4. NH Release of New PFAS Ambient Groundwater Quality Standards

For this health consultation, ATSDR used our scientifically based standard approach to screen and subsequently evaluate exposure doses. On September 30, 2019, NH released new ambient groundwater quality standards for four PFAS that include: 0.012 µg/L for PFOA, 0.015 µg/L for PFOS, 0.018 µg/L for PFHxS, and 0.011 µg/L for PFNA. Additional information regarding those values may be obtained from: https://www4.des.state.nh.us/nh-pfas-investigation/?p=1126. The NH ambient groundwater quality standards are water concentrations established by the state. ATSDR used our HBCVs to screen the well water concentration data for additional evaluation. If the NH ambient groundwater quality standards had been used to screen the data, rather than the ATSDR HBCVs, the dose calculations and conclusions in this health consultation would remain unchanged.

5. Public Health Implications of Exposure to PFAS in Drinking Water

If contaminant concentrations exceed HBCVs, ATSDR reviews exposure variables (such as duration and frequency), the toxicology of the contaminant, and epidemiology studies to determine the likelihood of possible health effects.

5.1. Evaluating Health Effects: Introduction

Humans and animals react differently to PFAS, and not all effects observed in animals may occur in humans. Scientists have ways to estimate how the exposure and effects in animals compare to what they would be in humans.

Some PFAS build up in the human body. The levels of some PFAS go down slowly over time when exposure is reduced or stopped. Scientists in multiple federal agencies are studying how different amounts of PFAS in the body might affect human health over time. Most existing research has focused on long-chain PFAS. These persist in the environment; bioaccumulate in wildlife and humans; and are toxic to laboratory animals, producing reproductive, developmental, and systemic effects in laboratory tests.
Long-chain PFAS comprise two sub-categories:

- perfluoroalkyl carboxylic acids (PFCAs) with eight or more carbons, including PFOA, and
- perfluoroalkane sulfonic acids (PFSAs) with six or more carbons, including
    - perfluorohexane sulfonic acid (PFHxS) and
    - perfluorooctane sulfonic acid (PFOS).

While persistent in the environment, PFCAs with fewer than eight carbons, such as perfluorohexanoic acid (PFHxA), and PFSAs with fewer than six carbons, such as perfluorobutane sulfonic acid (PFBS), are generally less bioaccumulative in wildlife and humans [EPA 2018b]. However, health effects of many short-chained PFAS and new PFAS alternatives have not been fully researched. See Table A-2 for a listing of PFAS chemical formulas and designated chain length.

5.1.1. What are Non-Cancer Health Effects of PFAS?

Many studies have examined possible relationships between levels of PFAS in blood and harmful health effects in people. However, not all studies involved the same groups of people, the same type of exposure, or the same PFAS, resulting in a variety of observed health outcomes.

Research in humans suggests that high levels of certain PFAS may lead to

- increased cholesterol levels
- changes in liver enzymes
- decreased vaccine response in children
- increased risk of high blood pressure or pre-eclampsia in pregnant women
- small decreases in infant birth weight [ATSDR 2020a]

One way to learn about whether PFAS will harm people is to do studies on lab animals.

- Most of these studies have tested doses of PFOA and PFOS that are higher than levels found in the environment
- These animal studies have found that PFOA and PFOS can cause damage to the liver and the immune system
- PFOA and PFOS have also caused birth defects, delayed development, and newborn deaths in lab animals

5.1.2. What are Cancer Health Effects of PFAS?

EPA [2016b] considers the evidence that PFOA is potentially carcinogenic in humans to be suggestive. The International Agency for Research on Cancer or IARC [2017] has determined that PFOA is possibly carcinogenic to humans. A recent review of PFOA carcinogenicity by Steenland et al. [2020] found the human (epidemiological) evidence remains supportive but not definitive for kidney and testicular cancers. Findings from the National Cancer Institute [Shearer et al. 2020] added to the evidence that PFOA might cause kidney cancer (renal cell carcinoma) in humans. Steenland et al. [2020] also found that human studies were inconsistent but suggestive of an association between PFOA and prostate cancer. In summary, some evidence is available from human studies that PFOA is associated with kidney, testicular, and prostate cancers.

Animals given PFOA orally have shown high rates of various cancers. We do not know if the cancers in animals result from a mode of action that is relevant to humans [ATSDR 2021]. A rat study from 2012 showed that PFOA exposure was associated with testicular cancers [Butenhoff et al. 2012]. More recent data from rats and mice suggest that lower PFOA doses than previously observed might be associated with liver and pancreatic cancers in male rats and liver, kidney, forestomach, and thyroid gland cancers in female rats [NTP 2018, 2020]. In summary, some evidence is available from animal studies that PFOA might cause several cancers, including liver, testicular, kidney, forestomach, thyroid, and pancreatic cancers. Of note, kidney and testicular cancers have been shown in both human and animal studies.

Epidemiology studies of PFOS-exposed workers reported an increased risk for some cancers; however, because of small sample sizes, the confidence intervals were wide, indicating considerable

uncertainty in the effect estimates [Alexander et al. 2003; Alexander and Olsen 2007; Grice et al. 2007; Olsen et al. 2004]. A causal association between cancer and PFOS exposures, based on human studies, remains uncertain. Animal studies have found limited but suggestive evidence of PFOS exposure and increased incidence of liver and thyroid tumors. However, there is uncertainty in these associations as the tumors did not show a direct relationship to dose and the mechanism of action may not be relevant to humans [ATSDR 2021].

While there is suggestive evidence that both PFOA and PFOS are carcinogenic, the science is too limited at this time to quantify risk.

5.1.3. How Does ATSDR Evaluate Non-Cancer and Cancer Health Effects?

For those residential wells with maximum PFAS values above ATSDR HBCVs, ATSDR compared estimated doses to the ATSDR Minimal Risk Levels (MRL). An MRL is an estimate of the amount of a chemical a person can eat, drink, or breathe each day without a detectable risk to health for non-cancer health effects. MRLs are a screening tool that help identify exposures that could be potentially hazardous to human health. MRLs help public health professionals determine areas and populations potentially at risk for health effects from exposure to a chemical. ATSDR has developed more than 400 human health MRLs. For those PFAS detected above an HBCV, ATSDR further evaluated the exposure by comparing the dose to the MRL by calculating a hazard quotient (HQ = ratio of exposure dose divided by the MRL). Finally, if the HQ is greater than one, ATSDR conducted an in-depth evaluation of the exposure. Moreover, to put these HQs into perspective, ATSDR calculated the MOE. The MOE is the effect level from the study used by ATSDR to derive the MRL, divided by the estimated exposure dose. The MOE measures how close an estimated residential exposure is to effect levels in animal studies used to derive ATSDR's MRL or other studies. The smaller the MOE, the closer the exposure dose is to an effect level.

Exposure above the MRLs does not mean that health problems will occur. Instead, it signals health assessors to look more closely at a site where exposures may be identified. MRLs do not define regulatory or action levels for ATSDR.

The way the MRL is calculated can change depending on the type and quality of data available. MRLs can be set for three different lengths of time people are exposed to the substance:

- Acute—about 1 to 14 days
- Intermediate—from 15 to 364 days
- Chronic—more than 365 days

MRLs are calculated for different exposure routes, for example: inhalation and ingestion. MRLs are developed for non-cancer health effectsFor PFAS, ATSDR developed MRLs for PFOS, PFOA, PFHxS, and PFNA ingestion based on intermediate duration oral animal studies. ATSDR is using these oral MRLs to screen and evaluate chronic exposures also [ATSDR 2021]. ATSDR's MRLs are developed for the most sensitive population (the fetus/neonate) and are protective for the entire population. In addition, ATSDR considered immune effects as these effects may be more sensitive than developmental effects.

Proposed MRLs undergo a rigorous review process. Following internal review by ATSDR's expert toxicologists and before being submitted for public comment, they are sent to an expert panel of external peer reviewers, an interagency MRL workgroup, with participation from federal agencies, such as CDC's National Center for Environmental Health and National Institute of Occupational Safety and Health, the National Institutes of Health's National Toxicology Program, and the EPA [ATSDR 2021].

An intermediate-duration (15 to 364 days), oral MRL of 3×10^{-6} milligrams per kilogram per day (mg/kg/day) was derived for PFOA based on neurodevelopmental effects (i.e., altered activity at age 5–8 weeks and skeletal alterations at age 13 to 17 months) in the offspring of mice fed a diet containing PFOA [Koskela et al. 2016]. The MRL is based on a human equivalent dose, lowest observed effect level ($LOAEL_{HED}$) of 8.21×10^{-4} mg/kg/day, and a total uncertainty factor of 300 (10 for use of a LOAEL, 3 for extrapolation from animals to humans, and 10 for human variability).

For PFOS, ATSDR derived an intermediate-duration oral MRL of 2×10^{-6} mg/kg/day based on developmental effects (i.e., delayed eye opening and transient decrease in body weight during lactation) in the offspring of rats administered PFOS [Luebker et al. 2005]. The MRL is based on a human equivalent dose for the no observed adverse effect level ($NOAEL_{HED}$) of 5.15×10^{-4} mg/kg/day and a total uncertainty factor of 30 (3 for extrapolation from animals to humans with dosimetric adjustments and 10 for human variability) and a modifying factor of 10 for concern that immunotoxicity may be a more sensitive endpoint than developmental toxicity) [ATSDR 2021]. The estimated $LOAEL_{HED}$ based on the Luebker et al. 2005 study is 2.1×10^{-3} mg/kg/day[7].

[7] HEDs not cited in the Final PFAS Toxicological Profile were calculated using the same process as was used for MRL derivation. This process is detailed in the introduction to the MRL worksheets (Appendix A of the 2021 Final PFAS Toxicological Profile). The inherent problem with PFAS is that one cannot extrapolate directly from dose to serum level. For this reason, ATSDR has taken the steps of estimating time-weighted average serum levels based on pharma-kinetic or PK models (for PFOA and PFOS) or measured serum levels (for PFHxS and PFNA) based on the trapezoid rule.

HED values are based on steady state serum concentrations. Ideally, this type of extrapolation from applied dose to HEDs would be possible, but it is not the case for PFAS. There is an intermediate step from applied dose to steady state serum concentrations to HEDs. Time-weighted average serum concentrations are estimated from the measured serum concentrations from the study of interest from the areas under the curve calculated using the trapezoid rule.

For PFHxS, ATSDR derived an intermediate-duration oral MRL of 2 x 10^{-5} mg/kg/day based on thyroid follicular cell damage, which is considered the most sensitive health outcome, in adult male rats administered PFHxS for a minimum of 42 days [Butenhoff et al. 2009; Hoberman and York 2003]. The MRL is based on a human equivalent dose NOAEL of 4.7 x 10^{-3} mg/kg/day, a total uncertainty factor of 30 (3 for extrapolation from animals to humans and 10 for human variability), and a modifying factor of 10 for database limitations. ATSDR added the modifying factor for database limitations to account for the small number and limited scope of studies examining PFHxS toxicity following intermediate-duration exposure, particularly studies examining immune effects, a sensitive endpoint for other PFAS, and general toxicity [ATSDR 2021]. ATSDR estimates the HED LOAEL for the above studies to be 7.3 x 10^{-3} mg/kg/day.

Currently, scientists are still learning about the health effects of exposures to mixtures of PFAS. In addition, investigators are actively studying whether being exposed to multiple PFAS at the same time increases the risk of health effects. Only two studies [Carr et al. 2013; Wolf et al. 2014] have shown that binary pairs of PFAS (i.e., comparing only two PFAS) show concentration and response additivity at lower concentrations, but deviate from additivity at higher concentrations [Wolf et al. 2014]. These possible interactions or dose additivity complicate the interpretation of the epidemiology data.

In the absence of data, chemical component-based approaches are used in risk assessment of chemical mixtures. Component chemicals, that are judged to be toxicologically similar, are evaluated by dose additive risk assessment methods that include the hazard index, relative potency factors, and toxicity equivalency factors. These methods are based on potency weighted dose addition and assume that there are no greater than or less than additive interactions among the chemicals in the dose region of interest. Because data are limited, ATSDR cannot assume any mixture effect besides additivity.

In the absence of other methods, ATSDR recommends a tiered approach to determine whether further evaluation of mixture effects is necessary [ATSDR 2018a]:

- In Tier 1, an HQ is calculated for each of the identified contaminants. For the PFAS assessed in this report, we can only evaluate mixtures using noncancer health guidelines.[8] Mixtures of contaminants with hazard quotients greater than 0.1 are carried forward for Tier 2 analysis.

[8] Intermediate MRLs based on noncancer effects are available for PFOA, PFOS, PFHxS, and PFNA. State reference doses based on noncancer effects are available for PFBA and PFBS. No official cancer slope factors exist for PFAS at the time of this report. Potential cancer effects are discussed later in this report.

- In Tier 2, for multi-component mixtures, all hazard quotients (regardless of the target organ) are summed to obtain a hazard index. Mixtures with a hazard index greater than 1 are carried forward to Tier 3 analysis. Tier 2 analysis assumes that doses are additive.

- Tier 3 analysis is a detailed analysis of potential mixture effects, considering, for example, shared target toxicities of each mixture component, sensitive subpopulations, or more refined estimates of potential exposure to the mixture.

ATSDR also conducted a qualitative analysis of the scientific literature to determine which PFAS might have similar target organ effects.

ATSDR considered several factors in evaluating if health effects are likely from current and past exposures, including the following:

- Potential effects of exposures to PFOA, PFOS, and PFHxS (individually)
- Potential effects of exposures to 6:2 FTS, EtFOSE, PFHpA, PFHpS, PFHxA, PFOSA, and PFPeA (individually)
- Potential effects of exposures to a mixture of PFAS
- Potential contributions from other sources
- Potential effects on susceptible populations: persons with pre-existing conditions and early development

ATSDR used the maximum detected concentration in each well as a health-protective approach when evaluating exposure from contaminated wells (see Appendix A, Table A-3). To estimate the exposure doses from past and current water consumption, ATSDR used default exposure scenario assumptions [ATSDR 2016a, 2016b]. ATSDR calculates exposure doses for each age group using average estimates of drinking water intake rates to determine the central tendency exposure (CTE). ATSDR also calculates the reasonable maximum exposure (RME) using reasonable maximum estimates of drinking water intake for each age group (see Appendix A, Table A-6 for description of exposure assumptions, and Equations 2 and 3 in Appendix A for how the CTE and RME were calculated).

5.2. Wells with Potential PFAS Hazards/Risks (5 wells: RES17, RES19, RES21, RES23, and RES37)

5.2.1 Evaluation of Past Exposures to PFAS with HBCVs

ATSDR used several measures to evaluate whether harmful effects are possible (i.e., whether there is an increased risk) from exposure to PFOA, PFOS, or PFHxS alone or combined. These include the

hazard index (HI), hazard quotient (HQ), and margin-of-exposure (MOE). The MOE measures how close a residential exposure is to effect levels from animal studies used to derive the MRL. The following public health evaluation discusses these measures and how they were used to determine whether harmful effects are possible for an individual PFAS exposure and exposure to a mixture of PFAS in each well evaluated. Table 2 summarizes the calculated measures for each of the residential wells with at least one of the maximum PFOA, PFOS, or PFHxS levels above an ATSDR HBCV (see Table 1). These measures are based on a health-protective scenario for a child (birth to 1 year old), based on an upper-percentile water intake (the reasonable maximum exposure or RME). The maximum concentrations detected in RES23 were collected at the wellhead. The PFOS, PFOA, and PFHxS levels detected in the faucet sample for RES23 were below ATSDR's HBCVs. However, exposures to the maximum levels detected could have occurred; therefore, ATSDR is evaluating these as actual exposures.

Table 2. Public health implication evaluation measures for users of private wells that have perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), or perfluorohexanesulfonic acid (PFHxS) above a health-based comparison value (HBCV), based on a reasonable maximum exposure (RME) dose for children ages birth to 1 year

Well ID	Hazard Quotient (HQ)			Margin-of-Exposure (MOE)*				Mixture Hazard Index (HI) †
	PFOS	PFOA	PFHxS	PFOS (developmental)	PFOS (immune)	PFOA	PFHxS	
RES03	1	1	<1	970	14-180	236	4581	2
RES17	41	5	3	25	<1-5	52	137	49
RES19	6	<1	<1	170	3-22	830	504	7
RES20	3	1	<1	381	8-100	270	672	4
RES21	3	1	<1	340	5-64	270	690	5
RES22	2	<1	<1	540	8-100	900	900	3
RES23	4	<1	<1	280	4-53	380	16796	5
RES25	1	<1	<1	1000	15-200	333	2519	2
RES37	9	<1	<1	110	2-21	400	512	11

Notes: *The MOEs are based on either developmental effects (PFOA and PFOS), immune effects (PFOS) or thyroid effects (PFHxS). Immune MOEs are based on the HED LOAELs from the Guruge et al. (2009) and Dong et al. (2011) animal studies of 3.1×10^{-5} mg/kg/day and 4.1×10^{-4} mg/kg/day, respectively.

† The mixture hazard index measures whether there is an increased risk of harmful effects beyond what might be expected from exposures to PFOS, PFOA, or PFHxS alone. Based on ATSDR's Mixtures Framework [ATSDR 2018a], only PFAS with an HQ ≥ 0.1 were included in the HI calculation. PFNA is only included in the HI calculations for RES03 and RES23 as PFNA was either not detected in other wells or the HQ was less than 0.1. PFHxS was included in all His calculations except for RES03 because the HQ was less than 0.1. PFBS and PFBA were not included in any of the HI calculations because the HQs were less than 0.1. Exposure to the mixture for all of these wells was further evaluated because their HIs were all greater than 1.0.

Abbreviations: HI = the sum of the hazard quotients for PFOS, PFOA, and PFHxS to evaluate mixtures; HQ = ratio of exposure dose divided by the MRL. For the mixture HI and HQ, if greater than 1.0, as the HI and HQ increase, so does the concern for potential mixture or individual health effects, respectively; MOE = health effect level used to derive the MRL divided by the exposure dose. The MOE measures how close a residential exposure is to effect levels from animal studies used to derive the MRL; an individual measure not applicable as water level not above a HBCV.

PFOA and PFOS. ATSDR compared estimated exposure doses with the MRLs for PFOA and PFOS. ATSDR calculated PFOS and PFOA exposure doses for each well using the maximum detected values. ATSDR used age group-specific exposure assumptions and calculated hazard quotients (HQ) for each estimated dose. An HQ is the ratio of the exposure dose divided by the MRL.

HQs for PFOS were greater than the HQs for PFOA. For RES17, all PFOS HQs for both the CTE and RME scenarios were elevated (HQ > 1.0) for all age groups and for pregnant and lactating women. For RES17, HQs for PFOA exposures were elevated for young children (birth to < 1 year) for both the CTE and RME scenarios but elevated only for the RME scenario for the other age and exposure groups. PFOA exposure HQs were all less than 1.0 for users of RES19, RES21, RES23, and RES37. The HQ for young children using the RME scenario for RES21 was 1.01.

(See Appendix A tables for HQ calculations: RES17-Tables A-7 to A-9; RES19-Table A-10; RES21-Tables A-11 and A12; RES23-Tables A-13 and A-14; RES37-Tables A-15 and A-16)

ATSDR calculated the MOE for RES17, RES19, RES21, RES23, and RES37. For RES17, the PFOS MOE for developmental effects was about 57 for the CTE scenario and 25 for the RME scenarios for the birth to < 1-year age group. To provide perspective to exposure doses and immune effects levels found in the scientific literature, MOEs were also calculated based on the Dong et al. [2011] and the Guruge et al. [2009] studies and an RME scenario (Table 2). Based on the current scientific literature, ATSDR believes that the immune effect levels from PFOS exposures lies somewhere between the HED LOAELs for these two studies (i.e., 4.1×10^{-4} mg/kg/day for the Dong study and 3.1×10^{-5} mg/kg/day for the Guruge study). Exposure doses near or exceeding the lower LOAEL HED from the Guruge et al. [2009] study would be considered potentially harmful. Therefore, historical PFOS exposures to young children (birth to < 1 year) from RES17 may result in harmful immune effects.

For RES17, the PFOA MOE for neurodevelopmental effects was about 120 for the CTE scenario and 52 for the RME scenario for a child, birth to < 1 year. The PFOS MOEs for adults and lactating and pregnant women ranged from 75 to 100 for the RME scenario and 160 to 300 for the CTE scenario. Based on this analysis, individual PFOS and PFOA exposures to these exposed groups using RES17 is not likely to have increased the risk for non-cancer health effects. These estimated exposures exclude possible PFOA and PFOS exposures from non-drinking water sources and other PFAS in their drinking water and from other sources.

For RES19, RES21, RES23, and RES37, the PFOS developmental effect MOEs for young children (birth to < 1 year) ranged from 110 to 340 for the RME scenario which is well below effect levels. As above, the MOEs for immune effects ranged from 2 to 5 when using the Guruge study and 21 to 64 when using the Dong study. Therefore, PFOS exposures to young children using these wells may increase the risk for non-cancer immune health effects, but other age groups and pregnant and lactating women are at a low increased risk.

(See Appendix A tables for MOE calculations based on studies used to derive the ATSDR intermediate MRL and for HQ calculations see RES17-Tables A-7 to A-9; RES19-Table A-10; RES21-Tables A-11 and A12; RES23-Tables A-13 and A-14; RES37-Tables A-15 and A-16.)

PFHxS. Only RES17 exceeded ATSDR's HBCV for PFHxS. The HQs for all exposed groups and ages were below 1.0 except for young children for the CTE (birth to < 1 year) and RME (birth to < 6 years) scenarios (see Appendix A, Table A-7). ATSDR calculated a PFHxS MOE to put these HQs into perspective. For RES17, assuming 100% of the PFAS exposure is from drinking water, a child younger than 1 year of age will have the highest PFHxS exposure doses. The MOE was about 307 for the CTE scenario and 137 for the RME scenario (see Appendix A, Table A-7). Based on this analysis, young children who consumed water at a higher daily intake rate (the RME scenario) would have a low increased risk of harmful non-cancer effects. However, the conclusions for PFHxS human health effects are limited as the number and scope of intermediate study duration studies are limited, especially for studies examining immune effects, a sensitive endpoint for other PFAS, and general toxicity [ATSDR 2021].

Mixture of PFOS, PFOA, and PFHxS.

For RES17, the HIs (based on an RME scenario) were greater than 1.0 for all age groups and pregnant and lactating women. The HIs for the other wells were greater than 1.0 only for young children (birth to < 1 year). Therefore, because of combined exposures to PFOA, PFOS, and PFHxS, all age groups that used RES17 might have increased risk for developmental, endocrine (thyroid), and immune effects greater than what might be expected from any one of these chemicals. Among users of other wells, only young children would have risk greater than what might be expected from exposure to any one of these PFAS alone. Harmful effects for other health outcomes shown to be associated with PFOA, PFOS, or PFHxS might also occur. The risk for harmful non-cancer effects to adult users of RES19, RES21, RES23, and RES37 from past exposure to the total mixture of PFAS (beyond PFOA, PFOS, and PFHxS) is uncertain because ATSDR lacks scientific information to evaluate this mixture.

(See Appendix A tables for HI calculations: RES17-Table A-21; RES19-Table A-22; RES21-Table A-23; RES23-Table A-24; RES37-Table A25)

5.2.2 Evaluation of Past Exposures to PFAS without HBCVs

In addition to PFOA, PFOS, and PFHxS exposures above HBCVs, people using wells RES17, RES19, RES21, RES23, and RES37 were exposed to the other PFAS at the maximum concentrations shown in Table 3. None of these wells had levels of PFBA nor PFBS above the Minnesota HBCVs. This section

evaluates exposure to those PFAS without HBCVs individually; it does not evaluate the mixture. ATSDR could not fully evaluate PFAS exposures because of the lack of scientific data. However, in this health consultation, ATSDR provides some health perspective on these PFAS exposures to owners of all wells. ATSDR has consulted with several well owners and remains available to consult with other individual well users on PFAS exposures in their wells.

Table 3. Maximum detected PFAS concentrations (other than PFOA, PFOS, and PFHxS) in Greenland and Newington, NH, private wells within 1 mile from the former Pease Air Force Base, Portsmouth, NH; concentrations in micrograms per liter (µg/L) 2014 to 2020

Well Identifier	6:2 FTS	EtFOSE	PFHpA	PFHpS	PFHxA	PFOSA	PFPeA
RES03	0.0068	0.009	0.013	0.0047	0.01	ND	0.01
RES09	ND	ND	0.012	ND	0.014	0.0048	0.024
RES17	0.041	ND	0.066	0.03	0.27	0.0043	0.14
RES19	ND	0.012	0.003	0.007	0.025	0.007	0.024
RES20	0.77*	ND	0.0038	0.0076	0.02	0.028	0.011
RES21	ND	ND	ND	ND	0.021	ND	0.02
RES23	ND	0.012	0.011	0.007	0.017	0.009	0.02
RES25	ND	ND	0.0063	ND	0.0078	0.017	0.0088

Note: ND = Not detected; * This well had an apparent anomaly–an elevated concentration of 0.77 µg/L. That concentration was never duplicated at that well; one other detection was much lower at 0.0059 µg/L

Sources AMEC 2014, AMECFW 2016, Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 16. Includes one file attachment with private well PFAS data from 2014 to 2017, and Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2020 September 9. Includes one file attachment with private well PFAS data through June 2020.

Abbreviations: 6:2 FTS = 6:2 fluorotelomer sulfonate; EtFOSE = N-ethyl perfluorooctane sulfonamidoethanol; PFHpA = perfluoroheptanoic acid; PFHpS = perfluoroheptane sulfonate; PFHxA = perfluorohexanoic acid; PFOSA = perfluorooctane sulfonamide; PFPeA = perfluoropentanoic acid.

PFAS, besides those shown in Table 3, also were found in these and other wells but were generally detected less frequently and at lower levels (see Appendix A, Table A-3). Table 4 below shows which health effects these PFAS have been associated with in either animal or human studies. A depiction, based on the best available scientific information, of the likely health effects for exposure to each compound shown in Table 3 is discussed below.

PFHxA. Although PFHxA, based on either animal or human studies, has been associated with several health outcomes, ATSDR determined that insufficient information exists to determine an MRL (ATSDR 2021). One animal study evaluated the chronic oral (ingestion) toxicity of PFHxA in laboratory animals [Klaunig et al. 2015]. Exposure of female rats to 200 mg/kg/day resulted in changes in blood (decreases in red blood cells and hemoglobin levels, and increases in reticulocyte counts), kidney effects (tubular degeneration, necrosis, increased urine volume, and reduced specific gravity), and liver effects (necrosis). No adverse changes were seen in female rats given doses of 30 mg/kg/day or in male rats given 100 mg/kg/day doses. In addition, ATSDR's PFAS

Toxicological Profile [ATSDR 2021] provides information on several intermediate duration studies with various organ effect levels (LOAELs) ranging from 100-500 mg/kg/day. The maximum site exposure dose is about 250,000 times below the lowest LOAEL from these studies. A major uncertainty related to this study is that researchers did not measure serum PFHxA levels which would allow ATSDR to calculate a human equivalent dose.

Based on the maximum detected concentration of PFHxA from RES17, the estimated RME dose for a child (birth to less than 1 year old) is 5.4×10^{-5} mg/kg/day (see Appendix A, Table A-20). This dose is about 500,000 times lower than the lowest NOAEL from the Klaunig et al. [2015] study. Exposures from other private wells with the highest detected levels of PFHxA (RES19) would produce even higher margins between exposure doses and effect levels, which would indicate less risk. Based on this study, harmful effects are unlikely. PFHxA has not been studied as extensively as the PFAS with ATSDR MRLs, especially for the most sensitive health endpoints, such as developmental and immune effects, and the only identified chronic study has limitations.

PFHpA, PFPeA, 6:2 FTS, PFHpS, PFOSA, and EtFOSE. The scientific literature has very limited information from animal studies relating to the health effects of exposure to perfluoroheptanoic acid (PFHpA), perfluoropentanoic acid (PFPeA), 6:2 fluorotelomer sulfonate (6:2 FTS), perfluoroheptane sulfonate (PFHpS), perfluorooctane sulfonamide (PFOSA), and n-ethyl perfluorooctane sulfonamidoethanol (EtFOSE). However, human studies relating to exposure to these PFAS are more numerous but still overall limited for making strong conclusions regarding their association with various health outcomes.

For PFHpA, ATSDR identified several human studies (e.g., for cardiovascular disease, development, immune system). However, overall, these studies found either no association, no consistent findings, or were too few to make definitive conclusions of an association. [ATSDR 2021]. No animal studies were identified for PFHpA.

For PFOSA, there is one animal study for acute oral exposure. No animal studies for intermediate or chronic exposures are available. The one acute animal study determined a hepatic and body weight no effect level (NOAEL) but did not determine a LOAEL. ATSDR identified several human studies of PFOSA exposures (about 12 studies) that either showed no association, no consistent findings, or were too few to make definitive conclusions of an association. One human study showed an association with breast cancer [ATSDR 2021; please note that ATSDR toxicological profile designates this PFAS as FOSA which is the same as PFOSA].

Studies have shown that EtFOSE is metabolized and degrades in the environment to PFOS. In animal studies, EtFOSE caused developmental effects similar to those associated with PFOS [DeWitt 2015].

Persons exposed to both PFOS and EtFOSE might have an increased risk for developmental effects, but ATSDR is unable to quantify this mixture effect with current knowledge.

No human studies were identified for exposures to 6:2 FTS. 6:2 FTS has been detected at low levels in some consumer products, drinking water, air, and fish. Human exposure might occur through any of these pathways. Some animal studies have shown that 6:2 FTS can cause kidney and liver toxicity, but it does not 1) cause damage to DNA, 2) act as a skin sensitizer, or 3) cause toxicity to reproductive organs or to the developing fetus [NASF 2019]. However, these studies are very limited, and no definitive conclusions can be drawn relating to potential effects of 6:2 FTS exposures in humans.

For all the PFAS discussed in this section, ATSDR determined that insufficient information exists to determine an MRL (ATSDR 2021). Moreover, none of the studies from the current scientific literature would allow ATSDR to calculate a human equivalent dose to compare the exposure dose from drinking private well water to effect levels. Therefore, ATSDR cannot evaluate these PFAS using its standard public health assessment approach. Additional analysis of the PFAS mixture in each well is provided below.

5.2.3 Evaluation of Cancer Health Effects from Past Exposures

Based on the recent human studies and the National Toxicology Program (NTP) animal studies discussed above, EPA and some state agencies are reassessing their PFOA CSFs. CSFs based on the more recent NTP studies might be different from the CSF previously derived by EPA for testicular cancer. For these reasons, ATSDR no longer recommends the use of the 0.07 $(mg/kg/day)^{-1}$ CSF to evaluate PFOA cancer risk.

EPA cites suggestive evidence that PFOS causes cancer, based on limited evidence of liver cancer in rats. However, the evidence was too limited to support a quantitative cancer assessment for PFOS [EPA 2016a]. EPA has not classified any other PFAS as potentially carcinogenic and has not derived oral CSFs for PFOS or other PFAS, mostly because animal and human data are insufficient. Therefore, similar to PFOA, ATSDR cannot calculate the estimated cancer risk from PFOS or other PFAS.

Until more definitive data are available, ATSDR is only able to evaluate the cancer risk posed by PFOA, PFOS, and other PFAS exposures qualitatively. Therefore, the actual cancer risk from PFOA, PFOS, other PFAS, or PFAS mixture exposures is uncertain.

5.2.4 Evaluation of Current Exposures to PFAS with HBCVs

No exposures above HBCVs have occurred since treatment systems were installed on wells RES17, RES19, RES21, and RES23, or since RES37 was abandoned. Therefore, no harmful effects are expected from current exposure to these PFAS. In addition, no harmful exposures are occurring from drinking water at RES19 and RES21 because these residents have been connected to public water in November 2019.

5.2.5 Evaluation of Current Exposures to PFAS without HBCVs

ATSDR evaluated the drinking water sampled from private wells with treatments systems. The samples were collected after going through the treatment system. During the period from 2017 through June 2020, there were very low concentrations detected for a few PFAS in samples from the faucet. For RES17, the PFAS detected in 2015 occurred shortly after the GAC treatment was installed in March 2015, with only one detection after that in 2018. The PFAS detected were below ATSDR's most conservative HBCV. For the other wells that have had a treatment system, there have been only a few instances of PFAS detections in treated water at the faucet, and the detections have been below ATSDR's most conservative HBCV. No current exposures are occurring to water from the seasonal well RES37, as it is no longer in use. In addition, no harmful exposures are occurring from drinking water at RES19 and RES21 because these residents have been connected to public water in November 2019.

5.2.6 Evaluation of Cancer Health Effects for Current Exposures

As stated in section 5.2.3, there is uncertainty with the current EPA CSF for PFOA. In addition, because of the lack of EPA CSFs for other PFAS (due to lack of the data), ATSDR cannot calculate the estimated cancer risk from other potentially carcinogenic PFAS exposures. Therefore, the actual cancer risk from all PFAS exposures from private wells is uncertain. However, because no or few PFAS at low levels have been detected in water from RES17, RES19, RES21, and RES23 since treatment systems were installed, ATSDR would expect no or a low increased risk for cancer. No harmful exposures are occurring from seasonal well RES37, which is no longer in use. In addition, no harmful exposures are occurring from drinking water at RES19 and RES21 because these residents were connected to public water in November 2019.

