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SUMMARY REPORT ON THE NEW HAMPSHIRE DEPARTMENT OF ENVIRONMENTAL SERVICES DEVELOPMENT OF MAXIMUM CONTAMINANT LEVELS AND AMBIENT GROUNDWATER QUALITY STANDARDS FOR PERFLUOROOCTANESULFONIC ACID (PFOS), PERFLUOROOCTANOIC ACID (PFOA), PERFLUORONONANOIC ACID (PFNA), AND PERFLUOROHEXANESULFONIC ACID (PFHxS)

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LIST OF COMMON ACRONYMS

AGQS – Ambient Groundwater Quality Standard

ATSDR – Agency for Toxic Substances and Disease Registry

CDC – Centers for Disease Control

COC – Contaminant of Concern

DWEL – Drinking Water Equivalency Level

EPA – United States Environmental Protection Agency

HED – Human Equivalent Dose

MCL – Maximum Contaminant Level

MRL – Minimum Risk Level

NHDES – New Hampshire Department of Environmental Services

NHDHHS – New Hampshire Department of Health and Human Services

NOAEL – No Observed Adverse Effect Level

PFAS – Per- and polyfluoroalkyl substances

PFHxS – Perfluorohexanesulfonic Acid

PFOA – Perfluorooctanoic Acid

PFOS – Perfluorooctanesulfonic Acid

PFNA – Perfluorononanoic Acid

PoD – Point of Departure

PWS – Public Water System

RfD – Reference Dose

RSC – Relative Source Contribution Factor

SDWA – Safe Drinking Water Act

UFs – Uncertainty Factors

1. Background

Perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS) are part of a large class of chemicals known as perfluorinated compounds (PFCs) and more broadly as per- and polyfluoroalkyl substances (PFAS). They have been widely used since the 1940s in commercial, industrial, and household products and applications, including production of water resistant materials, fire suppression foams, non-stick cookware, stain removers, etc. All four compounds have been detected in New Hampshire's groundwater and surface water. Because of their widespread use, persistence and mobility in the environment and bioaccumulative properties, these compounds have been detected in blood serum in humans and animals worldwide and have been studied for their toxicity and health effects. The health effects associated with PFAS exposure are currently being researched extensively by toxicologists and epidemiologists worldwide, resulting in numerous publications being released on a continuous basis. The New Hampshire Departments of Environmental Services (NHDES) and Health and Human Services (NHDHHS) continue to review and evaluate the toxicity and health effects of these compounds as research becomes available. According to the Centers for Disease Control's (CDC) Agency for Toxic Substances and Disease Registry (ATSDR), some, but not all, studies in humans have shown health effects possibly associated with PFAS exposure including:

- Altered growth, learning and behavior of infants and older children.
- Lowering a woman's chance of getting pregnant.
- Interference with the body's natural hormones.
- Increased cholesterol levels.
- Modulation of the immune system.
- Increased risk of certain cancers.

For additional information on the toxicity and health effects of these compounds, please visit the ATSDR webpage at: https://www.atsdr.cdc.gov/pfas/health-effects.html.

New Hampshire Chapter Laws 345 of 2018 (i.e., SB309, see Appendix 1) authorize NHDES to consult with NHDHHS and to initiate rulemaking to adopt maximum contaminant levels (MCLs) for PFOA, PFOS, PFHxS and PFNA by January 1, 2019. The legislation requires that NHDES consider, 1) the extent the contaminant is found in New Hampshire; 2) the ability to detect the compound; 3) the ability to treat the contaminant; 4) benefits associated with adopting an MCL; and 5) the costs associated with adopting an MCL. MCLs are water quality standards that apply to public water systems (PWS). Most MCLs , including those proposed in this report, are set for long-term, chronic exposure to a contaminant and only apply to non-transient public water systems (water systems serving 25 or more of the same population of people, six months of the year). Public water systems (PWS) sample all of their water sources for compounds with MCL standards, and submit the results to NHDES to demonstrate compliance with water quality standards.

Existing state law requires NHDES to adopt rules establishing Ambient Groundwater Quality Standards (AGQS) that are the same as any MCLs established by NHDES. Existing state law also requires that AGQS be the same or more stringent than any federal MCL or health advisory established under the federal Safe Drinking Water Act (SDWA). AGQS are the standards used to require site investigations and remedial action at and around contamination sites. AGQS are also used to identify where the provision of alternative drinking water is required when contaminated sites impact offsite private and/or public water supply wells. An AGQS also dictates the conditions under which wastewater and wastewater residuals may be discharged to groundwater. Although NHDES adopted an AGQS for PFOA and PFOS of 70 nanograms per Liter (ng/L) [or

parts per trillion (ppt)[1]] for these two compounds combined in May of 2016, the laws enacted in 2018 require NHDES to re-assess these standards and to also adopt AGQS for PFHxS and PFNA.

This report provides information on how New Hampshire's proposed MCLs and AGQSs for PFOA, PFOS, PFNA and PFHxS were developed to ensure they are protective of human health at all life stages. The report also provides information on the criteria that the law requires NHDES to consider when establishing MCLs including: occurrence in drinking water, the ability to detect the contaminant, the ability to treat to achieve compliance with the MCLs, and the costs and benefits to parties affected by establishing the standards.

It is important to note that New Hampshire, like most other states, has always relied on the U.S. Environmental Protection Agency (EPA) to set MCLs. EPA and the few other states that set drinking water standards employ a variety of experts who derive protective health-based standards (e.g., toxicologists and health risk assessors), economists trained in cost and benefit analysis, and chemists and engineers who can determine lab and treatment capabilities. SB309 included funding for a toxicologist and health risk assessor, who both began work at NHDES on October 12, 2018. NHDES was also able to engage the services of an outside expert to provide some additional assistance in the review of toxicological information. NHDES did not have resources to fully evaluate costs and benefits, as would have been done on the federal level, but has attempted to provide an analysis of each based upon available information.

The majority of the work NHDES has performed to date has been focused on deriving the individual standards for PFOA, PFOS, PFNA and PFHxS. During the rulemaking process, NHDES expects to continue researching health studies on these chemicals as well as risk management approaches that are scientifically valid and could address any compounding effects between chemicals when the chemicals are found in combination in a drinking water source. Further exploration on quantifying benefit to affected parties will also occur. This continued effort will be done in tandem with considering public comments received on the initial rule proposal.

2. Proposed MCLs and AGQSs

Establishing MCLs is done in accordance with guidance developed by EPA and other health agencies and programs. Details of how health protective drinking water standards are usually developed are presented in Appendix 2. The sequence of steps is summarized below:

- The most sensitive adverse effect that is thought to be relevant to humans is chosen. The lowest dose that has no significant toxic effect is the usual initial starting point (a no observed adverse effect level or NOAEL).

- The NOAEL or the *lowest* observed adverse effect level (LOAEL), if there is no NOAEL, is converted to a human equivalent dose (HED) through physiological models or other dose adjustment methods. The HED becomes the point of departure (PoD) for deriving the ultimate drinking water standard.

- The PoD is reduced by uncertainty factors (UFs) of either 10- or 3-fold to take into account incomplete knowledge regarding critical factors such as when there is incomplete knowledge of human variability and sensitivity; in cases where short-term studies are used to protect against

[1] Both the MCL and the AGQS are specified in nanograms per Liter (ng/L), a unit of concentration that is equivalent to parts per trillion (ppt) in water. In this document, concentrations are stated in ppt except in quoted references and tables that use ng/L.

effects from long-term exposure, and when the usual required studies to set a standard (e.g., reproductive effects studies, developmental studies or cancer studies) are missing.

- The toxicity value developed, which EPA refers to as a Reference Dose (RfD) and ATSDR refers to as a Minimal Risk Level (MRL), is converted to an equivalent dose in drinking water by selecting a sensitive human receptor and using their body weight and drinking water ingestion rate to calculate a drinking water equivalency level (DWEL). The DWEL is 100% of a dose not expected to cause any toxic effects to even the most sensitive subpopulation.

- For most chemicals, exposure from sources other than drinking water, such as from air, food and soil, is also possible. Therefore, the DWEL must be reduced by estimated doses coming from all other potential sources using a relative source contribution factor (RSC), so that the total exposure dose does not exceed 100% of the RfD, MRL or DWEL.

It is important to understand that drinking water standards for the same chemical often differ depending on the entity setting them. This is not unexpected, since standard setting guidance is not simply a mathematical formula and anticipates the need for professional judgment, which is involved in several stages of the standard setting process. Information about the relevancy of effects on animals to humans is often incomplete and contradictory, which will influence the toxic effect that is chosen. The selection of appropriate UFs is another area where judgment is critical. Whether a full UF of 10 or a partial one of 3 is used for an UF, it will change the resulting standard by just over 3-fold. The RSC chosen can also have a significant influence on the final standard. If one Risk Assessor determines that the data required to select an RSC are inadequate, EPA's guidance recommends using a default RSC of 20%. Another Assessor may determine the data on background exposure are adequate and choose an RSC of 60% based on them. The choice between those two RSCs will also change the standard selected by 3-fold. In a world of complete knowledge about a chemical's effects, relevance to humans and background exposure, health-protective drinking water standards calculated by different practitioners should be identical. However, in the real world, the lack of knowledge about a chemical and the appropriate degree of protectiveness to apply in the face of uncertainty results in differing choices, which can change the value selected for a standard.

In order to ensure that NHDES was aware of all the current, relevant health studies and information available in deriving the proposed MCLs/AGQSs, the agency solicited input from stakeholders through a series of public meetings held for this purpose. A list of the documents/references received following these meetings is available on the NHDES website at: https://www4.des.state.nh.us/nh-pfas-investigation/wp-content/uploads/2018/11/Draft_PFAS-Reference-List-as-of-11-07-18_For-Posting-to-Website.pdf. Comments received are available on the NHDES website at: https://www.des.nh.gov/organization/commissioner/max-contaminant-levels.htm. Studies selected and utilized in the derivation of the standards are listed in Appendix 8.

The following Table (Table 1) provides an overview of the proposed derived standards and the factors selected to derive the proposed MCL/AGQS. Appendices 4-7 include a description for each of the chemicals and how the standard was derived. These derivations were reviewed by Dr. Stephen M. Roberts, Ph.D., who also assisted NHDES with the review of ATSDR's Draft Toxicological Profile released in June 2018. In addition to the individual standards for PFOA and PFOS, the proposed rulemaking keeps the combined 70 ppt for PFOA and PFOS as an AGQS and also proposes that it be adopted as an MCL. This is consistent with existing law, which requires that an AGQS shall be no less stringent than an EPA health advisory.

Table 1: Summary of MCL Derivation Factors				
	PFOA*	PFOS*	PFHxS	PFNA
Health Effect Endpoint	Altered Liver Size/Function	Delayed Development	Impaired Reproduction	Altered Liver Size/Function
Animal Serum Dose (ng/mL)	4,351[a]	6,260[b]	27,200[c]	4,900[d]
Total Uncertainty Factor HUF x AUF x MF[e]	100 10 x 3 x 3	100 10 x 3 x 3	300 10 x 3 x 10	300 10 x 3 x 10
Target Human Serum Dose (ng/mL)	43.5	62.6	90.7	16.3
Human Half-life (years)	2.7[f]	3.4[f]	5.3[f]	2.5[g]
Dosimetric Adjustment Factor (L/kg/d)	$1.20E^{-04}$	$1.28E^{-04}$	$1.03E^{-04}$	$1.52E^{-04}$
Reference Dose (ng/kg/d)	5.2	8.0	9.3	2.5
Relative Source Contribution[h]	40%	50%	50%	50%
Water Ingestion Rate[i]	0.055 L/kg d	0.055 L/kg d	0.055 L/kg d	0.055 L/kg d
MCL/AGQS ppt (ng/L)	**38**	**70[j]**	**85**	**23**

[a] Loveless et al., 2006, NJ DWQI 2017, increased relative liver weight in mice;
[b] Luebker et al., 2005a, EPA 2016b, reduced pup weight and developmental delays in rats;
[c] Chang et al., 2018, reduced litter size in mice;
[d] Das et al., 2015, NJ DWQI 2018, increased relative liver weight in mice;
[e] HUF (Human-to-Human Uncertainty) x AUF (Animal-to-Human Uncertainty) x MF (Modifying Factor)
[f] Li et al., 2017, serum-derived half-life estimates from men and women exposed to PFAS via drinking water;
[g] Zhang et al., 2013, ATSDR 2018, urine-derived half-life from community exposure to PFNA;
[h] The RSC was derived using NH-specific blood data from high-exposed populations of Pease and Southern NH. This was calculated using the subtraction method described in the EPA 2000 Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health. Details about this approach are summarized in Appendices 4-7;
[i] EPA 2011 Exposure Factors Handbook, lactating women 95th percentile;
[j] PFOS rounded down to 70 ppt from 73 ppt, per the current EPA Health Advisory for PFOS.