5.3. Wells Where PFAS Hazard/Risk Cannot be Determined (30 wells)

5.3.1 Evaluation of Exposures to PFAS with HBCVs (RES03, RES09, RES20, RES22, and RES25)

Four wells (RES03, RES20, RES22, and RES25) had a maximum detection that exceeded the ATSDR HBCV for PFOS. Two maximum values for RES03 and RES20 were above the PFOA HBCV. None had maximum PFHxS levels that exceeded ATSDR's HBCV. None had combined PFOA and PFOS levels that exceeded the EPA health advisory. Table 2 shows the measures used to evaluate PFOS and PFOA.

PFOS. All CTE scenario HQs for all ages and exposure groups who consumed water from RES03, RES20, RES22, and RES25 were below 1.0. Exposures below an HQ of 1.0 indicate that no harmful effects from exposures to PFOS alone are expected. However, the RME scenario HQs for RES03, RES20, RES22, and RES25 were above 1.0 (from about 1.0 to 2.8) for a young child (birth to < 1 year). ATSDR also evaluated the MOE for each of these PFOS exposures. The RME scenario MOE for these wells ranged from 381 to 1,000 for young children (birth to < 1 year). The MOEs for all other age groups and pregnant and lactating women all exceeded 1124. Based on this analysis, no harmful non-cancer health effects are likely from PFOS exposures to users of these wells.

(See Appendix A tables for HQ and MOE calculations: RES03-Table A-17; RES20-Table A-18; RES22-no table, exposures are similar to RES20; RES25-Table A-19.)

PFOA. All CTE scenario HQs for all ages and exposure groups who consumed water from RES03 and RES20 were below 1.0. Exposures below an HQ of 1.0 indicate that no harmful effects from exposures to PFOS alone are expected. However, the RME scenario HQs for RES03 and RES20 were slightly elevated (1.01 to 1.16) for a young child (birth to < 1 year). ATSDR also evaluated the MOE for each of these PFOS exposures. The RME scenario MOE for these wells ranged from 236 to 270 for young children (birth to < 1 year). The MOEs for all other age groups and pregnant and lactating women all exceeded 795. Based on this analysis, no harmful non-cancer health effects are likely from PFOS exposures to users of these wells.

(See Appendix A tables for HQ and MOE calculations: RES03-Table A-17a and RES20-Table A-18a.)

Mixture of PFOS, PFOA, and PFHxS. No HIs were elevated for the CTE scenario. For RES03 and RES20, the HIs were slightly elevated between 3.3 to 4.3 for the RME scenario (see Table 2). These data do not provide enough evidence that the combined PFOS, PFOA, and PFHxS exposures to users of wells RES03 and RES20 significantly increase the risk of harmful non-cancer effects except for

what might be expected from exposure to any one of these PFAS alone. However, these wells also contained other PFAS. Further health perspective for the total mixture of PFAS found in these wells is provided below, and ATSDR is available to discuss these findings with the users.

(See Appendix A tables for HI calculations: RES03-Table A-26, and RES 20-Table A-27 and RES25-Table A-28. Although RES22 is not shown, HIs would be slightly less than for RES20).

5.3.2 Evaluation of Exposures to PFAS without HBCVs (See Table 5 below for listing of 30 wells)

In addition to PFOA, PFOS, and PFHxS exposures above HBCVs, people using wells RES03, RES09, RES20, RES22, and RES25 are also exposed to the other PFAS at the maximum concentrations shown in Table 3. None of these wells had levels of PFBA nor PFBS above the Minnesota HBCVs. In addition, 25 other wells detected PFAS with no HBCV. See above for the discussion of the known public health implications of exposure to PFAS without HBCVs. For all the PFAS detected in water from these wells, no animal or other studies were identified to allow ATSDR to compare the exposure dose from drinking private well water to effect levels (i.e., LOAELs).

5.3.3 Evaluation of Mixtures Exposure to PFAS without HBCVs

Aside from the HI approach for PFOA, PFOS, PFHxS, and PFNA, well-accepted scientific methods to calculate possible health effects of exposures to PFAS mixtures do not yet exist. In addition, not all PFAS share the same health outcomes nor have the same toxicity. Therefore, ATSDR evaluated the scientific literature to determine what health effects from the PFAS mixture found in these private wells might have similar health endpoints (see Table 4 below).

Table 4. PFAS and possible effects on organ systems

Specific PFAS	Cardiovascular	Developmental	Endocrine	Liver	Immune	Reproductive	Serum Lipid
6:2 FTS	○	○	○	○	○	○	○
8:2 FTS	○	○	○	○	○	○	○
EtFOSA	○	○	○	○	○	○	○
EtFOSE	○	●	○	○	○	○	○
PFBA	○	●	●	●	○	○	○
PFBS	○	●	●	○	○	●	○
PFDS	○	○	○	○	○	○	○
PFHpA	○	○	○	○	○	○	○
PFHpS	○	○	○	○	○	○	○
PFHxA	●	●	●	●	●	○	○
PFHxS	○	●	●	●	●	○	○
PFNA	○	●	○	○	●	○	●
PFOA	●	●	●	●	●	●	●
PFOS	●	●	●	●	●	●	●
PFOSA	●	○	○	○	○	○	○
PFPeA	○	○	○	○	○	○	○
PFTeDA	○	○	○	○	○	○	○
PFTrDA	○	○	○	○	○	○	○

Notes: ● = Indicates possible effects on this target organ system. ○=Indicates no effects/insufficient information. Only PFAS that have at least one detection in private wells are included in this table.

Abbreviation	Definition	Citation(s) for effects (if applicable)
6:2 FTS	6:2 fluorotelomer sulfonate	no effects or insufficient information on target organ systems
8:2 FTS	8:2 fluorotelomer sulfonate	no effects or insufficient information on target organ systems
EtFOSA	n-ethyl perfluorooctane sulfonamide	no effects or insufficient information on target organ systems
EtFOSE	n-ethyl perfluorooctane sulfonamidoethanol	DeWitt 2015
PFBA	perfluorobutanoic acid	[MDH] Minnesota Department of Health 2017a; ATSDR 2021
PFBS	perfluorobutane sulfonic acid	[MDH] Minnesota Department of Health 2017a; ATSDR 2021
PFDS	perfluorodecanesulfonic acid	no effects or insufficient information on target organ systems
PFHpA	perfluoroheptanoic acid	ATSDR 2021
PFHpS	perfluoroheptane sulfonate	no effects or insufficient information on target organ systems
PFHxA	perfluorohexanoic acid	Klaunig et al. 2015; Iwai and Hoberman 2014; ATSDR 2021
PFHxS	perfluorohexanesulfonic acid	Gleason et al. 2015; Grandjean et al. 2012; Morgensen et al. 2015; Viberg et al. 2013; Butenhoff et al. 2009
PFNA	perfluorononanoic acid	ATSDR 2021
PFOA	perfluorooctanoic acid	ATSDR 2021
PFOS	perfluorooctane sulfonic acid	ATSDR 2021
PFOSA (aka FOSA)	perfluorooctane sulfonamide	(ATSDR 2021
PFPeA	perfluoropentanoic acid	no effects or insufficient information on target organ systems
PFTeDA	perfluorotetradecanoic acid	no effects or insufficient information on target organ systems
PFTrDA	perfluorotridecanoic acid	no effects or insufficient information on target organ systems

As shown in Table 4, animal studies or human epidemiological studies have indicated that adverse health outcomes of concern for PFAS are typically associated with two or more compounds in the class. All target organ systems have at least three of the PFAS associated with that health outcome. Therefore, the combined exposures to PFAS from private wells may have increased the risk for some of these non-cancer health outcomes, but refined methods to evaluate these combined exposures are lacking.

For many of the PFAS listed in Table 4, ATSDR cannot evaluate these using its standard public health assessment approach. ATSDR used EPA's definition of long-chained PFAS [EPA 2018b] to calculate the percentage of long-chained PFAS, which are generally considered to be more bioaccumulative than short-chained PFAS (see Table A-1). The number of PFAS detected in these wells ranged from one (RES34 and RES54) up to 13-16 in a few wells (RES01, RES03, RES23, RES41 and RES49). Table A-1 shows that RES01, RES03, RES15, RES20, RES22, RES25, and RES41) had the highest total PFAS concentrations and number of different PFAS detected (based on at least nine PFAS detected and a total PFAS concentration greater than 0.1 μg/L or 100 ppt).

This information offers users of these wells some perspective on total PFAS concentrations, number of PFAS, and percentage of long-chained PFAS detected in their wells. Owners should also consider whether young children and women of childbearing age are being exposed to PFAS through the drinking water in their homes. ATSDR has consulted with several well owners and remains available to consult with other individual homeowners to explain the meaning of these results. However, we lack scientific information on the health effects of the combined exposures to these PFAS and refined methods to evaluate them. Therefore, ATSDR will not be able to definitively say if harmful effects are possible from exposures to users of these wells.

5.3.4. Evaluation of Cancer Health Effects

As stated in section 5.2.3, until more definitive data are available, ATSDR can only evaluate the cancer risk posed by PFOA, PFOS, and other PFAS exposures qualitatively. Therefore, the actual cancer risk from PFOA, PFOS, other PFAS, or PFAS mixture exposures for users of the 30 wells with an undetermined hazard/risk is uncertain.

5.4. Wells Where PFAS Hazard/Risk Unlikely or No Hazard (see Table 6 below for listing of 7 wells)

5.4.1 Evaluation of Exposures to PFAS with HBCVs

No PFAS with HBCVs were detected in RES30 and RES42; therefore, no harmful effects are expected. Only PFAS with HBCVs were detected in RES07 and RES27. All PFAS were below HBCVs, indicating that no harmful effects are expected.

5.4.2. Evaluation of Exposures to PFAS without HBCVs

No PFAS without HBCVs were detected in RES30 and RES42; therefore, no harmful effects are expected. For wells with only a few detections of PFAS (e.g., RES10, RES12, and RES13), the risk of harmful health effects is likely low as they were detected at low parts per trillion concentrations below or near ATSDR's lowest HBCV.

5.4.3. Evaluation of Cancer Health Effects

No increased risk of cancer is expected for exposures to user of RES30 and RES42 because no PFAS were detected. Although EPA does not have an oral cancer slope factor for PFOS or other PFAS because of the lack of data to calculate one, the cancer risk from PFAS exposures to users of RES07 and RES27 is likely to be low.

5.5. Other Public Health Considerations

5.5.1 Contributions from Other Sources

ATSDR does not have enough information to identify individual exposure sources and to estimate the background exposure level in persons whose private wells are contaminated. Those sources might include PFAS-contaminated food, such as certain types of fish and shellfish if nearby streams, rivers, or lakes are affected; hand-to-mouth transfer from surfaces previously treated with PFAS-containing stain protectants, with carpet being most significant for infants and toddlers; use of non-stick cookware (especially if manufactured before 2013); or eating food packaged in PFAS-containing material, such as popcorn bags, fast food containers, or pizza boxes.

5.5.2 Susceptible Populations: Persons with Pre-existing Health Conditions and Early Development

The available epidemiology data identify several potential targets of PFAS toxicity; people with pre-existing conditions may be unusually susceptible. For example, it appears that exposure to PFOA or PFOS may increase serum lipid levels, particularly cholesterol levels. Thus, an increase in serum cholesterol may result in greater health impact to persons with high levels of cholesterol or other existing cardiovascular risk factors. Similarly, increases in uric acid levels have been observed in persons with higher PFAS levels; increased uric acid may be associated with an increased risk of high blood pressure. Thus, people with hypertension may be at greater risk. The relationship between PFOA and PFOS exposure and increased risk for cardiovascular disease is inconclusive. Additional research is needed to understand how exposure to these chemicals might affect people with pre-existing risk factors (such as elevated cholesterol) for cardiovascular disease. The liver is a sensitive target in many animal species and might be a target in humans. Therefore, people with compromised liver function could be a susceptible population [ATSDR 2021]. Human studies have indicated that some PFAS may affect immune function [ATSDR 2021]. Therefore, immunocompromised persons may also be a susceptible population to PFAS exposures. In general, the clinical significance of the impact of PFAS exposures on people with pre-existing conditions is not well understood.

ATSDR recognizes that the unique vulnerabilities of fetuses, infants, and children merit special emphasis in communities affected by environmental contamination. A child's developing body systems can sustain damage if toxic exposures occur during critical growth stages. Children ingest a larger amount of water relative to body weight than adults, resulting in a higher intake of pollutants in proportion to body size. In addition, children exhibit hand-to-mouth behavior and could be exposed to PFAS from previously treated carpet materials and other treated fabrics. Reducing PFAS exposures to the developing fetus, infants, and young children is extremely important. As evidence for this concern:

- Formula-fed infants consuming formula mixed with contaminated water would have a higher exposure compared to adults because formula is their sole or primary food source and their smaller body weight.
- Evidence suggests that high serum PFOA or PFOS levels are associated with lower birth weights. Studies of populations with lower serum PFOA or PFOS levels have not found significant associations for birth weight. Although significant associations were found for the high serum group, decreases in birth weight were small and may not be biologically relevant [ATSDR 2021].

PFAS can be transferred from breast milk to nursing infants. Studies that measured PFAS in maternal serum and breast milk in matched mother-infant pairs found highly variable correlations [ATSDR 2021]. ATSDR considers mother and child health benefits of breastfeeding to outweigh the known risk from PFAS exposure through breastmilk. Information on breastfeeding is included elsewhere in this report.

5.5.3 Biomonitoring Results—NH Department of Health and Human Services Blood Sampling Program

The NH DHHS offered biomonitoring (blood testing) for any persons exposed to PFAS in drinking water at Pease International Tradeport, including those exposed to either PFOS or PFOA above the corresponding former EPA provisional health advisories from private wells tested because of the Pease PFAS investigation. Blood testing for PFAS is no longer available through the NH DHHS. NH DHHS has and will continue to provide information and recommendations to healthcare providers to help providers and patients make informed decisions about what PFAS exposure might mean for an individual's health (see also https://www.dhhs.nh.gov/dphs/pfcs/blood-testing.htm).

NH DHHS reported that body burdens of PFOA, PFOS, and PFHxS in persons who consumed water from the Pease Tradeport public water system and private wells were significantly higher than national levels reported in CDC's 2011–2012 National Health and Nutrition Examination Survey (NHANES) report [NH DHHS 2015]. In addition, since the release of the 2013–2014 NHANES data, NH DHHS revised its age-specific comparisons. For the age-specific comparisons, blood levels for all age groups where statistically above the general U.S. population for PFOS and PFHxS. For PFOA, only blood levels for persons 12 years and older were statistically elevated above the general U.S. population [NH DHHS 2017]. Please see ATSDR's health consultation evaluating public water at the Pease AFB for a summary of these findings [ATSDR 2020b]. It is important to note that the biomonitoring data reflects exposures received from all sources of PFAS in a person's environment, including their drinking water.

5.6. Summary of Public Health Implications Evaluation

There are several limitations and uncertainties when evaluating human health implications from PFAS exposures in drinking water (see below). Because of these limitations, ATSDR used a health-protective approach to evaluate the possibility for harmful non-cancer and cancer health effects. ATSDR used an approach that considered multiple exposures and factors. These included consideration of past body burdens, length of exposure, multiple PFAS in the water, contributions from other non-water sources, and similarity of health effects for various PFAS—all sources or factors which could contribute to the overall health effects of PFAS exposures. Although most of the

PFOA, PFOS, and PFHxS exposures were below health effect levels seen in the scientific literature (assuming a 100% contribution from drinking water), some of the estimated doses were above ATSDR's MRLs indicating a potential for concern and some doses approached effect levels. The following table summarizes the bottom-line findings from ATSDR's evaluation of the 42 private wells sampled and the following sections provide the basis for these determinations.

Table 5. Summary of Non-Cancer Public Health Findings for Private Drinking Water Wells in Newington and Greenland, NH sampled Near the Pease International Tradeport, Portsmouth, NH

Hazard (Risk) Determination	Private Drinking Water Wells
Wells with possible PFAS hazard/risk—see Conclusion 1	**5 Wells**: RES17, RES19, RES21, RES23, and RES37
Wells where PFAS hazard/risk cannot be determined—see Conclusion 2	**30 Wells**: RES01, RES02, RES03, RES04, RES05, RES06*, RES08, RES09, RES11, RES14, RES15, RES18*, RES20, RES22, RES24, RES25, RES29, RES31, RES34, RES38*, RES43, RES41, RES45, RES48, RES49, RES50, RES51, RES52, RES53, and RES54†
Wells where PFAS hazard/risk unlikely--Exposure—see Conclusion 3	**5 Wells**: RES07, RES10, RES12, RES13, and RES27
Wells with no PFAS hazard/risk—No Exposure—see Conclusion 3	**2 Wells**: RES30 and RES42

Notes: *Hazard cannot be determined for past exposures; however, sampling from these wells since March 2018 has either showed no detections or one detection at very low levels. †The one sampling event showed low levels of PFAS exposures indicating that a PFAS hazard/risk is unlikely. However, ATSDR placed this well in the hazard/risk cannot be determined category because of the limited data.

5.6.1. Wells with Possible PFAS Hazard/Risk (5 wells)

After evaluating multiple factors, ATSDR concludes that past exposure to drinking water with levels of PFOA, PFOS, and PFHxS measured in well RES17, in combination with exposure to other PFAS found in the RES17 water and other potential non-drinking water sources, could have increased the risk for harmful non-cancer health effects in all age and exposure groups, particularly young children and infants. The risks for harmful non-cancer effects were likely greater for young children who lived at RES17 or were born to mothers who used this well long-term for drinking water.

Adult users of wells RES19, RES21, RES23, and RES37/GBNWR are not likely to have increased risk for harm from their past exposures to PFOA, PFOS, and PFHxS in their private wells. However, the

risk of harmful non-cancer effects to adult users of RES19, RES21, RES23, and RES37 from past exposure to the total mixture of PFAS (beyond PFOA, PFOS, and PFHxS) is uncertain. There is a concern for exposures to young children who used water from these wells because of the combined PFOS, PFOA, and PFHxS exposures and other PFAS in their water. For some of these wells, especially RES17, the estimated exposure doses for PFOS were close to or above effect levels found in the animal studies ATSDR used to derive its MRL and from other animal studies of immune effects. Therefore, because PFOA and PFOS levels in RES19, RES21, RES23, and RES37/GBNWR were near or above the EPA health advisory, ATSDR agrees with actions to provide these residents with treatment systems or alternate water. No other private wells had PFOA and PFOS levels above the EPA health advisory.

5.6.2. Wells Where PFAS Hazard/Risk Cannot be Determined (30 wells)

Four wells (RES03, RES20, RES22, and RES25) had a maximum detection that exceeded the ATSDR HBCV for PFOS. Two maximum values for RES03 and RES20 were above the PFOA HBCV. No wells had maximum PFNA levels that exceeded ATSDR's HBCV. In addition, none of the combined PFOA and PFOS levels for these wells exceeded the EPA health advisory. PFHxS was not above its HBCVs in any other wells. The one high PFHxS level may be an anomaly because that concentration was never duplicated at that well. ATSDR's evaluation indicates that if this were an actual PFHxS exposure, young children may experience a slight increased risk of thyroid effects. If it were not an actual exposure, then ATSDR expects no harmful non-cancer effects to anyone using this well. ATSDR's evaluation of exposures to PFOA and PFOS alone indicate that no harmful effects are likely because the HQs were either below 1.0 or the estimated exposure doses were well below health effect levels shown in animals studies used to derive ATSDR's MRLs. ATSDR's evaluation of the exposure to the PFOA, PFOS, PFHxS, and PFNA mixture in these wells provided little information that the combined exposures to these PFAS appreciably increased the risk of harmful effects. Further health perspective for the total mixture of PFAS found in these wells is provided in the next section below. ATSDR is available to discuss these findings with the users of these wells.

For residential wells with no treatment systems, no harmful health effects are likely for exposures to PFOA, PFOS, PFHxS, or PFNA, either alone or combined. However, water from these wells also contained other PFAS with no HBCVs. We lack refined methods to evaluate the public health implications of exposure to the entire mixture of PFAS in water from these wells. For most of these other PFAS, except for those with HBCVs, little toxicological information is available to understand what harmful effects they might cause and at what exposure levels.

The number of PFAS detected in these 30 wells ranged from one (RES34 and RES54) up to 13 to 16 in a few wells (RES01, RES03, RES23, RES41 and RES49). Table A-1 shows that RES01, RES03, RES15,

RES20, RES22, RES25, and RES41) had the highest total PFAS concentrations and number of different PFAS detected (based on at least nine PFAS detected and a total PFAS concentration greater than 0.1 μg/L or 100 ppt).

This health consultation includes the limited information on what is known about the health effects of some of these PFAS. Longed-chained PFAS are generally considered to be more bioaccumulative than short-chained PFAS. (See Table A-1 for more information on which PFAS are short- or long-chained.) To help owners of wells with no treatment systems better understand what is in the water from their wells, ATSDR calculated the percentage of long-chained PFAS for the summed concentrations of all detected PFAS in water from each well (see Table A-1). Although that is a health-protective assumption, ATSDR is uncertain about the validity of adding these PFAS, because we do not know if they all have the same health endpoints. Besides PFAS exposures from drinking water, PFAS exposure from food (including some shellfish from Great Bay or liver from deer harvested in the area) and consumer products are possible contributors to the overall PFAS body burden.

5.6.3. Wells where PFAS Hazard/Risk Unlikely or No Hazard (7 wells)

No PFAS without HBCVs were detected in RES30 and RES42; therefore, no harmful effects are expected. For wells with only a few detections of PFAS (e.g., RES10, RES12, and RES13), the risk of harmful health effects is likely low as they were detected at low parts per trillion concentrations below or near ATSDR's lowest HBCV.

5.6.4 Additional Supporting Information

- Scientific information suggests an association between PFOA, PFOS, and PFHxS exposure and various health endpoints, including effects on serum lipids (not for PFHxS), immune responses, fetal growth and development, endocrine systems (thyroid), and the liver.
- A review of the scientific literature indicated children and neonates are considered sensitive to PFAS exposures and are the age group most likely to receive the highest exposures. In addition, persons with certain pre-existing health conditions (risk factors) such as elevated cholesterol or elevated blood pressure and those with compromised livers or who may be immunocompromised may be unusually susceptible to health effects associated with PFAS exposures. In general, the clinical significance of the impact of PFAS exposures on people with pre-existing conditions is not well understood.
- Well-accepted scientific methods to quantitatively evaluate the possible health impacts of the combined exposures to mixtures of PFAS do not exist. ATSDR determined that combined exposure to PFOA, PFOS, PFHxS and PFNA in these wells could have increased the risk of

developmental, endocrine (thyroid) and immune effects. Several other PFAS may adversely affect the same organ systems. Harmful effects for other health outcomes shown to be associated with PFOA, PFOS, or PFHxS may also occur. Therefore, the combined exposures to PFAS measured in these private wells may have increased the risk for some non-cancer health outcomes.

- Exposures to PFAS from non-drinking water sources, combined with exposure to other PFAS in private well water with limited scientific information, could increase the risk for some associated health effects.
- Research in humans suggest that high levels of certain PFAS may lead to an increased risk of kidney and testicular cancers. The EPA [2016b] considers the evidence that PFOA has the potential to be carcinogenic in humans to be suggestive, and IARC [2017] has determined that PFOA is possibly carcinogenic to humans. In a recent review of PFOA carcinogenicity by Steenland et al. [2020], the human (epidemiological) evidence remains supportive but not definitive for kidney and testicular cancers. Moreover, the findings from the U.S. National Cancer Institute [Shearer et al. 2020] of the association between PFOA and kidney cancer in humans is particularly suggestive. Steenland et al. [2020] conclude that there is some suggestive evidence for an association between PFOA and prostate cancer; however, the results are inconsistent. Animals given PFOA have shown higher rates of liver, testicular, and pancreatic tumors. We do not know if cancer at these three sites in animals results from a mode of action that is relevant to humans [ATSDR 2021].
- Based on the recent human studies and the NTP animal studies discussed above, EPA and some state agencies are reassessing their PFOA CSFs. CSFs based on the more recent NTP studies might be different from the CSF previously derived by EPA for testicular cancer. For these reasons, ATSDR no longer recommends the use of the 0.07 $(mg/kg/day)^{-1}$ CSF to evaluate PFOA cancer risk.
- Epidemiology studies of PFOS-exposed workers reported an increased risk for some cancers; however, because of small sample sizes, the confidence intervals were wide, indicating considerable uncertainty in the effect estimates [Alexander et al. 2003; Alexander and Olsen 2007; Grice et al. 2007; Olsen et al. 2004]. A causal association between cancer and PFOS exposures, based on human studies, remains uncertain. Animal studies have found limited but suggestive evidence of PFOS exposure and increased incidence of liver and thyroid tumors. However, there is uncertainty in these associations as the tumors did not show a direct relationship to dose, and the mechanism of action may not be relevant to humans [ATSDR 2021].
- Additional studies are needed to confirm the link between PFOA, PFOS, and other PFAS exposures and cancer. Therefore, although current data are very limited, some other PFAS might be carcinogenic, and some might not.

- Until more definitive data are available, ATSDR can only evaluate the cancer risk posed by PFOA, PFOS, and other PFAS exposures qualitatively. Therefore, the actual cancer risk from PFOA, PFOS, other PFAS, or PFAS mixture exposures is uncertain.

6. Community Concern: Breastfeeding Exposures and Health Implications

Community members, especially mothers who were exposed to PFAS from the Pease International Tradeport site, have expressed concerns about the health implications of PFAS exposure to infants who breastfeedStudies have shown PFAS to transfer to nursing infants. Comparisons of serum concentrations of women who breastfed their infants with those who did not showed that breastfeeding significantly decreases maternal serum concentrations of PFAS [Mogensen et al. 2015]. The decrease was estimated to be 2% to 3% per month of breastfeeding. Concentrations of PFAS in breast milk also decrease with breastfeeding duration [ATSDR 2021].

Breastfeeding provides many health and nutritional benefits to a child, such as a reduced risk of ear and respiratory infections, asthma, obesity, and sudden infant death syndrome. In addition, breastfeeding can also help lower a mother's risk of high blood pressure, type 2 diabetes, and ovarian and breast cancer [CDC 2019].

In general, CDC and the American Academy of Pediatrics recommend breastfeeding, despite the presence of chemical toxicants [CDC 2015; AAP 2012]. A woman's decision to breastfeed is a personal choice, made in consultation with her healthcare provider. It is a choice made after consideration of many different factors, many unrelated to PFAS exposure, specific to the mother and child

7. Limitations and Uncertainties of Human Health Risks from PFAS Exposures

7.1 Multiple Exposure Sources

In addition to drinking water exposures, community members likely have additional PFAS exposures from other sources unrelated to AFFF releases at the former Pease AFB. These could include food, dust, air, and consumer products. Exposures might also occur by touching surfaces treated with a stain protector and then touching one's mouth or touching food that is eaten. All sources add to the amount of chemicals in one's body and potential health effects. ATSDR was not able to assess the impact of these sources on possible health effects.

7.2 Lack of Historical Exposure Data

ATSDR does not know exactly how long and at what concentrations workers and children were exposed to PFAS in private wells near the Pease International Tradeport. Historical sampling data are unavailable. Exposures might have occurred for years as PFAS moved through groundwater. PFAS accumulate and remain in the body for years before they are eliminated. Past and current exposures contribute to the overall health risks from PFAS.

7.3 Inadequate Methods to Fully Assess Human Health Implications

Methods are available to evaluate the public health implications of exposure to some but not all PFAS. People who use private well water are potentially exposed to a mixture of PFAS. Methods used to assess exposure to other environmental mixtures have not been developed for PFAS or might be appropriate only for PFAS with established health guidelines. Consistent with ATSDR Cancer Framework [ATSDR 2018a], ATSDR used the approach of adding hazard quotients to get a hazard index which is often used to assess risk to multiple chemicals. However, this approach may not provide an appropriate solution for all PFAS. Only compounds with similar toxicological endpoints should be combined (i.e., PFOS, PFOA, PFHxS, and PFNA). Moreover, standard risk assessments methods have limitations.

7.4 Other General Limitations

Humans and experimental animals differ in how their bodies absorb and react to PFAS. That leaves questions about the relevance of effects in animals to humans. ATSDR also has limited toxicity data for many PFAS from human and animal studies [Butenhoff JL and Rodricks JV 2015]. The health consequences of PFAS in the body are uncertain. Significant uncertainty exists about the lowest concentration at which toxic effects might occur in people exposed to PFAS for many years.

The HBCVs for PFOS, PFOA, PFHxS, and PFNA in drinking water were calculated by ATSDR using the best available scientific information. These values allow ATSDR to assess the potential risk from drinking water exposures. ATSDR HBCVs and MRLs are based on the most current PFAS science; however, the overall scientific knowledge on PFAS is still evolving. Toxicity information for other PFAS is limited.

Because of these limitations, ATSDR used a health-protective approach to evaluate health risks for non-cancer health effects until better methods are developed. For non-cancer health effects, ATSDR calculated hazard quotients for PFOS, PFOA, PFHxS, and PFNA, the most thoroughly investigated

PFAS. In a qualitative way, ATSDR considered other source contributions, other PFAS in the mixture, and past exposures in evaluating health risks.

7.5 Incomplete Information on the Type of AFFF Used at the Former Pease AFB and Specific PFAS Formulations

One of the challenges to evaluating exposures from an AFFF source is that we do not know which PFAS were present in the AFFF formulations used at Pease AFB. Data on AFFF-impacted groundwater indicate that about 25% of the PFAS remain unidentified [Houtz et al. 2013]. A study by Barzen-Hanson et al. (2017) resulted in the discovery of 40 novel classes of PFAS and the detection of 17 classes of previously reported PFAS, adding over 240 individual PFAS to the previous list that can now be associated with AFFF. Little is known about the newly discovered PFAS regarding the subsurface remediation strategies, transport, and toxicity [Barzen-Hanson et al. 2017].

8. Conclusions

ATSDR evaluated the public health implications of past and current PFAS exposure to the users of private wells near the Pease Tradeport and reached four conclusions. These conclusions are limited by several uncertainties. The specific PFAS formulation in the AFFF used at the former Pease AFB is not known. ATSDR used a health-protective approach to evaluate concentrations of 23 PFAS in drinking water wells. However, there may be PFAS in the water that were not measured. ATSDR's conclusions are based on evaluation of other PFAS that were measured in the water.

Conclusion 1—Wells with Possible PFAS Hazard/Risk

Past PFAS exposures may have increased the risk of harmful non-cancer health effects, especially to young children, who drank water from RES17, RES19, RES21, RES23, and RES37 or were born to mothers who did. The cancer risk from past exposures to all PFAS in these wells is uncertain. No current or future harmful exposures are expected for residents using these five water supply wells because actions have been taken to reduce or eliminate their exposures. However, there might be PFAS in the water that were not measured.

Basis for conclusion

The combined past exposures to PFOA, PFOS, and PFHxS to users of RES17, RES19, RES21, RES23, and RES37 approached health effect levels from animal studies. Thus, these exposures may have increased the risk of harmful non-cancer health effects, especially for developmental, endocrine (e.g., thyroid), and immune effects, in young children. Harmful effects for other health outcomes shown to be associated with PFOA, PFOS, or PFHxS may also occur, such as, effects on cholesterol and the liver. Harmful non-cancer health effects for adults are only a concern for users of RES17. The risk of harmful effects to adult users of the other wells (RES19, RES21, RES23, and RES37) is uncertain because of the limited scientific information to evaluate the public health implications of the combined exposures to all PFAS in these wells.

Human studies provide some evidence that PFOA is associated with kidney, testicular, and prostate cancers. Animals given PFOA orally have shown high rates of various cancers (liver, testicular, kidney, stomach, thyroid, and pancreatic). However, it is not known if the way these cancers occur in animals is relevant to humans. Human and animal studies have shown an association with both kidney and testicular cancers. Suggestive evidence that PFOS causes cancer is based on limited evidence of liver cancer in rats. However, the evidence is too limited to support a quantitative cancer assessment for PFOS. Therefore, although there is suggestive evidence that both PFOA and PFOS are carcinogenic, the science on PFOA, PFOS, and other PFAS is too limited at this time to quantify risk.

Limited data exist on the potential of other PFAS to cause cancer. ATSDR cannot calculate the estimated cancer risk for other past PFAS exposures or a total cancer risk from all potentially cancer-causing PFAS exposures. Therefore, the total cancer risk from past PFAS exposures from these private wells is uncertain.

Exposure to PFAS from food (including some shellfish from Great Bay and deer liver from the area) and consumer products, and to other PFAS in the water, likely contribute to the overall amount of PFAS in a person's body. Some pre-existing risk factors might increase the risk for harmful effects (e.g., persons with compromised immune systems or liver function).

Conclusion 2—Wells Where PFAS Hazard/Risk Cannot be Determined

The risk of harmful health effects (non-cancer and cancer) from past and current exposures to mixture of all PFAS in drinking water from 30 wells without treatment systems (see Table 5 for list of wells), now or in the past, cannot be determined.

Basis for Conclusion

The public health implications of past or current exposures to users of these 30 wells cannot be determined because we lack health information on the entire mixture of PFAS in these wells and the cancer risk from past and current exposure to all PFAS in these wells is uncertain because of the limited data on the potential for these PFAS to cause cancer.

Exposure to PFOS, PFOA, and PFHxS individually or combined in drinking water from these 30 wells were evaluated and determined to not likely result in an increased risk of harmful non-cancer health effects. However, other PFAS were detected in wells which could not be evaluated because of the lack of scientific information on the health effects. Moreover, for all 30 wells, the number of PFAS detected in these wells ranged from one (RES34 and RES54) up to 13 to 16 in a few wells (RES01, RES03, RES23, RES41, and RES49). Table A-1 shows that RES01, RES03, RES15, RES20, RES22, RES25, and RES41 had the highest total PFAS concentrations and number of different PFAS detected (based on at least nine PFAS detected and a total PFAS concentration greater than 0.1 micrograms per liter (µg/L) or 100 parts per trillion (ppt). In addition to PFAS exposures from drinking water, PFAS exposure from food (including some shellfish from the Great Bay and deer liver from the area) and consumer products likely contribute to the overall amount of PFAS in a person's body. See Section 2.3 (Surface Water and Biota Issues) for links to the NH DES reports on shellfish and deer sampling.

Conclusion 3—Wells where PFAS Hazard/Risk Unlikely or No Hazard

Past and current exposure to PFAS in drinking water from 7 wells without treatment systems is unlikely to result in an increased risk of harmful health effects.

Basis for conclusion

For these 7 wells, harmful effects are not expected because either no PFAS have been detected above an HBCVs or, if detected, were below or near ATSDR's lowest HBCV.

No PFAS without HBCVs were detected in RES30 and RES42; therefore, no harmful effects are expected. For wells with only a few detections of PFAS (e.g., RES07, RES10, RES12, RES13, and RES27), the risk of harmful health effects is likely low as they were detected at low parts per trillion concentrations below or near ATSDR's lowest HBCV.

Conclusion 4—Breastfeeding remains a healthy option

Current scientific information suggests that the health and nutritional benefits of breastfeeding outweigh the potential risks associated with PFAS in breastmilk.

Basis for conclusion

Community members, particularly mothers who have been exposed to PFAS from the Pease International Tradeport site, have expressed concern about the health implications of PFAS exposures to breastfed infants. Studies have shown that infants can be exposed to PFAS during pregnancy by transfer through the mother to the fetus and through breastfeeding. However, breastfeeding provides clear health and nutritional benefits. Some of the many benefits for infants include a reduced risk for ear and respiratory infections, asthma, obesity, and sudden infant death syndrome. Breastfeeding can also help lower a mother's risk for high blood pressure, type 2 diabetes, and ovarian and breast cancer. In general, CDC and the American Academy of Pediatrics recommend breastfeeding despite the potential presence of chemical contaminants in breast milk.

9. Recommendations

ATSDR recommends that EPA, NHDES, and the USAF continue their investigations to characterize PFAS groundwater contamination at the site and continue monitoring the private drinking water supply wells (treated and non-treated), including the identification of any affected wells that were not part of the original inventory plan. In addition, the USAF is encouraged to consider prioritizing their efforts and research into better understanding the types and the formulations of AFFF used at Pease and other facilities to better inform future monitoring efforts and health evaluations.

The USAF preferred long-term remedy for the four residences currently with water treatment systems is to connect them to the Pease Tradeport public water supply. ATSDR recommends that the USAF with EPA and NHDES regulators continue their efforts to implement a long-term remedy, which will permanently stop exposure to contaminated private drinking water sources that have PFAS above EPA or other applicable state health-based drinking water guidelines and reduce exposures to PFAS compounds that have no HBCVs. In addition, because the PFAS drinking water regulatory standards are continuing to evolve, these agencies should implement a long-term monitoring program that evaluates PFOS, PFOA, PFHxS and other PFAS that may be found in private wells. This will allow the agencies to stop exposures to contaminated private drinking water sources containing PFAS above applicable health-based drinking water standards.

If individuals want to reduce their exposure to PFAS in their water, they can use an alternative or treated water source for drinking, food preparation, cooking, brushing teeth, and any activity that might result in ingestion of water. Using contaminated water for bathing or showering, washing dishes, and doing laundry is not expected to result in significant exposure to PFAS.

ATSDR recommends that residents using wells where ATSDR has determined a hazard exists for past exposures (Conclusion 1) or where current exposures cannot be determined (Conclusion 2) should

consider not consuming shellfish from certain areas of Great Bay and not consume liver harvested from deer caught in the Great Bay area.

ATSDR recommends, based on several health benefits of breastfeeding for both mother and child, that nursing mothers continue to breastfeed. If formula is used (either exclusively or as a supplement to breastfeeding), then caregivers should use pre-mixed formula or reconstitute dry formula with water sources not containing PFAS. Infant feeding decisions should be made in consultation with a healthcare provider**.** More Information to guide healthcare providers is available from: https://www.atsdr.cdc.gov/pfas/docs/clinical-guidance-12-20-2019.pdf.

10. Public Health Action Plan

10.1 Completed Actions

- The USAF tested private wells located within one mile of the former Pease AFB boundary for PFAS.
- The USAF installed whole house activated carbon treatment systems at RES17, RES19, and RES21 to treat water with exceedances of the EPA health advisory. As a health-protective action, the USAF also installed a whole house activated carbon treatment system at RES23 because the combined PFOA and PFOS concentrations in the most recent sample taken in April 2016 was close to reaching the EPA health advisory. The USAF also provided bottled water for the seasonal users of RES37/GBNWR and this well is no longer in use. In November 2019, public water was provided to users of RES19 and RES21 whereas RES17 and RES23 still have whole-house treatment systems maintained and monitored by the USAF.NHDES collaborated with the NH Department of Health & Human Services (DHHS) to provide health information about PFAS in a document titled *Frequently Asked Questions: Perfluorochemicals (PFCs) in the Pease Tradeport Water System.* This can be found on the DHHS webpage: Pease Tradeport Water System Investigation available from: http://www.dhhs.nh.gov/dphs/investigation-pease.htm.
- In November 2017, ATSDR released a feasibility assessment for conducting a study to evaluate potential health effects of the population exposed to PFAS at the Pease Tradeport. The report is available from: https://www.atsdr.cdc.gov/pfas/docs/pease/pease-feasibility-assessment-november-2017-508.pdf.
- On July 15, 2020, ATSDR presented the findings of this report to the affected residents and community members and answered their questions. ATSDR will attempt to contact previous residents who lived in homes with contaminated wells.
- ATSDR provided health education information related to PFAS in private residential drinking water wells to the affected residents and community members. General information related

to PFAS in drinking water for residents, community members, and health professionals is available from: https://www.atsdr.cdc.gov/PFAS/.

10.2 Ongoing Actions

- The USAF will maintain whole house activated carbon treatment system at RES17. The users of well RES23 have opted to take over their filter system.
- The USAF is investigating the source and migration pathway of PFAS from former Pease AFB Site 8 to off-site wells to determine strategies to mitigate contaminant migration.
- Investigations by applicable agencies will proceed under CERCLA and the signed Federal Facility Agreement; further decisions will be based on risk as determined by a Human Health Risk Assessment using accepted toxicity values.
- NHNH DHHS offered biomonitoring (blood testing) for any persons exposed to PFAS in drinking water at Pease International Tradeport, including those exposed to either PFOS or PFOA above the corresponding former EPA provisional health advisories from private wells tested because of the Pease PFAS investigation. Blood testing for PFAS is no longer available through the NH DHHS. NH DHHS has and will continue to provide information and recommendations to healthcare providers to help providers and patients make informed decisions about what PFAS exposure might mean for an individual's health (see also https://www.dhhs.nh.gov/dphs/pfcs/blood-testing.htm).
- ATSDR and the CDC are conducting a health study of children and adults exposed to PFAS-contaminated drinking water at the Pease International Tradeport and from nearby private wells. The study will evaluate associations between PFAS blood levels and signs of changes in the body (e.g., cholesterol levels, kidney and thyroid function, and the development of specific diseases) and will serve as the first site in CDC/ATSDR's Multi-site Health Study looking at the relationship between PFAS drinking water exposures and health outcomes. ATSDR has funded seven cooperative agreement partners as principal investigators for the Multi-site Health Study.
- ATSDR and CDC are working to address the concerns of community members regarding potential associations between PFAS exposure and cancer. ATSDR and CDC are conducting analyses that use previously collected data to look at rates of certain health outcomes, including many adult and pediatric cancers, in communities that have been exposed to PFAS through drinking water and those that have not. These are exploratory analyses (hypothesis-generating and ecologic) and any observed associations will require further study. ATSDR and CDC are also developing plans for a study of PFAS and selected adult cancers using data from an existing study population (cohort).+
- ATSDR and CDC have conducted exposure assessments in communities near current and former military bases and that are known to have had PFAS in their drinking water. The

exposures assessments will provide information to communities about the levels of PFAS in their bodies. Using this information, public health professionals provide guidance to help people reduce or stop exposure.

- ATSDR is also providing technical assistance to tribal, state, local, and territorial health departments nationwide so they can effectively evaluate PFAS exposure in contaminated communities. ATSDR is also providing educational materials to the public to better understand PFAS and the health implications of PFAS exposures (see https://www.atsdr.cdc.gov/pfas/health-effects/index.html).
- ATSDR will work with the USAF and Town of Newington to make every effort to provide the findings of this report to the prior owners/residents of the affected properties.
- ATSDR has consulted with several individual well users to provide them additional health perspective on the PFAS exposures in their drinking water. ATSDR will work with the USAF and Town of Newington to make every effort to present the findings of this report to the prior owners/residents of the affected properties. ATSDR remains available to consult with well users. Contact ATSDR at 800-CDC-INFO (800-232-4636) or at https://wwwn.cdc.gov/dcs/ContactUs/Form to arrange a consultation with ATSDR scientists.

ATSDR recognizes that additional information is needed about the types of PFAS in AFFF and the type of AFFF used at Pease. Standard laboratory methods capable of detecting a broader range of PFAS in environmental samples are also needed. As more information becomes available, ATSDR will incorporate it into future assessments of exposure to PFAS from sites associated with the use of AFFF.

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Appendix A–Figures, Tables, and Equations

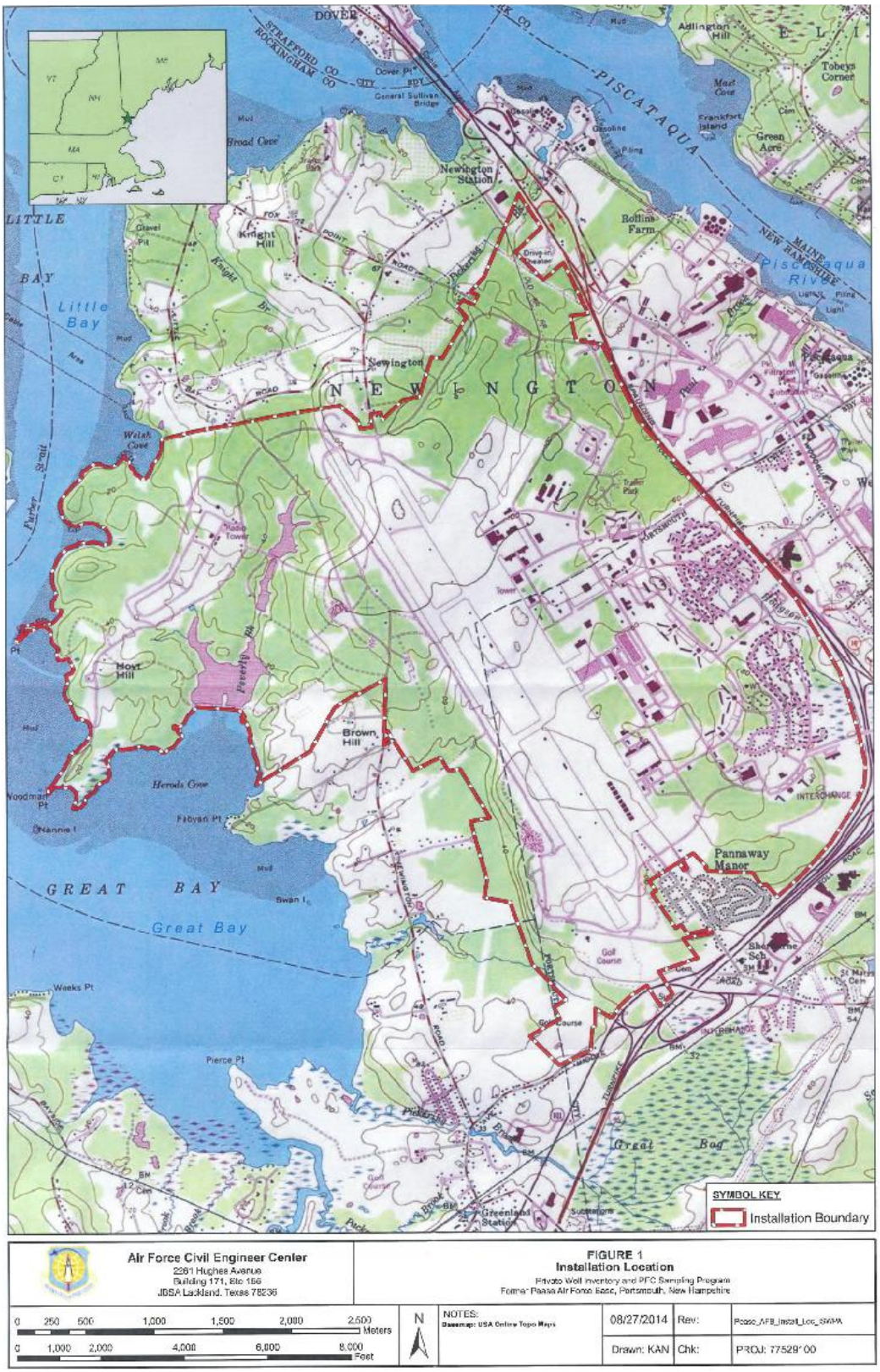


Figure A-1. Location and vicinity of Pease International Tradeport (former Pease Air Force Base). **Source**: AMEC. 2014.

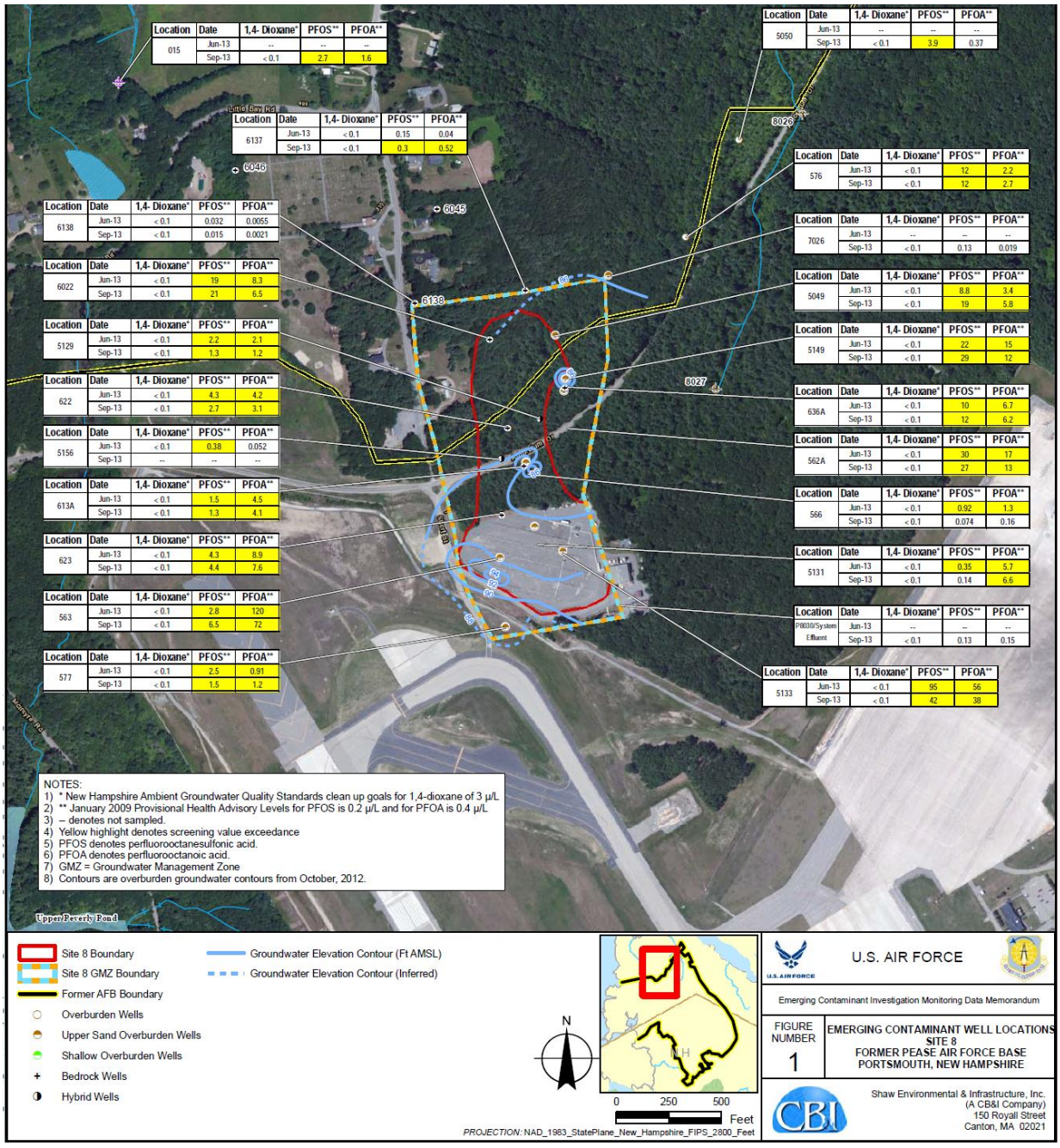


Figure A-2. Former Pease Air Force Base/Pease International Tradeport detail and location of site 8. **Source**: CB&I. 2015.

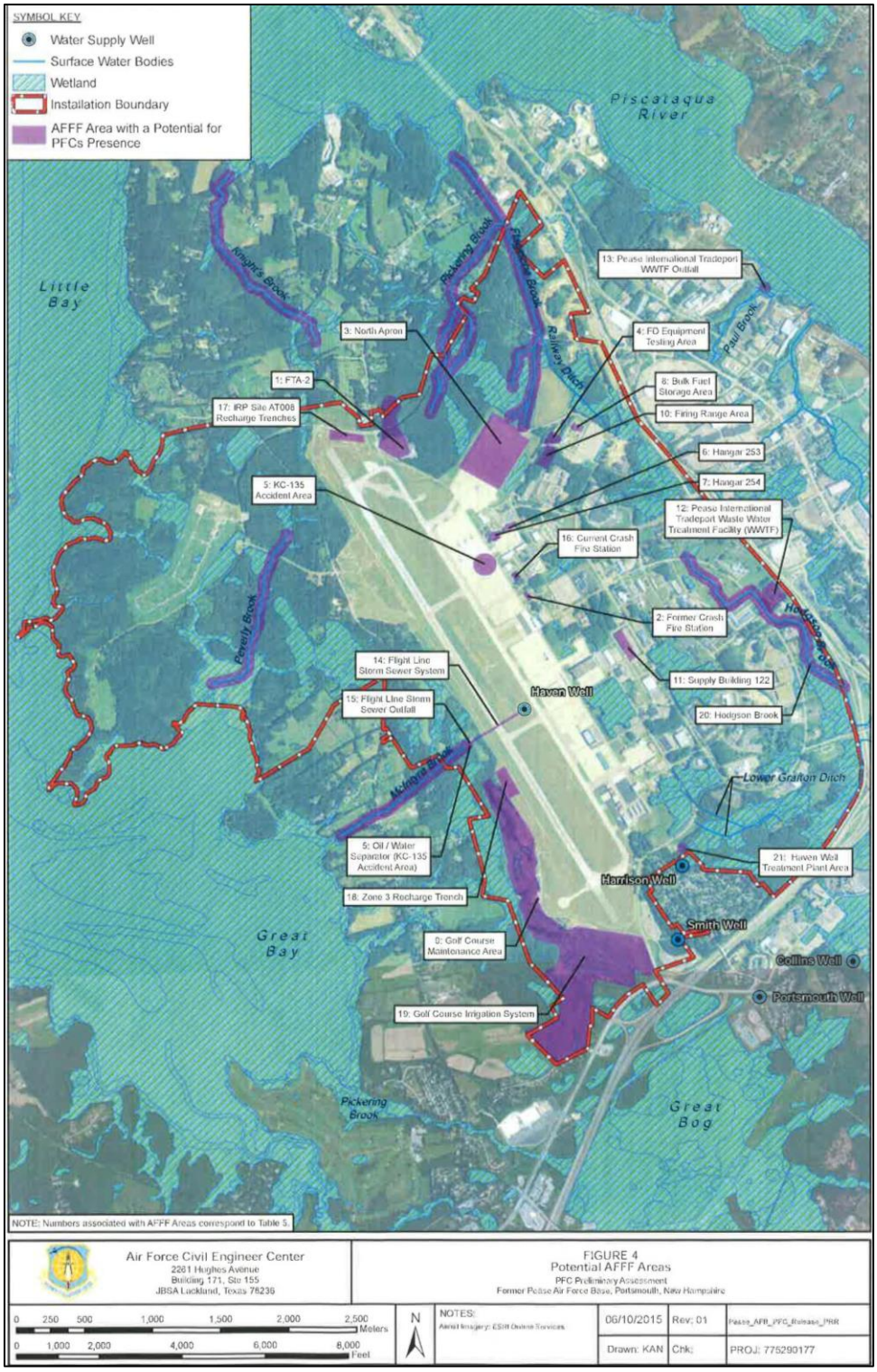


Figure A-3. Potential aqueous film-forming foam areas. **Source**: AMECFW 2015.

Table A-1. Total PFAS concentration (Including and excluding the perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS, number of different PFAS detected, and percentage of detected PFAS that were long chain from Untreated Private drinking water wells located within 1 mile from the former Pease Air Force Base, Portsmouth, NH. Concentrations in micrograms per liter (µg/L)

	Includes PFHxS, PFNA, PFOA, PFOS			Excludes PFHxS, PFNA, PFOA, PFOS		
Well ID	Total PFAS concentration	# PFAS	% Long Chain*	Total PFAS concentration	# PFAS	% Long Chain*
RES01	0.1144	15	73%	0.0742	11	64%
RES02	0.0785	9	56%	0.0431	6	33%
RES03	0.1287	13	69%	0.0748	9	56%
RES04	0.0216	5	80%	0.0106	2	50%
RES05	0.0398	5	100%	0.0277	3	100%
RES06	0.0762	9	56%	0.0488	6	33%
RES07	0.0059	1	100%	0	0	0%
RES08	0.0327	5	100%	0.0248	4	100%
RES09	0.0901	8	63%	0.0668	5	40%
RES10	0.0136	2	100%	0.0084	1	100%
RES11	0.0359	4	75%	0.0189	2	50%
RES12	0.0157	3	100%	0.0157	2	100%
RES13	0.0139	2	100%	0.0139	2	100%
RES14	0.0556	8	50%	0.0324	5	20%
RES15	0.1203	9	56%	0.0349	6	33%
RES17	2.129	15	73%	0.729	11	54%
RES18-W1	0.0241	5	80%	0.0083	2	50%
RES19	0.3409	13	77%	0.132	10	70

Note: PFAS = per and polyfluoroalkyl substances *% Long Chain = percent of PFAS detected in this well that are classified as long chain PFAS. Long-chain PFAS comprise two sub-categories: long-chain perfluoroalkyl carboxylic acids with eight or more carbons, and perfluoroalkane sulfonates with six or more carbons [EPA 2018].

Table A-1. (continued)

Well ID	Includes PFHxS, PFNA, PFOA, PFOS			Excludes PFHxS, PFNA, PFOA, PFOS		
	Total PFAS concentration	# PFAS	% Long Chain*	Total PFAS concentration	# PFAS	% Long Chain*
RES20	1.004	11	64%	0.8696	8	50%
RES21	0.296	11	64%	0.105	8	50%
RES22	0.1428	10	70%	0.049	7	57%
RES23	0.194	16	75%	0.103	12	67%
RES24-W1	0.0426	8	75%	0.0289	5	60%
RES25	0.1098	9	56%	0.0588	6	33%
RES27	0.0059	1	0%	0.0059	1	0%
RES29	0.0508	8	50%	0.0348	6	33%
RES31	0.0394	6	67%	0.0319	5	60%
RES34	0.033	1	100%	0.033	1	100%
RES37	0.2743	7	57%	0.0313	4	25%
RES38	0.0319	5	80%	0.0116	2	50%
RES41	0.149	16	75%	0.1195	13	69%
RES43	0.0225	6	50%	0.0131	4	25%
RES45	0.0588	7	57%	0.0343	4	25%
RES48	0.0914	10	60%	0.0453	7	43%
RES49	0.0738	13	69%	0.0526	10	60%
RES50	0.042	9	56%	0.0157	6	33%
RES51	0.0224	4	50%	0.0095	3	33%
RES52	0.0159	4	50%	0.0093	3	33%
RES53	0.0585	7	47%	0.0241	4	0%
RES54	0.0013	1	100	0	0	0%

Note: PFAS = per and polyfluoroalkyl substances No detections were identified in RES30 and RES42. *% Long Chain = percent of PFAS detected in this well that are classified as long chain PFAS. Long-chain PFAS comprise two sub-categories: long-chain perfluoroalkyl carboxylic acids with eight or more carbons, and perfluoroalkane sulfonates with six or more carbons [EPA 2018].

Table A-2. PFAS analyzed in water supply wells during April 2014 to December 2020

Specific PFAS	Abbreviation	Chemical Formula*	Type†
8:2 fluorotelomer sulfonate	8:2 FTS	$C_{10}H_4F_{17}O_3S$	Long
6:2 fluorotelomer sulfonate	6:2 FTS	$C_8H_4F_{13}O_3S$	Long
n-ethyl perfluorooctane sulfonamide	EtFOSA	$C_{10}H_6F_{17}NO_2S$	Long
n-ethyl perfluorooctane sulfonamidoethanol	EtFOSE	$C_{12}H_{10}F_{17}NO_3S$	Long
n-methyl perfluorooctane sulfonamide	MeFOSA	$C_9H_4F_{17}NO_2S$	Long
n-methyl perfluorooctane sulfonamidoethanol	MeFOSE	$C_{11}H_8F_{17}NO_3S$	Long
perfluorobutanesulfonic acid	PFBS	$C_4HF_9O_3S$	Short
perfluorobutanoic acid	PFBA	$C_4HF_7O_2$	Short
perfluorodecanesulfonic acid	PFDS	$C_{10}HF_{21}O_3S$	Long
perfluorodecanoic acid	PFDA	$C_{10}HF_{19}O_2$	Long
perfluorododecanoic acid	PFDoA	$C_{12}HF_{23}O_2$	Long
perfluoroheptane sulfonate	PFHpS	$C_7HF_{15}SO_3$	Long
perfluoroheptanoic acid	PFHpA	$C_7HF_{13}O_2$	Short
perfluorohexanesulfonic acid	PFHxS	$C_6HF_{13}O_3S$	Long
perfluorohexanoic acid	PFHxA	$C_6HF_{11}O_2$	Short
perfluorononanoic acid	PFNA	$C_9HF_{17}O_2$	Long
perfluorooctane sulfonamide (aka FOSA)	PFOSA	$C_8H_2F_{17}NO_2S$	Long
perfluorooctanesulfonic acid	PFOS	$C_8HF_{17}O_3S$	Long
perfluorooctanoic acid	PFOA	$C_8HF_{15}O_2$	Long
perfluoropentanoic acid	PFPeA	$C_5HF_9O_2$	Short
perfluorotetradecanoic acid	PFTeDA	$C_{14}HF_{27}O_2$	Long
perfluorotridecanoic acid	PFTrDA	$C_{13}HF_{25}O_2$	Long
perfluoroundecanoic acid	PFUnA	$C_{11}HF_{21}O_2$	Long

Note*:* PFAS = per and polyfluoroalkyl substances

*available from: https://pubchem.ncbi.nlm.nih.gov/ and https://comptox.epa.gov/dashboard/chemical_lists/pfastrier

†Long-chain PFAS comprise two sub-categories: long-chain perfluoroalkyl carboxylic acids with eight or more carbons, and perfluoroalkane sulfonates with six or more carbons [EPA 2018].

Table A-3. Maximum detected PFAS concentrations in Greenland and Newington, NH private wells within 1 mile from the former Pease Air Force Base, Portsmouth, NH. Concentrations in micrograms per liter (µg/L) 2014 to 2020

Specific PFAS ==> / Sample ID / HBCV ==>	PFOS (0.014)*	PFOA (0.021)*	6:2FTS (none)	8:2FTS (none)	EtFOSA (none)	EtFOSE (none)	PFBA (7.0)†	PFBS (2.0)†
RES01	0.013 J	0.011 J	0.0078	0.0059 J	ND	ND	0.0087 J	0.011 J
RES02	0.013 J	0.0094 J	ND	ND	ND	ND	0.0091 J	0.006 J
RES03	0.015 J	0.024	0.0068	ND	ND	0.009 J	0.0086 J	0.012 J
RES04	0.0045 J	0.0013 J	ND	ND	ND	ND	ND	0.0059 J
RES05	0.0043 B	ND	0.0067J	ND	0.01 J	ND	ND	ND
RES06	0.0068 J	0.011 J	ND	ND	ND	ND	0.0079 J	0.0057 J
RES07	ND	ND	ND	ND	ND	ND	ND	ND
RES08	ND	ND	ND	ND	ND	ND	ND	ND
RES09	0.0068 J	0.0078 J	ND	ND	ND	ND	0.012 J	ND
RES10	0.0052 B	ND	ND	ND	0.0084 J	ND	ND	ND
RES11	0.0074 J	ND	ND	ND	ND	ND	ND	0.011 J
RES12	ND	ND	ND	ND	ND	ND	ND	ND
RES13	ND	ND	0.009 J	ND	ND	ND	ND	ND
RES14	0.0047 B	0.0055J	ND	ND	ND	ND	0.0093 J	ND
RES15	0.0094 J	0.014 J	ND	ND	ND	ND	0.0037 J	0.01 J
RES17	0.57	0.11	0.041 J	ND	ND	ND	0.032	0.06
RES17TRT	ND	ND	ND	ND	ND	ND	ND	ND
RES18-W1	0.0053 B	0.0068 J	ND	ND	ND	ND	ND	0.0027 J
RES19	0.089	0.02	ND	ND	0.014	0.012	ND	0.02 J
RES19TRT	ND	ND	ND	ND	ND	ND	ND	ND
RES20	0.038	0.021 J	0.77	ND	ND	ND	0.0092 J	0.02 J

Notes: PFAS = per and polyfluoroalkyl substances. Only PFAS with at least one detection are shown in this table. ND = Not detected. RES17 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on October 18, 2014. RES17TRT = Samples after the treatment system were ND. RES19 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on July18, 2014. RES19TRT = Samples after the treatment system were ND. Shaded indicate concentration of individual PFAS or summed PFAS exceeds a HBCV. Gaps in numbering between residential wells indicates the numbers are attached to non-potable wells used for irrigation or open springs.

Sources: AMEC 2014, AMECFW 2016, Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 16. Includes one file attachment with private well PFAS data from 2014 to 2017, and Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2020 September 9. Includes one file attachment with private well PFAS data through June 2020.

*ATSDR HBCV. †MDH Minnesota Department of Health Risk Limit. B = This compound was detected in an associated blank by the laboratory. J = Analyte was identified, but the concentration was estimated.