*The derivation of the 70 ppt standard for PFOA and PFOS combined is based on the U.S. Environmental Protection Agency's November 2016 Health Advisory (https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos)

Each MCL/AGQS was calculated through a risk assessment process that: 1) assessed sensitive and human-relevant health effects of each PFAS in rodent models, 2) evaluated non-cancer endpoints due to uncertainty about cancer endpoints observed in rodent models, and 3) estimated health-protective doses for exposure to individual compounds across sensitive life stages. Under State law, development of MCLs necessitates evaluation of, and possible modification based on, the availability and accuracy of detection and treatment technology, as well as the costs associated with compliance. While these factors were considered, NHDES has determined that, for these compounds at this time, adjustments to the standards based on detection/treatment technology or projected compliance costs are not warranted, as both technology challenges and compliance costs can be addressed by means other than standards that do not adequately protect health. Therefore, NHDES has proposed the health-protective levels calculated using the science-based process as both the drinking water standard and the ambient groundwater standard for New Hampshire.

Animal studies, namely rodents, served as the basis for the derived dose of each MCL/AGQS. Human epidemiology studies were evaluated to identify relevant health effects observed in rodent models, but did not serve as the basis for dose calculation. The use of animal studies for risk assessment is consistent with the approach of other states (e.g., Minnesota, New Jersey, and New York) and federal agencies (EPA and ATSDR). Due to differences in methodology, exposure history and data reporting, the existing human epidemiological studies alone were determined to be insufficient for deriving the dose for MCL/AGQS in a manner that would be consistent with other drinking water standards. Although a novel method for epidemiology-based risk assessment has been applied by a single European agency (European Food Safety Authority 2018), this approach is self-acknowledged to either overestimate or underestimate reference doses and has not been adopted by other U.S. regulatory bodies.

The critical health effects selected from the toxicology literature were non-cancer endpoints, including liver enlargement (PFOA and PFNA), delayed development (PFOS) and impaired reproduction (PFHxS). Recognizing that epidemiological studies have identified associations between certain PFAS and cancer, NHDES also considered the feasibility of deriving a MCL/AGQS for a cancer endpoint using its standard risk assessment approach. Of the four PFAS assessed by NHDES, only PFOA had a study for consideration of a cancer-based endpoint. However, this study (Butenhoff et al., 2012) had technical limitations that hinder extrapolation of serum doses, as well as uncertainty regarding the biological relevance to humans. Thus, it was determined that there was insufficient information to conduct an accurate risk assessment for a cancer endpoint given the existing scientific literature. This has similarly been studied by both EPA and ATSDR, and both determined that if a cancer endpoint would have been chosen, the resulting standard would have been at a higher (less protective) level and therefore, the endpoint chosen is fully protective for all health effects.

Due to the current lack of information on the toxicity of PFAS mixtures, NHDES conducted its risk assessment for each compound on an individual basis. There is emerging evidence that suggests various PFAS may affect similar organ systems, but these effects occur at differing doses depending on experimental design and their relative potency has not been quantified. To address this concern for mixture effects, other states have exercised a risk management strategy, instead of risk assessment, by applying a combined standard for the sum total of multiple PFAS. While perceived as protective, this risk management strategy lacks a scientific basis as the combined toxicity of multiple PFAS is poorly understood. As there is uncertainty about the specific health effects of PFAS and the growing number of different PFAS identified in the environment, the scientific and practical merits of any risk management approach should be carefully

evaluated as an alternative to standard risk assessment. NHDES continues to study developments in scientifically based approaches to regulating combinations of PFAS.

Consistent with the previous points, Michigan recently released a report summarizing the challenges for deriving health-based standards for PFAS under the current risk assessment paradigm. This report was prepared by an independent panel of scientists from government and academic institutions with technical expertise on PFAS health effects, exposure and remediation. Given the current limitations of animal studies and human epidemiology, the expert panel recommended developing regulatory approaches that consider both of these lines of scientific evidence. Yet they did not provide technical guidance on how that might be achieved. The panel also stated that the non-cancer endpoint of PFAS seem to be more sensitive than cancer endpoints and may be more important for setting regulatory limits. Furthermore, the panel emphasized caution in using combined regulatory approaches due to the lack of quantitative evidence for assuming similar potency of different PFAS. Additional discussion of these technical issues and their relation to the derivation of the proposed MCL/AGQS are detailed in Appendices 3-7.

Finally, it is important to note the toxicity values for the MCL/AGQS were derived from the lowest doses in animal studies that were determined to be relevant to human health. This included selection of health effects associated with developmental delays from *in utero* exposure (i.e. PFOS), or other effects that occur at lower doses than those that induce developmental defects in animals (i.e., liver toxicity for PFOA and PFNA, and impaired reproduction for PFHxS). To afford additional protection for chronic exposure, daily water intake was assumed to be that of the 95th percentile for lactating women, which is the highest water in-take rate for adults (i.e., for a 175 lb. person, this would equal about 4.4 liters of water consumed each day. By using this rate of water intake to calculate the MCLs, the levels are expected to be safe for pregnant mothers and their fetuses, lactating mothers and their infants, and all children, adolescents, and adults). This high intake rate was assumed "through life" as a protective measure.

3. Occurrence, Ability to Reliably Quantify and Ability to Treat

The statute concerning how the State develops MCLs was amended in 2018 to clarify that New Hampshire's process should align with the process followed by EPA and most of the few other states that set MCLs. This section addresses three of the criteria that the law now requires be considered in the development of an MCL. It is important to note that no additional resources were provided to NHDES to produce information on these considerations or for cost and benefit estimates. Accordingly, NHDES used available data and work done under other investigations/projects or by others to address these aspects of determining a MCL.

3.1 Occurrence in Drinking Water

In New Hampshire, two contaminated sites, one involving contamination of Portsmouth, New Hampshire's municipal water system wells at the Pease Tradeport and another involving contamination of wells used as a source of water for Merrimack Village District in Merrimack, New Hampshire, raised awareness of these compounds and led NHDES and others to perform state-wide sampling at public water systems and other suspected sites. Based on these data, PFOA, PFOS, PFHxS, and PFNA occur in drinking water, groundwater and surface water in New Hampshire in proximity to releases of these contaminants to the environment. The following table describes the results of analysis for these chemicals at 402 of the 1,880 sources of drinking water that supply non-transient public water systems in New Hampshire.

Table 2: PFAS Concentrations Detected in Sources of Drinking Water for Non-Transient Public Water Systems (data provided by NHDES Sampling or PWS voluntary sampling conducted March 2016 to December 2018)

	Number of PFAS Sources			
Concentration (ppt)	**PFHxS**	**PFNA**	**PFOS**	**PFOA**
Not Detected	357	390	336	253
Detected at less than 10 ppt	35	6	47	125
10-20 ppt	2	3	14	13
20-40 ppt	7	3	2	8
40-60 ppt	1	0	2	0
Greater than 60 ppt	0	0	1	3

3.2 Ability to Reliably Quantify in Drinking Water

The following excerpt from the Association of State Drinking Water Administrator's PFAS Lab Testing Primer (https://www.asdwa.org/wp-content/uploads/2018/10/ASDWA-PFAS-Lab-Testing-Primer-10-10-18-Final.pdf) describes the current status of the ability to reliably quantify PFAS, including the four subject compounds, in drinking water:

"Laboratory analytical methods with reporting limits (RL) of at least 2-4 nanograms per liter (ng/L) parts-per-trillion (ppt) should be utilized. Many commercial labs are achieving reporting limits of less than 1 ng/L ppt. Additional health studies are rapidly evolving and some states have determined that PFAS health advisory concentrations in drinking water should be based on the additive effect of PFAS compounds. Obtaining water quality results with low RL will improve the utility of the data in the event health guidance or standards are changed or that the state you are in develops health guidance or standards based on the additive effects of PFAS.

It is important to understand the difference between a reporting limit (RL) and a detection limit (DL). An RL or reporting detection limit is the limit of detection in which the concentration of a contaminant can be reliably quantified. In contrast, the DL or method DL is lower than the RL and is below the point of calibration such that results reported below the RL are unreliable and as such, must be qualified as estimated values by carrying a "J" or "E" (NELAP) qualifier/flag."

Typical PFAS Reporting Limits	
Method 537	Range from 2.9 to 14 ng/L
Isotope Dilution	Varies by lab and compound but can be: • Below 1 ng/L for some compounds and • Up to 3 ng/L for others

3.3 Ability to Treat Drinking Water

Based on published literature, PFOA, PFOS, PFNA and PFHxS can be removed from drinking water with varying success using a number of treatment options. The most common treatment for PFAS removal, both in the literature and in practice, including at wells in New Hampshire, is granulated activated carbon (GAC). Data from a variety of sites, including at full-scale and fully operational municipal wells, clearly demonstrate that compliance with the proposed MCLs can be achieved using GAC or other approaches such as combining GAC with resin.

4. Costs to Affected Parties

NHDES used available water quality data to estimate potential costs to affected parties of compliance with the MCLs/AGQSs. For certain types of waste and groundwater discharge sites, this involved determining the frequency of exceeding the proposed standards for the sites sampled and applying that to the universe of sites. For other types of sites for which there are limited data, a qualitative description of anticipated costs is provided. As noted previously, with existing resources and expertise, NHDES was unable to analyze costs in keeping with EPA and Office of Management and Budget guidance, which entails determining costs associated with a number of different potential standards and capturing marginal costs.

For affected parties such as public water systems, landfill and hazardous waste site owners, and groundwater discharge permittees, NHDES had sufficient sampling data to estimate a cost range associated with setting these standards. In the case of affected public water systems that have already made significant investment in meeting the current AGQS, these costs were not included as new costs resulting from setting the standards. In the case of waste and discharge sites, where only initial sampling has occurred, the costs of compliance with the existing and new standards are included. The assumptions and analysis used to derive costs is included as an appendix to this report.

4.1 Estimated Costs to Public Water Systems to Comply with New MCLs

The MCLs for PFOA, PFOS, PFNA and PFHxS will apply to PWSs that serve residential populations (community PWSs) and those that serve the same 25 or more people each day for at least 6 months of the year (non-transient, non-community PWSs), such as schools and places of work with their own wells. There are currently 1,880 sources of water for PWSs that would be subject to the adoption of these MCLs. The costs incurred by these PWSs include the cost of routine sampling, the frequency of which will depend on compliance with the MCLs. For public water systems that exceed any of the MCLs based on a running annual average, the costs will also include treatment such as GAC, and operation and maintenance costs associated with the installed treatment. The methodology and assumptions made for estimating each of these costs is contained in Appendix 9. To summarize, NHDES estimated the following:

The initial cost of sampling for PWSs is estimated to be $1,102,500 - $2,836,000. Based on the anticipated percentage of detections, the costs of sampling for non-transient PWSs in year 2 thru 9 after the MCLs are established are estimated to be $73,055 - $184,825.

To date, sampling has occurred at 402 of the 1,880 sources of non-transient public drinking water in New Hampshire (see Table 2 in the Occurrence in Drinking Water subsection). Comparing these analytical results to the proposed standards allows estimation of the number of public water systems that will require treatment. The cost of treatment at PWSs associated with these standards is estimated to range from $1,800,000 - $5,200,000.

NHDES utilized operation and maintenance estimates from PWSs that have developed cost estimates for maintaining PFAS treatment systems under construction to comply with the current PFOA and PFOS 70 ppt combined AGQS to estimate operation and maintenance costs associated with the new MCLs. Operation and maintenance costs are estimated to range from $114,912 - $223,439 per year.