Table A-3. (CONTINUED)

Sample ID / Specific PFAS ==> / HBCV ==>	PFOS (0.014)*	PFOA (0.021)*	6:2FTS (none)	8:2FTS (none)	EtFOSA (none)	EtFOSE (none)	PFBA (7.0)†	PFBS (2.0)†
RES21	0.043	0.021	ND	ND	ND	ND	0.0033	ND
RES21TRT	ND	ND	ND	ND	ND	ND	ND	ND
RES22	0.029	0.0088 J	ND	ND	ND	0.0079 B	ND	0.014 J
RES23	0.055	0.016	ND	ND	ND	0.012	0.011	0.014
RES23TRT	ND	ND	ND	ND	ND	ND	ND	ND
RES24-W1	0.0069	0.0011	0.011 J	ND	ND	0.0051 B	ND	0.0045 J
RES25	0.014 J	0.017 J	ND	ND	ND	ND	0.0069 J	0.012 J
RES27	ND	ND	ND	ND	ND	ND	ND	0.0059 J
RES29	ND	0.0083 J	0.007	ND	ND	ND	0.0072 J	0.0046 J
RES30	ND	ND	ND	ND	ND	ND	ND	ND
RES31	ND	ND	0.0083	ND	0.0089 J	ND	ND	0.0054 J
RES34	ND	ND	0.033 J	ND	ND	ND	ND	ND
RES37/GBNWR	0.13	0.014 J	ND	ND	ND	ND	ND	0.0054 J
RES38	0.005 J	0.01 J	ND	ND	ND	ND	0.0074 J	ND
RES41	0.0095	0.01 J	ND	ND	0.016	0.0095	0.0073	0.0087 J
RES42	ND	ND	ND	ND	ND	ND	ND	ND
RES43	ND	0.002	0.0083 J	ND	ND	ND	ND	0.0014
RES45	0.0081 J	0.0095 J	0.0079	ND	ND	ND	0.012 J	0.0082 J
RES48	0.0041 B	0.02 J	ND	ND	ND	ND	0.0019	0.0086 J
RES49	0.0013	0.0099 J	0.007 J	ND	0.0076 J	ND	0.0008	0.0058
RES50	0.0095	0.007	ND	ND	ND	0.01 J	0.0027	0.0007
RES51	0.0021	0.0011	0.0079	ND	ND	ND	0.0027	ND
RES52	ND	0.0066	0.0076	ND	ND	ND	0.0013	0.0004
RES53	0.0094 J	0.014	ND	ND	ND	ND	0.0073 J	0.005 J
RES54	ND	ND	ND	ND	ND	ND	ND	ND

Notes: PFAS = per and polyfluoroalkyl substances. Only PFAS with at least one detection are shown in this table. ND = Not detected. RES21 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on September 1, 2016. RES21TRT = Samples after the treatment system were ND. RES23 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on July 18, 2016. RES23TRT = Samples after the treatment system were ND. Shaded indicate concentration of individual PFAS or summed PFAS exceeds a HBCV. Gaps in numbering between residential wells indicates the numbers are attached to non-potable wells used for irrigation or open springs.

Sources AMEC 2014, AMECFW 2016, Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 16. Includes one file attachment with private well PFAS data from 2014 to 2017, and Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2020 September 9. Includes one file attachment with private well PFAS data through June 2020.

*ATSDR HBCV. †MDH Minnesota Department of Health Risk Limit.

B = This compound was detected in an associated blank by the laboratory. J = Analyte was identified, but the concentration was estimated.

Table A-3. (CONTINUED)

Sample ID	Specific PFAS ==> HBCV ==>	PFDS (none)	PFHpA (none)	PFHpS (none)	PFHxA (none)	PFHxS (0.14)*	PFNA (0.021)*	PFOSA (none)	PFPeA (none)	PFTeDA (none)	PFTrDA (none)
RES01		ND	0.0039 J	0.005 J	0.008 J	0.0095 J	0.0067 J	0.007 J	0.0058 J	0.006 J	0.0051 J
RES02		ND	0.0047 J	0.0048 B	0.0075 J	0.013 J	ND	ND	0.011 J	ND	ND
RES03		ND	0.013 J	0.0047 J	0.01 J	0.011 J	0.0039 J	ND	0.01 J	ND	ND
RES04		ND	ND	0.0047 B	ND	0.0052 J	ND	ND	ND	ND	ND
RES05		ND	ND	ND	ND	0.0078 J	ND	0.011 J	ND	ND	ND
RES06		ND	0.007 J	0.0044 B	0.0098 J	0.0096 J	ND	ND	0.014 J	ND	ND
RES07		ND	ND	ND	ND	0.0059 J	ND	ND	ND	ND	ND
RES08		ND	ND	ND	ND	0.0079 J	ND	0.0052J	ND	ND	ND
RES09		ND	0.012 J	ND	0.014 J	0.0087	ND	0.0048 J	0.024 J	ND	ND
RES10		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
RES11		ND	ND	ND	ND	0.0096 J	ND	0.0079 J	ND	ND	ND
RES12		ND	ND	0.0045 B	ND	ND	ND	ND	ND	0.0072 J	ND
RES13		ND	ND	0.0049 J	ND	ND	ND	ND	ND	ND	ND
RES14		ND	0.0017J	ND	0.011 J	0.013 J	ND	ND	0.0088 J	ND	ND
RES15		ND	0.0059 J	ND	0.0065 J	0.062	ND	0.0053 J	0.0035 J	ND	ND
RES17		0.0056 J	0.066	0.03 J	0.27	0.53	0.00083J	0.0043J	0.14	0.005 J	ND
RES17TRT		0.0056 J	ND	0.0049 J	ND	ND	ND	ND	ND	0.005 J	ND
RES18-W1		ND	0.0056 J	ND	ND	0.0037 J	ND	ND	ND	ND	ND
RES19		ND	0.0033J	0.0073	0.025	0.1	ND	0.007	0.024	0.012	0.0073J
RES19TRT		ND	ND	ND	ND	ND	ND	ND	ND	0.0039J	ND
RES20		ND	0.0038 J	0.0076 J	0.02 J	0.075	ND	0.028	0.011 J	ND	ND

Notes: PFAS = per and polyfluoroalkyl substances. Only PFAS with at least one detection are shown in this table. ND = Not detected. RES17 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on October 18, 2014. RES17TRT = Samples after the treatment system were ND. RES19 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on July18, 2014. RES19TRT = Samples after the treatment system were ND. Shaded indicate concentration of individual PFAS or summed PFAS exceeds a HBCV. Gaps in numbering between residential wells indicates the numbers are attached to non-potable wells used for irrigation or open springs.

Sources: AMEC 2014, AMECFW 2016, Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 16. Includes one file attachment with private well PFAS data from 2014 to 2017, and Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2020 September 9. Includes one file attachment with private well PFAS data through June 2020.

*ATSDR HBCV. †This well had an apparent anomaly–an elevated concertation of 0.96 µg/L. That concentration was never duplicated at that well.

B = This compound was detected in an associated blank by the laboratory.

J = Analyte was identified, but the concentration was estimated.

Table A-3. (CONTINUED)

Sample ID	Specific PFAS ==>	PFDS	PFHpA	PFHpS	PFHxA	PFHxS	PFNA	PFOSA	PFPeA	PFTeDA	PFTrDA
	HBCV ==>	(none)	(none)	(none)	(none)	(0.14)*	(0.021)*	(none)	(none)	(none)	(none)
RES21		ND	0.0094	0.0096	0.021	0.1	ND	ND	0.02	ND	ND
RES21TRT		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
RES22		ND	0.0056 J	0.0041 J	0.0099 J	0.056	ND	ND	0.0039 J	ND	ND
RES23		ND	0.011	0.007	0.017	0.014	0.0056	0.0093	0.02	0.0003	0.0003
RES23TRT		ND	ND	ND	ND	ND	ND	0.0042J	ND	ND	ND
RES24-W1		ND	ND	ND	0.0014	0.0057 J	ND	0.0069	ND	ND	ND
RES25		ND	0.0063 J	ND	0.0078 J	0.02 J	ND	0.017 J	0.0088 J	ND	ND
RES27		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
RES29		ND	0.0065 J	ND	0.0055 J	0.0077 J	ND	ND	0.004 J	ND	ND
RES30		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
RES31		ND	ND	0.0045 B	ND	0.0075 J	ND	ND	0.0048 J	ND	ND
RES34		ND	ND	ND	ND	0.002	ND	ND	ND	ND	ND
RES37/GBNWR		ND	ND	0.0078 J	0.013 J	0.099	ND	ND	0.0051 J	ND	ND
RES38		ND	ND	ND	ND	0.0053 J	ND	0.0042 J	ND	ND	ND
RES41		0.01	0.002	ND	0.014 J	0.013 J	ND	0.013	0.01 J	ND	0.004
RES42		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
RES43		ND	ND	ND	0.0021	0.0074 J	ND	ND	0.0013	ND	ND
RES45		ND	ND	ND	ND	0.0069 J	ND	ND	0.0062 J	ND	ND
RES48		ND	0.0011	ND	0.028	0.022	ND	ND	0.0051 J	0.0003	ND
RES49		ND	0.0005	ND	0.00074	0.01 J	ND	0.029	0.00063	0.0003	ND
RES50		ND	0.0005	ND	0.0009	0.0099 J	ND	ND	0.0008	ND	ND
RES51		ND	ND	ND	0.0004	0.0082 J	ND	ND	ND	ND	ND
RES52		ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
RES53		ND	ND	ND	0.0076 J	0.011	ND	ND	0.0077 J	ND	ND
RES54		ND	ND	ND	ND	0.0013 J	ND	ND	ND	ND	ND

Notes: PFAS = per and polyfluoroalkyl substances. Only PFAS with at least one detection are shown in this table. ND = Not detected. RES21 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on September 1, 2016. RES21TRT = Samples after the treatment system were ND. RES23 = Samples collected at the faucet before the activated carbon whole house treatment system which was installed on July 18, 2016. RES23TRT = Samples after the treatment system were ND. Gaps in numbering between residential wells indicates the numbers are attached to non-potable wells used for irrigation or open springs.

Sources: AMEC 2014, AMECFW 2016, Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2018 February 16. Includes one file attachment with private well PFAS data from 2014 to 2017, and Walton R (Air Force Civil Engineer Center), email to Gary Perlman (ATSDR), 2020 September 9. Includes one file attachment with private well PFAS data through June 2020.

*ATSDR HBCV.

B = This compound was detected in an associated blank by the laboratory.

J = Analyte was identified, but the concentration was estimated.

Table A-4. Exposure Pathways, Off-Site Private Wells, Surface Water and Biota, Former Pease Air Force Base, Newington, NH

Pathway	Source	Media	Exposure Point	Exposure Route	Exposed Population	Time	Pathway Completion Status
Private Wells	Pease AFB–Fire Dept. Training Area 2 (Site 8)	Drinking Water	Off-Base Residential Wells	Ingestion	Residents with Contaminated Private Wells	Past	Complete-But we do not know when exposure began because there are no well sampling data before June 2014
Private Wells	Pease AFB–Fire Dept. Training Area 2 (Site 8)	Drinking Water	Off-Base Residential Wells	Ingestion	Residents with Contaminated Private Wells	Present and Future	Complete-PFAS detected in 37 wells. Five wells above HBCVs However, a point-of-entry (POE) water treatment system was installed at RES17 in October 2014, eliminating their exposure. POE water treatment systems were installed at three other residences in July and August 2016; the two with exceedances and another slightly below the EPA health advisory. Bottled water was provided to seasonal users of Great Bay National Wildlife Refuge well.
Private Wells	Pease AFB–Fire Dept. Training Area 2 (Site 8)	Shower or Bath Water	Off-Base Residential Wells	Dermal Absorption and Inhalation of PFAS as vapors	Residents with Contaminated Private Wells	Past	Incomplete. PFAS are not volatile and inhalation of PFAS as vapor is an incomplete pathway
Private Wells	Pease AFB–Fire Dept. Training Area 2 (Site 8)	Shower or Bath Water	Off-Base Residential Wells	Dermal Absorption and Inhalation of PFAS as vapors	Residents with Contaminated Private Wells	Present and Future	Incomplete. PFAS are not volatile and inhalation of PFAS as vapor is an incomplete pathway. The 22 residential wells and the seasonal Refuge well users without POEs– But the non-drinking water exposure routes contribute negligible additional intake based on current concentrations in drinking water [ATSDR 2021, ATSDR 2018b]
Private Wells	Pease AFB–Fire Dept. Training Area 2 (Site 8)	Drinking Water	Off-Base Residential Wells	Ingestion	Pregnant Women and Women of child bearing age who breastfeed	Past	Completed
Private Wells	Pease AFB–Fire Dept. Training Area 2 (Site 8)	Drinking Water	Off-Base Residential Wells	Ingestion	Breast feeding infants	Past, Present, and Future	Completed

Table A-4. (CONTINUED)

Pathway	Source	Media	Exposure Point	Exposure Route	Exposed Population	Time	Pathway Completion Status
Biota (Fish Deer)	Pease AFB–Fire Dept. Training Area 2 (Site 8)	Biota	On or off base where fish, shellfish, or deer are caught	Ingestion	Consumers of fish, shellfish, or deer meat	Past, Present, and Future	Potential
Surface Water	Surface water-Great Bay	Surface Water	Swimming, wading	Dermal, ingestion	Recreational swimmers/wader	Past, Present, and Future	Potential

Table A-5. Health-based comparison values used to screen water quality for PFAS. Concentrations in micrograms per liter (µg/L)

Specific PFAS	Health-Based Comparison Value Source	Value (µg/L)
PFBA	MDH HRL	7
PFBS	MDH HRL	2
PFHxS	ATSDR EMEG	0.14
PFNA	ATSDR EMEG	0.021
PFOA	ATSDR EMEG	0.021
PFOS	ATSDR EMEG	0.014

Notes: There were no HBCVs for the following: PFOSA, 6:2 FTS, 8:2 FTS, EtFOSA, EtFOSE, MeFOSA, MeFOSE, PEPeA0, PFDA, PFDoA, PFDS, PFHpA, PFHpS, PFHxA, PFTeDA, PFTrDA, or PFUnA

Abbreviations: PFAS = per and polyfluoroalkyl substances. ATSDR = These values were derived by ATSDR for children's exposures. This value is called an Environmental Media Evaluation Guide (EMEG) and is an estimated contaminant concentration that is not expected to result in adverse noncarcinogenic health effects based on ATSDR evaluation. EMEGs are based on ATSDR MRLs and health-protective assumptions about exposure, such as intake rate, exposure frequency and duration, and body weight. Child drinking water EMEGs are based on an infant (age birth to one year old) weighing 7.8 kg and an intake rate of 1.113 liters per day; HBCV = health-based comparison value; MDH = Minnesota Department of Health Risk Limit (HRL) [MDH 2017a, 2017b, 2017c. 2017d].

Table A-6 Exposure assumptions used for dose calculations

Exposure Assumptions			
	Daily drinking water intake rate		Body weight
	CTE	RME	
Age groups	L/day	L/day	kg
Birth to <1 year	0.504	1.13	7.8
1 to <2 years	0.308	0.893	11.4
2 to <6 years	0.376	0.977	17.4
6 to <11 years	0.511	1.404	31.8
11 to <16 years	0.637	1.976	56.8
16 to <21 years	0.77	2.444	71.6
Adults (≥21 years)	1.227	3.092	80
Pregnant women	0.872	2.589	73
Lactating women	1.665	3.588	73

Abbreviations: CTE = central tendency exposure; kg = kilogram; L = liter; RME = reasonable maximum exposure

Table A-7. Environmental exposure assumptions and estimated exposure doses for perfluorohexanesulfonic acid (PFHxS) from private drinking water well identified as RES17 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFHxS= 0.37 µg/L		Hazard quotient for PFHxS (dose divided by the Intermediate MRL)		Margin of exposure for PFHxS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	2.4E-05	5.4E-05	1.20	2.68	307	137
1 to <2 years	1.0E-05	2.9E-05	0.50	1.45	734	253
2 to <6 years	8.0E-06	2.1E-05	0.40	1.04	918	353
6 to <11 years	5.9E-06	1.6E-05	0.30	0.82	1235	449
11 to <16 years	4.1E-06	1.3E-05	0.21	0.64	1769	570
16 to <21 years	4.0E-06	1.3E-05	0.20	0.63	1845	581
Adults (≥21 years)	5.7E-06	1.4E-05	0.28	0.72	1293	513
Pregnant women	4.4E-06	1.3E-05	0.22	0.66	1661	559
Lactating women	8.4E-06	1.8E-05	0.42	0.91	870	404

Note: Shaded = Exceedance of health-based comparison value.

*Margin of exposure for PFHxS (based on HED effect level from study used to derive MRL divided by the dose).

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-8. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES17 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose* based on the maximum concentration of PFOS= 0.57 µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)†	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	3.7E-05	8.3E-05	18.4	41.3	57	25
1 to <2 years	1.5E-05	4.5E-05	7.7	22.3	140	47
2 to <6 years	1.2E-05	3.2E-05	6.2	16.0	170	66
6 to <11 years	9.2E-06	2.5E-05	4.6	12.6	230	83
11 to <16 years	6.4E-06	2.0E-05	3.2	9.9	330	110
16 to <21 years	6.1E-06	1.9E-05	3.1	9.7	340	110
Adults (≥21 years)	8.7E-06	2.2E-05	4.4	11.0	240	95
Pregnant women	6.8E-06	2.0E-05	3.4	10.1	310	100
Lactating women	1.3E-05	2.8E-05	6.5	14.0	160	75

Notes: Shaded = Exceedance of health-based comparison value. *The maximum value was from samples collected at the faucet before the whole house activated carbon treatment system was installed on October 18, 2014.
†Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-9. Environmental exposure assumptions and estimated exposure doses for perfluorooctanoic acid (PFOA) from private drinking water well identified as RES17 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose* based on the maximum concentration of PFOA= 0.11 µg/L		Hazard quotient for PFOA (dose divided by the Intermediate MRL)		Margin of exposure for PFOA (effect level used to derive MRL divided by the dose)†	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	7.1E-06	1.6E-05	2.37	5.31	120	52
1 to <2 years	3.0E-06	8.6E-06	0.99	2.87	280	95
2 to <6 years	2.4E-06	6.2E-06	0.79	2.06	350	130
6 to <11 years	1.8E-06	4.9E-06	0.59	1.62	460	170
11 to <16 years	1.2E-06	3.8E-06	0.41	1.28	670	210
16 to <21 years	1.2E-06	3.8E-06	0.39	1.25	690	220
Adults (≥21 years)	1.7E-06	4.3E-06	0.56	1.42	490	190
Pregnant women	1.3E-06	3.9E-06	0.44	1.30	620	210
Lactating women	2.5E-06	5.4E-06	0.84	1.80	330	150

Notes: *The maximum value was from samples collected at the faucet before the whole house activated carbon treatment system was installed on October 18, 2014. Shaded = Exceedance of health-based comparison value.
†Margin of exposure for PFOA (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-10. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES19 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOS= 0.086 µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	5.6E-06	1.2E-05	2.8	6.2	380	170
1 to <2 years	2.3E-06	6.7E-06	1.2	3.4	900	310
2 to <6 years	1.9E-06	4.8E-06	0.9	2.4	1100	430
6 to <11 years	1.4E-06	3.8E-06	0.7	1.9	1500	550
11 to <16 years	9.6E-07	3.0E-06	0.5	1.5	2200	700
16 to <21 years	9.2E-07	2.9E-06	0.5	1.5	2300	720
Adults (≥21 years)	1.3E-06	3.3E-06	0.7	1.7	1600	630
Pregnant women	1.0E-06	3.1E-06	0.5	1.5	2000	690
Lactating women	2.0E-06	4.2E-06	1.0	2.1	1100	500

Note: Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-11. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES21 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOS= 0.043µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	2.8E-06	6.2E-06	1.4	3.1	760	340
1 to <2 years	1.2E-06	3.4E-06	0.6	1.7	1800	620
2 to <6 years	9.3E-07	2.4E-06	0.5	1.2	2300	870
6 to <11 years	6.9E-07	1.9E-06	0.3	0.9	3000	1100
11 to <16 years	4.8E-07	1.5E-06	0.2	0.7	4400	1400
16 to <21 years	4.6E-07	1.5E-06	0.2	0.7	4500	1400
Adults (≥21 years)	6.6E-07	1.7E-06	0.3	0.8	3200	1300
Pregnant women	5.1E-07	1.5E-06	0.3	0.8	4100	1400
Lactating women	9.8E-07	2.1E-06	0.5	1.1	2100	990

Note: Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-12. Environmental exposure assumptions and estimated exposure doses for perfluorooctanoic acid (PFOA) from private drinking water well identified as RES21 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOA= 0.021 µg/L		Hazard quotient for PFOA (dose divided by the Intermediate MRL)		Margin of exposure for PFOA (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	1.4E-06	3.0E-06	0.45	1.01	610	270
1 to <2 years	5.7E-07	1.6E-06	0.19	0.55	1400	500
2 to <6 years	4.5E-07	1.2E-06	0.15	0.39	1800	700
6 to <11 years	3.4E-07	9.3E-07	0.11	0.31	2400	890
11 to <16 years	2.4E-07	7.3E-07	0.08	0.24	3500	1100
16 to <21 years	2.3E-07	7.2E-07	0.08	0.24	3600	1100
Adults (≥21 years)	3.2E-07	8.1E-07	0.11	0.27	2500	1000
Pregnant women	2.5E-07	7.4E-07	0.08	0.25	3300	1100
Lactating women	4.8E-07	1.0E-06	0.16	0.34	1700	800

Note: Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOA (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-13. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES23 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

	Dose based on the maximum concentration of PFOS= 0.052 µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)*	
Age groups	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	3.4E-06	7.5E-06	1.7	3.8	630	280
1 to <2 years	1.4E-06	4.1E-06	0.7	2	1500	520
2 to <6 years	1.1E-06	2.9E-06	0.56	1.5	1900	720
6 to <11 years	8.4E-07	2.3E-06	0.42	1.1	2500	910
11 to <16 years	5.8E-07	1.8E-06	0.29	0.9	3600	1200
16 to <21 years	5.6E-07	1.8E-06	0.28	0.89	3800	1200
Adults (≥21 years)	8.0E-07	2.0E-06	0.4	1	2600	1000
Pregnant women	6.2E-07	1.8E-06	0.31	0.92	3400	1100
Lactating women	1.2E-06	2.6E-06	0.59	1.3	1800	820

Notes: Shaded = Exceedance of health-based comparison value. Sample obtained from the wellhead. The faucet concentrations were lower. This calculation was conducted since the wellhead data drove the decision to provide an alternative water source for RES23.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-14. Environmental exposure assumptions and estimated exposure doses for perfluorooctanoic acid (PFOA) from private drinking water well identified as RES23 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOA= 0.015 µg/L		Hazard quotient for PFOA (dose divided by the Intermediate MRL)		Margin of exposure for PFOA (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	9.7E-07	2.2E-06	0.32	0.72	850	380
1 to <2 years	4.1E-07	1.2E-06	0.14	0.39	2000	700
2 to <6 years	3.2E-07	8.4E-07	0.11	0.28	2500	970
6 to <11 years	2.4E-07	6.6E-07	0.08	0.22	3400	1200
11 to <16 years	1.7E-07	5.2E-07	0.06	0.17	4900	1600
16 to <21 years	1.6E-07	5.1E-07	0.05	0.17	5100	1600
Adults (≥21 years)	2.3E-07	5.8E-07	0.08	0.19	3600	1400
Pregnant women	1.8E-07	5.3E-07	0.06	0.18	4600	1500
Lactating women	3.4E-07	7.4E-07	0.11	0.25	2400	1100

Note: Sample obtained from the wellhead. The faucet concentrations were lower. This calculation was conducted since the wellhead data drove the decision to provide an alternative water source for RES23.

*Margin of exposure for PFOA (based on HED effect level from study used to derive MRL divided by the dose).

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-15. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES37/GBNWR located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOS= 0.13 µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	8.4E-06	1.9E-05	4.2	9.4	250	110
1 to <2 years	3.5E-06	1.0E-05	1.8	5.1	600	210
2 to <6 years	2.8E-06	7.3E-06	1.4	3.6	750	290
6 to <11 years	2.1E-06	5.7E-06	1.0	2.9	1000	370
11 to <16 years	1.5E-06	4.5E-06	0.7	2.3	1400	460
16 to <21 years	1.4E-06	4.4E-06	0.7	2.2	1500	470
Adults (≥21 years)	2.0E-06	5.0E-06	1.0	2.5	1100	420
Pregnant women	1.6E-06	4.6E-06	0.8	2.3	1400	460
Lactating women	3.0E-06	6.4E-06	1.5	3.2	710	330

Notes: The intermediate exposure scenario for these well users include the following: seven days per week for eight weeks. This was established since the supplied residents is only seasonal (i.e., eight summer weeks). Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-16. Environmental exposure assumptions and estimated exposure doses for perfluorohexanesulfonic acid (PFHxS) from private drinking water well identified as RES37/GBNWR located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFHxS= 0.099 µg/L		Hazard quotient for PFHxS (dose divided by the Intermediate MRL)		Margin of exposure for PFHxS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	6.4E-06	1.4E-05	0.32	0.72	1147	512
1 to <2 years	2.7E-06	7.8E-06	0.13	0.39	2744	946
2 to <6 years	2.1E-06	5.6E-06	0.11	0.28	3431	1320
6 to <11 years	1.6E-06	4.4E-06	0.08	0.22	4614	1679
11 to <16 years	1.1E-06	3.4E-06	0.06	0.17	6611	2131
16 to <21 years	1.1E-06	3.4E-06	0.05	0.17	6894	2172
Adults (≥21 years)	1.5E-06	3.8E-06	0.08	0.19	4834	1918
Pregnant women	1.2E-06	3.5E-06	0.06	0.18	6207	2091
Lactating women	2.3E-06	4.9E-06	0.11	0.24	3251	1508

Note: The intermediate exposure scenario for these well users include the following: seven days per week for eight weeks. This was established since the supplied residents is only seasonal (i.e., eight summer weeks).

*Margin of exposure for PFHxS (based on HED effect level from study used to derive MRL divided by the dose).

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-17. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES03 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOS = 0.015 µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	9.7E-07	2.2E-06	0.5	1.1	2200	970
1 to <2 years	4.1E-07	1.2E-06	0.2	0.6	5200	1800
2 to <6 years	3.2E-07	8.4E-07	0.2	0.4	6500	2500
6 to <11 years	2.4E-07	6.6E-07	0.1	0.3	8700	3200
11 to <16 years	1.7E-07	5.2E-07	0.1	0.3	12000	4000
16 to <21 years	1.6E-07	5.1E-07	0.1	0.3	13000	4100
Adults (≥21 years)	2.3E-07	5.8E-07	0.1	0.3	9100	3600
Pregnant women	1.8E-07	5.3E-07	0.1	0.3	12000	3900
Lactating women	3.4E-07	7.4E-07	0.2	0.4	6100	2800

Note: Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-17A. Environmental exposure assumptions and estimated exposure doses for perfluorooctanoic acid (PFOA) from private drinking water well identified as RES03 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOA = 0.024 µg/L		Hazard quotient for PFOA (dose divided by the Intermediate MRL)		Margin of exposure for PFOA (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	1.6E-06	3.5E-06	0.52	1.16	529	236
1 to <2 years	6.5E-07	1.9E-06	0.22	0.63	1266	437
2 to <6 years	5.2E-07	1.3E-06	0.17	0.45	1583	609
6 to <11 years	3.9E-07	1.1E-06	0.13	0.35	2129	775
11 to <16 years	2.7E-07	8.3E-07	0.09	0.28	3050	983
16 to <21 years	2.6E-07	8.2E-07	0.09	0.27	3181	1002
Adults (≥21 years)	3.7E-07	9.3E-07	0.12	0.31	2230	885
Pregnant women	2.9E-07	8.5E-07	0.10	0.28	2864	965
Lactating women	5.5E-07	1.2E-06	0.18	0.39	1500	696

Note: Shaded = Exceedance of health-based comparison value.

*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-18. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES20 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOS= 0.038 µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	2.5E-06	5.5E-06	1.2	2.8	855	381
1 to <2 years	1.0E-06	3.0E-06	0.5	1.5	2045	705
2 to <6 years	8.2E-07	2.1E-06	0.4	1.1	2557	984
6 to <11 years	6.1E-07	1.7E-06	0.3	0.8	3439	1252
11 to <16 years	4.3E-07	1.3E-06	0.2	0.7	4928	1589
16 to <21 years	4.1E-07	1.3E-06	0.2	0.6	5139	1619
Adults (≥21 years)	5.8E-07	1.5E-06	0.3	0.7	3603	1430
Pregnant women	4.5E-07	1.3E-06	0.2	0.7	4626	1558
Lactating women	8.7E-07	1.9E-06	0.4	0.9	2423	1124

Note: Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-18a. Environmental exposure assumptions and estimated exposure doses for perfluorooctanoic acid (PFOA) from private drinking water well identified as RES20 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOA= 0.021 µg/L		Hazard quotient for PFOA (dose divided by the Intermediate MRL)		Margin of exposure for PFOA (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	1.36E-06	3.04E-06	0.45	1.01	605	270
1 to <2 years	5.67E-07	1.65E-06	0.19	0.55	1447	499
2 to <6 years	4.54E-07	1.18E-06	0.15	0.39	1809	696
6 to <11 years	3.37E-07	9.27E-07	0.11	0.31	2433	885
11 to <16 years	2.36E-07	7.31E-07	0.08	0.24	3486	1124
16 to <21 years	2.26E-07	7.17E-07	0.08	0.24	3635	1145
Adults (≥21 years)	3.22E-07	8.12E-07	0.11	0.27	2549	1012
Pregnant women	2.51E-07	7.45E-07	0.08	0.25	3273	1102
Lactating women	4.79E-07	1.03E-06	0.16	0.34	1714	795

Note: Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-19. Environmental exposure assumptions and estimated exposure doses for perfluorooctane sulfonic acid (PFOS) from private drinking water well identified as RES25 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Age groups	Dose based on the maximum concentration of PFOS= 0.014 µg/L		Hazard quotient for PFOS (dose divided by the Intermediate MRL)		Margin of exposure for PFOS (effect level used to derive MRL divided by the dose)*	
	CTE mg/kg/day	RME mg/kg/day	CTE unitless	RME unitless	CTE unitless	RME unitless
Birth to <1 year	9.0E-07	2.0E-06	0.5	1.0	2300	1000
1 to <2 years	3.8E-07	1.1E-06	0.2	0.5	5600	1900
2 to <6 years	3.0E-07	7.9E-07	0.2	0.4	6900	2700
6 to <11 years	2.2E-07	6.2E-07	0.1	0.3	9300	3400
11 to <16 years	1.6E-07	4.9E-07	0.1	0.2	13000	4300
16 to <21 years	1.5E-07	4.8E-07	0.1	0.2	14000	4400
Adults (≥21 years)	2.1E-07	5.4E-07	0.1	0.3	9800	3900
Pregnant women	1.7E-07	5.0E-07	0.1	0.2	13000	4200
Lactating women	3.2E-07	6.9E-07	0.2	0.3	6600	3100

Note: Shaded = Exceedance of health-based comparison value.
*Margin of exposure for PFOS (based on HED effect level from study used to derive MRL divided by the dose).
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-20. Environmental exposure assumptions and estimated exposure doses for perfluorohexanoic acid (PFHxA) from private drinking water well identified as RES17F located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Exposure Assumptions				Dose Based on the Maximum Concentration PFHxA 0.23 µg/L*	
	Daily Drinking Water Intake Rate		Body Weight		
	CTE	RME		CTE	RME
Age groups	L/day	L/day	kg	mg/kg/day	mg/kg/day
Birth to < 1 year	0.504	1.113	7.8	1.49E-05	5.4E-05
1 to < 2 years	0.308	0.893	11.4	6.21E-06	2.9E-05
2 to < 6 years	0.376	0.977	17.4	4.97E-06	2.1E-05
6 to < 11 years	0.511	1.404	31.8	3.70E-06	1.6E-05
11 to < 16 years	0.637	1.976	56.8	2.58E-06	1.3E-05
16 to < 21 years	0.77	2.444	71.6	2.47E-06	1.3E-05
Adults (≥21 years)	1.227	3.092	80	3.54E-06	1.4E-05
Pregnant Women	0.872	2.589	73	2.75E-06	1.3E-05
Lactating Women	1.665	3.588	73	5.26E-06	1.8E-05

Note: *The maximum value was from samples collected at the faucet before the whole house activated carbon treatment system was installed.

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-21. Combined perfluorohexanesulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) hazard index for private drinking water well identified as RES17F located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

	Exposure assumptions				
	Daily drinking water intake rate		Body weight	Hazard index (HI) for combined PFHxS, PFOA, and PFOS	
Age groups	CTE L/day	RME L/day	kg	CTE unitless	RME unitless
Birth to <1 year	0.504	1.13	7.8	21.98	49.28
1 to <2 years	0.308	0.89	11.4	9.19	26.65
2 to <6 years	0.376	0.98	17.4	7.35	19.10
6 to <11 years	0.511	1.4	31.8	5.47	15.02
11 to <16 years	0.637	1.98	56.8	3.81	11.83
16 to <21 years	0.77	2.44	71.6	3.66	11.61
Adults (≥21 years)	1.227	3.09	80	5.22	13.15
Pregnant women	0.872	2.59	73	4.06	12.06
Lactating women	1.665	3.59	73	7.76	16.72

Notes: Shaded = exceedance of an HI of 1. Estimated exposure doses assume 100% of exposure is from drinking water ingestion.

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; HI = hazard index is the combined hazard quotients for PFHxS, PFOA and PFOS combined; kg = kilogram; L = liter; RME = reasonable maximum exposure.