New Hampshire does not require drinking water not supplying public water systems to comply with MCLs. However, it is anticipate that homeowners and others with private wells will incur costs to ensure

their drinking water meets health based standards. NHDES estimates that 3,125 of the 250,000 private wells in New Hampshire will have drinking water that exceeds the MCLs. The cost of point-of-entry treatment for those wells is estimated to be $9,375,000, with an annual maintenance cost of $2,812,500.

4.2 Estimated Costs to Comply with New and Existing AGQS

4.2.1 Municipal Solid Waste Facilities (Groundwater Management/Release Detection Permits)

The vast majority of the unlined/lined solid waste disposal facilities or synthetic lined waste water treatment lagoons in New Hampshire are municipally owned, and as such, the municipality is responsible for maintaining the water quality systems and monitoring water quality associated with a permit. There are roughly 200 of these facilities that currently have groundwater release detection or groundwater management permits that have been issued by NHDES, in accordance with its administrative rules. These permits prescribe programs for periodic groundwater quality monitoring and reporting, provide for groundwater remediation either through active measures or natural attenuation, specify performance standards for remedies, and describe procedures for performing site investigations and implementing remedial action plans.

NHDES has required sampling for PFAS at all of these sites. To date, 58% have sampled and approximately 42% of those have exceedances of the current AGQS for PFOA and/or PFOS. Based on the proposed MCLs, 44% are estimated to have exceedances. NHDES has assumed that 25% to 50% of these sites will require either an expansion of the existing groundwater management zone where PFAS is already an established contaminant of concern (COC) or will require investigation where PFAS will become a new COC. The capital costs are estimated to be in the range of $380,000 - $755,000, and the annual operating costs could range from $260,000 - $390,000 per year. This includes assumptions concerning the cost to install additional monitoring wells, comply with permit sampling and reporting requirements, sample private wells and provide treatment to some percentage of the private wells tested, and administration of the permits. The worksheet that includes the assumptions and unit costs is provided in Appendix 10.

4.2.2 Hazardous Waste Remediation Sites (Groundwater Management Permits)

Hazardous waste remediation sites include all sites where a hazardous substance or waste has been released, and often have a long-term remediation and management component prescribed and regulated through an NHDES-issued groundwater management permit or remedial action plan. There are roughly 515 waste sites, including State-listed hazardous waste, CERCLA, and brownfields sites, that have an open status and are currently regulated by NHDES.

NHDES has required waste sites that meet certain criteria to complete an initial screening for the presence of PFAS. To date, 27% have sampled and approximately 49% of those have exceedances of the current AGQS for PFOA and/or PFOS. Based on the proposed MCLs, 53% are estimated to have an exceedance. NHDES has assumed that 25% to 50% of these sites will require either an expansion of the existing groundwater management zone where PFAS is already an established COC or will require investigation where PFAS will become a new COC. Assuming these percentages of non-compliance for the universe of waste sites, with the exceptions noted below, the capital costs are estimated to be in the range of $1,150,000 - $2,310,000 and the annual operating costs could range from $570,000 - $1,020,000 per year. Not included in the estimate above are costs associated with a few unprecedented, large-scale site investigations and associated response actions currently ongoing in southern New Hampshire to mitigate PFAS-contaminated drinking water. Response

actions at these sites have included providing treatment or alternative water sources to affected properties. Based on site-specific data collected to date, it is estimated that the proposed MCLs will result in an expanded area requiring investigation and additional properties requiring sampling and treatment. The additional capital costs unique to these southern New Hampshire sites are estimated to be in the range of $1.52M - $2.53M and the additional annual operating costs could range from $220,000 - $365,000 per year.

The cost estimates for waste sites include assumptions concerning the cost to install additional monitoring wells, comply with permit sampling and reporting requirements, sample private wells and provide treatment to some percentage of the private wells tested, and administration of the permits. The worksheet that includes the assumptions and unit costs is provided in Appendix 10.

4.2.3 Oil Remediation Sites (Groundwater Management Permits)
Oil remediation sites include all sites where long-term remediation and management of petroleum contamination occurs primarily through a NHDES-issued groundwater management permit or remedial action plan. There are approximately 1,500 active petroleum sites, including, but not limited to, leaking underground/above ground storage tank sites, and spill sites that have an open status and are currently regulated by NHDES.

NHDES has recently undertaken an initiative requesting a small initial subset of these petroleum sites to voluntarily complete an initial screening for the presence of PFAS. To date, only an estimated 1% of all petroleum sites have sampled for PFAS. The data indicate that some percentage of sites will have exceedances of the proposed MCLs. However, based on the limited nature of information and the types of releases/release mechanisms associated with petroleum sites, the capital and annual costs associated with the proposed MCLs is indeterminate at this time.

4.2.4 Wastewater Disposal to Groundwater (Groundwater Discharge Permits)
A number of municipalities and some private entities dispose of wastewater to the ground through such practices as discharges to lagoons, rapid infiltration basins, spray irrigation systems and very large leach fields. There are 96 of these facilities that currently have a groundwater discharge permit, which allows the discharge in accordance with rules that protect against impact to other properties and wells. NHDES has required sampling for these and other PFAS at all of these sites. To date, 44% have sampled and, of those, 29% have exceeded one or more of the proposed MCLs. Assuming this same percentage of non-compliance for the universe of sites, the capital costs are estimated to be approximately $1,100,000 and the annual operating costs are estimated in the range of $200,000 - $400,000. This includes assumptions concerning the cost to install additional monitoring wells at these sites, sample private wells and provide treatment to some percentage of the private wells tested. Given the variety of groundwater discharge sites and that wastewater discharge volumes at many permitted facilities are on the order of hundreds of thousands of gallons per day, available treatment technologies would not suitably treat these flows in a manner that is cost effective. The worksheet that includes the assumptions and unit costs is provided in Appendix 11.

4.2.5 Biosolids and Sludge Processing and Application Sites and Septage Land Spreading.
Biosolids are produced by municipally owned wastewater treatment facilities when they receive a sludge quality certification from NHDES approving the material for beneficial use as a fertilizer in New Hampshire. Some industrial sludge, such as short paper fiber or water treatment residuals, may also be approved for land application for their organic content or ability to bind phosphorous,

respectively. Before biosolids or sludge can be applied to the land for agricultural purposes, they must receive a Sludge Quality Certification that ensures that over 159 potential contaminants are at acceptable levels, following strict screening guidelines that protect groundwater and human contact. Until a leaching standard (the amount that can be in the biosolid or sludge without its land application resulting in an exceedance of AGQS) is set for these four PFAS, it is impossible to quantify the costs resulting from establishing these standards. In some cases, biosolids and sludge that are now being applied for beneficial purposes (i.e., fertilizer or organic material) may no longer be able to be used and communities and industry may see a rise in their biosolid and sludge disposal costs. A similar cost increase could occur at the five domestic septage (i.e., material pumped from residential septic tanks) land spreading sites if PFOA, PFOS, PHNA, PFHxS are found to leach into groundwater at unacceptable levels (i.e., causes an exceedance of AGQSs set for the four PFAS).

At the present time, New Hampshire has only one biosolids processing site that must sample and comply with the four PFAS AGQSs that are established as a result of setting the MCLs. This facility is currently sampling for PFAS, specifically to comply with the existing combined standard for PFOA and PFOS of 70ppt. The new AGQSs may require the installation of new sampling wells and modification of the facility to protect groundwater by controlling and treating runoff, etc. These costs are unknown at this time. This facility primarily serves municipalities and any increase in costs is likely to be reflected in increased tipping fees paid for by the New Hampshire municipalities who utilize this facility.

4.2.6 Fire Station/Fire Foam Sites

A known source of PFAS in the environment is the use of certain formulations of firefighting foams, referred to as Class B foam or aqueous film-forming foam (AFFF), which contains PFAS. Certain fire training areas and discrete locations across the state where AFFF has been applied historically are currently undergoing remedial investigation and/or cleanup of PFAS-contaminated groundwater. The recent discovery of contamination in drinking water wells at fire stations has prompted additional sampling in the vicinity of those fire departments, and has resulted in the detection of elevated PFAS concentrations in nearby private and public drinking water supply wells. Of the 16 fire departments that have sampled their private water supply wells and provided results to NHDES, five (or 31%) would exceed the proposed MCLs.

Based on review of available information, there are an estimated 293 fire stations in New Hampshire of which potentially just over 175 may be serviced by a private water supply well. Furthermore, information suggests that there are over 120 active public water supplies and potentially over 4,600 private wells within 1000 feet of a known fire station. Given the limited information, the capital and annual costs associated with the existing AGQS and the proposed MCLs is indeterminate at this time.

4.2.7 Air Deposition Sites

In addition to instructing NHDES to set MCLs, which in turn become AGQSs, for PFOA, PFOS, PFNA, PFHxS, SB 309 also require the agency to limit air emissions from facilities that cause or contribute to an exceedance of an AGQS and otherwise address the contamination caused. It is not possible to determine the number of facilities that have emissions that cause or contribute to contamination above the AGQS(s) or the costs associated with treatment, investigation and remediation.

NHDES has identified one current and one former industrial facility that have emissions that resulted in the exceedance of the current AGQS for PFOA and PFOS and is evaluating Best Available Control

Technology for PFAS emissions for the current facility. Estimated capital costs for the control devices under consideration range from $2,000,000 - $3,000,000 with annual operating costs of $200,000 - $400,000. In addition, the facility would be subject to air emission stack testing that could cost approximately $100,000 per test, depending on testing methodologies employed. Other potentially affected parties include:

1. Facilities with evaporators used to reduce the volume of liquid wastes if the liquid contains PFAS compounds.

2. Landfill gas (LFG) emissions at solid waste landfills, if it is determined that LFG contains PFAS. Further study as to the effectiveness of combustion of LFG in boilers, engines, turbines or flares as well as current treatment occurring at some LFG to energy facilities would be necessary to identify the impact from this potential source.

3. Other industrial facilities identified as using PFAS where emissions to air might be of concern. Specifically, this could be chrome plating operations that historically used PFAS mist suppressants.

4.2.8 Miscellaneous Sources

Highly fluorinated chemicals can be found in commercially available products and that are used in households, institutions and commercial and industrial facilities. Examples of items that *may* contain PFAS include but are not limited to:

1) Paints.
2) Sealants, including products used on grout, countertops and floor treatments.
3) House cleaners and stain removers.
4) Floor wax removers.
5) Stain-resistant textiles (or chemicals used to treat textiles in homes and businesses) including, but not limited to, carpets, shoes and clothing.
6) Furniture with stain-resistant fabric.
7) Water proof textiles.
8) Food cooking ware and utensils.
9) Ski and boat waxes.
10) Dental floss, cosmetics, sunscreen and other personal care products.
11) Construction materials, including caulk sealants and plumbing sealants.
12) Pesticides.
13) Treated paper.
14) Chemical coatings for metal roofing.
15) Solar panels.
16) Purchased garden soils.
17) Automotive supplies, including waxes, cleaners, windshield wipers and additives to fluids used in automobiles.
18) Camping and other outdoor gear.
19) Spray- and grease-based lubricants.
20) Inks.

The possible presence of PFAS in these items not only presents other exposure potential for PFAS to individuals in the home and at businesses, but also another potential source of contamination to

wastewater, groundwater, storm water and/or surface water. NHDES lacks sufficient data to estimate the potential costs to facility owners of addressing contaminated sites that result from the use of these products.

5. Benefits to Affected Parties

In general, it is difficult to quantify the monetized benefits for environmental and public health standards, and often the case is made that EPA's guidance on deriving benefits for MCLs underestimates benefit, particularly in the area of indirect costs such as reduced quality of life for both the sick individual and their family caregivers. *Contingent valuation,* which is a survey-based economic method for valuing non-market resources (e.g., asking people what they would pay to lower the risk of an adverse health outcome) is a widely accepted economic method to evaluate benefits in such cases as establishing a MCL when reduction in risk can be reasonably quantified. Contingent valuation is based on the economic principle that value equates to willingness to pay. Unfortunately, the type of information needed to use contingent valuation is not yet available for PFAS. While PFOA, PFOS, PFHxS and PFNA have clearly been associated with numerous adverse health outcomes in animals, the mechanism for, and risks related to, similar outcomes in humans are not well understood. Accordingly, NHDES currently has no quantified value of benefit, although there is likely significant benefit to reducing exposure to these compounds through drinking water given the findings of the few previous direct exposure studies and the emerging findings from current epidemiological studies. Qualitatively, given the potential for direct health care treatments costs, associated losses of economic production and income of those impacted, and associated impacts to families and caregivers, limiting exposure to PFOA, PFOS, PFNA and PFHxS at unsafe levels may result in numerous and significant avoided costs.