Table A-22. Environmental exposure assumptions and calculated hazard indexes for combined perfluorohexanesulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) for private drinking water well identified as RES19 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Exposure Assumptions				Hazard Indexes (HI) for combined PFHxS, PFOA, and PFOS	
	Daily Drinking Water Intake Rate		Body Weight		
	CTE	RME		CTE	RME
Age groups	L/day	L/day	kg	unitless	unitless
Birth to < 1 year	0.504	1.113	7.8	3.25	7.28
1 to < 2 years	0.308	0.893	11.4	1.36	3.94
2 to < 6 years	0.376	0.977	17.4	1.09	2.82
6 to < 11 years	0.511	1.404	31.8	0.81	2.22
11 to < 16 years	0.637	1.976	56.8	0.56	1.75
16 to < 21 years	0.77	2.444	71.6	0.54	1.72
Adults (≥21 years)	1.227	3.092	80	0.77	1.94
Pregnant Women	0.872	2.589	73	0.60	1.78
Lactating Women	1.665	3.588	73	1.15	2.47

Note: Shaded = Exceedance of health-based comparison value.
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-23. Environmental exposure assumptions and calculated hazard indexes for combined perfluorohexanesulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) for private drinking water well identified as RES21 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Exposure Assumptions				Hazard Index (HI) for combined PFHxS, PFOA, and PFOS	
	Daily Drinking Water Intake Rate		Body Weight		
	CTE	RME		CTE	RME
Age groups	L/day	L/day	kg	unitless	unitless
Birth to < 1 year	0.504	1.113	7.8	2.08	4.66
1 to < 2 years	0.308	0.893	11.4	0.87	2.52
2 to < 6 years	0.376	0.977	17.4	0.69	1.81
6 to < 11 years	0.511	1.404	31.8	0.52	1.42
11 to < 16 years	0.637	1.976	56.8	0.36	1.12
16 to < 21 years	0.77	2.444	71.6	0.35	1.10
Adults (≥21 years)	1.227	3.092	80	0.49	1.24
Pregnant Women	0.872	2.589	73	0.38	1.14
Lactating Women	1.665	3.588	73	0.73	1.58

Note: Shaded = Exceedance of health-based comparison value.
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-24. Environmental exposure assumptions and calculated hazard indexes for combined perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) for private drinking water well identified as RES23 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Exposure Assumptions				Hazard Index (HI) for combined PFHxS, PFOA, PFNA, and PFOS	
	Daily Drinking Water Intake Rate		Body Weight		
	CTE	RME		CTE	RME
Age groups	L/day	L/day	kg	unitless	unitless
Birth to < 1 year	0.504	1.113	7.8	2.3	5.0
1 to < 2 years	0.308	0.893	11.4	0.9	2.8
2 to < 6 years	0.376	0.977	17.4	0.8	1.9
6 to < 11 years	0.511	1.404	31.8	0.6	1.6
11 to < 16 years	0.637	1.976	56.8	0.4	1.2
16 to < 21 years	0.77	2.444	71.6	0.4	1.2
Adults (≥21 years)	1.227	3.092	80	2.3	5.0
Pregnant Women	0.872	2.589	73	0.9	2.8
Lactating Women	1.665	3.588	73	0.8	1.9

Notes: Shaded = Exceedance of health-based comparison value. Sample obtained from the wellhead. The faucet concentrations were lower. This calculation was conducted since the wellhead data drove the decision to provide an alternative water source for RES23.

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-25. Environmental exposure assumptions and calculated hazard indexes for combined perfluorohexanesulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) for private drinking water well identified as RES37/GBNWR located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Exposure Assumptions				Hazard Index (HI) for combined PFHxS, PFOA, and PFOS	
	Daily Drinking Water Intake Rate		Body Weight		
	CTE	RME		CTE	RME
Age groups	L/day	L/day	kg	unitless	unitless
Birth to < 1 year	0.504	1.113	7.8	4.82	10.81
1 to < 2 years	0.308	0.893	11.4	2.02	5.84
2 to < 6 years	0.376	0.977	17.4	1.61	4.19
6 to < 11 years	0.511	1.404	31.8	1.20	3.29
11 to < 16 years	0.637	1.976	56.8	0.84	2.60
16 to < 21 years	0.77	2.444	71.6	0.80	2.55
Adults (≥21 years)	1.227	3.092	80	1.14	2.88
Pregnant Women	0.872	2.589	73	0.89	2.65
Lactating Women	1.665	3.588	73	1.70	3.67

Notes: The intermediate exposure scenario for these well users include the following: seven days per week for eight weeks. This was established since the supplied residents is only seasonal (i.e., eight summer weeks). Shaded = Hazard index exceeded 1.0.

Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-26. Combined perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) hazard index for private drinking water well identified as RES03 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

	Exposure assumptions				
	Daily drinking water intake rate		Body weight	Hazard index (HI) for combined PFOA, PFNA, and PFOS	
Age groups	CTE L/day	RME L/day	kg	CTE unitless	RME unitless
Birth to <1 year	0.504	1.13	7.8	1.1	2.4
1 to <2 years	0.308	0.89	11.4	0.5	1.3
2 to <6 years	0.376	0.98	17.4	0.4	1.0
6 to <11 years	0.511	1.4	31.8	0.3	0.7
11 to <16 years	0.637	1.98	56.8	0.2	0.6
16 to <21 years	0.77	2.44	71.6	0.2	0.6
Adults (≥21 years)	1.227	3.09	80	1.1	2.4
Pregnant women	0.872	2.59	73	0.5	1.3
Lactating women	1.665	3.59	73	0.4	1.0

Notes: Shaded = exceedance of an HI of 1. Estimated exposure doses assume 100% of exposure is from drinking water ingestion.
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; HI = hazard index is the combined hazard quotients for PFHxS, PFNA, PFOA and PFOS combined; kg = kilogram; L = liter; RME = reasonable maximum exposure.

Table A-27. Environmental exposure assumptions and calculated hazard indexes for combined perfluorohexanesulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) for private drinking water well identified as RES20 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Exposure Assumptions				Hazard Indexes (HI) for combined PFHxS, PFOA, and PFOS	
	Daily Drinking Water Intake Rate		Body Weight		
	CTE	RME		CTE	RME
Age groups	L/day	L/day	kg	unitless	unitless
Birth to < 1 year	0.504	1.113	7.8	1.92	4.31
1 to < 2 years	0.308	0.893	11.4	0.80	2.33
2 to < 6 years	0.376	0.977	17.4	0.64	1.67
6 to < 11 years	0.511	1.404	31.8	0.48	1.31
11 to < 16 years	0.637	1.976	56.8	0.33	1.03
16 to < 21 years	0.77	2.444	71.6	0.32	1.02
Adults (≥21 years)	1.227	3.092	80	0.46	1.15
Pregnant Women	0.872	2.589	73	0.36	1.06
Lactating Women	1.665	3.588	73	0.53	1.14

Note: Shaded = Exceedance of health-based comparison value.
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Table A-28. Environmental exposure assumptions and calculated hazard indexes for combined perfluorohexanesulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) for private drinking water well identified as RES25 located within 1 mile from the former Pease Air Force Base, Portsmouth, NH

Exposure Assumptions				Hazard Index (HI) for combined PFHxS, PFOA, and PFOS	
	Daily Drinking Water Intake Rate		Body Weight		
	CTE	RME		CTE	RME
Age groups	L/day	L/day	kg	unitless	unitless
Birth to < 1 year	0.504	1.113	7.8	0.88	1.98
1 to < 2 years	0.308	0.893	11.4	0.37	1.07
2 to < 6 years	0.376	0.977	17.4	0.30	0.77
6 to < 11 years	0.511	1.404	31.8	0.22	0.60
11 to < 16 years	0.637	1.976	56.8	0.15	0.48
16 to < 21 years	0.77	2.444	71.6	0.15	0.47
Adults (≥21 years)	1.227	3.092	80	0.21	0.53
Pregnant Women	0.872	2.589	73	0.16	0.48
Lactating Women	1.665	3.588	73	0.31	0.67

Note: Shaded = Exceedance of health-based comparison value.
Abbreviations: µg/L = micrograms per liter; CTE = central tendency exposure; kg = kilogram; L = liter; mg/kg/day = milligrams of chemical per kilogram of body weight per day; RME = reasonable maximum exposure.

Equations

Equation 1. Reasonable maximum exposure (RME) concentration calculation approach.

$$\text{Reasonable maximum exposure} = \frac{\text{Upper Percentile Drinking Water Intake } \left(\frac{\text{L}}{\text{day}}\right) \text{ x Exposure point concentration } \left(\frac{\mu\text{g}}{\text{L}}\right)}{\text{Body weight (kg) x 1,000}}$$

Equation 2. Central tendency exposure (CTE) concentration calculation approach.

$$\text{Central tendency exposure} = \frac{\text{Mean Drinking Water Intake } \left(\frac{\text{L}}{\text{day}}\right) \text{ x Exposure point concentration } \left(\frac{\mu\text{g}}{\text{L}}\right)}{\text{Body weight (kg) x 1,000}}$$

Appendix B–Chemical Specific Health-Based Comparison Values Discussion

Perfluorobutanoate (PFBA)

In 2017, Minnesota developed a health risk value for PFBA of 7 µg/L for chronic non-cancerous health effects. This PFBA health risk value is based on a reference dose of 0.0014 mg/kg/day and NOAEL of 60 mg/kg/day. The critical effects end point observed in laboratory animals include liver weight changes, morphological changes in liver and thyroid gland, decreased T4, decreased red blood cells, decreased hematocrit and hemoglobin. The Minnesota health risk value includes an uncertainty factor of 300 (3 for interspecies differences, 10 for intraspecies variability, and 10 for database uncertainty) [MDH 2017c].

Perfluorobutane sulfonate (PFBS)

In 2011, Minnesota developed a health risk value for PFBS of 2 µg/L for chronic non-cancerous health effects. This health risk value for PFBS is based on a reference dose of 0.0043 mg/kg/day and human equivalent dose of 0.129 mg/kg/day. The critical effects were kidney epithelial and tubular/ductal hyperplasia. The co-critical effects include focal papillary edema and necrosis in the kidney The Minnesota health risk value includes an uncertainty factor of 300 (3 for interspecies differences (for toxicodynamics), 10 for intraspecies variability, 3 for database uncertainty (concerns regarding neurological effects and persistent effects observed following in utero only exposure), and 3 for use of a subchronic study for the chronic duration [MDH 2017d, 2017e].

Appendix C—Responses to Public Comments by Section

ATSDR released this health consultation for public comment on April 30, 2020. The public comment period ended on July 30, 2020. The public comments received and ATSDR responses, organized by the major headings of the health consultation, are shown below. Some commenters provided references with their comments--these are shown at the end of this section along with any references provided by ATSDR in response to these public comments. Some references may be listed here and in the primary reference section of this health consultation.

Summary

Comment: The Summary section (@ pg ii discloses a significant gap--of nearly 2 1/2 years between the last date (DEC 2017) sampling data from the wells was considered and the issuance of the Consultation in mid-2020. The implications, if any, of this potential staleness in the data that forms the basis of the Consultation needs to be addressed in the Summary.

RESPONSE: ATSDR requested these additional private well sampling data from the USAF and the final health consultation has been updated with these data and any analysis, conclusions, or recommendations have been updated as needed. Here is a summary of the changes made to ATSDR's original conclusions regarding the hazard/risk posed by past or current private well PFAS exposures:

All well hazard/risk designations remain the same except for:

RES06: Hazard still cannot be determined for past exposures, but all sampling since March 2018 has been non-detect.

RES08: Previous category was no hazard with exposure, now cannot be determined.

RES09: The USAF informed ATSDR high detection of 0.96 µg/L was reported incorrectly by the laboratory. The lab corrected the result to 0.005 µg/L. The USAF is following up to determine if the homeowner was notified of the reporting error.

RES18: Hazard still cannot be determined for past exposures, but sampling since March 2018 has only one detection of PFOA at 4.6 ppt.

RES34: Previous category was no hazard with exposure, but now 6:2 FTS value has increased from 7 to 33 ppt; changed category to hazard cannot be determined.

RES38: Hazard still cannot be determined for past exposure, but all sampling since March 2018 has been non-detect.

RES51: Previous category was no hazard with exposure, but now more PFAS detected so changed category to cannot determine hazard.

RES52: Previous category was no hazard with no exposure, but now several PFAS detected above lowest ATSDR CV so changed to hazard cannot be determined.

RES53: New well that was not reported in public comment health consultation release was identified, so no previous category; new hazard category cannot be determined.

RES54: New well that was not reported in public comment health consultation release was identified, so no previous category; new hazard category cannot be determined because only one round of sampling conducted to date.

ATSDR has updated the dose calculations for RES03 and RES20 because of new maximum highs for PFOA and/or PFOS. One PFAS, 6:2 FTS, was detected at 770 ppt in RES20; however, all other sampling except for one detection of this PFAS at 5.9 ppt was non-detect. This one detection of 6:2 FTS could be an anomaly. The hazard category for these wells remains as cannot be determined.

Comment: The Summary and the full report should more explicitly explain the evaluation standard ATSDR applied in evaluating the data and reaching its conclusions and recommendations and most importantly how it compares/ relates to EPA and State of NH promulgated drinking water standards for PFAS. In that regard the issue mentioned in our Zoom call regarding the status of NH's more protective standards has been resolved as Governor Sununu on July 23rd signed the legislation incorporating the lower maximum PFAS standards earlier promulgated by the NH Dept of Environmental Services. Especially where the potential for significantly different standards may exist w/ emerging contaminants such as PFAS, it is very important that the public be able to easily appreciate the Agency's standard and how it may differ from other applicable standards, especially if they are stricter.

RESPONSE: ATSDR uses health-based comparison values (HBCVs) as screening values to determine if further evaluation is needed. HBCVs are not a final determinant of whether harmful effects are possible. HBCVs are developed based on data from the epidemiologic and toxicological literature. Many uncertainty factors, sometimes known as safety factors, are applied to ensure that the HBCVs amply protect human health. Once a contaminant is selected for further evaluation, ATSDR estimates exposure doses. If exposure doses are above the health guideline (e.g., MRLs), ATSDR then evaluates several factors to determine if the exposure doses

may result in harmful health effects. ATSDR's evaluation process was explained in the public comment version of this health consultation. When no federal HBCVs are available, ATSDR uses applicable State values. Contaminants for which there were no federal or State HBCVs are retained for further evaluation. ATSDR used six HBCVs in the evaluations of PFAS exposures. Four of the ATSDR-derived HBCVs (PFHxS, PFNA, PFOA, and PFOS) were used. The remaining two HBCVs were derived by the Minnesota Department of Health (PFBA and PFBS). Given ATSDR's approach, if the NH Ambient Groundwater Quality Standards had been used instead of the ATSDR HBCVs, the dose calculations and comparisons to effect levels would remain the same. The conclusions would also remain the same.

Comment: (Conclusion 1, Next steps and study, first bullet point) Add ATSDR will make every effort to present the findings of this report to the prior owners/residents of the affected properties. Residential properties have changed ownership during the years between when the contamination occurred and the testing dates. Research through town records and the Rockingham Registry of Deeds can determine prior property owners. Residents of those properties anytime between 1974 – the present are affected residents.

RESPONSE: ATSDR will work with local town officials and the USAF to share the findings of the Health Consultation with prior owners/residents of the affected properties. This information has been added to the 'Next Steps' section of the summary and public health action plan.

Comment: (Conclusion 1, Next steps and study, fourth bullet point) Add ATSDR and CDC are working to address the concerns of community members regarding any potential associations between PFAS exposure and reduced response to immunizations. Reduced responses to immunizations are a neurological impact that is of concern to parents in regard to the routine immunizations that protect children from many diseases. The current pandemic with Covid 19 brings this concern to all children and adults and vaccines are currently being developed to protect from this Coronavirus. Studies have shown that adults and children with higher levels of certain PFAS chemicals were associated with weaker responses to vaccines as noted in ATSDR's releases "Potential interaction between PFAS exposure and Covid-19."

RESPONSE: CDC/ATSDR understands that many of the communities are concerned about how PFAS exposure may affect their risk of COVID-19 infection. ATSDR agrees that this is an important question.

CDC/ATSDR recognizes that exposure to high levels of PFAS may impact the immune system. There is evidence from human and animal studies that PFAS exposure may reduce antibody responses to vaccines [Grandjean et al. 2017a and 2017b; Looker et al. 2014] and may reduce infectious disease resistance [NTP 2016]. Because COVID-19 is a new public health concern,

there is still much that is unknown. More research is needed to understand how PFAS exposure may affect illness from COVID-19.

Because COVID-19 is a new public health concern, any and all work around understanding this virus is occurring in a very dynamic environment, where things change and evolve each day. Questions about the relationship between the vaccine and PFAS exposure are certainly on our radar and we may be able to investigate them in the future.

All that said, ATSDR is collaborating with CDC to assess the intersection between PFAS exposure and COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). For instance, CDC is currently implementing a study that will look at COVID-19 among healthcare personnel and first responders. As part of this study, PFAS serum concentrations will be measured in participants to help determine the association between serum PFAS concentrations and the risk of SARS-CoV-2 infection and subsequent COVID-19. The study will also evaluate the association of PFAS levels and antibody response to SARS-CoV-2 infection and waning of antibodies over time, which may shed light on the potential impact of PFAS exposure on vaccine response and potential duration of vaccine protection.

CDC and ATSDR are also exploring how to incorporate investigator-initiated COVID-19 research into the current multi-site PFAS study.

ATSDR is also developing a study to evaluate the intersection between PFAS exposure and susceptibility to viral infection, including but not limited to COVID-19, that will recruit participants from existing ATSDR PFAS cohorts for whom we already have PFAS serum measurements.

Comment: (Conclusion 2, Next steps) CHANGE the word – applicable to the most current NH DES in the sentences between the first two bullet points.

RESPONSE: ATSDR accepted this text change.

Comment: Page iii – In the basis for conclusion the document describes "Human and animal studies suggest a link between PFOA exposure and higher rates of several cancers. Animal studies suggest a link between PFOS exposure and several cancers; although, human studies have yet to confirm a link between cancer and PFOS exposures." The prior health consultation by ATSDR for Pease and the provisional Toxicological Profile for Perfluoroalkyls (ATSDR, 2018) provide explanations that differ from this summary. We suggest that the agency review their own text and language relative to "links" between cancer, associative studies and animal models. One approach to address this is to lead the paragraphs (half-way down, page iii) with ATSDR's determination of "The cancer risk from past exposures to all PFAS in these wells is uncertain" instead of the uncertainty of animal studies.

RESPONSE: Based on the most current information on PFOA carcinogenicity and the uncertainty regarding the EPA cancer slope factor for PFOA, ATSDR has updated the text relating to potential PFAS carcinogenicity. In addition, ATSDR no longer reports a numeric cancer risk based on the current EPA cancer slope factor for PFOA testicular cancer risk.

Comment: Page viii – The definition for the acronym "NOAEL HED" should read "Human Equivalent Dose for NOAEL" to be consistent with the definition for the LOAEL HED. Also, the description for EtFOSE should read "N-ethyl perfluorooctane sulfonamidoethanol".

RESPONSE: ATSDR accepted these text changes.

Comment: <u>Conclusions limited by several uncertainties:</u>

- ***One of the biggest limitations is not knowing what was in the AFFF, how many different types of PFAS were in it, their relative concentrations, and characteristics. I understand that PFASs are an emerging area of study but one of the greatest limitations is understanding the components of AFFFs. If we do not know what went into the ground to begin with, it is nearly impossible to determine what is still is the well water and how it impacts human health.***
- ***Has the ATSDR received any information from the Air Force about the AFFFs used at Pease –beyond just the locations on a map of where PFASs might have been released?***
- ***The USAF had dragged its feet about determining the components of AFFF – lost records, no records, trade secrets, big black box, other priorities to triage and prioritize ….. That is not helpful at all when trying to understand and report on the impacts to human health. I would like to see a recommendation in this study with "more teeth" about the necessity of characterizing AFFF components in order to understand potential health impacts.***
- ***As a bare minimum, can the ATSDR request that a study be done to look at the PFAS components of AFFFs now on the market? Those are readily accessible, and information should be available on their components. As a government health agency concerned with human health, "trade secrets" and "brand name" issues should not stand in the way of understanding human health impacts.***

RESPONSE: ATSDR agrees that there are many uncertainties relating to the amount, type, and formulation of the AFFF used at the former Pease AFB and those uncertainties are described in the public comment version of this health consultation. Standard laboratory methods capable of detecting a broader range of PFAS in environmental samples are also needed. As more information becomes available, ATSDR will incorporate it into future assessments of exposure to PFAS from sites associated with the use of AFFF. In addition, ATSDR has revised this health consultation to recommend to the USAF that they should consider doing additional work and

research to better understand the type and formulations of AFFF used at Pease and other facilities to inform future monitoring efforts and health assessments.

Comment: <u>Conclusion #1 – Based on data from June 2014 through December 2017 found elevated risk of harmful non-cancer health effects for children who drank water from 5 residential wells (17, 19, 21, 23, 37).</u>

- ***The current residents at two of these well locations are not the people who were living there during the period of exposure, e.g., 20 years, or more, before June 2014. The previous residents should be notified of ATSDR's findings and get a chance to speak with you about PFAS and the potential health issues to them and their children based on this conclusion.***
- ***Due to privacy concerns, the USAF has made it very difficult to find information beyond the RES code numbers to understand which wells and which people may have been impacted. Ask them to supply a list of all residents at the impacted properties for 20 years before June 2014. Good luck with that. The USAF has been tying itself in knots trying to explain how confidentiality trumps the need for public understanding and disclosure. Does it also trump the rights of the people who lived there to know that their health may have been impacted by drinking the well water? Or to limit ATSDR's ability to speak with them about your findings?***
- ***This public comment may include personal identifying information that has been redacted due to privacy issues.***

RESPONSE: Thank you for the suggestions on how to locate former Newington residents where ATSDR has determined that past PFAS exposures from their private drinking water wells may result in harmful health effects. ATSDR will evaluate this information and work with local town officials and the USAF to share the findings of the Health Consultation with prior owners/residents of the affected properties. ATSDR has added information indicating this in the 'Next Steps' section of the summary and public health action plan. Please note that some information provided in this comment may violate the privacy of these former Newington residents; therefore, this information has been redacted.

Comment: <u>Conclusion 2 – Risks to human health from mixtures of PFAS in 24 wells cannot be determined.</u>

- ***The importance of this issue is underscored by the results of a non-targeted PFAS study presented at Pease last Fall. At Site 8, which is the main contamination site for well water in Newington, Dr. Higgins found 48 PFAS compounds in the groundwater on his list of suspected targets. He believes there are likely 150 different PFAS compounds, or more, in the water but most of them cannot be specifically tested because no assays exist.***

- ***See attached slide deck from Christopher Higgins of the Colorado School of Mines, who presented at the Pease Restoration Advisory Board meeting – see www.youtube.com/watch?v=xYvn3NDXmlM). Dr. Higgins gave permission for me to share his slide deck with you. He has been speaking with Rachel Rodgers at ATSDR. He asks that the slide deck not be posted on any websites.***
- ***The 4 PFAS compounds that you were able to assess in this Health Consultation are clearly just the tip of the iceberg based on the presence of 150+ PFAS compounds thought to be at Site 8 that could have migrated into Newington well water. Under Next Steps, it would be very helpful to discuss how this issue should be addressed.***
- ***The EPA, USAF, and City of Portsmouth water department have been focusing their efforts only on the 24+ PFAS compounds that they can test for and track. Ignoring 125, or more, of other PFASs that cannot be tested directly is like burying your head in the sand and hoping it all turns out OK in the end.***
- ***I think a next step recommendation from ATSDR for the EPA, NHDES, and USAF to develop a way to use non-targeted analysis (or something similar) to study and identify the groundwater contamination from these other 124 PFAS compounds would be very prudent.***

  At the very least, samples of water from all the well testing locations should be collected and archived until such time as additional PFAS compounds in them can be directly tested.

  Also, the ability of granulated charcoal and other resins to remove ALL types of PFAS compounds needs to be determined. The Portsmouth public drinking water system is using both charcoal and resin to remove PFASs. I don't have any information on what is happening for the private wells, other than the use of charcoal.

RESPONSE: ATSDR agrees that the work of Dr. Higgins and others to identify the constituents of various AFFF formulations is important to understand exposures to residents and workers around Pease and elsewhere in the U.S. Moreover, ATSDR is aware of the non-target analysis work being conducted to help achieve this goal. ATSDR is supportive of these efforts and those to derive methods to detect and quantify other AFFF-related PFAS in water (and other media). Finally, even if ATSDR was able to analyze and quantify all of the other AFFF-related PFAS, for this health consultation, ATSDR would not be able to conduct a health evaluation of them because of the lack of animal and human health data.

ATSDR evaluated the drinking water sampled from private wells with treatment systems (called granular activated carbon systems or GACs). The samples were collected after going through the treatment system. During the period from 2017 through June 2020, there were very low

concentrations detected for a few PFAS in samples from the faucet. The following were detected after the treatment systems in these three wells (at low levels - units are µg/L):

RES17 from faucet after GAC
2015
PFDA=0.0037
PFDS=0.0056
PFHpS=0.0049
PFTeDA=0.005

2018
PFOSA=0.0043

RES19 from faucet after GAC
2018
PFTeDA=0.0039

RES21 from faucet after GAC
No detections

RES23 from faucet after GAC
2018
PFOSA=0.0042

For RES17, the PFAS detected in 2015 occurred shortly after the GAC treatment was installed on March 17, 2015, with only one detection after that in 2018. The PFAS detected were below ATSDR's most conservative HBCV. For the other wells that have had a treatment system, there have been only a few instances of PFAS detections in treated water at the faucet and these have been below ATSDR's most conservative HBCV. Overall, the systems appear to be working well, and this information does not change any of ATSDR's conclusions or recommendations in this health consultation.

1. Background and Statement of Issues

Comment: (Page 3, Section 1 Background and Statement of Issues) On page 3 (second paragraph), the ATSDR Health Consultation provided for public comment cites the "current EPA health advisory of 0.07 µg/L." This needs to be correctly stated in the first mention of this "health advisory" as the EPA "lifetime drinking water health advisory."

RESPONSE: No change was made because the U.S. EPA uses the term "health advisory" and no longer uses the term "lifetime drinking water health advisory."

Comment: (Section 1, Second paragraph, page 3) Confirm correct acronym for Provisional Health Advisory; document adds "Level" and resulting acronym is PHAL versus PHA. Conversely Lifetime Health Advisory is LHA.
Recommendation: Global change to acronyms to PHA.

RESPONSE: ATSDR will use the term provisional health advisory and not abbreviate it, thereby avoiding confusion with the ATSDR term public health assessment (PHA).

Comment: (Background and Statement of Issues, page 4, line 9) The text separated by dashes, — potentially PFAS contaminated — seems clunky especially since the next word areas, goes with the adjective contaminated.
Recommendation: Remove both.

RESPONSE: ATSDR accepted these text changes.

Comment: (Background and Statement of Issues, page 4, line 12) Since you explicitly talk about 21 sites, and mention 11 are being investigated, the sentence, "Ten sites currently are not the focus of additional investigations [AMECFW 2017]." Seems redundant.
Recommendation: Recommend removing the sentence.

RESPONSE: ATSDR will maintain the current wording for clarity.

Comment: (Background and Statement of Issues, page 4, line 13) "Since about 2014" awkward wording, is the actual date not known?
Recommendation: Recommend "In 2014", or if not known "Around 2014".

RESPONSE: "In 2014" will be used.

Comment: At page 4 the study area includes only those residential wells in the Town of Newington located w/in approximately 1 mile from the former Pease AFB. This area was designated by USAF on the recommendation of its consultant AMEC, 6 years ago when little was known about the significant amount/extent of PFAS in ground water in the Town coming from the former firefighting site @ the north end of the base where the one mile radius begins. Currently it now is known that there are plumes of PFAS contaminated ground water emanating from the firefighting site into the residential areas of the Town. While a further site investigation is expected to define the full extent of the spread of the contamination, it appears clear that the entire area of the residentially zoned portion of the Town, including Fox Point which is currently considered outside the study area, should have any wells sampled

and considered in further consultations or follow up. The Consultation should clearly note the limitation on its scope resulting from this potentially outdated limitation of the study area.

RESPONSE: ATSDR used the private drinking water well locations provided by the USAF and included two additional wells added to the inventory since late 2017. ATSDR agrees that there are limitations in knowing the full extent of the PFAS plume.

2. Groundwater PFAS Contaminant History

Comment: (Section 2.3, page 5) It states: "Some community members noticed foam floating on the surface waterways where they used to play." This may be important, but without details or supporting documentation it seems out of place in a scientific paper. Recommendation: Specify how many community members reported this, when and how they reported it, and add a citation.

RESPONSE: ATSDR learned about those observations while listening to residents during several meetings. Those meetings included a 12-hour public availability session as well as two Newington Town Selectmen board meetings. Additional details were not provided.

Comment: (Section 2.3, page 5 and 8) More recent data exists for the surface water and biota pathways. After conclusion of the Expanded Site Inspection, the State of NH Environmental Health Program evaluated potential shellfish exposures using State derived reference doses to conclude that no unacceptable risk from shellfish consumption currently exists. http://www4.des.state.nh.us/IISProxy/IISProxy.dll?ContentId=4824416 Recommendation: Include discussion of actual results and try to avoid breaking section 2.3 with insertion of Figures 1 and 2.

RESPONSE: The split text has been repaired. The paragraph will be modified to the following:

Some community members noticed foam floating on the surface waterways where they used to play. ATSDR cannot confirm that the foam observed by the community was AFFF. If AFFF impacted the surface water bodies, residents in the area may have been exposed to PFAS while playing in the nearby waterways.

The NH DES evaluated PFAS exposures from eating shellfish. Their observations are provided below.

"Based on the currently available data and reported concentrations in shellfish, the ... [Environmental Health Program] has determined a shellfish consumption advisory is not necessary. Using conservative ... exposure assumptions ... and the highest PFOS concentration, a tissue consumption limit ... would exceed the recognized shellfish consumption rates for people residing in the Northeastern U.S. ... Although some PFOS tissue concentrations exceed the more conservative NHDES [Screening Levels or SLs] in certain samples, they do not present a significant risk of exposure for the typical consumer of shellfish including oysters, clams and mussels. Additionally, these sites are subject to existing restrictions on recreational shellfish harvesting that further reduces potential exposure risk from the measured concentrations.

The EHP notes that the revised draft report detected three other PFAS in shellfish samples including: Perfluorooctane sulfonamide (PFOSA, about 23% of samples), Perfluorobutanoic acid (PFBA, about 34% of samples) and Perfluoropentanoic acid (PFPeA, 100% of samples). At this time, neither the U.S. EPA, [the] Agency for Toxic Substances and Disease Registry (ATSDR, 2018), or NHDES have toxicity values for these PFAS and therefore cannot determine SLs for site investigations. If toxicity values are developed for these PFAS, the EHP will reassess the available data and may adjust its recommendation(s) accordingly."
Source: https://www4.des.state.nh.us/IISProxy/IISProxy.dll?ContentId=4824416

Based on NHDES' evaluation, it appears that any exposures that might have occurred to PFAS (primarily PFOS) in shellfish from the Great Bay are not likely to result in harmful effects. The existing restrictions in place would further reduce the potential for any exposures. NHDES could not evaluate all PFAS present in shellfish because of the lack of toxicity data. Moreover, the NHDES indicated that PFOS detections occurred in shellfish collected from the Broad Cove at the mouth of Knights Brook, Great Bay at the Mouth of McIntyre Brook, and Trickys Cove at the mouth of Pickering Brook. If any residents with contaminated wells in Newington consumed shellfish from these areas, they that would have added to the PFAS exposures they are receiving from the private wells and other sources. ATSDR recommends that residents using wells where ATSDR has determined a hazard exists for past exposures or where current exposures cannot be determine should consider not consuming shellfish from these areas.

3. ATSDR's Evaluation Process

Comment: (Page 12, Table 1) Table 1 of the ATSDR Health Consultation provided for public comment is presented as binary outcomes (i.e., yes or no). The commenter recommends that the actual values also be presented in parentheses in this table for each of these wells. Otherwise, the reader must find these data in the appendices.

RESPONSE: The information in Table 1 was provided to the reader for a quick review of exceedances with all of the maximally detected values clearly shown in Table 1.

Comment: (Section 3.2, page 10) It states: "…other characteristics can affect how a person's body responds to an exposure." It is unclear what is meant by "other characteristics."
Recommendation: Either delete "other characteristics" or provide an example. Anthropometric variables, such as height or body fat percentage, may be examples of other characteristics.

RESPONSE: There are many characteristics which could be listed, but the main ones were listed for emphasis.

Comment: (Section 3.3, page 11) The second paragraph references Table A-5 but not Appendix B.
Recommendation: Add a reference to Appendix B at the end of this section.

RESPONSE: The last sentence was modified to the following: "Table A-5 shows the HBCVs used in this evaluation. Please see Appendix B for details on the ATSDR process."

Comment: (Section 3.3, first sentence, page 11) Document states that HBCVs as "screening values" which per section 3.2 are "based on contaminant concentrations many times lower than levels at which no effects were observed". HBCVs are used throughout the document similar to a reference dose for determining potential non-cancer health effects.
Recommendation: Clarify whether HBCVs are truly screening values per the definition.

RESPONSE: ATSDR HBCV's are media-specific values used to compare to environmental levels to determine if further evaluation is needed. Exceedances of HBCVs do not mean non-cancer health effects will occur. ATSDR's HBCVs are derived from various health guidelines, such as ATSDR MRLs and EPA RfDs. Health guidelines are in dose units (e.g., mg/kg/day). After a contaminant is selected for further evaluation using an HBCV, ATSDR will then calculate an exposure dose which is then compared to a health guideline. If an exposure dose is above a health guideline, ATSDR will evaluate how close the dose is to effect levels along with other factors to determine if harmful health effects are possible.

Comment: (Section 3.3 and 7.3, page 11 and 38) Current text at 3.3 notes: "As a first step in the evaluation process, ATSDR uses health-based comparison values (HBCVs) as screening values… When no federal HBCVs are available, ATSDR uses applicable state values… ATSDR

used six HBCVs in the evaluations of PFAS exposures. Four of the ATSDR-derived HBCVs (PFHxS, PFNA, PFOA, and PFOS) were used. The remaining two HBCVs were derived by the Minnesota Department of Health (PFBA and PFBS)." Similar text appears at 7.3.

In its review of previous drafts, the Air Force recommended the ATSDR Health Assessment not use state HBCVs without formal ATSDR review, a recommendation that has not changed. The Air Force also notes that EPA has published peer reviewed toxicity values for PFBS, and question why, if the ATSDR hierarchy described in the document is to use state HBCVs when federal values are unavailable, ATSDR continues to use HBCVs derived by Minnesota Department of Health. It is understood that revised toxicity values for PFBS have been proposed by EPA and may be revised before being finalized in the Federal Register, and that EPA has other PFAS actions on-going including the Systematic Review Protocol for PFDA, PFNA, PFHxA, PFHxS and PFBA for Integrated Risk Information System (IRIS) assessments, but the existing EPA peer reviewed toxicity value for PFBS remains valid and should be considered before defaulting to a state value without formal review.

Recommendation: The Air Force recommends ATSDR use valid toxicity values developed by other federal agencies such as EPA when ATSDR-derived HBCVs are not available and reiterates the recommendation that state HBCVs without formal ATSDR review are not to be used.

RESPONSE: ATSDR considers state screening values when appropriate ATSDR or EPA screening values are not available. ATSDR scientists vetted the MN screening values used by ATSDR for screening in this health consultation. In general, ATSDR does not use draft guidance values from other agencies. The former PFBS EPA Regional Screening Level (RSL) for drinking water, based on a draft EPA reference dose (RfD), was 400 µg/L. The current RSL for PFBS of 6 µg/L is based on a final EPA RfD. The EPA RSL is above the MN PFBS value of 2 µg/L used by ATSDR for screening in this health consultation. The use of either of these values would not have resulted in ATSDR screening in PFBS for further evaluation. Therefore, ATSDR's conclusions would not have changed.

Comment: Page 11 – HBCVs for PFBS and PFBA – The agency should provide more explanation for the selection of these HBCVs for screening purposes at this site. The document details the role of HRLs and MRLs used by ATSDR and their difference from regulatory values. Without additional clarification there may be confusion regarding the application of ATSDR's MRLs and values derived by state regulatory agencies under the EPA's risk assessment process. On page 39 the authors note that these values were not fully reviewed by ATSDR. We support the additional consideration of other PFAS compounds, but the differences in these types of risk

assessment tools (e.g., RfD-derived drinking water values versus MRL-based screening values) should be made more explicit. An example of possible miscommunication is the interpretation of ATSDR using the MDH values for PFBS and PFBA, but not utilizing their lower value for PFHxS nor the lower value of 18 ng/L recommended by NHDES. While Appendix B provides a brief explanation of their derivation, it lacks text that defines their differences from a traditional MRL and implications for risk assessment.

RESPONSE: As a general rule, ATSDR will first use screening values derived from its own MRLs. Therefore, for PFHxS, ATSDR used 140 ng/L as the screening value. Even if ATSDR were to use the lower NHDES value of 18 ng/L, it would not have changed the conclusions as ATSDR does not use a screening value as an indication that harmful effects are likely to occur if the screening value is exceeded. However, ATSDR does support prudent public health actions to reduce exposures to users of private wells in Newington to the below NH's regulatory values. Also, please see the response above to comments on ATSDR's use of MN's PFBS value.

4. NH release of new PFAS Ambient Groundwater Quality Standards

Comment: Page 13 – Section 4. NH release of new PFAS Ambient Groundwater Quality Standards – There are two errors with the draft in this section. The first is that an incorrect value is stated for perfluorohexane sulfonic acid (PFHxS) as 18 µg/L and should read 0.018 µg/L (or 18 ng/L). Secondly, the standards for PFOA, PFOS, PFHxS and PFNA are currently under injunction pending additional legal review. As such, there are only enforceable Ambient Groundwater Quality Standards (AGQS) for 2 of the PFAS; perfluorooctanoic acid (PFOA), 0.07 µg/L, and perfluorooctane sulfonic acid (PFOS), 0.07 µg/L, or the sum of PFOA and PFOS at 0.07 µg/L. This issue may or may not be settled by the time ATSDR has completed its health consultation, and therefore you may want to refer to the water values from NHDES (NHDES, 2019) as health-based comparison values in the revision if it is intended for release prior to the court's final decision.

RESPONSE: It is ATSDR's understanding this issue has been settled and these PFAS Ambient Groundwater Quality Standards are now promulgated. ATSDR has corrected the error in the NH standard value reported for PFHxS to state it as 0.018 µg/L.

5. Public Health Implications of Exposure to PFAS in Drinking Water

Comment: (Pages 13 – 14, Section 5.1.1, Non-Cancer Health Effects) The public comment version of the ATSDR Health Consultation alludes to a range of non-cancer health effects potentially associated with "high levels of certain PFAS" in humans. These include increased cholesterol levels, changes in liver enzymes, decreased vaccine response in children, increased risk of high blood pressure or pre-eclampsia in pregnant women, and small decreases in infant birth weight. The Health Consultation does not include a detailed discussion of these potential health effects but rather cites the 2018 ATSDR Draft Toxicological Profile for Perfluoroalkyls as the sole reference for these potential associations. It is important to recognize that the 2018 ATSDR Toxicological Profile remains a DRAFT document. It is not cited as such within the written text of the Health Consultation (only cited as a draft in the reference citation). This results in a misleading characterization of the ATSDR 2018 reference to the reader of the text as a final document. It is not. The commenter recommends citations to the draft ATSDR 2018 Toxicological Profile be written in the text as "draft ATSDR 2018".

The draft state of the ATSDR 2018 Toxicological Profile is important because, in August 2018, ATSDR received, at its request, over 60 public comments from various stakeholders (including from the commenter) during the public comment period. To date, ATSDR has not addressed any of these public comments nor has it issued a revised draft or a finalized Toxicological Profile. In addition, many studies have been published since the release of the draft 2018 ATSDR Toxicological Profile that this ATSDR Health Consultation should consider when discussing the potential health effects of PFAS exposure.

For those reasons and the reasons described further below, the commenter disagrees with much of the ATSDR Health Consultation's interpretation of the epidemiologic and toxicologic research pertaining to the five health outcomes on which the Health Consultation focuses (see attachment to this response to comments for health outcome specific comments from this reviewer).

RESPONSE: The draft Toxicological Profile has gone through three external peer-review and three public comment periods. ATSDR has addressed all of the comments received and made changes as needed. The PFAS Toxicological Profile was finalized in May 2021; public comments received as well as ATSDR's responses were finalized and are available in the public docket as well. Responses to concerns regarding the five health outcomes that ATSDR has determined are associated with PFAS exposures are provided below after each specific health outcome.

Increased cholesterol levels

Although several observational epidemiological studies have reported an association between PFOA exposure and increased cholesterol levels, these findings are inconsistent with experimental studies which have observed decreased cholesterol levels with markedly higher PFOA concentrations. These experimental studies now include a Phase 1 clinical trial in humans (Convertino et al. 2018) and a transgenic mouse model that mimics human lipoprotein metabolism (Pouwer et al. 2019). A primate study on PFOS (Chang et al. 2017), not included in the draft ATSDR Toxicological Profile (2018), also presents observations inconsistent with the assertion that PFOS would result in increased cholesterol levels. Summaries of these three studies are presented immediately below.

- ***Convertino et al. (2018) was a phase 1 dose-escalation study, conducted by oncologists in Scotland, that assessed the chemotherapeutic potential of ammonium perfluorooctanoate (APFO) in forty-nine primarily solid-tumor cancer patients who had failed standard therapy. The study participants received weekly APFO doses (50– 1200 mg) for 6 weeks. The main limitation of the study was that it included cancer patients who had failed conventional treatments and whose metabolic activity may have differed from healthy individuals. However, according to Convertino et al., there was no evidence that any of the cancers involved or treatments received prior to the study had systematic effects of the metabolic function studied. Baseline values prior to PFOA treatment were also recorded to determine measurable differences over the course of treatment. No more than one subject showed dose limiting toxicity at any dose; therefore, the protocol-defined maximum tolerated dose was not reached. Standard clinical chemistries were assessed including total cholesterol, LDL, HDL, ALT and other liver enzymes as well as liver function (e.g., prothrombin time), TSH and free thyroxine, creatine and uric acid. There was strong evidence that showed PFOA concentrations were associated with a reduction of total cholesterol as there was a clear transition in shape and range of the probability distribution functions for a decrease in total cholesterol. The reduction of total cholesterol was with the LDL cholesterol, not the HDL fraction. This transition occurred approximately between 175,000 and 230,00 ng/mL PFOA which are concentrations several orders of magnitude higher than reported in the general population, communities exposed through drinking water such as the mid-Ohio River Valley community, or occupational workers. The findings at these high concentrations are, in fact, contrary to the positive association between considerably much lower PFOA and total cholesterol observed in epidemiological cross-sectional studies.***

- ***Pouwer et al. (2019) used a genetically engineered APOE*3-Lieden.CETP mouse model that mimics human lipoprotein metabolism and confirmed the lipid lowering high-dose PFOA findings from the phase 1 clinical trial in humans (Convertino et al. 2018). This mouse model is designed to assess cholesterol ester transfer protein (CETP) expression***

and a delayed apolipoprotein B (apoB) clearance. CETP is responsible in both humans and in this mouse model for the transfer of cholesterol ester from HDL to the apoB-containing lipoproteins in exchange for triglyceride. In three different experiments lasting 4 to 6 weeks, Pouwer et al. fed these mice a Western-type diet that had four doses of PFOA (control, 10 ng/g/d, 300 ng/g/d, and 30,000 ng/g/d) that resulted in plasma PFOA concentrations of approximately < 1.0 ng/mL, 50 ng/mL, 1500 ng/mL, and 90,000 – 144,000 ng/mL, respectively. These four resulting plasma concentrations reflect, in increasing order, general population, environmental, occupational, and toxicological exposures. Also reported at this high dose group in the Pouwer et al. study were increased liver weight and elevated ALT. The plasma lipid change at the high dose was explained through a decrease in very low-density lipoprotein (VLDL) production and increased VLDL clearance by the liver via increased lipoprotein lipase activity. The increase in HDL was mediated by a decrease CETP and changes in protein expression involving HDL metabolism. This APOE*3-Leiden.CETP mouse model has considerably higher concentrations of CETP than what is found in humans.

- ***<u>Chang et al. (2017)</u> undertook a six-month oral dose study with PFOS administered to male and female cynomolgus monkeys, with scheduled clinical assessments through 1 year, in order to evaluate markers for coagulation, lipids, hepatic, renal, electrolytes, and thyroid-related hormones. There was a time-matched control group as well as 4 weeks of baseline values for the dosed groups. The low dose group (n = 6/sex) received 1 single K+PFOS dose (9 mg/kg) with the highest mean serum concentration measured at 68000 ng/mL. The high-dose group (n = 4-6/sex) received 3 separate doses (11 – 17.2 mg/kg) during the six-month treatment phase with the highest mean serum concentration measured at 165000 ng/mL. Liver needle biopsies performed two months after completion of the study showed the highest mean liver PFOS concentrations at 112000 ng/g. At the end of the study, all the animals were considered healthy, had gained weight, and were released back to the colony. Throughout the entire study, there were no K+PFOS treatment-related changes in serum liver enzymes, serum BUN or creatinine. There was a decrease in serum total thyroxine without a concomitant change in in the clinically-relevant TSH and free T4. Authors considered the decreased total thyroxine observed was likely due to competitive displacement by PFOS with thyroxine and its subsequent increased metabolism and elimination. The most notable observation in this study was after treatment serum total cholesterol decreased by approximately 4–12% at 1 and 3 weeks post-dose when compared with mean time-matched control or baseline values. The reduction in cholesterol was used to determine a lower-bound fifth percentile benchmark concentration (BMCL1SD) of 74000 and 76000 ng/mL in male and female monkeys, respectively.***

Additionally, as mentioned above, new studies have been published since the ASTDR draft Toxicological Profile was released in 2018. While the following comments do not provide a comprehensive overview of papers published post-ATSDR's draft Toxicological Profile (2018), the commenter highlights the study below to illustrate the point that individual studies must be carefully evaluated.

Li et al. (2020) studied associations between the perfluoroalkyls PFOS and PFHxS (and to a lesser degree PFOA) and serum lipids in Ronneby, Sweden, where one of two waterworks had been contaminated from aqueous film forming foams (AFFF). The original exposure occurred sometime after the mid-1980s and ceased in 2013 when a GAC filter was installed. Three populations were reported: 1) a control population (N =130) in a neighboring community that had not been exposed; 2) a recently exposed population (N = 1160) who lived in Ronneby anytime between 2005 to 2013; and 3) a non-recent/uncertain exposure group (N = 655) who lived in the contaminated waterworks distribution area in Ronneby before 2005 but not after as well as participants who lived in the non-contaminated waterworks area in Ronneby anytime between 1985 to 2013. All participants were between 20 and 60 years of age. Median serum concentrations (ng/mL) for the control, non-recent/uncertain, and recently exposure groups were, respectively: PFOS 4.8, 45, 240; PFHxS 0.98 40, 210; and PFOA 1.6, 3.5, 13. Comparing the control to total (combined) exposure group revealed a significant increase in total and LDL cholesterol but not HDL, triglycerides or the total/HDL ratio.

Analyzing each separately, the strongest positive lipid associations were reported for the recently exposed. Even among the controls, there were modest associations with PFOS and PFHxS. Similar to Steenland et al. (2009), decile analyses suggested the strongest associations (slopes) were observed at the lowest concentrations (up to about the 40th percentile). The recently exposed group had the largest odds ratio for high cholesterol. Li et al. concluded that their findings provided evidence of a causal association between PFAS, including PFHxS, and serum lipids as their results were not necessarily confounded by the reabsorption of bile acids and the categorization levels of serum PFAS. However, Li et al. acknowledged some important limitations including another cross-sectional study design reported in the literature, disparate socioeconomic status (SES) differences between the exposed and control populations (the latter having the higher SES), the lack of information on cholesterol lowering medications, and unknown dietary habits of the population. Also, there was a preference by the authors to cite literature that supported their position of a causal association. For example, Li et al. stated that humans may be less active than the rodent to the lipid lowering effects of PPARα, but neither the Pouwer et al. nor Convertino et al. studies were mentioned in the Li et al. paper. Li et al. also cited Fletcher et al. 2013 that had promoted the idea of a "hypercholesterolemic environment" with PFOA through its effect on the expression of genes

involved in human cholesterol transport and metabolism (Fletcher et al. 2013) yet they chose not to cite the evidence presented against the Fletcher et al. hypothesis as published by Vanden Heuval (2013).

It is also worth noting that, in 2018, the EFSA Scientific Panel on Contaminants in the Food Chain (CONTAM Panel) released a provisional tolerable weekly intake (TWI) for PFOA and PFOS based on cross-sectional epidemiological studies that reported positive associations between serum cholesterol and PFOA/PFOS (Knutsen et al. 2018). However, after careful consideration of the experimental evidence, the EFSA CONTAM Panel (2020, see https://www.efsa.europa.eu/en/consultations/call/public-consultation-draft-scientific-opinion-risks-human-health) has acknowledged the uncertainty regarding its cholesterol assessment to be larger than what was assumed in 2018. Specifically, on page 148 of the draft EFSA CONTAM Panel Opinion (2020), EFSA stated:

> ***"In the previous opinion (EFSA CONTAM Panel, 2018), the CONTAM Panel used the effects on serum cholesterol levels to derive TWIs for both PFOS and PFOA. Those TWIs were also protecting towards the other potential critical endpoints. Although the association with increased cholesterol was observed in a large number of studies, the CONTAM Panel now considers the uncertainty regarding causality larger. This is primarily due to a postulated biological process around the enterohepatic cycling of both PFASs and bile acids, the latter affecting serum cholesterol levels."***

In conclusion, the experimental evidence discussed above suggests a decrease in cholesterol with high concentrations of PFOA in humans and humanized mice. The low dose associations between cholesterol and PFOA/PFOS noted in certain observational epidemiologic studies are likely due to yet-to-be-discovered mode of actions or unaccounted confounding factors. The commenter encourages the authors of this ATSDR Health Consultation to review the most recent paper published on the alternative explanation that involves the interaction of cholesterol, PFAS, and bile acids (Salihovic et al. 2019).

RESPONSE: The Convertino et al. (2018) study was published after the literature search for the updated toxicological profile was conducted (May 2016); the results of the Convertino et al. (2018) study were added to the profile. ATSDR considers the results of this study supportive of its suggestion that the dose-response curve may be biphasic, since the decreasing serum cholesterol levels in the Convertino et al. (2018) study were associated with very high serum PFOA levels (similar to those observed in animal studies). Moreover, the Agency agrees with Convertino's statement that plausible biologic modes of action that support positive associations between serum PFOA levels and cholesterol levels at low serum PFOA levels and inverse associations at higher serum PFOA levels. Thus, increased environmental exposures could increase serum cholesterol, which is a risk factor for cardiovascular disease.

The Chang et al. (2017) study was also added to the profile. ATSDR characterized this study as an acute-duration study since the monkeys were dosed only 1 or 3 times. The results of the study did not impact the intermediate-duration MRL because it was an acute-duration study and did not examine sensitive endpoints observed in rodents such as developmental toxicity or immunotoxicity.

ATSDR's determination of an association between PFOS exposure and increases in serum lipids is based on a number of epidemiological studies. Findings from PFOA epidemiological studies suggest that the relationship between serum PFOA and serum cholesterol might be U-shaped with lower serum PFOA levels resulting in increases in serum cholesterol levels and higher serum PFOA levels associated with decreasing serum cholesterol levels. There are limited data to make a similar assessment for PFOS.

ATSDR disagrees that there is insufficient evidence to conclude an association between serum PFOS and serum lipids and considers the epidemiological data suggestive of an association. Moreover, a recent review of the PFOA findings from the C8 Science Panel by Steenland et al. (2020) concluded that there is consistent evidence of a positive association between PFOA and increased cholesterol, but no evidence of an association with heart disease (which ATSDR did not include in the list of possible PFAS-related health outcomes). Any study that was released after the literature review for the 2021 PFAS Toxicological Profile will be reviewed for possible inclusion in future updates to the profile.

Changes in liver enzymes

The commenter refers the authors of this Health Consultation to the commenter's detailed public comments to the draft ATSDR Toxicological Profile regarding liver enzymes and liver disease that were submitted in August 2018. The commenter also refers to a conclusion of the C8 Science Panel statement in 2012 on liver enzymes as they interpreted their own research (http://www.c8sciencepanel.org/pdfs/Probable_Link_C8_Liver_29Oct2012.pdf).

> ***"From our studies of patterns of diagnosed liver disease there is no evidence of any increased risk of liver disease in relation to PFOA exposure. Based on our studies of liver enzymes and inconsistent findings in reported literature there is some evidence of small shifts in liver function, mainly within the normal physiologic range, being associated with increasing PFOA exposure. It is uncertain if PFOA is the cause of the association, but if so there is no evidence that this is reflected in any increase in overall incidence of diagnosed liver disease. Therefore, the Science Panel does not find a probable link between exposure to PFOA and liver disease."***

Furthermore, this line of reasoning by the C8 Science Panel is in agreement with the draft 2018 ATSDR Toxicological Profile (see page 24) which stated,

> ***"It should be noted that although the data may provide strong evidence of an association, it does not imply that the observed effect is biologically relevant because***

the magnitude of the chance may be within the normal limits or not indicative of an adverse health outcome."

In sum, the commenter is unaware of an association between PFOA or PFOS with human liver disease including enlarged liver, fatty liver, or cirrhosis. This should be included in the bullet point regarding liver enzymes. Small percentage changes in ALT have been reported, albeit inconsistently in epidemiology studies across vastly different perfluoroalkyl concentrations but are within normal physiological ranges. This small magnitude of change, if it is even present, does not indicate liver damage by any standard clinical practice of medicine. Confounding cannot be ruled out as a possible explanation for this observation due to the many factors that can influence ALT. Thus, there is insufficient evidence of an association with ALT.

RESPONSE: ATSDR agrees with the comment that the available community, occupational, and epidemiological data do not support an association between PFOA or PFOS exposure and an increased risk of liver disease. Nowhere in the public comment version of the health consultation does ATSDR suggest that PFAS are associated with liver damage based on human studies.

Although there are limitations to interpreting the serum enzyme data, ATSDR stills considers the data suggestive of an association with PFAS exposure. It is noted that associations were found in the studies that adjusted for a number of potential confounders. For example, Gallo et al. (2012) adjusted for age, physical activity, body mass index (BMI), average household income, educational level, race, alcohol consumption, and cigarette smoking and found significant correlations between serum PFOA and alanine aminotransferase (ALT) levels. The study also found an increased risk of elevated ALT levels (≥45 IU/L in men and 34 IU/L in women) in participants with serum PFOA levels in the third decile or higher. ATSDR's interpretation of the current human data suggest that some PFAS are associated with:

- Increase in serum hepatic enzymes, particularly ALT, and decreases in serum bilirubin levels (PFOA, PFOS, PFHxS);
- Increase in serum enzymes and decreases in serum bilirubin, observed in studies of PFOA, PFOS, and PFHxS, are suggestive of liver alterations; and,

The recent review of the PFOA findings from the C8 Science Panel by Steenland et al. (2020) concluded that there is evidence of an association with liver enzymes, but not with liver disease. Any study that was released after the literature review for the 2021 PFAS Toxicological Profile will be reviewed for possible inclusion in future updates to the profile.

Decreased vaccine response in children

Excluding the very recently published results from Abraham et al. (2020) due to their failure to provide confidence intervals, there have been 11 studies that have examined vaccine antibody response with exposure to PFOS and PFOA (see the table below).

Percent change to tetanus antibody or diphtheria antibody per increase in PFOS or PFOA have been the outcomes most reported.

Vaccine type	Number of studies	Reference(s)
Tetanus	6	Grandjean et al. (2012); Grandjean et al. (2017a); Grandjean et al. (2017b); Granum et al. (2013); Kielsen et al. (2016); Mogenson et al. (2015)
Diphtheria	5	Grandjean et al. (2012); Grandjean et al. (2017a); Grandjean et al. (2017b); Granum et al. (2013); Mogenson et al. (2015)
Rubella	3	Granum et al. (2013); Pilkerton et al. (2018); Stein et al. (2016b)
Measles	2	Granum et al. (2013); Stein et al. (2016b)
Influenza A (H1N1)	2	Looker et al. (2014); Stein et al. (2016a)
Influenza B	1	Looker et al. (2014)
Haemophilus influenza type b	1	Granum et al. (2013)
Influenza A (H1N2)	1	Looker et al. (2014)
Mumps	1	Stein et al. (2016b)
Enterovirus (EV71)	1	Zeng et al. (2019)
Coxsackievirus (CA16)	1	Zeng et al. (2019)

Based on the forest plots below, there appears to be inconsistent evidence to suggest an association with reduced tetanus antibody response for either PFOS or PFOA (Figure 1A and Figure 1B). There is imprecise evidence suggestive of an association between decreased diphtheria antibody response and increased serum concentrations of PFOS or PFOA (Figure 2A and Figure 2B).

Figure 1A:

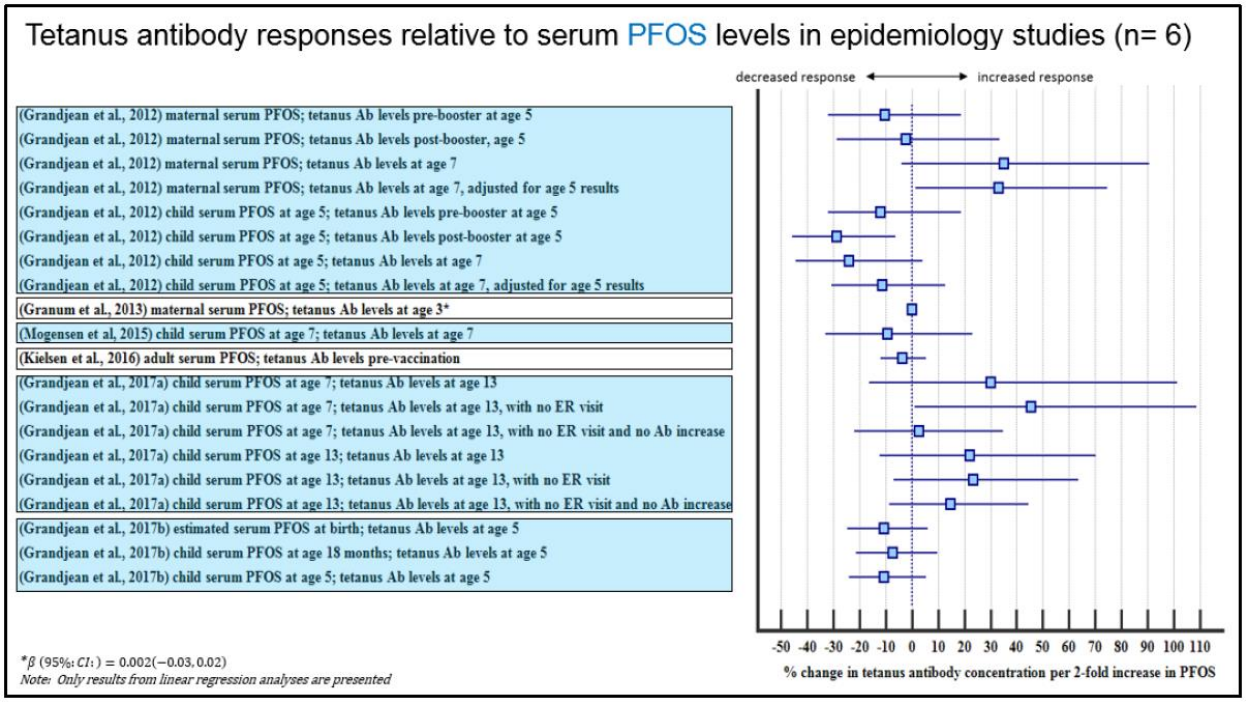


Figure 1B:

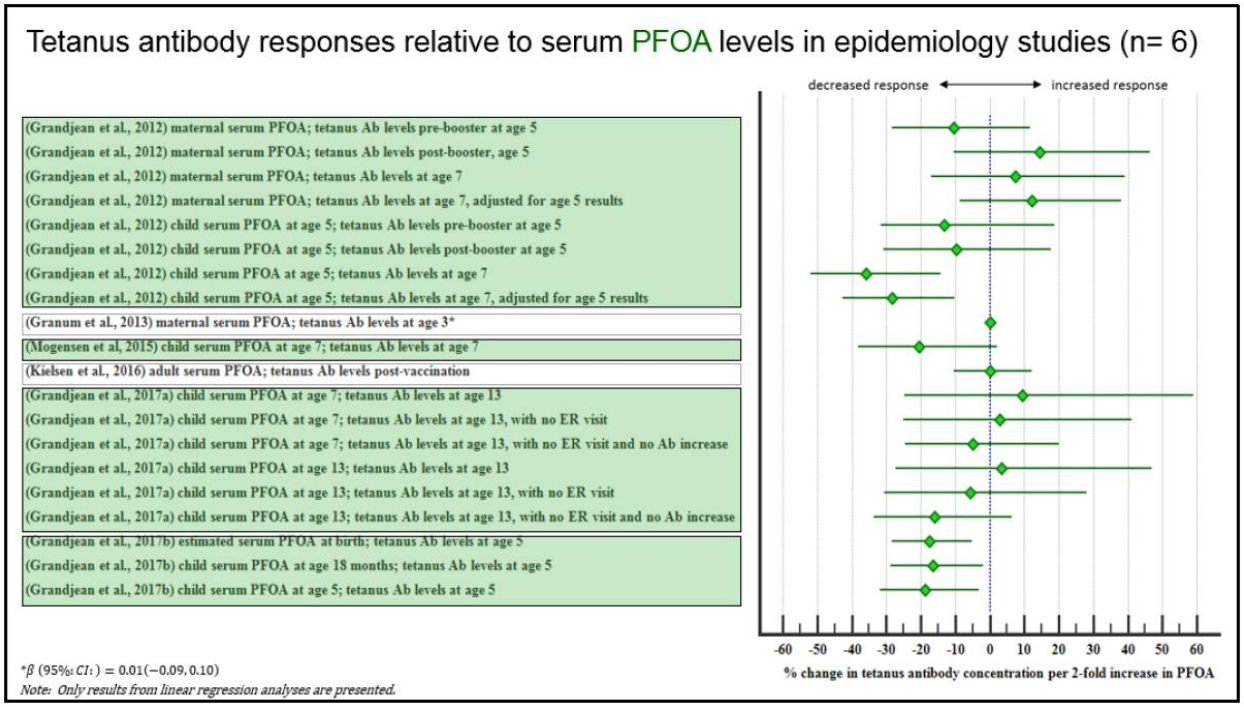


Figure 2A:

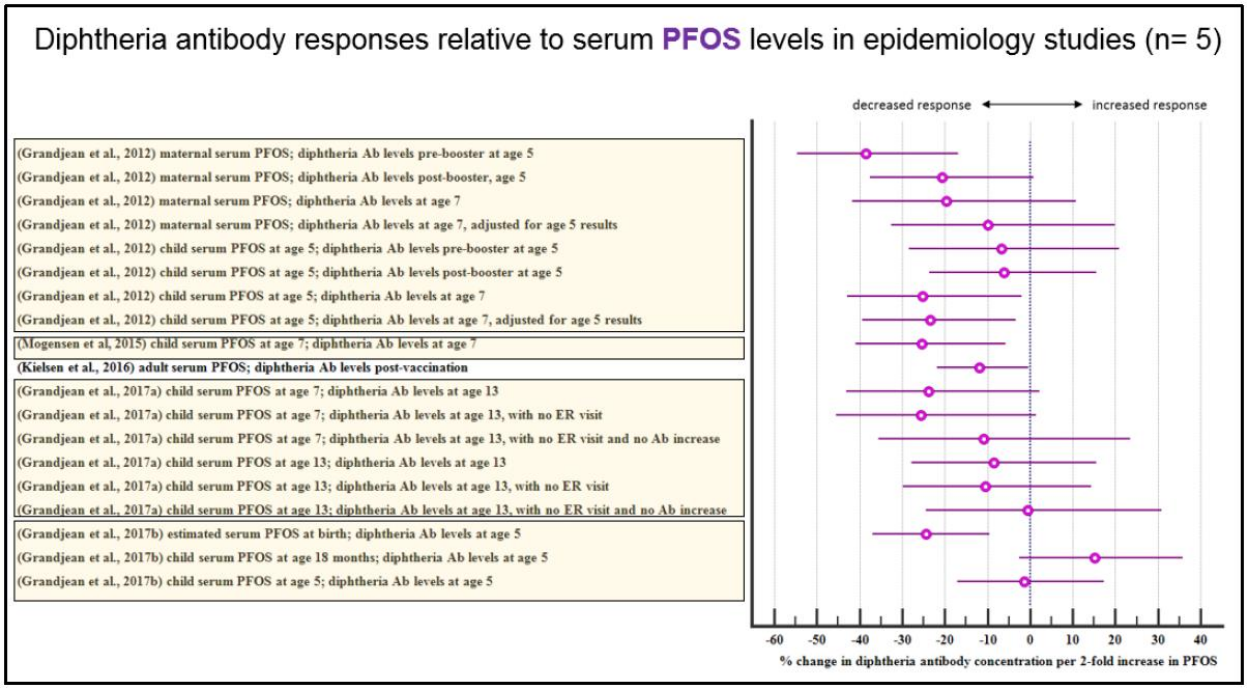
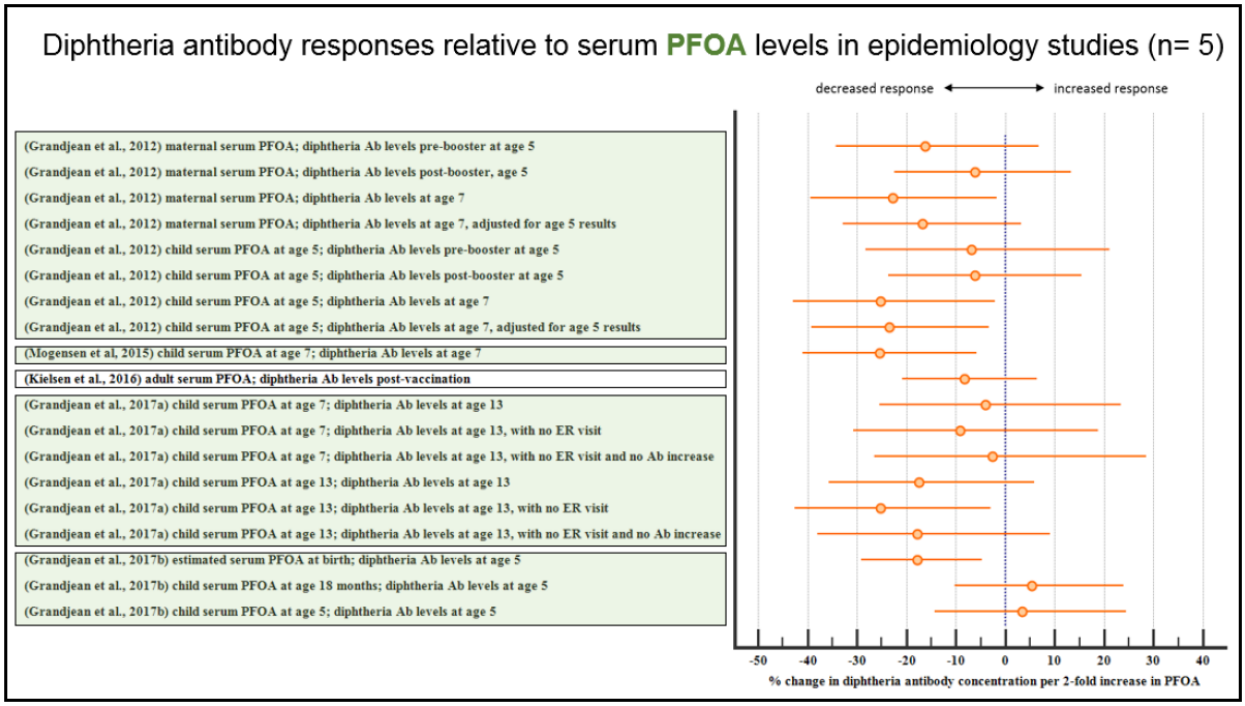


Figure 2B:



Commercially available vaccines differ depending on the nature of the vaccine antigen. Tetanus and diphtheria, for example, are toxoid vaccines whereas measles, mumps and rubella are live attenuated vaccines. Influenza vaccines are inactivated (killed), conjugate or live attenuated depending on the strain and method of administration (e.g., intranasal, injectable). Consequently, each vaccine type elicits an immune response through various

molecular and cellular mechanisms of the immune system. Additionally, all vaccines contain various excipients including adjuvants to improve the antibody response, preservatives, stabilizers, and vehicles for delivering the vaccine which may differ substantially depending on the vaccine (Baxter 2007).