NHDES researched the subject of benefit quantification and spoke with experts, including a group of professors and researchers at the University of New Hampshire (UNH), with whom NHDES recently contracted to quantify the benefits of reducing the arsenic MCL. NHDES intends to further evaluate the possibility of quantifying benefit of these standards with the group at UNH to see whether studies exist or emerge that would allow the department to do so. In addition, through previous stakeholder engagements, a number of stakeholder groups have been engaging with other research institutions throughout the United States to find recent methods or studies that can help quantify the benefits.

APPENDICES

Appendix 1: Senate Bill 309-FN- Final Version

Below is an image of the final bill text of Senate Bill (SB) 309-FN- Final Version. Please visit the following webpage for an HTML or PDF version of the final bill text: http://gencourt.state.nh.us/bill_status/Results.aspx?q=1&txtbillnumber=SB309&txtsessionyear=2018

CHAPTER 368
SB 309-FN - FINAL VERSION

03/08/2018 0973s
12Apr2018... 1310h
26Apr2018... 1580h

2018 SESSION

18-2838
08/10

SENATE BILL ***309-FN***

AN ACT regulating groundwater pollution caused by polluting emissions in the air and relative to standards for perfluorochemicals in drinking water, ambient groundwater, and surface water.

SPONSORS: Sen. Innis, Dist 24; Sen. Bradley, Dist 3; Sen. Avard, Dist 12; Sen. Fuller Clark, Dist 21; Sen. Gannon, Dist 23; Sen. Ward, Dist 8; Sen. Carson, Dist 14; Sen. Birdsell, Dist 19; Sen. Feltes, Dist 15; Rep. Messmer, Rock. 24; Rep. H. Marsh, Rock. 22; Rep. Emerick, Rock. 21; Rep. Bean, Rock. 21; Rep. Murray, Rock. 24

COMMITTEE: Energy and Natural Resources

AMENDED ANALYSIS

This bill:

I. Allows the department of environmental services to make rules regarding air pollution and the deposit of such pollutants on soils and water.

II. Regulates devices emitting or having the potential to emit air pollutants that may harm soil and water through the deposit of such pollutants.

III. Clarifies the basis for and requires periodic review of ambient groundwater quality standards.

IV. Directs the department to evaluate the ambient ground water quality standards for perfluorooctanoic acid (PFOA) and perfluoroctanesulfonic acid (PFOS) and set ambient groundwater quality standards for perfluorononanoic acid (PFNA) and perfluorohexanesulfonic acid (PFHxS).

V. Establishes the criteria for setting maximum contaminant limits for public drinking water and directs the department to set maximum contaminant limits for perfluorooctanoic acid (PFOA), perfluoroctanesulfonic acid (PFOS), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS).

VI. Establishes a toxicologist position and a human health risk assessor position in the department of environmental services and makes an appropriation to fund the positions.

VII. Directs the department to develop a plan, including a schedule and cost estimates, for establishing surface water quality standards for perfluorooctanesulfonate (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS) in class A and class B waters.

CHAPTER 368
SB 309-FN - FINAL VERSION

Explanation: **Matter added to current law appears in *bold italics.***
Matter removed from current law appears [~~in brackets and struckthrough.~~]
Matter which is either (a) all new or (b) repealed and reenacted appears in regular type.

CHAPTER 368
SB 309-FN - FINAL VERSION

03/08/2018 0973s
12Apr2018... 1310h
26Apr2018... 1580h

18-2838
08/10

STATE OF NEW HAMPSHIRE

In the Year of Our Lord Two Thousand Eighteen

AN ACT regulating groundwater pollution caused by polluting emissions in the air and relative to standards for perfluorochemicals in drinking water, ambient groundwater, and surface water.

Be it Enacted by the Senate and House of Representatives in General Court convened:

368:1 New Subparagraph; Rulemaking; Air Contaminant Impacts on Soil and Water. Amend RSA 125-C:4, I by inserting after subparagraph (s) the following new subparagraph:

(t) The determination of air contaminants subject to regulation, applicability thresholds, determination of best available control technology, and procedures to determine potential impacts of the deposit of such contaminants from the air on soils or water resources to implement RSA 125-C:10-e.

368:2 New Section; Requirements for Air Emissions of Perflourinated Compounds Impacting Soil and Water. Amend RSA 125-C by inserting after section 10-d the following new section:

125-C:10-e Requirements for Air Emissions of Perfluorinated Compounds Impacting Soil and Water.

I. For the purposes of this section:

(a) "Best available control technology" means "best available control technology" as defined in RSA 125-C:10-b, I(a).

(b) "Ambient groundwater quality standard" means "ambient groundwater quality standard" as defined in RSA 485-C:2, I.

(c) "Surface water quality standard" means "surface water quality standard" established in or pursuant to RSA 485-A.

(d) "Perfluorinated Compounds" or "PFCs" means the list of compounds identified in paragraph 1.1 of Environmental Protection Agency Document #: EPA/600/R-08/092 Method 537. "Determination of Selected Perfluorinated Alkyl Acids in Drinking Water by Solid Phase Extraction and Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS)", Version 1.1 (September 2009).

(e) "Precursor" means any substance that has been shown by sound science to be transformed into a PFC under ambient conditions reasonably expected to occur in New Hampshire.

II. A device that emits to the air any PFCs or precursors that have caused or contributed to an exceedance of an ambient groundwater quality standard or surface water quality standard as a result of the deposition of any such PFCs or precursors from the air, shall be subject to the determination and application of best available control technology. Within 6 months of the department determining that the device is subject to such control technology, the owner of the device shall submit to the department an application for a permit. Within 12 months of permit issuance, the applicant shall complete construction and installation of controls consistent with the permit. Operation of the source may continue through the permitting, construction, and installation time period. A source which can demonstrate to the department that its device no longer contributes to an exceedance of an ambient groundwater quality standard or surface water quality standard shall be exempt from this section.

III. The construction, installation, or modification of any device that has the potential, based on an applicability threshold adopted by the department, to cause or contribute to an exceedance of an ambient groundwater quality standard or surface water quality standard as a result of the deposition of any PFCs or precursors from the air, shall be prohibited without first applying for and obtaining a permit from the department that establishes emission limitations for such device based on best available control technology.

IV. Part of the initial application for a permit under this section shall include an analysis of best available control technology for controlling emissions. Any permit issued shall contain inspection, testing, and reporting requirements, as applicable, to ensure the conditions of the permit are met.

V. Any determination of best available control technology under this section shall be subject to the following:

(a) In no event shall application of best available control technology result in:

(1) Emission of any air contaminant that would exceed the emissions allowed by any applicable standard under RSA 125-C or RSA 125-I or rules adopted pursuant to either chapter.

(2) Emission of any air contaminant subject to this section in an amount disproportionate to the emissions of such air contaminant from other similar air pollution control devices for that air contaminant at facilities using similar technology.

(3) Emission of any air contaminant subject to this section which causes or contributes to or has the potential to cause or contribute to an exceedance of an ambient groundwater quality standard or surface water quality standard, as a result of the deposition of the contaminant from the air.

(b) If the department determines that the facility has more than one device

that emits air contaminants subject to this section, the department shall determine best available control technology emission limitations for each such device.

VI. This section shall only pertain to PFCs for which at least one study has been conducted in accordance with generally accepted scientific principles that demonstrates that the PFC of concern is known to cause or may reasonably be anticipated to cause acute, chronic, mutagenic, reproductive, or developmental health effects in humans as a result of exposure to such PFC. The implementation of this section shall only rely upon standards that are based on federal maximum contaminant levels, health advisories, provisional health advisories, standards that are derived from federally published toxicological data, or more restrictive New Hampshire state standards.

368:3 New Subparagraph; Statement of Purpose. Amend RSA 485:1, II by inserting after paragraph (h) the following new subparagraph:

(i) Adopt primary drinking water standards by establishing maximum contaminant limits or treatment techniques.

368:4 Drinking Water Rules. Amend RSA 485:3, I(b) to read as follows:

(b) ***After consideration of the extent to which the contaminant is found in New Hampshire, the ability to detect the contaminant in public water systems, the ability to remove the contaminant from drinking water, and the costs and benefits to affected parties that will result from establishing the standard, a*** specification for each contaminant of either:

(1) A maximum contaminant level that is acceptable in water for human consumption[~~, if it is feasible to ascertain the level of such contaminant in water in public water systems~~]; or

(2) One or more treatment techniques or methods which lead to a reduction of the level of such contaminant sufficient to protect the public health, if it is not feasible to ascertain the level of such contaminant in water in the public water system; and

368:5 New Subdivision; Perfluorochemicals. Amend 485 by inserting after section 16-d the following new subdivision:

Perfluorochemicals

485:16-e Perfluorochemicals. By January 1, 2019, the commissioner shall, in consultation with the commissioner of the department of health and human services and other interested parties, initiate rulemaking in accordance with RSA 541-A to adopt a maximum contaminant limit for perfluorooctanoic acid (PFOA), perfluoroctanesulfonic acid (PFOS), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS).

368:6 Ambient Groundwater Quality Standards. Amend RSA 485-C:6 to read as follows:

485-C:6 Ambient Groundwater Quality Standards.

I. The commissioner shall establish and adopt ambient groundwater quality standards for regulated contaminants which adversely affect human health or the environment. Ambient groundwater standards shall apply to all regulated contaminants which result from human operations or activities, but do not apply to naturally occurring contaminants. ***Where state maximum contaminant levels have been adopted under RSA 485:3, I(b), ambient groundwater quality standards shall be equivalent to such standards.*** Where federal maximum contaminant level or health advisories have been promulgated under the Federal Safe Drinking Water Act or rules relevant to such act, ambient groundwater quality standards shall be [~~equivalent to~~] ***no less stringent than*** such standards. ***The commissioner may adopt standards more stringent than federal maximum contaminant levels or health advisories if, accounting for an adequate margin of safety to protect human health at all life stages, including but not limited to pre-natal development, the commissioner determines federal standards are insufficient for protection of human health.*** Where such standards are ***established*** based upon ***health advisories that address*** cancer risks, the ambient groundwater quality standards shall be equivalent to that exposure which causes a lifetime exposure risk of one cancer in 1,000,000 exposed population. Where no federal ***or state*** maximum contaminant level or health advisory has been issued, the commissioner may adopt ambient groundwater quality standards on a basis which provides for an adequate margin of safety to protect human health and safety.

II. ***Health advisories that are adopted as ambient groundwater quality standards shall be reviewed by the department at least every 5 years to determine if new research warrants revising the current ambient groundwater quality standard. If the department finds a revision is necessary it shall conduct rulemaking to adopt the revised standard.***

III. Ambient groundwater quality standards shall be the water quality basis for issuance of groundwater discharge permits under RSA 485-A: 13.

[~~III.~~] ***IV.*** Except for discharges of domestic wastewater regulated under RSA 485-A:13 and RSA 485-A:29, no person shall violate ambient groundwater quality standards.

V. By January 1, 2019, the commissioner shall, in consultation with the commissioner of the department of health and human services and interested parties, initiate rulemaking to adopt ambient groundwater quality standards for perfluorononanoic acid (PFNA) and perfluorohexanesulfonic acid (PFHxS).

VI. By January 1, 2019, the commissioner shall, in consultation with the commissioner of the department of health and human services and interested parties, conduct a review to determine whether current research warrants revising the existing ambient groundwater quality standards for perfluorooctanoic acid (PFOA) and

perfluorooctanesulfonic acid (PFOS).

368:7 Department of Environmental Services; Positions Established; Appropriation. There is established within the department of environmental services one classified toxicologist position and one classified human health risk assessor for the purposes of developing appropriate standards to protect groundwater and drinking water quality under RSA 485-C. The sum necessary to pay the salary, benefits, and other costs related to the positions established in this section is hereby appropriated to the department of environmental services for the biennium ending June 30, 2019. This appropriation shall be in addition to any other appropriations made to the department in the biennium. The governor is authorized to draw a warrant for said sum out of any money in treasury not otherwise appropriated.