Given the minimum evidence of increased infectious disease susceptibility, it is questionable whether the imprecise decreases in antibody response, as seen in Figures 2A and 2B for diphtheria, are clinically relevant for this disease. Examination of the WHO incidence time series data between 1995 and 2017 indicates very few cases diagnosed in the United States during this time period, likely due to the consequence of the high prevalence of vaccinations (https://apps.who.int/immunization_monitoring/globalsummary/incidences?c=USA). During a similar interval of time (2000 – 2016) since the announced phase-out of perfluorooctanyl chemistry by the commneter and the US EPA PFOA Product Stewardship program, PFOS and PFOA concentrations have declined in the general population by approximately 80 and 70 percent, respectively (CDC NHANES 2019; Olsen et al. 2017).

It is worth noting that PFOS and PFOA have high degrees of binding affinity with serum albumin proteins, therefore, there might be a potential interference between these compounds and the ELISA assay components used to determine serum antibody titers, which normally consist of protein-based buffers and diluents. We are currently unaware of any research that has examined this question.

RESPONSE: The altered responses to different vaccines were considered to collectively suggest an association with serum PFAS levels. ATSDR does not consider the available human data for infectious disease sufficient to assess whether there is an association with serum PFAS levels. ATSDR only suggests an association with antibody responses to vaccines and does not make a general assessment regarding immune function. ATSDR also notes that NTP (2016) concluded that there is a moderate level of evidence from studies in humans that PFOA and PFOS suppress the antibody response.

As discussed in NTP's (2016) systematic review of immunotoxicity associated with exposure to PFOA, there are limited laboratory animal data on antigen-specific IgG antibody response. DeWitt et al. (2008) reported an increase in IgG response to sRBC at mid-dose levels, but not at the higher dose. Yang et al. (2002) reported increases in the primary IgG response to horse red blood cells. The DeWitt et al. (2016) study did not measure IgG response.

ATSDR notes that its statements that the epidemiological data suggest that there is an association between PFOA exposure and altered response to vaccines statement and that laboratory animal data suggest that immunotoxicity is a sensitive endpoint are supported by the NTP (2016) statements that "there is moderate confidence that exposure to PFOA is associated with suppression of the antibody response in humans based on the available

studies" and that "there is high confidence that exposure to PFOA is associated with suppression of the antibody response in animals based on consistent suppression of the primary antibody response in experimental studies in mice."

Finally, for PFOA, the recent review of the PFOA findings from the C8 Science Panel by Steenland et al. (2020) concluded that there is evidence that PFOA is associated with immune response, but uneven evidence for an association with infectious disease.

Although there are inconsistencies in the epidemiological data, ATSDR considers the data to be suggestive of an association between serum PFOS and decreased response to antibodies. Immune effects have been observed in laboratory animals in the absence of overt signs of toxicity such as decreases in body weight.

It is also noted that in its systematic review of immunotoxicity associated with exposure to PFOS, NTP (2016) concluded that "there is moderate confidence that exposure to PFOS is associated with suppression of the antibody response in humans based on the available studies. The results present a consistent pattern of findings that higher prenatal, childhood, and adult serum concentrations of PFOS were associated with suppression in at least one measure of the anti-vaccine antibody response to common vaccines across multiple studies."

In general, the epidemiological studies identify the immune system as a target of PFAS toxicity. The strongest evidence of the immunotoxicity of PFAS in humans comes from epidemiological studies finding associations evaluating the antibody response to vaccines. Associations have been found for PFOA, PFOS, PFHxS, and PFDA. There is also some limited evidence for decreased antibody response for PFNA, PFUnA, and PFDoDA, although many of the studies did not find associations for these compounds. Any study that was released after the literature review for the 2021 Final PFAS Toxicological Profile will be reviewed for possible inclusion in future updates to the profile.

Increased risk of high blood pressure or pre-eclampsia in pregnant women

There is insufficient evidence of an association between PFOA (or any other PFAS) exposure and pregnancy-induced hypertension or pre-eclampsia in pregnant women. Four studies from the mid-Ohio River Valley community studied the association between PFOA exposure and pregnancy-induced hypertension, and they have reported mixed results. Two of these studies (Nolan et al. 2010 and Savitz et al. 2012) showed no associations. The third study by Stein et al. (2009) described modest associations (although not statistically significant) between preeclampsia and exposure to PFOA and PFOS. The fourth study, Darrow et al. (2013), showed significant positive associations with pregnancy-induced hypertension and exposure to PFOA and PFOS but when categorized by quintiles such associations did not increase monotonically (in other words, effects were not shown to increase continuously as serum levels increased).

The draft 2018 ATSDR Toxicological Profile essentially relied on the inconsistent findings from the C8 Science Panel reports to arrive at this conclusion with PFOA when this exposure was estimated through historic exposure modelling for pregnancies in this mid-Ohio River Valley community. The draft 2018 ATSDR Toxicological Profile did cite the one major Norwegian population where PFOA or PFOS were actually measured in mid-gestation (Starling 2014). This study did not confirm an association with pre-eclampsia. Actual measurements during the course of pregnancy were not done in the C8 Science Panel studies.
Not stated in this ATSDR Health Consultation is the fact that in the last two years there have been six papers published examining this association with measured PFOA or PFOS involving 6 other sets of investigators using different populations: five papers have essentially not reported associations between measured (not modelled) PFOA/PFOS and pregnancy-induced hypertension or preeclampsia (Bangma et al. 2020; Borghese et al. 2020; Huang et al. 2019; Rylander et al. 2020; Souza et al. 2020) and one report showed a statistical association for PFOS but not for PFOA (Wikström et al. 2019). This ATSDR Health Consultation should take into consideration the more recently available literature that has been published since the draft ATSDR Toxicological Profile to more fully comprehend the inconsistent evidence that exists in the literature on pregnancy-induced hypertension or pre-eclampsia with exposure to PFOA or PFOS.

RESPONSE: Several studies have evaluated the possible associations between serum PFAS and pregnancy-induced hypertension and pre-eclampsia. Pregnancy-induced hypertension, also referred to as gestational hypertension, is the onset of hypertension after the 20th week of pregnancy and pre-eclampsia is pregnancy-induced hypertension accompanied signs of damage to another organ system, often elevated levels of protein in the urine.

ATSDR acknowledges there are limitations to interpreting the results of the studies examining pregnancy-induced hypertension and/or pre-eclampsia which include inconsistencies in the results, uncertain exposure estimates, misreporting the disease, some studies reliance on self-reported diseases, and a limited number of examined populations. However, the Agency concluded that, overall, the data suggest an association between PFOA and PFOS exposure and an increased risk of pregnancy-induced hypertension/pre-eclampsia. Any study that was released after the literature review for the 2021 Final PFAS Toxicological Profile was completed will be reviewed for possible inclusion in future updates to the profile.

<u>Small decreases in infant birth weight</u>
The ATSDR Health Consultation's assertion that high levels of certain PFAS may lead to small decreases in infant birth weight is not supported by the scientific evidence. Most epidemiologic studies have centered on the association between measured maternal (or cord blood) PFOA and PFOS concentrations and lower birthweight. The epidemiological association for decreases in birthweight has been demonstrated to be the result of confounding or

reverse causation by maternal glomerular filtration rate (GFR). The following brief comments focus on this reported association and why it is clearly not supported by the scientific evidence. Given the amount of published PFAS literature, the draft ATSDR 2018 Toxicological Profile is already out-of-date. Below is a brief review of some of the research on PFOA and PFOS impacts on infant birth weight. In particular, the Health Consultation should review the two most recent publications on infant birth weight and PFOA (Steenland et al. 2019) and PFOS (Dzierlenga et al. 2020).

- ***Johnson et al. (2014) originally concluded in their meta-analysis of epidemiology studies that there was an association between measured maternal (or cord blood) PFOA concentrations and lower birthweight. This analysis, however, did not directly consider the possibility of confounding by the maternal GFR.***
- ***Several months later, Verner et al. (2015) reported findings from their PBPK model/Monte Carlo simulation models and a meta-analysis of a similar collection of epidemiologic studies. The work by Verner et al. was based on a study by Morken et al. (2014) who observed an association between GFR and fetal growth which meant that GFR could potentially confound an association between fetal growth and measured PFOA or PFOS concentrations. Indeed, Verner et al. (2015) found such confounding by the GFR as it biased upwards, up to 50 percent, in their modeling efforts of the association between fetal growth and measured maternal PFOA or PFOS concentrations. Furthermore, the authors reported that confounding by GFR was observed only in the second and third trimesters, not the first trimester, likely because the effect of GFR would be subsequent to the well-known plasma volume expansion that occurs during the first trimester.***
- ***Another meta-analysis was subsequently published by Negri et al. (2017) which expanded to 16 epidemiologic studies. Based on their sensitivity analyses, there were stronger associations from studies conducted in Asia and significant heterogeneity was observed when the measurement of PFOS was done later in the pregnancy or using cord blood. The latter is consistent with the simulation PBPK modelling done by Verner et al. (2015) as it relates to the potential confounding influence of maternal GFR with the timing of when PFOS is measured during pregnancy. Negri et al. also concluded that the animal data showed similar dose-response trends, but the effective serum concentrations in rodents were 100 to 1000 times higher than in humans based on the epidemiological evidence. This led Negri et al. to increase their degree of uncertainty as to the biological plausibility of a causal relationship between PFAS exposure and lower birthweight in humans. This doubt led these authors to suggest there might be some, not yet identified, confounding factors that lead to this spurious association of lower birth weight and perfluoroalkyl measurements in humans.***
- ***Steenland et al. (2018) recognized the distinction in timing of when the PFOA maternal measurement was made based on the findings from the Verner et al. (2015) study. They also elaborated upon the Negri et al. (2017) study by conducting a meta-analysis***

of 24 epidemiologic studies. They stratified their results as to whether the maternal PFOA concentration was measured in the first or the combined second and third trimesters. When maternal PFOA was measured during the first trimester, Steenland et al. (2018) reported a -3.3 gram (95% CI -9.6, 3.0) reduction in birthweight per ng/mL PFOA. When PFOA was measured during second/third trimester, there was a -17.8 gram reduction (95 CI -25.0, -10.6) in birthweight per ng/mL PFOA. Steenland et al. (2018) concluded "restriction to studies with blood sampling conducted early in pregnancy or shortly before conception showed little or no association such that these results are consistent with confounding and /or reverse causation being responsible for the inverse association seen in studies with low background exposure levels and blood sampling conducted later in pregnancy, when confounding and/or reverse causality are likely to be more important."

- ***A very recent (June 2020) published meta-analysis on PFOS and birthweight by Dzierlenga et al. (2020) is consistent with the conclusion offered by Steenland et al. on PFOA and birthweight. Dzierlenga et al. conducted a meta-analysis of 29 published studies and reported the random effects summary was −3.22 g/ng/ml PFOS (95% confidence interval [CI] = −5.11, −1.33). In a subgroup analysis stratified by when in pregnancy the PFOS concentration was measured, the summary for the early group was −1.35 (95% CI = −2.33, −0.37) and for the latter group was −7.17 g/ng/ml (95% CI = −10.93, −3.41). In a meta-regression model including a term for timing of blood draw, the intercept was slightly positive but essentially zero (0.59 g/ng/ml, 95% CI = −1.94, 3.11). In other words, the model indicated that when blood was drawn at the very beginning of pregnancy, there was no relation of birth weight to PFOS. Similar to Negri et al. 2017, Dzierlenga et al. also reported a stronger inverse association in Asian studies that they could not completely explain by their blood draws being from later in pregnancy. Dzierlenga et al. concluded the evidence was weakly or not supportive of a causal association between birthweight and PFOS.***

In conclusion, the essential message from the multiple meta-analyses that have now been conducted, to date, indicate physiological aspects of pregnancy, including plasma volume expansion, GFR, and the timing when the maternal PFAS measurement was made during gestation, are critical points to evaluate. The association between birthweight (few gram reduction) and maternal serum PFOA and PFOS is likely not causal, but rather consistent with confounding and/or reverse causation via increased maternal GFR as a consequence of plasma volume expansion during first trimester.

RESPONSE: Concerning PFOA and birth weight, Steenland et al. (2018) state that "present human evidence provides only modest support for decreased birthweight with increasing PFOA." They do not say that there is no evidence. Steenland et al. go on to say that "…studies with blood sampled early in pregnancy, showed little or no association of PFOA with

birthweight. These are studies in which confounding and reverse causality would be of less concern." The concern with this statement is that although this evidence—blood sampled early in pregnancy showing little effect on birth weight—is consistent with reverse causation because of pregnancy hemodynamics, it is also true that for exposures to air pollutants, solvents, and disinfection byproducts, (to name only a few chemical exposures where the following is the case), the impact on birth weight is most often seen from second and third trimester exposures, not early in pregnancy. So, the evidence that early PFOA blood measurements have little effect on birth weight is also consistent with findings for other chemical exposures; that is, the impact is greater for exposures measured later in pregnancy. Dzierlenga et al. (2020) found that "in a subgroup analysis stratified by when in pregnancy the PFOS concentration was measured, the summary for the early group (pre-pregnancy, 1st and 2nd trimester) was −1.35 (−2.33, −0.37) and for the later group (2nd and 3rd trimester cord blood) was −7.17 (−10.93, −3.41). When blood was drawn at the very beginning of pregnancy, there was essentially no relationship of birth weight to PFOS concentration." The simulations in Verner et al. (2015) produced similar findings. The conclusion in the Verner et al. (2015) paper is that pregnancy hemodynamics may account for some (not clear how much) but not all the effect of PFOA and PFOS on birth weight. So, the question is whether the evidence is consistent with reverse causation/confounding by eGFR (due to pregnancy hemodynamics) or consistent with what happens with other chemical exposures (i.e., the impact occurs with later in pregnancy exposures) or both. ATSDR is not aware of any studies that measure both eGFR and serum PFAS later in pregnancy and birth weight. Such studies might, more definitively, answer this question. Until further evidence is forthcoming, ATSDR believes that it is safe to say that the evidence for an effect of PFOA and PFOS on birth weight is modest.

Second, before claiming that confounding (or reverse causation) exists, it is important to provide evidence that the risk factor doing the confounding is actually a risk factor for birth weight and if so, the magnitude of the effect of the risk factor. If the risk factor has only slight or moderate effects on birth weight, it would require an extremely strong association with PFAS to have appreciable confounding/reverse causation impact. ATSDR's review of the evidence so far did not identify much impact of eGFR on birth weight unless the woman has preeclampsia. For women without preeclampsia, there seems to be little if any evidence for an impact of eGFR on birth weight (regression coefficient = 0.2 grams), and even including women with preeclampsia, the partial correlation was a small, r= 0.07 [Morken et al. 2014]. This finding is contrary to what is stated (and used) in the Verner et al. (2015) study. If there is confounding or reverse causation, it appears to be rather minimal so far. A study by Sagiv et al. (2018) saw no evidence of reverse causation or confounding, but the study measured PFAS and eGFR early in pregnancy. Moreover, the effect of eGFR on PFAS serum levels would be slightly early in pregnancy as would the effect of PFAS measured early in pregnancy on birth weight if PFAS

exposure (like other chemical exposures) impacts birth weight mostly when exposures are measured later in pregnancy.

Third, there is some evidence that parity and sex of the child modify the effect of PFAS on birth weight. Why this happens is not understood (see for example, Kashino et al. Environ Int 2020, March 136:105355). But this effect modification should not be ignored and provides additional evidence for a PFAS effect on birth weight for vulnerable subpopulations.

ATSDR has different interpretation of the available data that suggest no association between serum PFOA/PFOS and birth weight but acknowledges that there is some uncertainty.

Comment: (5.1.2 Cancer Health Effects) Based on a weight-of-evidence approach to evaluate epidemiologic studies, the draft 2018 ATSDR Toxicological Profile did not list cancer as a potential health effect associated with perfluoroalkyl exposure (ATSDR 2018), but cited both IARC (2017) and EPA (2016a; 2016b) conclusions of the carcinogenic potential of PFOA and PFOS.

> ***"The International Agency for Research on Cancer (IARC 2017) concluded that PFOA is possibly carcinogenic to humans (Group 2B) and EPA (2016e, 2016f) concluded that there was suggestive evidence of the carcinogenic potential of PFOA and PFOS in humans. Increases in testicular and kidney cancer have been observed in highly exposed humans."***

It is important to note that IARC considered PFOA to be a 'possible' human carcinogen based, in part, on limited epidemiologic evidence on testicular and kidney cancer but could not rule out chance, bias or confounding with reasonable confidence in its evaluation of the literature (Benbrahin-Tallaa 2014).

RESPONSE: As a general rule, ATSDR relies on the other agencies' determination of carcinogenicity. ATSDR's current language in this health consultation includes the correct designation by IARC that PFOA is a possible human carcinogen. Moreover, in their review of the available epidemiology data, IARC (2017) concluded that the evidence for testicular cancer was "considered credible and unlikely to be explained by bias and confounding, however, the estimate was based on small numbers." Similarly, IARC (2017) concluded that the evidence for kidney cancer was also credible but noted that chance, bias, and confounding could not be ruled out with reasonable confidence. They considered that there was limited evidence in humans for the carcinogenicity of PFOA. See additional comments below regarding the association of PFOA and kidney and prostate cancers and the current knowledge of the association of PFOS with bladder cancer in human studies and the possible association of PFOS with liver, thyroid, and mammary tumors from animal studies.

Kidney cancer

Steenland and Woskie (2012), a DuPont worker cohort mortality study, is often cited as evidence of an association with kidney cancer; however, Steenland and Woskie only examined kidney cancer mortality – not kidney cancer incidence. PFOA (ammonium salt) was used as a processing aid in the polymerization of tetrafluoroethlyene (TFE) to make polytetrafluoroethylene (PTFE). TFE is a known renal carcinogen in rats. Steenland and Woskie did not consider the potential confounding exposure of tetrafluoroethylene (TFE) at this DuPont West Virginia plant due to the explosive nature of TFE. ATSDR needs to appreciate the fact that the lower explosion limit for TFE is 110,000 ppm (ACGIH 2001; Olsen 2015). The 8-hour time weighted average for worker exposure to TFE is 2 ppm. Thus, TFE exposure would have occurred at the DuPont plant but considerably below the lower explosion limit. Therefore, the confounding effect of TFE exposure was not considered by Steenland and Woskie (2012) yet it should have been. ATSDR should be aware of Consonni et al. (2013), who concluded they could not "disentangle' the association between TFE and PFOA in their multiple cohort mortality study of TFE exposures (which included the DuPont West Virginia plant). A study by Barry et al. (2013) did not find an association with kidney cancer incidence in a subset of DuPont workers from the C8 Science Panel community worker cohort study. The studies by Leonard et al. (2006; 2008) are the same kidney cancer deaths as discussed in Steenland and Woskie (2012) as both studies discuss 12 male kidney cancer deaths. The Leonard et al. study did not report kidney cancer incidence cases. Raleigh et al. (2014) studied both kidney cancer mortality and incidence at the 3M Cottage Grove PFOA manufacturing plant that had near absence of exposure to TFE (unlike the DuPont worker population) yet reported some of the highest exposures to PFOA. Raleigh et al. did not see an increase in kidney cancer with increasing categorical exposures of PFOA.

Prostate cancer

This ATSDR Health Consultation opines that epidemiologic data suggested a "link" between PFOA and prostate cancer. This opinion is not supported by two reviews of the epidemiology data: 1) the lack of a "probable link" determination review for prostate cancer provided by the C8 Science Panel https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3855514/pdf/ehp.1306615.pdf and 2) by IARC (2017) that judged the human evidence association between PFOA and prostate cancer to be "inadequate." This ATSDR Health Consultation does not describe how it arrived at their contrary opinion of the epidemiology data. None of the largest epidemiologic studies conducted, to date, whether those with the highest PFOA occupational exposures (Steenland and Woskie et al. 2012, Barry et al. 2013; Steenland et. al. 2015; Raleigh et al. 2014) or of an exposed mid-Ohio River Valley community through consumption of drinking water containing

PFOA (Barry et al. 2013) provided evidence to suggest an association exists in these studies with prostate cancer mortality (Steenland and Woskie et al. 2012; Raleigh et al. 2014) or incidence (Barry et a.2013; Steenland et al. 2015; Raleigh et al. 2014) with PFOA. Depending on the study, <u>estimates</u> of exposure were calculated as cumulative serum µg/mL-years or cumulative exposure µg/m3-years. The C8 Science Panel stated their strongest evidence from their own research that led them to conclude there was not a probable link for prostate cancer was their community worker cohort incidence study of 32,541 individuals that reported identical 10-year lags of hazard ratio trends of 0.98 for logged estimated cumulative PFOA serum concentration of prostate cancer risk in both the community (p = 0.58) and occupational (p = 0.83) groups (Barry et al. 2013). Analyzing a similar subset of occupational workers that Barry et al. observed, Steenland et al. reported a 10-year lagged trend in hazard ratios for prostate cancer incidence quartiles (p = 0.10) but this was not seen when analyzed as log cumulative exposure (p = 0.91). The only other possible evidence by the C8 Science Panel was a geographical analysis of the community by Viera et al. (2013) that showed a higher adjusted odds ratio (OR = 1.5, 95% CI 0.9, 2.5) for prostate cancer in the Ohio water district that had the highest concentration of PFOA in the drinking water. Many of these prostate cancer cases were included in the Barry et al. study. Higher level PSA tests were not shown to be associated with PFOA exposure in the affected community (Ducatman et al. 2015). In a different occupational population of highly exposed PFOA manufacturing workers, Raleigh et al. did not observe an exposure trend in quartile hazard ratios for prostate cancer incidence (1.0 reference other non-exposed workers, 0.80, 0.85, 0.89., 1.11). A total of 461 prostate cancer cases were included in this analysis. A study in a Danish general population study with serum concentrations orders of magnitude below the above occupational or affected community studies reported an adjusted incidence rate ratio trend of 1.03 (95% CI 0.99, 1.07) for prostate cancer. A case-control study of a different general population with low PFOA exposure reported an association between prostate cancer and PFOA > median with a first degree relative (OR = 2.6, 95% CI 1.2, 6.0) that was based on 24 cases (Hardell et al. 2014). Keeping the concept of dose response in mind, the above collective evidence clearly does not support the conclusion in this ATSDR Health Consultation that a "link" exists between exposure to PFOA and prostate cancer mortality or incidence.

RESPONSE: Recently, Steenland et al. (2020) reviewed the evolution of evidence on the PFOA and health findings following the assessment of the C8 Science Panel. Below are their findings:

"Overall, we found 19 epidemiologic studies of PFOA and cancer, six of which were of occupational cohorts (of which two were updates of the original cohorts) (see Table S1). In 2012, the Science Panel concluded that there was a probable link between PFOA and both testicular and kidney cancers (C8 Science Panel 2012). The modest evidence that has accumulated since that time does not generally strengthen the conclusion that PFOA is

carcinogenic for any given site, also there is somewhat stronger evidence for kidney cancer. Despite these caveats, we believe the evidence for an association of PFOA with testicular cancer is suggestive overall, with two Science Panel studies, one cohort (Barry et al. 2013), one ecological/case-control (Viera et al. 2013), having found a relatively strong positive exposure–response for this cancer, supported by animal studies (ATSDR 2018). Testicular cancer is rare and generally not fatal (American Cancer Society 2020), and only Science Panel studies have reported on its relation to PFOA, limiting conclusions (Leonard et al. 2008 also reported on testicular cancer mortality but had only 1 death). The evidence for kidney cancer, also implicated by the Science Panel in their community (Barry et al., 2013) and worker (Steenland and Woskie 2012) cohorts, also remains suggestive although not consistent in newer studies. Kidney cancer was not found in a high-exposure occupational cohort of 3 M workers (Raleigh et al. 2014) based on mortality or incidence, although the number of kidney cancers was small (16 exposed incident cases). Mastrantonio et al. (2017), in an ecologic study in the Veneto region of Italy, comparing areas with PFOA-contaminated drinking water (as well as some other PFAS) with areas with non-contaminated water, did not find an excess of kidney cancer overall, although some excess among women (SMR 1.32(95% CI 1.06–1.65)). Finally, a recent population-based case-control study by U.S. National Cancer Institute investigators, with 324 renal cancer cases and 324 individually matched controls, found a positive exposure–response trend with renal cancer for several PFAS including PFOA, perfluorooctane sulfonic acid, and perfluorohexane sulfonic acid. Only the association with PFOA remained apparent after adjustment for all three chemicals (Shearer et al. 2020). It should be noted that this general population study had much lower exposure contrasts than other studies. There is little evidence for a relationship of PFOA with either liver or pancreatic cancer, tumors of which are associated with PFOA in animal studies (ATSDR 2018), with the exception of an increased risk for liver cancer, recently seen in Italian workers exposed occupationally to PFOA (Girardi and Merler, 2019). In our view there is some suggestive evidence for prostate cancer (positive Lundin et al. 2009; some suggestion Vieira et al. 2013, Hardell et al. 2014, Steenland et al. 2015; largely negative Ericksen et al. 2009, Steenland and Woskie 2012, Barry et al., 2013), but results are inconsistent. This inconsistent evidence has led other reviewing bodies such as IARC (IARC, 2018), ATSDR (ATSDR 2018), and EFSA (EFSA Contamination Panel 2018), to similarly conclude the evidence for PFOA carcinogenicity remains suggestive but not conclusive."

The bottom-line conclusion from Steenland et al. (2020) is that, for cancer, the epidemiological evidence remains supportive but not definitive for kidney and testicular cancers. Moreover, ATSDR believes that the findings from the U.S. National Cancer Institute [Shearer et al. 2020] of the association between PFOA and kidney cancer in humans is particularly suggestive. In addition, as stated above, Steenland et al. conclude that there is some suggestive evidence for

an association between PFOA and prostate cancer; however, the results are inconsistent. ATSDR agrees with these conclusions and has updated this health consultation accordingly.

Bladder cancer

The ATSDR Health Consultation misinterprets the series of events that resulted in several epidemiologic studies conducted by 3M and/or the University of Minnesota. Specifically, the ATSDR Health Consultation wrote (see page 15): "Epidemiology studies of PFOS-exposed workers reported an increased risk for some cancers; however, because of small sample sizes, the results were not statistically significant (Alexander et al. 2003; Alexander and Olsen 2007; Grice et al. 2007; Olsen et al. 2004)." In fact, the original study by Alexander et al. reported a large, highly imprecise, but nevertheless statistically significant SMR for bladder cancer (SMR = 12.77; 95% CI 2.63 to 37.35). In a series of investigations that followed, Olsen et al. analyzed health claims data for the Decatur manufacturing site. They reviewed 204 inpatient and 34,053 outpatient claims for the 652 chemical plant employees and 237 inpatient and 40,174 outpatient claims for the adjacent film plant employees to ascertain any additional prevalent bladder cancer cases let alone other cancer and non-cancer claims data. No bladder cancer claims were found for workers in the chemical plant and 1 bladder cancer claim was found in the film plant. Another follow-up study, as reported by Alexander and Olsen (2007), examined medically validated self-reported incidence of bladder cancer of current and former Decatur employees who worked one year or longer. A total of 11 bladder cancer cases were identified (8.6 expected, SIR = 1.28 (95% CI 0.64-2.29)). The expected numbers were based on NCI SEER data. Compared with employees in the lowest cumulative exposure category, the relative risk of bladder cancer was 0.83 (95% CI 0.15-4.65), 1.92 (95% CI 0.30-12.06), and 1.52 (95% CI 0.21-10.99). Alexander and Olsen concluded these results did not confirm the high excess risk of bladder cancer that was reported in the mortality study by Alexander et al. but the possibility remained for a smaller risk in the higher exposed workers. However, the limited size of the population prohibited a conclusive exposure response analysis. The paper by Grice et al. examined other self-reported data including bladder calculi and cystitis. These associations were not observed by Grice et al. Not cited by the ATSDR Health Consultation was a population-based bladder cancer incidence study conducted in Denmark (sponsored by the International Institute of Epidemiology who received funds from 3M). A total of 332 bladder cancer cases were identified over an approximate 10-year time period. Based on 5th to 95th percentile plasma PFOS samples that ranged in this general population between men (17.4 – 60.9 ng/mL) and women (14.0 – 58.1 ng/mL) yielding respective geometric means of 35.1 ng/mL and 32.1 ng/mL, Eriksen et al. (2009) reported on their adjusted incidence rate ratios for the three upper quartiles of plasma concentration compared with the lowest quartile. For PFOS, these incidence rate ratios were: 1.00 (reference); 0.76 (95% CI 0.50-1.16); 0.93 (95% CI 0.61-1.41), and 0.70 (0.46-1.07). The Eriksen et al. findings did not support the

hypothesis that PFOS might be associated with bladder cancer at general population levels of PFOS. Finally, the commenter notes there was not an increased risk of bladder tumors in a 2-year bioassay of Sprague Dawley rats (Butenhoff et al. 2012). In conclusion, the commenter recommends that the ATSDR Health Consultation correctly interpret this series of events as it relates to bladder cancer and PFOS that occurred at the Decatur plant.

RESPONSE: ATSDR has revised the statement referred to in this comment to:
Epidemiology studies of PFOS-exposed workers reported an increased risk for some cancers; however, because of small sample sizes, the confidence intervals were wide, indicating considerable uncertainty in the effect estimates [Alexander et al. 2003; Alexander and Olsen 2007; Grice et al. 2007; Olsen et al. 2004].

The bottom-line conclusion that "a causal link between cancer and PFOS exposures, based on human studies, remains uncertain" was not changed.

Comment: (Page 15, section 5.1.2 and Page 41, conclusion 1: The Health Consultation had made the following statements: "Animal studies have found limited but suggestive evidence of PFOS exposure and increased incidence of liver, thyroid, and mammary tumors" (page 15) and "Animal studies suggest a link between PFOS exposure and several cancers" (page 41).) The assertions above are only partially incorrect and reflect a lack of understanding of the context of the studies on which they rely.

1. ***In laboratory rats, the only chronic study with PFOS (Butenhoff et al. 2012) reported increased incidence of benign liver adenomas; however, subsequent detailed mechanistic evaluations demonstrated that the activation of hepatic nuclear receptor such as PPAR and CAR in rodents can lead to the development of liver tumors (Elcombe et al. 2012a; Elcombe et al. 2012b; Klaunig et al. 2003; Klaunig et al. 2012; Gonzales et al. 1998). More importantly, extensive research studies have shown that this pathway is unlikely to occur in humans due to species difference (Gonzales and Shah 2008; Elcombe et al. 2014; Corton et al. 2014). Therefore, the development of liver tumors in humans with exposure to PFOS would not be expected; and no association has been reported in epidemiological studies.***
2. ***From the same chronic study by Butenhoff et al., there was no increased incidence of thyroid tumor in rats that had received PFOS treatment for two years, nor was there a significant trend in thyroid tumors across treatment groups (control and four PFOS dietary dose groups at 0.5, 2, 5, and 20 ppm). At the end of the two-year study period, there was a statistically significant increase in thyroid follicular cell adenoma in male rats that received 20 ppm dietary PFOS for one year followed by another year of control diet, the finding was considered spurious given that similar observation was***

not reported for male rats or female rats that had received 20 ppm dietary PFOS for the entire two years.

3. ***From the same chronic study by Butenhoff et al., there were statistically significant <u>decreased</u> trends in the incidences of mammary fibroadenoma and combined mammary adenoma and fibroadenoma in PFOS-treated female rats compared to control. The decreased (not increased) trend in mammary adenoma is in direct contrast to what the Health Consultation had stated above.***

RESPONSE: From ATSDR's Final Toxicological Profile (2021), an increase in hepatocellular adenomas was observed in male rats exposed to dietary PFOS for 2 years; thyroid follicular cell adenomas were observed in rats exposed to PFOS for 1 year and allowed to recover for an additional year. Moreover, from U.S. EPA (2016a), "in the only chronic oral toxicity and carcinogenicity study of PFOS in rats, liver and thyroid tumors (mostly adenomas) were identified in both the controls and exposed animals at levels that did not show a direct relationship to dose." Therefore, animal studies have found limited but suggestive evidence of the association of PFOS exposures and liver and thyroid tumors. The commenter is correct about mammary gland tumors; this is, according to ATSDR (2021), "In females, there were also significant negative trends for mammary adenoma and fibroadenoma carcinoma combined." Because of this information, ATSDR has deleted the suggestion that mammary gland tumors have been associated with PFOS exposures in animal studies. Finally, ATSDR has added a statement that there is uncertainty in these associations as the tumors did not show a direct relationship to dose and the mechanism of action may not be relevant to humans.
With that, ATSDR is not discounting the animal studies but is acknowledging the limitations especially with relevance to humans.

Comment: (Pages 16 - 17, section 5.1.3: The Health Consultation had made the several inaccurate / inconsistent statements on the provisional MRLs for PFOA, PFOS, and PFHxS which were released for public comments in 2018 by ATSDR.) Because the draft ATSDR 2018 Toxicological Profile is a draft document, this ATSDR Health Consultation should cite the MRLs as proposed MRLs as the final (non-draft) document has not been issued by the ATSDR.

The high-level summary provided in this section for PFOA, PFOS, and PFHxS provisional MRLs was not only inconsistent within the same paragraph itself, it also was inconsistent when compared to the draft PFAS Toxicological Profile released by ATSDR in 2018. These included:

1) ***According to the draft PFAS Toxicological Profile, the provisional LOAELHED for PFOA based on Koskela et al. 2016 study was 8.21 x 10-4 mg/kg/day. This provisional LOAELHED (8.21 x 10-4 mg/kg/day) was mentioned in current Health Consultation in the beginning of the third paragraph on page 16; however, at the end of that very same paragraph, it stated "The estimated LOAELHED based on the Koskela et al. 2006***

study is 2.1 × 10-3 mg/kg/day." The inconsistency in the data presentation is not only misleading, but also confusing to the readers. Further clarification is required.

2) ***Based on the draft PFAS Toxicological Profile, only HED NOAEL was proposed for PFHxS (as 4.7 x 10-3 mg/kg/day based on a POD of 1 mg/kg/day). There was no mentioning of a HED LOAEL or LOAELHED for PFHxS. It was not clear why the current Health Consultation stated that "ATSDR estimates that the HED LOAEL for the above studies to be 7.3 x 10-3 mg/kg/day."***

   If the current Health Consultation's intent was to calculate the MOE based on HED LOAEL (as it later stated and showed in the document), then the inferred HED LOAEL for PFHxS should be 3 times higher than the HED NOAEL because the critical study's NOAEL and LOAEL were 1 mg/kg/day and 3 mg/kg/day, respectively. Therefore, the inferred HED LOAEL for PFHxS should be 14.1 x 10-3 mg/kg/day, not 7.3 x 10-3 mg/kg/day.

RESPONSE: ATSDR's approach for MRLs developed based on a draft toxicological profile is to designate them as "provisional". The same approach was taken for MRLs based on the 2018 draft PFAS Toxicological Profile. However, because the PFAS Toxicological Profile has been finalized, the word "provisional" is no longer needed and was deleted in the final version of the health consultation. For comment #1, the reference here should be the Leubker (2005) study for PFOS, and not the Koskela et al. (2016) study. This has been corrected.

For comment #2, HEDs in this health consultation were calculated using the same process as was used for MRL derivation. This process is detailed in the introduction to the MRL worksheets (Appendix A of the 2021 Final PFAS Toxicological Profile). The inherent problem with PFAS is that one cannot extrapolate directly from dose to serum level. For this reason, ATSDR has taken the steps of estimating time-weighted average serum levels based on pharmacokinetic or PK models (for PFOA and PFOS) or measured serum levels (for PFHxS and PFNA) based on the trapezoid rule.

HED values are based on steady state serum concentrations. Ideally, this type of extrapolation from applied dose to HEDs would be possible, but it is not the case for PFAS. There is an intermediate step from applied dose to steady state serum concentrations to HEDs. Time-weighted average serum concentrations are estimated from the measured serum concentrations from the study of interest from the areas under the curve calculated using the trapezoid rule. The serum concentrations for the 1 mg/kg/day dose group were 80.97mg/L after 14 days and 89.12 mg/L after 42 days. On the other hand, for the 3 mg/kg/day dose group, the concentrations were 143.05 mg/L after 14 days and 128.67 mg/L after 42 days. As can be seen, a 3-fold increase in dose does not result in a 3-fold increase in serum levels.

Therefore, the HED LOAEL should not necessarily be 3 times higher than the HED NOAEL. ATSDR has re-checked and verified these calculations.

A footnote has been added to the final health consultation explaining how ATSDR calculated HEDs that were not reported in the Final 2021 PFAS Toxicological Profile.

Comment: (Page 17, section 5.1.3: The Health Consultation's approach using dose additive risk assessment methods in evaluating mixtures of PFAS.)

The current Health Consultation has analyzed the mixture effect by additivity assuming that the compounds (in the mixture) are toxicologically similar. This assumption is incorrect and it is in direct contrast to the draft ATSDR Toxicological Profile (2018) in which it clearly acknowledged that approaches such as toxic equivalency factor approach would not be suitable for perfluoroalkyls. In addition, while the Health Consultation stated that "ATSDR also conducted a qualitative analysis of the scientific literature to determine which PFAS might have similar target organ effects", it did not report to what (ATSDR's) findings were on the analysis **mentioned above.**

RESPONSE: ATSDR assumes additivity if there is insufficient evidence to the contrary. For the four PFAS with ATSDR MRLs, ATSDR's default approach of additivity was used and there is nothing in the literature yet to suggest that this approach is incorrect. The approach taken by ATSDR in this health consultation to evaluate mixtures is not a toxic equivalency factor (TEF) approach for this class of chemicals—ATSDR is not currently recommending using a TEF approach for PFAS.

Comment: (Page 19, Table 2: The Health Consultation's calculation on HQ, MOE, and HI for selected wells.)
The calculations presented in Table 2 on the Health Consultation need to be clarified.

1) ***The inferred HED LOAEL for PFOS on the developmental effect was not stated anywhere in this document. This information should be added.***
2) ***Similarly, the HED LOAEL for PFOS on the immune effects, based on the studies by Guruge et al. (2009) and Dong et al. (2011) should also be provided for the readers. While the 2018 draft ATSDR PFAS Toxicological Profile did specify what LOAELs were, the HED LOAELs for these two studies were not mentioned at all.***
3) ***As stated above, the current Health Consultation should clarify the source for the HED LOAEL for PFHxS.***

RESPONSE: See response above relating to a similar comment on how ATSDR calculated HEDs that were not presented in the Final 2021 PFAS Toxicological Profile.

Comment: (5.5.3 Biomonitoring results)
This ATSDR Health Consultation does not provide any data in this section. It references itself (ATSDR 2020) by providing a web address (for itself) which provides no human biomonitoring data. Tabular or graphical data should be presented in this section for this Pease area community as well as corresponding NHANES data. A web address should also be provided for the NH citation.

RESPONSE: The reference below was used in this health consultation to refer readers of this consultation to a summary of the biomonitoring data and findings. The reference cited is not this health consultation on private wells near the Pease Tradeport, but the final ATSDR health consultation on the Pease Tradeport public water system that assessed the public health implications of PFAS exposures to persons who drank water from that system. Any resident who wants to review ATSDR's summary of the biomonitoring data relating to the Pease community should use the link below.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2020. Health Consultation - Final Version - Per and Polyfluoroalkyl Substances (PFAS) in the Pease Tradeport Public Water System. EPA PWS ID: 1951020 Portsmouth, Newington, and Greenland, NH EPA Facility ID: NH7570024847. Agency for Toxic Substances and Disease Registry. March 20, 2020. [updated 2020 March 30; accessed 2020 March 30]. Available from: https://www.atsdr.cdc.gov/HAC/pha/pease/Pease_Air_Force_Base_HC-508.pdf.

Comment: (What are the Cancer Health Effects of PFAS?, page 15, line 4) "Epidemiologic data suggest a link between PFOA exposure and elevated rates of kidney, prostate, and testicular cancers."
Recommendation:
Add a citation(s) to support this assertion.

RESPONSE: ATSDR has added in the following references to support this statement for the association between PFOA and kidney, prostate, and testicular cancers:

IARC (2017). IARC monographs on the evaluation of carcinogenic risks to humans. Some chemicals used as solvents and polymer manufacture. Vol. 110. IARC Press, Lyon. http://monographs.iarc.fr/ENG/Monographs/vol110/mono110.pdf.

Shearer JJ, Callahan CL, Calafat AM, Huang W, Jones RR, Sabbisetti VS, Freedman ND, Sampson JN, Silverman DT, Purdue MP, Hofmann JN. 2020. Serum concentrations of per- and polyfluoroalkyl substances and risk of renal cell carcinoma, *JNCI: Journal of the National Cancer Institute*, djaa143. [updated 2020 September 18; accessed 2020 December 21]. Available from: https://doi.org/10.1093/jnci/djaa143

Steenland K, Fletcher T, Stein CR, Bartell SM, Darrow L, Lopez-Espinosa MJ, Barry Ryan P, Savitz DA. Review: Evolution of evidence on PFOA and health following the assessments of the C8 Science Panel. Environ Int. 2020 Dec;145:106125. http://doi: 10.1016/j.envint.2020.106125. E-pub 2020 Sep 18.

See additional ATSDR responses to similar comments above.

Comment: (Section 5.2, page 18) The title of this section Wells with Potential PFAS Hazards/Risks lists five wells, though Table 2 includes ten.
Recommendation:
Relocate Table 2 to after Section 5.3 or at the end of the document.

RESPONSE: Table 2 presents the public health implication measures calculated by ATSDR to help determine if a potential hazard exists or risks of harmful effects are possible. This table evaluated any private well that had at least one PFAS above an ATSDR HBCV. In the final analysis, five of the 10 wells with data presented in Table 2 were determined to be a hazard—the remaining wells were then evaluated in other sections to determine if ATSDR could make a health determination based on the entire mixture of PFAS presented in any given well.

Comment: (Section 5.2.1, page 18) Hazard Index and Hazard Quotient have very specific meaning and resultant actions under CERCLA when exceeding 1.0. As the HBCVs have not yet met even Tier 3 of the USEPA Hierarchy of Toxicity Values appropriate for calculation of HI and HQ, recommend an alternate terminology be used.
Recommendation:
For HI and HQ, use only toxicity values meeting the Hierarchy established for use under CERCLA; ratios in comparison to HBCVs should be given alternate titles.

RESPONSE: ATSDR does not calculate any ratio measures that compares a media-specific exposure concentration to an HBCV. In this health consultation, ATSDR only calculated HQs and HIs in relation to dose measures with ratios calculated based on the exposure dose and associated MRL. ATSDR's guidance indicates that health assessors calculate HQs based on applicable MRLs or EPA RfDs. If an HQ is above 1.0, then ATSDR further evaluates that exposure to determine if harmful effects are possible. If a mixtures evaluation is conducted, then ATSDR

uses these same HQs to calculate HIs for further evaluation of the public health implications of the mixture. See ATSDR's mixture guidance at:

> ATSDR 2018. Framework for Assessing Health Impacts of Multiple Chemicals and Other Stressors. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Agency for Toxic Substances Disease Registry. https://www.atsdr.cdc.gov/interactionprofiles/index.asp

Comment: (Section 5.2.1 & Table 2, page 18 and 19) Margin of Exposure is introduced and then presented in Table 2 prior to any context as to what the numbers mean. Embedding in a table of HI/HQ, where a higher number, typically means more risk while the opposite is true for MOE, needs to be explained prior to presentation.
Recommendation:
Either move definition of Margin of Exposure earlier in the document or relocate Table 2 to after section 5.3.

RESPONSE: ATSDR has revised the text to define margin of exposure before the presentation of Table 2.

Comment: (Page 20, 4th paragraph) Margin of Exposure is defined here.
Recommendation:
Either move definition to 5.2.1 where concept is first introduced or move Table 2 to after section 5.3.

RESPONSE: ATSDR has revised the text to define margin of exposure before the presentation of Table 2.

.

Comment: (Page 20, 4th paragraph) Last sentence states that MOE was calculated for five listed wells, but it was actually calculated for 10.
Recommendation:
Relocate or split Table 2 to present information for different sub-sets of wells.

RESPONSE: The sentence from the health consultation mentioned in the comment is in *Section 5.2 Wells with Potential PFAS Hazards (RES17, RES19, RES21, RES23, and RES37).* Therefore, the sentence referring to five wells is correct. Please see response to other comment above about what is presented in Table 2.

Comment: (Page 20, line 12, PFOA and PFOS) "HQs for PFOS were greater than for PFOA" missing word.

Recommendation:
Add "HQs" after "than".

RESPONSE: Suggested edit accepted.

Comment: (Page 20, line 17, PFOA and PFOS) "However, the HQ of 1.01 was slightly elevated for young children using the RME scenario for RES21." Is this finding meaningful, the article states that those HQs equal to or less than 1.00 are likely not associated with adverse health outcomes.
Recommendation:
Recommend rewording, "The RME scenario for RES21 had an HQ of 1.01." Understand that this was the highest one but calling it "elevated" has connotation that it could be an action level.

RESPONSE: Edit accepted.

Comment: (Section 5.2.2 Evaluation of Past Exposures without HBCVs, Page 24, Para 5) "Persons exposed to both PFOS and EtFOSE might have an increased risk for developmental effects, but ATSDR is unable to quantify this mixture effect with current knowledge."
A conservative assumption to make for exposures to EtFOSE would be to consider it as PFOS, essentially because it will either degrade or be metabolized into it. Although I can't speak as to the exact amount that would be metabolized, assuming a 100% degradation/metabolic rate would be protective.
Recommendation:
Recommend performing a risk calculation using combined concentrations of EtFOSE and PFOS. With sufficient caveats regarding the uncertainties of EtFOSE metabolism/degradation, it would add a more complete picture of the risks related to PFOS exposure specifically.

RESPONSE: ATSDR reviewed the EtFOSE toxicity and pharmacokinetics information in the Final ATSDR Toxicological Profile for PFAS to determine if it is appropriate to treat it as PFOS in a mixtures evaluation or to determine if such an approach is health protective. Based on this review, ATSDR is not aware of any strong data to support using PFOS as a proxy for EtFOSE. Therefore, ATSDR does not currently know whether making such an assumption would be protective, and given the uncertainties involved, ATSDR does not believe it would give a more complete understanding of the risks posed by PFOS than what is currently available.

Comment: (Section 5.2.5 Evaluation of Current Exposures without HBCVs, Page 26, Para 3) It would be useful to include the PFAS that were detected post-treatment here.

Recommendation:
Include the information here to indicate how close the concentration came to the HBCV and which PFAS were detected.

RESPONSE: ATSDR evaluated the drinking water sampled from private wells with treatment systems (called granular activated carbon systems or GACs). The samples were collected after going through the treatment system. During the period from 2017 through June 2020, there were very low concentrations detected for a few PFAS in samples from the faucet. The following were detected after the treatment systems in these three wells (at low levels - units are µg/L):

RES17 from faucet after GAC
2015
PFDA=0.0037
PFDS=0.0056
PFHpS=0.0049
PFTeDA=0.005

2018
PFOSA=0.0043

RES19 from faucet after GAC
2018
PFTeDA=0.0039

RES21 from faucet after GAC
No detections

RES23 from faucet after GAC
2018
PFOSA=0.0042

For RES17, the PFAS detected in 2015 occurred shortly after the GAC treatment was installed on March 17, 2015, with only one detection after that in 2018. The PFAS detected were below ATSDR's most conservative HBCV. For the other wells that have had a treatment system, there have been only a few instances of PFAS detections in treated water at the faucet and these have been below ATSDR's most conservative HBCV. Overall, the systems appear to be working

well, and this information does not change any of ATSDR's conclusions or recommendations in this health consultation.

Comment: (Section Evaluation of Cancer Health Effects, page 30, line 34) EPA does not have an oral cancer slope factor for PFOS or other PFAS because the animal data do not show a measurable or dose-response relationship.
Recommendation:
Add a citation(s) to support this assertion.

RESPONSE: It is unclear from the comment if the reviewer would like ATSDR to prove a negative that EPA has not developed any cancer slope factors for PFOS or other PFAS (besides PFOA) or if the reviewer is commenting on the reason why EPA has not developed a cancer slope factor for other PFAS besides PFOA. Based on a review of various EPA databases and publications, EPA has only proposed a cancer slope factor for PFOA. Although one of the reasons to not derive a cancer slope factor is that the animal data do not show a measurable or dose-response relationship, there are other reasons why EPA might not have developed a cancer slope factor for PFOS or other PFAS (besides PFOA). For this reason, ATSDR is deleting the possible reason why EPA has not developed a cancer slope factor.

It is important to note that based on the recent human studies and the National Toxicology Program (NTP) animal studies discussed above, EPA and some state agencies are reassessing their PFOA CSFs. CSFs based on the more recent NTP studies might be different from the CSF previously derived by EPA for testicular cancer. For these reasons, ATSDR no longer recommends the use of the 0.07 $(mg/kg/day)^{-1}$ CSF to evaluate PFOA cancer risk.

Comment: (Section 5.5.1, page 31) Many non-water sources of PFAS are enumerated, but non-stick cookware is not.
Recommendation:
Consider adding "use of non-stick cookware (especially if manufactured before 2013)" to this list.

RESPONSE: ATSDR added in "use of non-stick cookware (especially if manufactured before 2013)" to the list of possible non-water sources of PFAS exposures.

Comment: Page 24 – There is a grammatical error and "associated" should be "association" with breast cancer. Furthermore, there have been more recent epidemiological reports on

such associations, or lack thereof, to PFOSA and other PFAS since the draft toxicological profile's release (ATSDR, 2018).

RESPONSE: Grammatical error corrected.

7. Limitations and Uncertainties of Human Health Risks from PFAS Exposures

Comment: (Section 7.1, page 38) Clarity is needed concerning "other sources" in the first sentence.
Recommendation:
Suggest adding "unrelated to AFFF releases at the former Pease AFB" after "other sources."

RESPONSE: Suggested edit accepted.

Comment: (Section 7.4, first paragraph, last line, Page 39) The conclusion "Therefore, people exposed for many years could be an increased health risk" does not follow from the preceding text that addresses relevant in animals to humans, uncertainty in health consequences, and effects and low concentrations.
Recommendation:
Either add information to support this conclusion or revise the conclusion to fit the information actually presented in the paragraph.

RESPONSE: ATSDR has deleted the sentence that does not appear to follow the preceding text.

8. Conclusions

Comment: (Conclusion 1—Wells with Possible PFAS Hazard/Risk, Page 40, Para 3)
It's fairly easy to misread the title of this conclusion and assume that risks are ongoing, when in fact there is little reason to think there is a current or future hazard thanks to steps that have already been taken.
Recommendation:
Recommend altering the conclusion title to be more specific that the hazards were due to past exposures.

RESPONSE: The draft for public comment health consultation clearly indicates that actions have been taken to mitigate the exposures to the five wells that ATSDR has identified may pose a

possible hazard/risk. The PFAS evaluated by ATSDR to determine if a hazard exists for these five wells have long half-lives in the body. Therefore, ATSDR cannot say with certainty that just because exposure to PFAS in private well water has been mitigated/interrupted, that these past exposures still do not present a hazard/risk to these exposed persons.

Comment: (Conclusion 2 — Wells Where PFAS Hazard/Risk Cannot be Determined, Page 41, Para 5)
"The cancer risk from current and past exposure to all PFAS in these wells is uncertain because of limited data on the potential for these PFAS to cause cancer."
While this is accurate for the mixture as a whole, PFOA is a possible carcinogen. This should mean that the cancer risk at least due to PFOA in wells RES03, RES20, RES22, and RES25 should be quantifiable.
Recommendation:
Recommend that the ATSDR calculates risk due to PFOA exposure in these wells and includes it here to clarify that cancer risk may exist due to the mixture of PFAS but likely not due to PFOA alone based on limited knowledge of the carcinogenicity of the other PFAS.

RESPONSE: ATSDR has updated its approach to using the current EPA PFOA cancer slope factor based on testicular cancer and revised this health consultation by adding the following text:

> Based on the recent human studies and the National Toxicology Program (NTP) animal studies discussed above, EPA and some state agencies are reassessing their PFOA CSFs. CSFs based on the more recent NTP studies might be different from the CSF previously derived by EPA for testicular cancer. For these reasons, **ATSDR no longer recommends the use of the 0.07 (mg/kg/day)$^{-1}$ CSF to evaluate PFOA cancer risk**.
>
> EPA cites suggestive evidence that perfluorooctane sulfonate (PFOS) causes cancer, based on limited evidence of liver cancer in rats. However, the evidence was too limited to support a quantitative cancer assessment for PFOS [EPA 2016a]. EPA has not classified any other PFAS as potentially carcinogenic and has not derived oral CSFs for PFOS or other PFAS, mostly because animal and human data are insufficient. Therefore, similar to PFOA, ATSDR cannot calculate the estimated cancer risk from PFOS or other PFAS.
>
> Until more definitive data are available, ATSDR can only evaluate the cancer risk posed by PFOA, PFOS, and other PFAS exposures qualitatively. Therefore, the actual cancer risk from PFOA, PFOS, other PFAS, or PFAS mixture exposures is uncertain.

Comment: (Conclusion 2 — Wells Where PFAS Hazard/Risk Cannot be Determined, Page 41, Para 5)
"In addition to PFAS exposures from drinking water, PFAS exposure from food and consumer products might contribute to the overall amount of PFAS in a person's body."
This language downplays the ubiquity of PFAS - a large portion of PFAS exposure in a typical person usually comes from exposures via food for example. Elimination of PFAS from drinking water likely won't completely eradicate PFAS exposure for most people.
Recommendation:
Suggest that ATSDR strengthen the language here to indicate that PFAS levels in the body are likely a result of multitude of exposures, including food, dust, and of course drinking water.

RESPONSE: Edit accepted here and elsewhere in the health consultation with similar language.

Comment: (Page 41, first paragraph on page) The text as written is misleading as it may cause a reader to believe there is a confirmed link between human PFOA exposure and higher rates of cancer. The text states human and animal studies suggest a link between PFOA exposure and higher rates of several cancers. The second sentence also states animal studies suggest a link for PFOS exposure but then states human studies have not confirmed a link between cancer and PFOS exposure, which could be misconstrued as the line for PFOA being "confirmed".
Recommendation:
Revise second sentence in paragraph to clarify what it means to "suggest a link" as was stated for PFOA compared to "confirm a link" as was stated for PFOS.

RESPONSE: See ATSDR's responses to other public comments on section 5, Public Health Implications of Exposure to PFAS in Drinking Water, relating to the language on the association between PFOA and PFOS exposures and the evidence from human and animal studies. Also, see changes to sections 5.1.2 and 5.2.3 in this final health consultation.

9. Recommendations

Comment: (Page 43, first sentence) The recommendation to "continue their investigations to characterize PFAS groundwater contamination at the site" is inappropriate for this document. Investigations will proceed under CERCLA and the signed Federal Facility Agreement and further decisions will be based on risk as determined by a Human Health Risk Assessment using accepted toxicity values.
Recommendation:
Remove recommendation for further investigations.

RESPONSE: ATSDR did not revise the recommendations to EPA, NHDES, and USAF; however, ATSDR added the action language suggested in the comment to Next Steps for Conclusion 2 in the Summary and to the Public Health Action Plan—Ongoing Actions section.

Comment: (Page 43) The breastfeeding recommendation is confusing. It reads as if ATSDR recommends both breastfeeding and formula use. It also fails to mention the role of the healthcare provider.
Recommendation:
Suggested rewrite: "ATSDR endorses the policy statement of the American Academy of Pediatrics promoting exclusive breastfeeding (https://pediatrics.aappublications.org/content/129/3/e827.full#content-block). This applies regardless of the PFAS concentration of the water supply, as the benefits of breastfeeding in this context appear to outweigh the risks. If formula is used (either exclusively or as a supplement to breastfeeding), then caregivers should use pre-mixed formula or reconstitute dry formula with water sources not containing PFAS. Infant feeding decisions should be made in consultation with a healthcare provider."

RESPONSE: This recommendation is linked to Conclusion 4 (Breastfeeding remains a healthy option). In that conclusion, ATSDR mentions both the CDC and American Academy of Pediatrics recommendations so there is no need to mention them again here. The conclusion and this recommendation are clear that breastfeeding has benefits over other feeding choices. However, if a mother chooses not to breastfeed, then ATSDR recommends that water sources not containing PFAS be used to develop infant formula. Although ATSDR mentions the potential role of a mother's healthcare provider in these decisions, ATSDR agrees with the comment that the recommendation leaves out this point. The last sentence in the comment has been added to this recommendation.

Appendix A
Comment: (Tables A-7 through A-32) In the main text, for example Table 2, hazard quotients and hazard indices are presented at 1 significant figure. However, the tables in Appendix B use 3 significant digits and apply shading indicating an exceedance of a health-based value. Therefore, a hazard index of 1.01 is viewed as "different" from a hazard index of 1. The text (Section 3.3) states "Estimated doses that are below health guidelines are not expected to cause adverse health effects." This would lead a reader to understand that a shaded hazard quotient or hazard index of 1.01 could be expected to cause an adverse health effect" even though this does not seem to be how the hazard quotients and hazard indices are presented in the main text.

For the tables presenting hazard indices, it is not clear what "health-based comparison value" has been exceeded as the hazard index is a sum of hazard quotients. Hazard indices exceeding 1 are not segregated by target effect. Based in the information presented in the text, it does not seem the MRL for PFHxS (thyroid follicular cell damage) is the same as for PFOS and PFOA (developmental, albeit different endpoints). No note is provided to the tables to explain what a hazard quotient or hazard index greater than 1 may mean with regards to noncancer health effects.

Recommendation:
Either revise the number of significant digits to align with presentation in the main text or add a note to all tables providing context for what an "exceedance" may mean with respect to adverse health effects and how significant digits are used and reported in the main text. Clarify what "health-based comparison value" is intended and used in calculating the hazard quotients and hazard indexes.

If the target effect is the same for all chemicals contributing to the hazard index, then clarify in the note. Otherwise, the note should clarify the target systems are not the same.

RESPONSE: The significant digits have been adjusted to one. Health-based comparison values usage and determinations have been previously discussed. The addition of separate hazard quotients to generate hazard indices use similar endpoint toxicities.

Comment: (Table A-33) Cancer risk is shown at two significant digits. EPA guidance (RAGS A) recommends reporting cancer risk at one significant figure only.
Recommendation:
Revise to present cancer risk at one significant digit.

RESPONSE: ATSDR agrees with this comment; however, all cancer risk estimates have been deleted from this health consultation.

Comment: (Table A-4, page A-8) Table A-4, Exposure pathway biota – In the past year, sampling of shellfish and deer from the Great Bay region has been completed and should be revisited as a part of this assessment. The low levels of PFAS likely represent a minor to insignificant exposure pathway depending on the methods used by ATSDR, but none-the-less are available for consideration.

RESPONSE: As mentioned in a response to a similar comment above about shellfish sampling from the Great Bay, based on NHDES' evaluation, it appears that

- any exposures that might have occurred to PFAS (primarily PFOS) in shellfish from the Great Bay are not likely to result in harmful effects;
- the existing restrictions in place would further reduce the potential for any exposures; and
- evaluation of all PFAS present in shellfish could not be done because of the lack of toxicity data.

Moreover, the NHDES indicated that PFOS detections occurred in shellfish collected from the Broad Cove at the mouth of Knights Brook, Great Bay at the Mouth of McIntyre Brook, and Trickys Cove at the mouth of Pickering Brook. If any residents with contaminated wells in Newington consumed shellfish from these areas, this would have added to their PFAS exposures they have received from the private wells and other sources.

In addition to the shellfish sampling from the Great Bay, in 2019, the NH Department of Fish and Game sampled muscle and liver of deer in the Great Bay area. Their report is available from: https://www.wildlife.state.nh.us/hunting/deer-pfas.html

Here is a summary of their findings:

During the 2019 Great Bay Deer Hunt, successful hunters were asked to provide muscle and liver tissue samples from their harvested deer for PFAS testing. US Fish and Wildlife Service staff assisted in collecting tissue samples for the Department during the registration process. These samples were then sent to a lab at the University of Connecticut to screen for PFAS chemicals. Sixteen (16) deer were sampled, yielding 16 muscle samples and 15 liver samples for a total of 31 tissue samples collected and tested. Each sample was tested for 14 PFAS compounds with the following results:

- ***PFOS was the only PFAS chemical detected in any of the 31 tissue samples.***
- ***3 of 15 liver samples (20%) were positive for PFOS, 80% of liver samples were negative for PFOS.***
- ***15 liver samples (100%) were negative for any of the other 13 PFAS compounds tested.***
- ***16 muscle samples (100%) were negative for any of 14 PFAS compounds tested.***

No PFAS chemicals were detected in any of the muscle tissue samples tested, suggesting venison consumption likely represents a low risk for PFAS exposure. While PFAS levels detected in deer livers were considered moderately low, the Department still recommends

hunters do not consume deer liver. The liver is a filtering organ and therefore has potential to have high levels of a number of contaminants.

ATSDR recommends that residents using wells where ATSDR has determined a hazard exists for past exposures or where current exposures cannot be determined should consider not consuming shellfish from these areas of concern from the Great Bay or deer liver in the Great Bay area.

Comment: (Table A-6, page A-10) RME Table A-6 – The agency should clarify the source of its assumed drinking water ingestion rates (i.e., ATSDR's 2016 guidance document or the more recent update to the EPA Exposure Factors Handbook). EPA recently revised body weight and drinking water intake rate assumptions and it is unclear which values served as the basis for the RME calculations. This could be addressed with a footnote and proper citations.

RESPONSE: This health consultation used the body weights and drinking water intake rates based on ATSDR's 2016 Exposure Dose Guidance for Water Ingestion [ATSDR 2016]. This guidance is based on data and information from the 2011 EPA Exposure Factors Handbook (EFH) [U.S. EPA 2011]. ATSDR is currently reviewing updates to the EFH that relate to water ingestion to determine if any changes to ATSDR's guidance are needed.

References cited in this appendix:

Abraham K, Mielke H, Fromme H, Volkel W, Menzel J, Peiser M, Zepp F, Willich SN, Weikert C. 2020. Internal exposure to perfluoroalkyl substances (PFASs) and biological markers in 101 healthy 1-year-old children: associations between levels of perfluorooctanoic acid (PFOA) and vaccine response. Arch Toxicol.

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Alexander BH, Olsen GW, Burris JM, Mandel JH, Mandel JS. 2003. Mortality of employees of a perfluorooctanesulphonyl fluoride manufacturing facility. Occup Environ Med 60:722–9.

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