368:8 Department of Environmental Services; Surface Water Quality Standards. The commissioner of environmental services shall develop a plan, including a schedule and cost estimates, to establish surface water quality standards for perfluorooctanesulfonate (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorohexanesulfonic acid (PFHxS) in class A and class B waters for all designated uses. The commissioner shall submit the plan upon its completion, but no later than January 1, 2020, to the house resources, recreation, and development committee and the senate energy and natural resources committee.

368:9 Effective Date.

I. Sections 1 and 2 of this act shall take effect 60 days after its passage.

II. The remainder of this act shall take effect upon its passage.

Approved: July 10, 2018
Effective Date:
I. Sections 1 and 2 shall take effect September 8, 2018.
II. Remainder shall take effect July 10, 2018.

Appendix 2: The Basic Steps Used by NHDES Environmental Health Program to Propose Health Based Drinking Water Standards for Perfluoroalkyl Substances

The Basic Steps Used by NHDES Environmental Health Program to Propose Health Based Drinking Water Standards for Perfluoroalkyl Substances

Contact with questions or comments:
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Step 1:

Find a **no observed adverse effect level** (**NOAEL**) or **lowest observed adverse effect** (**LOAEL**) for the **critical health effect** in an animal study. Usually in units of milligrams of chemical/kilograms of animal body weight/ day (mg/kg/day).

NOAEL/LOAEL = To be protective against all other toxic effects, the critical effect (s) occurring at the lowest NOAEL is usually chosen. If even the lowest dose in the animal study has an effect, then the LOAEL must be used.

Critical health effect = adverse health effect in animal that is relevant to humans; generally occurs at very low exposures.

Step 2:

NOAEL/LOAEL dose (mg/kg/day) goes into a **pharmacokinetic model** = **point of departure (PoD in mg/kg/day)**

Pharmacokinetic model = model to convert an animal dose to a human exposure dose based on physiological parameters of each and knowledge of how chemicals act in the body (metabolism)

PoD = human dose (mg/kg/day) that is starting point for developing a toxicity value (100% of the safe chemical dose)

If no pharmacokinetic model exists, 2nd choice is a **dosimetric adjustment factor (DAF)** to go from NOAEL/LOAEL to PoD.

DAF = ratio of human half-life of chemical in the blood to the animal half-life of chemical in the blood.

Step 3:

PoD (human dose in mg/kg/day)/total uncertainty factors (UFs) = Reference Dose (RfD) or Minimal Risk Level (MRL in (mg/kg/day).

RfDs and MRLs are the same. Just different terminology used by EPA and ATSDR.

UFs = adjustment factors used when knowledge about a chemical's toxicity or effect on animal and human's is incomplete. UFs are usually either 10 or 3. Examples of common UFs: going from an animal study to a human exposure; accounting for human variability and sensitivity; if the lowest dose in an animal study still has an effect (no NOAEL); if a short-term study is used to develop a drinking water standard to protect against effects from long-term exposure, if the usual required studies such as developmental or cancer studies to understand how a chemical affects different life stages are missing (called a database deficiency UF).

RfD/MRL = the total safe non-cancer dose of a chemical to a human (mg/kg/day)

Step 4:

RfD/MRL (mg/kg/day) X Receptor (exposure factors) = drinking water equivalency level (DWEL in micrograms per liter (µg/L)

Receptor (exposure factors) = the sensitive exposed person used in the calculations (infant, young child, adult, pregnant or lactating woman) and their applicable bodyweight in kilograms and water ingestion rate in Liters/day.

DWEL (µg/L) = 100% of the safe dose expressed as the concentration in water for the receptor chosen.

Step 5:

DWEL (µg/L) /relative source contribution factor (RSC) = proposed drinking water standard (µg/L)

RSC = accounts for exposure to the chemical from sources other than drinking water. Examples are exposure from air, food, soil, non-ingestion drinking water exposure, such as breathing in the chemical when bathing (if the chemical is volatile) and absorption through the skin when bathing.

EPA guidance states that the highest RSC should be 80% (ceiling) and the lowest RSC should be 20% (floor). If there are sufficient data to calculate an RSC, one should be calculated. If data are insufficient, EPA recommends using the floor of 20% as a default value.

If data exist to calculate an RSC, EPA guidance recommends using **average** exposure values, not high-end.

For PFAS and some other chemicals, data on background exposure to humans has been collected and analyzed. CDC conducts the National Health and Nutrition Examination Survey (NHANES) to determine the nutritional and health status of the U.S. population. From blood samples of randomly selected volunteers, NHANES analyzes for several chemicals. In general, blood is not collected from the very young (less than 6 years of age). PFOA, PFOS, PFHxS, and PFNA are among the chemicals analyzed in blood serum by NHANES.

NHANES data are one of the best sources of background chemical exposure data for calculating an RSC. This is especially true for PFAS because of the long half-lives in human blood for many PFAS. Examples – PFOA half-life = 2.3 to 3.8 years; PFOS half-life = 5.4 years; PFHxS half-life = 8.5 years; PFNA half-life = 2.5 years).

NHANES has PFAS blood data results analyzed from 1999 through 2013-14. Because use of PFOA and PFOS has been phased out over time in the U.S., the concentrations found in the U.S. population by NHANES have been declining for years. See the Table below for the first and most recent PFAS sample results:

Concentrations in blood serum in micrograms per liter (µg/L = parts per billion (ppb))

Collection year	PFOA		PFOS	
	Geometric Mean Concentration	95th Percentile Concentration	Geometric Mean Concentration	95th Percentile Concentration
1999-2000	5.2	11.9	30.4	75.6
2013-2014	1.94	5.57	4.99	18.5

Geometric mean = 50% of the results are above and 50% are below this value. 95th percentile = 95% of the results are below and 5% are above this value.

Appendix 3: Technical Considerations for Health-Based Risk Assessment & References

Appendix 3: Technical Considerations for Health-Based Risk Assessment & References

The following is a summary of certain technical factors considered by NHDES in the derivation of the MCL/AGQS for PFOA, PFOS, PFHxS and PFNA. It should be noted that NHDES conducted a focused review of the existing information based on recent reports from state and federal agencies, public comments from technical workshops and recently published studies. Appendices 3-7 are not an exhaustive summary of all studies evaluated by NHDES; rather, they are a summary of critical information needed to understand the process by which the proposed MCL/AGQS values were derived. As the study of PFAS is an evolving area of science, NHDES is monitoring for emerging studies that would change the current understanding of PFAS-related health effects. NHDES will reevaluate the proposed standards if studies are published that demonstrate new and strong evidence for re-evaluating the toxicity values used to derive the currently proposed values.

In deriving the standards, there were two major technical considerations that influenced the NHDES evaluation of studies and selection of health effects. The first is discussion of issues related to the mechanism(s) of action associated with effects in animals and in vitro human models. The second was the determination to utilize non-cancer endpoints given the limited amount of information available for carcinogenicity of these specific PFAS.

Mechanism of Action

A mechanism of action is the biochemical process that allows a chemical to cause a physiological response. Mechanisms of action vary between chemicals and could include: interactions with receptors, interference of enzymes, mimicking of hormones or the formation of chemical bonds with biomolecules like cellular proteins or DNA. For toxicologists, knowledge about a chemical's mechanism of action is crucial for evaluating toxicity and relevance toward human health. Some mechanisms of action are unique to certain species or groups of animals and may have limited relevance to human health. If the mechanism of action is unknown, it is difficult to demonstrate a causal relationship between a chemical and a human health effect, even if there are associations.

Currently, there is no consensus in the scientific literature for the mechanism of action by which PFAS elicit their effects. There are two categories that the suspected mechanisms and their underlying studies can be classified into. The first mechanism is the activation of nuclear receptors, such as the peroxisome proliferator-activated receptor subtype alpha (PPARα). Activation of PPARα leads to peroxisome proliferation and oxidative stress in rodents, and altered lipid metabolism in humans. The second proposed mechanism is the induction of cellular stress and mitochondrial dysfunction independent of PPARα. The current literature presents evidence for both pathways, with more publications that focus on PPARα activation. Recent studies have sought to evaluate the role of PPARα-independent pathways in PFAS-related effects. It should be noted that the following summary does not seek to define a known mechanism of action for PFAS, as this is beyond the scope of the NHDES risk assessment. Rather, it is an overview of the issues surrounding the mechanism of action, which are critical to selecting appropriate health effects for risk assessment.

PPAR and Nuclear Receptor Mediated Effects

Peroxisome proliferator-activated receptor (PPAR) activation is the presumed mechanism of action for several forms of PFAS-induced toxicity in rodents. There are multiple isoforms of PPAR including subtypes alpha (α), beta (β) and gamma (γ), where PPARα is one of the most commonly studied isoforms in mammals. As nuclear receptors, PPARs are capable of initiating gene expression, thereby producing proteins that regulate lipid and energy metabolism (Issemann and Green, 1990; Lee et al., 1995). This includes elevating enzyme levels responsible for enzymatic-oxidation, ketogenesis, and lipoprotein metabolism (reviewed by Sertznig et al., 2007). Rodent studies demonstrate that PFAS exposure is associated with increased transcription of PPARα-regulated genes, palmitoyl CoA oxidase activity and perturbed lipid homeostasis and peroxisome proliferation (Perkins et al., 2004; Loveless et al., 2006; Rosen et al., 2007, 2008, 2017; Das et al., 2017; reviewed by ATSDR, 2018). An adverse side effect of this metabolic pathway is the generation of reactive oxygen species (ROS) that damage cellular structures and organelles, culminating in pathological effects observed in animal studies. PPARα activation in humans does not result in the same peroxisome proliferation effects, but does induce changes in lipid metabolism and gene transcription.

The role of PPARα in PFAS toxicity continues to be a major criticism against the use of rodent studies for human risk assessment (Klaunig et al., 2012). This criticism is based on quantitative and qualitative differences between rodent and human PPARα biology. When compared to humans, rodents overexpress PPARα by an approximate factor of 10 in certain tissues, namely the liver (Palmer et al., 1998; Corton et al., 2014). This overexpression of PPARα in rodents creates more molecular targets, thereby enhancing their sensitivity to PFOA and other PPARα agonists. Along with quantitative differences in the abundance of PPARα, structural differences between human and rodent PPARα enhance the sensitivity of rodents to certain PPARα agonists (Klaunig et al., 2003; Gonzalez and Shah, 2008; Tyagi et al., 2011). In light of these differences, *responses that are exclusively mediated by PPARα in rodents may overestimate toxicity for humans*.

The low expression of PPARα and other PPARs is not to be mistaken for lack of a functional role in human physiology. Human PPARs are involved in lipid and energy metabolism and are primarily expressed in liver, muscle, adipose tissues and certain cell types in the immune system (Tyagi et al., 2011). Hypolipidemic drugs such as fibrates act on human PPARs to manage clinically-high cholesterol levels (Brunton et al., 2011; Ferri et al., 2017). Some in vitro evidence shows that PFAS can activate human PPAR, albeit with less efficiency than rodent PPARs (Wolf et al., 2008). Additional studies are required to understand what role, if any, that PPARs play in human responses to PFAS.

Evidence from gene knock-out studies in mice (i.e., PPARα-null) and primates indicates that there are potentially PPARα-independent mechanisms of PFAS toxicity that involve other nuclear receptors (reviewed by Li et al., 2017a). The constitutive androstane receptor (CAR), estrogen receptor subtype-α (ERα), farnesoid X receptor (FXR), retinoid X receptor (RXR) and pregnane-X receptor (PXR) contribute to PFAS toxicity in wild-type and knock-out mice (Vanden Heuvel et al., 2006; Bjork et al., 2011; Rosen et al., 2017); albeit to a lesser degree in human cell models (Behr et al., 2018). Activation of these nuclear receptors can be influenced by activation of PPARα as ligand-bound nuclear receptors can form heterodimers (e.g. PPARα and RXR) with each other to initiate changes in gene expression (Evans and Mangelsdorf, 2014; Cave et al., 2016). Given the uncertainty about nuclear receptor and co-activator protein interactions, further research is needed before the role of other nuclear receptors in PFAS toxicity can be clearly demonstrated or refuted.

Non-Nuclear Receptor Mediated Effects

Aside from nuclear receptors, there is growing evidence that PFAS induce cellular dysfunction via PPARα-independent mechanisms. The alternative mechanisms with limited evidence include disruption of the: *i*) nuclear factor kappa(κ) B (NFκB) pathway, *ii*) intercellular gap-junction communication, *iii*) lipid membrane stability, and *iv*) mitochondrial signaling pathways (EPA 2016ab; Li et al., 2017a; ATSDR, 2018). Of these, recent evidence from rodent exposures and human cell lines points to disrupted mitochondrial signaling as a plausible PPARα-independent mechanism of PFAS toxicity.

Mitochondria are primarily responsible for maintaining chemical energy levels within cells through the production of ATP. Disruption of the mitochondrial membrane or proteins facilitating ATP production results in imbalanced energy metabolism and the formation of ROS. In response to this stress, cells will undergo programed cell death (apoptosis). In human HepG2 (hepatoma) cells, PFOA induces apoptosis that is preceded by ROS formation, loss of mitochondrial membrane potential and activation of the apoptosis regulating protein known as caspase-9 (Shabalina et al., 1999; Panaretakis et al., 2001; Yao and Zhong, 2005). Eriksen et al. (2010) reported a pronounced effect of PFOA and PFOS on ROS generation in HepG2 cells, but only PFNA was associated with DNA damage. In non-cancerous cell lines, Li et al. (2017b) documented dose-dependent apoptosis in HL-7702 (human liver) cells treated with PFOA (2,500-7,500 ppt). At these same doses they also observed increased production of caspase-9 and the formation of 8-hydroxydeoxyguanosine (8-OHdG), a marker of ROS damage to DNA. While the exact mechanism for mitochondrial dysfunction in human cells remains unidentified, there is evidence that both abnormal (i.e., cancerous) and normal *in vitro* cell lines are responsive to PFAS.

Beyond human cell lines, the mitochondrial effects of PFOA have been documented across a variety of *in vivo* models in the presence and absence of PPARα activation. Similar to human liver cells, PFOA-treated mice showed a dose-responsive increase in hepatic production of caspase-9 and 8-OHdG (Li et al., 2017b). Proteomic analysis of these mice found that ROS formation was independent of PPARα and likely due to suppression of proteins involved with ATP formation in the electron transport chain (ETC). Of note, these effects were observed following a 28-day *in vivo* exposure with average PFOA serum concentrations of 970 ng/mL. This pathway was associated with hepatic hypertrophy and signs of apoptosis.

In vitro animal studies have further substantiated PFAS-associated mitochondrial dysfunction. Suh et al. (2017) reported impaired mitochondrial metabolism combined with ROS formation in a rat pancreatic β-cell line exposed to PFOA. Mitochondria isolated from the livers of male rats and treated with various PFAS showed reduced membrane potential that was attributed to destabilization of lipid structures and subsequently enhanced ion exchange; however, this was at concentrations above extreme occupational exposures for individual PFAS (Starkov and Wallace, 2002). Compared to other PFAS, PFOS showed the most potent inhibitory effect on mitochondrial respiration in an isolated system (Wallace, 2013). In isolated rat mitochondria, Mashayekhi et al (2015) found that PFOA increased ROS generation, interfered with ETC complexes I, II and III activity and contributed to collapse of mitochondrial membrane potential. Additionally, there is some evidence for mitochondrial effects across broader classes of vertebrates including fish (Hagenaars et al., 2013; Cui et al., 2015). The ubiquity and conservative evolution of mitochondria makes this pathway potentially more relevant to human health than PPARα, but further research is needed before this can be confirmed, or excluded, as a mechanism of action for PFAS.

Conclusions

Current evidence suggests that the effects of PFAS in animal models may be due to various mechanisms of action, where activation of PPAR is critical for advanced toxicity observed in rodents. The latter PPAR-independent pathways have only recently received as much research attention as PPARα and *require further investigation*. As stated by EPA's own Health Advisory for PFOA (2016a) and PFOS (2016b), there is no known unifying mechanism of action for the wide-array of effects associated with PFOA, PFOS and other PFAS. Yet, there is some evidence that these compounds affect biological targets in animals and humans and thus does not preclude the necessity for assessment of the myriad of health effects observed through animal studies and human epidemiology.

If all PFAS shared an identical molecular mechanism of action, a class-based MCL/AGQS would be a scientifically reasonable method for risk management. Such approaches have been applied to other chemical classes where there is a known and common mechanism of action (e.g., polychlorinated biphenyls). However, based on current literature, the only demonstrated common target for PFAS appears to be the activation of PPARα. If this is true for all PFAS, then rodent-derived toxicity values for a class of "PPARα activators" are 3-10x more protective, given the overexpression and sensitivity of PPARα in rodents relative to humans. However, this would mean that the Animal-to-Human Uncertainty Factor (discussed in the Derivation Appendices) of 3 that is used to derive the human doses may overestimate human sensitivity. As there is currently evidence for compound-specific effects through other nuclear receptors and PPAR-independent pathways, NHDES assessed the health impacts of each PFAS individually.

It should be noted that in conducting this assessment NHDES observed a potential bias in the current understanding of the mechanism(s) of action for PFAS. In older animal studies, there is a tendency to focus on PPARα-related enzyme activity without measuring other biochemical processes that would substantiate, or rule-out, other mechanisms of action. This is, in part, due to an under-utilization of methods for identifying mechanisms of action. This is not unreasonable, as current approaches for identifying pathways were once very cost prohibitive. High-throughput approaches that are readily applied in today's research laboratories were not well standardized until quite recently. Now, the rapidly changing technologies in molecular biology, and the fairly recent application of these tools for toxicological studies, are allowing a better understanding of subtle biological processes. *Although not currently available, NHDES expects that future studies will provide important information about the mechanism(s) of action that will be critical to identifying relevant human health risks associated with PFOA, PFOS, PFHxS, PFNA and other PFAS*.

Non-Cancer Versus Cancer Endpoints

NHDES risk assessment of PFOA, PFOS, PFHxS and PFNA used non-cancer health effects for derivation of toxicity values and subsequent MCL/AGQS values. This is due to a current lack of adequate information to derive reliable cancer-based toxicity values from animal studies. Human epidemiological studies show some associations between these PFAS and certain cancers, but these associations are inconsistent with limited data on serum concentrations required to confidently develop health-based guidance values. Of the four PFAS, the most information is available for PFOA and PFOS and is discussed below. To the best of NHDES' knowledge, there are currently no peer-reviewed rodent studies that evaluate the carcinogenicity of either PFNA or PFHxS. This precludes risk assessment for cancer-based endpoints for PFNA and PFHxS at this current time.

PFOA is classified as possibly carcinogenic to humans (IARC, 2016) based on evidence from the C8 Study population (Barry et al., 2013) and a limited number of toxicology studies that identified kidney and testicular tumors in rats (Butenhoff et al., 2012; Biegel et al., 2001). In the 2016 Drinking Water Health Advisory document, EPA found suggestive evidence of carcinogenic potential in humans (EPA, 2016a). In humans, Barry et al. (2013) found an increased risk of testicular cancer with estimated exposure to PFOA in a highly exposed population, but others have reported no association with testicular cancer (Vieira et al., 2013). Steenland and Woskie (2012) reported an increase in kidney cancer associated with modeled exposure to PFOA, whereas others have found no association (Leonard, 2006; Leonard et al., 2008; Barry et al., 2013; Raleigh et al., 2014). Inconsistencies in the epidemiological evidence are likely due to the limited information regarding PFOA exposure, which is modeled in some studies to address a lack of exposure history. Additional sources of variation likely include differences between populations in lifestyle and background exposure to other environmental agents. However, these studies are associative and cannot demonstrate causation for increased or decreased risks making these studies ill-suited for deriving toxicity values. Therefore, risk assessment for PFOA currently would rely on evidence from more controlled animal studies to determine a cancer-based toxicity value for MCL/AGQS derivation.

While the animal studies provide limited support for PFOA-induced testicular tumors, the study that includes a dose-response relationship suitable for risk assessment did not measure serum concentrations (Butenhoff et al., 2012). Due to the profound differences in the half-lives of PFAS between rodents and humans, this omission introduces a large measure of uncertainty, since orally-administered doses of PFOA do not result in the same serum levels across species. Different approaches for estimating the serum concentrations from this study result in vastly different toxicity value and subsequent health advisory numbers (EPA, 2016a; NJ DWQI, 2017). Furthermore, there is no known mechanism of action for the carcinogenic potential of PFOA, and some potential pathways have questionable relevance to human health. Thus, NHDES found the existing database to be inadequate for assessing carcinogenic potential of PFOA and utilized non-cancer endpoints.

Currently, there is little evidence linking PFOS to a specific human cancer with inconsistent associations reported from epidemiological studies. For example, PFOS was associated with breast cancer in a study of Inuit women in Greenland (Bonefeld-Jørgensen et al., 2011), yet a later study of a larger Danish cohort did not substantiate the association (Bonefeld-Jørgensen et al., 2014). A single animal study that evaluated carcinogenicity in rats observed an increased incidence of hepatocellular adenomas at the highest dose, as well as a small number of thyroid tumors that did not display a dose-response relationship. As PFOS is shown to be a PPAR-activator, the hepatic tumors are unlikely to be relevant to human health assessment (Klaunig et al., 2003; Corton et al., 2014), and are not supported by epidemiological evidence (Eriksen et al., 2009). Given this and the EPA conclusion that there was insufficient evidence to pursue a cancer endpoint for PFOS (2016b), NHDES did not select cancer as an endpoint for risk assessment of PFOS.

In its 2018 draft, ATSDR identified on-going studies sponsored by the National Institute of Environmental Health Sciences (NIEHS) that aim to identify the carcinogenic potential of PFOA. To date, NHDES is unaware of other research teams that are investigating the carcinogenicity of other PFAS. Related to this, an independent panel of scientists commissioned by the state of Michigan noted that:

> "Although cancer often receives more attention than other potential adverse health effects that may result from a toxicant exposure, based in part on the presumption that it is the most sensitive outcome, this is not always the case. Indeed, for PFOA and PFOS, developmental and immune

> effects seem to be among the most sensitive in both animal and human studies and may be more important for setting advisory and regulatory limits on exposure. Developmental, immune, and liver effects were often drivers for determining the recent advisory levels of PFOA and PFOS from EPA, ATSDR, and state agencies." - Michigan PFAS Science Advisory Panel (2018)

If additional studies are published that demonstrate human-relevant mechanisms for carcinogenicity, combined with sufficient data for reliable and accurate extrapolation, NHDES recommends re-assessment of the proposed toxicity values.

Appendix 4: PFOA Derivation

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Toxicity Endpoint: **Altered Liver Weight and Function**

Of the four PFAS for which MCL/AGQS values were derived, PFOA has the largest body of scientific literature for evaluation. Despite a large number of epidemiological studies showing a variety of associated health effects, these studies did not provide sufficient information for derivation of reference doses based on the recommended guidelines used by NHDES. However, NHDES did evaluate the human health literature to identify health endpoints with the greatest weight of evidence to narrow its search to animal studies with similar effects.

In humans, prolonged exposure to PFOA has been associated with alterations in markers of hepatic function and lipid metabolism. In the 2018 draft report, ATSDR found current epidemiological studies provide adequate evidence for alterations in serum levels of hepatic enzymes, as well as elevations in serum lipids (i.e., total and LDL cholesterol). A recent analysis of the current epidemiological literature by a team at the Australian National University found inadequate evidence for altered liver function in response to PFAS, but identified sufficient evidence for association between PFOA and PFOS exposure with hypercholesterolemia (Kirk et al., 2018). Most recently, an independent panel of academic and government scientists agreed with ATSDR's assessment of associations between PFAS exposure and liver enzyme levels (Michigan PFAS Science Advisory Panel, 2018), although additional research is needed to determine if such changes in these clinical markers translate into liver disease following chronic exposure.

As a critical health effect, altered liver weight and function are potentially adaptive, meaning they are expected to recede in the absence of the stimulating chemical. Hall et al. (2012) contend that such adaptive effects should not serve as the basis for risk assessment as the effect is dependent on continuous exposure. Kirk et al. (2018) suggest that any adverse effect related to changes in cholesterol metabolism and downstream effects may not be of public health relevance due to treatability. However, the NHDES risk assessment process assumed that the MCL/AGQS should allow for prolonged water consumption without the need for recovery from an adaptive response in the liver or associated effects on lipid metabolism. Furthermore, the relatively long half-lives of PFOA, and other PFAS, in humans prolong exposure on a scale of months to years making such depurations suspect. Thus, the NHDES risk assessment of PFOA evaluated and selected increased relative liver weight in rodents as a sensitive precursor effect for altered liver function and changes in lipid metabolism.

Several research teams have evaluated the hepatotoxicity of PFOA in non-human primates, rodents and other non-mammalian model organisms. Hepatotoxicity is of particular interest as PFOA concentrations are frequently higher in the liver than circulating serum levels. Furthermore, considerable resources have been dedicated to investigating the hepatic effects of PFOA across *in vitro*, *in vivo* and epidemiological studies. This is due to concern for prolonged liver damage and its implications for chronic diseases, such as non-alcoholic fatty liver disease. However, indicators of hepatotoxicity in animal models may be overly sensitive when compared to human biology due to PPARα activation, making outcomes like liver cancer in rodents less relevant to human health (Hall et al., 2012). Given the suggestive evidence for liver impacts in humans, NHDES evaluated the consistency of adverse hepatic outcomes across animal studies and their relevance to human health as determined by PPARα-independent effects.

One the most consistently documented responses to PFOA across rodent models is hepatic hypertrophy. As reviewed by Hall et al. (2012), hepatic hypertrophy has various connotations including increases in the i)

organ weight, ii) average size of hepatocytes, and iii) expression levels or activity of hepatic enzymes (also referred to as functional hypertrophy). The occurrence of any one of these forms of hepatic hypertrophy alone may not indicate liver toxicity. This is due to rodent-specific sensitivity in the activation of cellular responses that are mediated by the PPARα pathway. Thus, the presence of multiple forms of hepatic hypertrophy in animals and evidence for a non-PPARα mechanism of action would suggest hepatotoxicity that is relevant to humans. Regarding PFOA, there is evidence for multiple forms of hepatic hypertrophy in animal models, summarized below. As mentioned in Appendix 3, the mechanism of action was evaluated and it was determined that liver hypertrophy could be associated with non-PPARα mechanisms.

Several studies have demonstrated that exposure to PFOA through food or water induces increased liver weights in mice and rats (reviewed by EPA 2016 and ATSDR, 2018, and references therein). This is associated with changes in hepatocellular structure that include hepatocellular hypertrophy, cytoplasmic vacuolization, necrosis, signs of apoptosis and persistent changes in liver structure following prenatal exposure (Griffith and Long, 1980; Butenhoff et al., 2004a; Loveless et al., 2008; Son et al., 2008; Cui et al., 2009; Elcombe et al., 2010; Yahia et al., 2010; Wang et al., 2013; Quist et al., 2015; Li et al., 2017b). Changes in clinical chemistry markers, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), can be observed after exposure to drinking water laced with PFOA (21-d; Son et al., 2008). Others reported no changes in ALT and AST despite the occurrence of liver necrosis in rodents (Kennedy et al., 1985), suggesting that AST and ALT may not be accurate indicators for chronic disease in rodents (Hall et al., 2012). Additionally, hepatic hypertrophy from PFOA is associated with reductions in circulating cholesterol levels in rodents (Haughom and Spydevold, 1992; Loveless et al., 2006, 2008; Elcombe et al., 2010; Quist et al., 2015ab). While hypocholesterolemia is the opposite effect of that generally seen in epidemiological studies, hypercholesterolemia has been observed in PFOA-exposed rodents that are also fed a high-fat or Westernized diet (Tan et al., 2013; Rebholz et al., 2016).

As discussed in Appendix 3, recent studies indicate that there are PPARα-independent pathways associated with altered liver size and function making the hepatic effects in rodents relevant to human health risk assessment.

In primates, Butenhoff et al. (2004b) used male cynomolgus monkeys to assess liver toxicity from ammonium perfluorooctanoate (APFO) at 3, 10 and 30 mg/kg/d over the course of 26 weeks. They observed increased absolute liver weights, although relative liver weight (liver weight relative to body weight) was only significantly elevated at the highest dose, along with serum triglycerides and thyroid hormones. Consistent with other primate studies using cynomolgus monkeys (Thomford, 2001) and Rhesus monkeys (Griffith Long, 1980), no histological changes were observed in the liver. A lack of change in hepatic palmitoyl CoA oxidase activity at all but the highest dose led the authors to conclude that peroxisome proliferation did not play a role in the observed toxicity. The authors also noted that:

> "increase in liver weights seen following the administration of APFO to cynomolgus monkeys was, at least in part, due to hepatocellular hypertrophy (as demonstrated by decreased hepatic DNA content) which in turn may be explained by mitochondrial proliferation (as demonstrated by increased succinate dehydrogenase activity)." - Butenhoff et al. (2004b)

The strength of these observations is limited by inherent challenges with primate research including a limited sample size combined with high inter-individual variability in wild-caught animals (as referenced by the need to determine age by dentition). Additional issues in this study add greater scrutiny, such as

changes in the high-dose treatment mid-way through the experiment and attrition of animals from what were assumed to be non-treatment-related causes (Butenhoff et al., 2004b).

Consideration of Other PFOA-Related Effects from Animal Studies

As outlined by EPA (2016), National Toxicology Program (NTP 2016) and the draft assessment by ATSDR (2018), PFOA has also been shown to affect the functions of the immune, thyroid and reproductive systems, along with effects on early growth and development. The sensitivity of early life stages requires additional consideration regarding developmental effects associated with PFOA. As discussed below, EPA based its 2016 Health Advisory for PFOA on developmental delays in mice following an in utero exposure to PFOA (Lau et al., 2006; EPA, 2016). Another developmental endpoint of concern is delayed mammary gland development, which has been a contentious endpoint in recent health-based risk assessments of PFOA. Most regulatory bodies have deferred from its use as a critical health endpoint given uncertainty about its functional significance and relevance to human health. Given concerns for developmental outcomes, NHDES decided it was important to detail its decision not to use these health endpoints as the basis for PFOA's reference dose.

Early-life exposure to PFOA elicits responses from a variety of physiological systems and age-dependent-processes. Rodent responses to in utero, perinatal, lactational or peripubertal exposures include: pre- and post-birth loss of pups, reduced neuro-motor activity, delays in developmental hallmarks, reduced bone ossification and impaired growth (Butenhoff et al., 2004a; Lau et al., 2006; White et al., 2007; Wolf et al., 2007; Hu et al., 2010; Onishchenko et al., 2011; White et al., 2011; Albrecht et al., 2013; Cheng et al., 2013; Quist et al., 2015ab; Koskela et al., 2016). The variety of developmental endpoints reflects experiments using both standardized and non-traditional toxicological endpoints. The use of different rodent strains, routes of administration and exposure periods makes it difficult to discern common effects. However, a meta-analysis of seven fetal growth studies estimated a negative relationship between PFOA and rodent pup weight, where body mass is reduced by 0.23 g per 1 mg/kg/d increase in PFOA (Koustas et al., 2014). Together, there is evidence that PFOA is detrimental to growth and development in rodent models.

EPA and ATSDR considered certain developmental impacts of PFOA to be sufficient critical effects for their derivation of final and draft reference doses, respectively. The developing fetus is often more sensitive to chemical insults meaning that standards based upon developmental exposures in mice or rats, spanning gestation and subsequent window of lactation, are considered protective for sensitive subpopulations (EPA, 2016a). In both cases, EPA and ATSDR selected studies that reported alterations in bone development, along with additional developmental effects unrelated to the skeletal system. However, there were stark differences between these studies in their suitability for human health risk assessment.

Lau et al. (2006) evaluated the pre- and post-natal effects of in utero PFOA exposure in CD-1 mice. Developmental effects were observed in pups across all doses (1-40 mg/kg/d), where the lowest dose was associated with reduced bone ossification, precocious male puberty, and increased weight gain in later life. Higher doses (10-20 mg/kg/d) were associated with increased incidence of full fetal reabsorption, microcardia, delayed eye-opening, as well as reductions in fetal survival, birth weight. At 40 mg/kg/d there was a complete loss of pregnancy in all treated mice. Lau et al. (2006) concluded that reduced ossification of the forelimb phalanges (long-bones of the paw) was the most sensitive endpoint in prenatally-exposed pups. A weakness of this study was the lack of information regarding PPARα activity, or other biochemical

measures, that might have pointed to a mechanism of action for developmental toxicity. A good experimental design, adequate sample sizes and thorough characterization of fetal growth and survival were strengths of the study, making it a credible basis for risk assessment.

Another developmental study, presented across two publications (Onischenko et al., 2011, Koskela et al., 2016), reported behavioral and skeletal changes in C57BL/6 mice. This study used a single dose level of PFOA (0.3 mg/kg/d) based on the lowest effect doses estimated by Lau et al. (2006), and exposed the mice throughout gestation (Onischenko et al., 2011). It is not explicitly stated when, but, somewhere between 5-8 weeks of age the mice were evaluated for locomotor activity and changes in circadian rhythms, then again at 3-4 months for coordination and muscle strength. Onischenko et al. (2011) found that PFOA exposure was associated with a decrease in the number of inactive periods in group social settings. However, there was no effect on other endpoints including novelty exploration, anxiety and coordination. In a subsequent analysis of the bones from these same mice, Koskela et al. (2016) reported changes in bone morphology in the PFOA-exposed mice when compared to controls. These effects were subtle, and the authors even acknowledged that these morphological changes might be due to increased body-weight of PFOA-treated mice. They augmented their study with a dose-response experiment using *in vitro* osteoblast cells that showed some PFOA-induced changes in metabolism, altered nuclei features and relative gene expression (Figures 5 and 6 of Koskela et al., 2016). The observations for morphological features, organ weights and birth defects were poorly characterized in this study, only reporting a significant increase in the absolute liver weight of PFOA-exposed pups (Onischenko et al., 2011) and significant body weight gains in treated adults (Koskela et al., 2016). At best, this study demonstrated that the lowest effect dose estimated by Lau et al. (2006) for neonatal survival can be considered a LOAEL for behavioral, skeletal and liver weight effects of PFOA. The combined lack of a dose-response relationship, questionable statistical power and inadequate study design precluded these combined works from further consideration by NHDES.

It is noteworthy that the study by Onischenko et al. (2011) and Koskela et al. (2016) selected their PFOA singular dose based on the low doses for effects estimated by Lau et al. (2006). Of the biological effects observed in pups and their dams, the most sensitive response was the increased maternal liver weight and not the developmental delays observed in pups (Lau et al., 2006). Given PFOA's effects on hepatic function, oxidative stress and cholesterol metabolism, it is not unreasonable to question if these responses in the dam contributed to the developmental effects observed in pups. Thus, increased liver weight of the dam was the most sensitive response from a gestational exposure, not the developmental delays observed in pups.

Other animal studies provide limited insight into the developmental toxicity and teratogenicity of PFOA. Most studies have focused on morphological endpoints with little to no anchoring in biochemical or histological changes observed in exposed pups. This lack of molecular details with these observations raises challenges for interpreting their relevance for human health. The exception to this has been work by the National Toxicology Program that has evaluated the effects of PFOA on mammary gland development in mice.

Nine studies have evaluated altered mammary gland development in female mice following exposure to PFOA either during gestation, nursing/lactation or puberty (White et al., 2007; Yang et al., 2009; White et al., 2009; Zhao et al., 2010; Macon et al., 2011; White et al., 2011; Zhao et al., 2012; Albrecht et al., 2013; Tucker et al., 2015). All but one (Albrecht et al., 2013) have reported altered timing of mammary gland development in response to PFOA. This suggests a consistent biological effect in an animal model that is commonly used to study mammary gland development.

Mammary gland development starts in the fetus, followed by a second window of maturation during puberty in response to hormonal changes, and undergoes a third period of maturation in preparation for lactation (Rudel et al., 2011; Osborne et al., 2015). In animal models, this has been evaluated through subjective scoring of whole-mount tissues, as well as quantitative measures of gland-specific tissue structures such as tubules, terminal end buds and duct ends. Altered developmental timing of the mammary gland is a proposed susceptibility factor for an increased risk of mammary gland-related diseases, such as breast cancer (Rudel et al., 2011; Tiede and Kang, 2011; Macon and Fenton, 2013; Osborne et al., 2015). It should be noted that these references are not studies that demonstrate PFOA-associated delays in mammary gland development are a risk factor for breast cancer; rather, they are primarily reviews and perspectives of why this should be investigated. Aside from cancer outcomes, there is concern for detrimental impacts of altered mammary gland development on lactation and ability to adequately support nursing offspring.

In utero exposure to PFOA delays mammary gland development in female mice. White et al. (2007) evaluated fetal windows of susceptibility toward PFOA-induced delay in mammary gland development. They found that exposure to PFOA delayed mammary gland development in both pups and dams. In a follow-up study, White et al. (2009) demonstrated that intrauterine and/or lactational exposure to PFOA (5 mg/kg/d) delayed mammary gland development in CD-1 mice, emphasizing the sensitivity of the mammary gland during pre- and post-natal development. In a third publication, White et al. (2011) showed that gestational and chronic life exposure to PFOA (1, 5 mg/kg/d; some animals supplemented with 5 ppb-laced drinking water) leads to delayed mammary gland development in daughters and granddaughters of exposed CD-1 mice. From a functional standpoint, this had no significant effect on lactational support of their offspring despite the observed changes in gland structure (White et al., 2011) and milk-related gene expression (White et al., 2007). A related study characterized the internal dosimetry of PFOA treated CD-1 mice, showing that PFOA crosses the placenta and leads to delayed mammary gland development at relatively low serum concentrations (Macon et al., 2011).

Strain- and age-specific differences in mice affect whether there is a delay, acceleration or no effect on mammary gland development. Tucker et al. (2015) evaluated strain differences between CD-1 and C57BL/6 mice for susceptibility towards delayed mammary gland development after gestational exposure to PFOA (0.01-1 mg/kg/d). They found that both strains were susceptible to delayed mammary gland development but at different doses. Yang et al. (2009) compared strains of mice (Balb/c and C57BL/6 mice) for differences in PFOA's effect on peri-pubertal development of the mammary ducts, uterus and estrus cycling. Balb/c mice experienced delayed mammary duct development, and liver hypertrophy, whereas C57BL/6 mice experienced accelerated mammary gland development at 5 mg/kg/d and delayed development at higher doses. This effect has been speculated to be the result of differences between *in utero* and peri-pubertal exposure (Yang, 2009; Tucker et al., 2015).

This effect is possibly due to PPAR activation in mice. PPAR-associated binding proteins have been implicated in mammary duct development in mice models, as their inactivation results in delayed mammary gland development. Peroxisome proliferator-activated receptor-binding protein (PBP) is a transcription factor that supports the activation of PPARs, as well as other nuclear receptors (Zhu et al., 1997). Jia et al. (2005) showed that PBP is involved in normal mammary gland development in mice, and that its inactivation results in impaired gland function and responsiveness to hormone signals, as well as delayed development. This same research group reported that another PPAR coactivator protein was involved in delayed mammary gland development and impaired milk production in mice (Qi et al., 2004). Yang et al. (2006)

demonstrated that PPARα activation leads to delays in mammary gland development following treatment with a PPARα activator, or constitutive activation of PPARα in transgenic mice. Curiously, this same study found no delays in gland development of PPARα-null mice indicating that PPARα-activation is not necessary for normal mammary gland development. More recently, Albrecht et al. (2013) reported no effect of PFOA on mammary gland development in mice with normal PPAR function, humanized PPAR function or a loss of PPAR function (knock-out mice). This would suggest that the rodent-specific sensitivity of the PPAR pathway might be responsible for this critical effect. To date, the role of these proteins and PPAR-signaling on PFOA-induced delays in mammary gland development has not been clearly studied, nor is it clear if PPAR-activation during mammary gland development is of direct relevance to human health.

Aside from potential detriments to lactation, there is a concern for increased cancer risks due to abnormal mammary gland development. Rudel et al. (2011) argued that enhanced cancer susceptibility can be induced by delays in mammary gland development that lead to a higher number of terminal end buds, such as those seen within rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (Brown et al., 1998; Fenton et al., 2002). There is also evidence for concern from accelerated mammary gland development (reviewed by Tiede and Kang, 2011; Macon and Fenton, 2013; Osborne et al., 2015; and references therein). The problem with applying this is that PFOA is associated with a reduced number of terminal end buds, but the TCDD model is associated with an increased number of terminal end buds. This does not appear to align with mechanisms proposed in other reviews (Tiede and Kang, 2011; Macon and Fenton, 2013; Osborne et al., 2015). To date, we are unaware of any study that links the observed structural delays seen in mice after PFOA exposure with enhanced susceptibility toward carcinogenesis. If future evidence arises that addresses the shortcomings of this health endpoint and identifies clear linkage to human relevance, this endpoint should be re-assessed as a potential critical health effect of PFOA.

Other state agencies, including Texas and New Jersey, have considered delayed mammary gland development as a critical health effect towards setting regulatory limits. However, the two agencies reached starkly different numbers with this same biological endpoint. The New Jersey Drinking Water Quality Institute (NJ DWQI) calculated a reference dose that would have resulted in an MCL of < 1.0 ppt, although NJ DWQI ultimately selected increased relative liver weight and arrived at an MCL of 14 ppt. The NJ DWQI Subcommittee found the delay in mammary duct development concerning in their health-based risk assessment, but determined the limited existing information only supported justification of using a modifying factor of 10 out of precaution for this and other developmental impacts. The Texas Commission on Environmental Quality (CEQ) derived a protective concentration level (PCL) of 290 ppt based on delayed mammary gland development, although their estimations rely on the orally-administered dose instead of serum concentrations. EPA (2016) concluded there was insufficient evidence demonstrating that delays in mammary gland development resulted in a permanent adverse effect, thus excluded this critical effect for calculation of the current health advisory level of 70 ppt.

Animal Serum Dose: **4,351 ng/mL**

The reference study used to derive the animal serum dose was Loveless et al. (2006) that reported the responses of rodents (rats and mice) toward i) linear PFOA, ii) branched PFOA and iii) a mixture of linear and branched isoforms. PFOA was administered in the form of ammonium perfluorooctanoate (APFO) via oral gavage with APFO-treated water. All three forms of PFOA displayed hepatotoxic responses in male mice and

rats. Given the occurrence of different PFOA isoforms in the environment, it was decided that this study was well-suited for characterizing response to a relevant mixture of PFOA isoforms.

Loveless et al. (2006) reported serum concentrations for PFOA for both the LOAEL and NOAEL. When feasible, it is recommended to utilize benchmark dose (BMD) modeling to address technical uncertainties related to the use of NOAELs for determining a point of departure from animal studies (EPA 2002). Given the time required for *de novo* development and appropriate validation of BMD models, we deferred to the BMD model described by the NJ DWQI for the same study by Loveless et al. (2006) (methodology is summarized in NJ DWQI, 2017). Briefly, BMD analysis estimated the serum dose for a 10% increase in relative liver weight from a branched and linear mixture of PFOA. The average serum concentration for the lower 95% confidence limit (the BMDL) from the two best fit models was determined to be 4,351 ng/mL (NJ DWQI, 2017).

Uncertainty Factors (UF): Total UF of 100

A full UF of 10 was applied to account for differences in sensitivity and toxicokinetics (e.g., half-lives and elimination rates) across the human population. Given the uncertainty surrounding the exact mechanism(s) of action for PFOA, a partial UF of 3 was applied for rodent-to-human differences in toxicodynamics to account for unknown differences in sensitivity between humans and rodents for PPARα-independent effects. In practice, an additional UF can be applied to account for suspected differences in toxicokinetics between rodents and humans (i.e., half-life); however, the use of a dosimetric adjustment factor can replace this UF of 3. A UF of 3 was applied due to evidence for associated effects on other physiological systems including immune function observed in animal and human epidemiological studies.

UF 10 (Human-to-Human) x UF 3 (Animal-to-Human) x UF 3 (Other Toxicities) = Total UF 100

Note that an UF of 3 is a simplification of a half-log unit ($10^{0.5}$ = 3.16), where $10^{0.5}$ x $10^{0.5}$ = 10.

Dividing the Animal Serum Dose by the Total Uncertain give the Target Serum Level in humans.

Target Serum Level = Animal Serum Dose ÷ Total uncertainty Factor

43.5 ng/mL = 4,351 ng/mL ÷ 100

Dosimetric Adjustment: $1.20E^{-04}$ L/kg/d, assuming 2.7-year half-life

The dosimetric adjustment factor (DAF) estimates an externally administered (ingested) dose corresponding to the internal serum dose of concern (i.e., the Human Equivalent Dose). This is a necessary step since the half-lives of PFAS in rodents are profoundly shorter than the half-lives in humans. The NHDES approach is similar to the EPA method used for deriving the reference dose for PFOA (EPA, 2016). This approach requires a volume of distribution (V_d; 0.17 L/kg, Thompson et al. 2010) and the chemical's half-life ($t_{½}$) in humans.

$DAF = V_d$ x (Ln(2) ÷ $t_{½}$)

*DAF = 0.17 L/kg x (Ln(2) ÷ (2.7 y * 365 d/y)) = $1.1954E^{-04}$ L/kg/d*

The half-life for PFOA was assumed to be 2.7 years, based on a recent study by Li et al. (2018). This study evaluated the half-lives of PFOA, PFOS and PFHxS in a population that was exposed to these compounds via drinking water. The strengths of this study included its sample size, relevance to drinking water exposure, inclusion of a broad age range (15-50) and balanced representation of both sexes. Amongst the 106 participants of the study, the average (± SD) serum concentration of PFOA was 21.1 ± 14.7 ng/mL. No difference was detected between the average half-life of PFOA in men and women from this study (Li et al., 2018).

Reference Dose (RfD): 5.2 ng/kg/d

The RfD is calculated as:

RfD = (Animal Serum Dose / Total UF) x DAF

RfD = (4,351 ng/mL ÷ 100) x 1.20E^{-04} L/kg/d = 5.2 ng/kg/d

This RfD is less than EPA's current RfD for PFOA (20 ng/kg/d) and greater than ASTDR's draft MRL for PFOA (3.0 ng/kg/d). This difference from both agencies in not unexpected as the NHDES assessment utilized a different study, a lower total uncertainty factor (100 versus 300 for both EPA and ATSDR) and a longer half-life for PFOA estimated from a non-occupational exposure.

It should be noted that in the RfD calculation there is no term that adjusts for the proportion of PFOA actually absorbed following ingestion. This is because NHDES assumed that 100% of the PFOA ingested from environmental sources is absorbed within the gastrointestinal tract. Although ingestion is the primary route of exposure to PFAS, the mechanisms and efficiency of uptake is poorly understood. This is a health-protective assumption as the actual uptake efficiency is currently unknown in humans (summarized by ATSDR, 2018), but may be less than 100% as indicated by animal studies following exposure through food or water.

Exposure Assumptions: Relative Source Contribution of 40%,
Water consumption rate for lactating women

The relative source contribution (RSC) for drinking water is typically set between 20-80%. When possible, the RSC is calculated using quantitative information for exposure from other sources such as air, food and soil. However, sufficient information is currently unavailable for accurate estimation of daily exposure to PFOA from non-drinking water sources such as food and inhalation. Thus, the cumulative background exposure to PFOA is estimated from serum concentrations in the general population.

In this assessment, the RSC was derived using the subtraction method in conjunction with the EPA decision tree for RSC determination (EPA, 2000). The subtraction method derives a RSC from the background level of exposure and the target serum level, where:

RSC = (Target Serum Level – Background exposure level) ÷ Target Serum Level

When population-specific data for background exposure are not available, it is recommended to utilize the average from datasets such as NHANES. The 2013-2014 NHANES report shows an average PFOA serum

concentration of 1.9 ng/mL for all ages, with a high end estimate (95th percentile) of 5.6 ng/mL for those age 12 years or older (NH HEALTH WISDOM, accessed December, 2018; ATSDR 2018). Utilizing either the average or the 95th percentile for exposure from the 2013-2014 NHANES data would result in an RSC >80%. However, more recent and population-specific data for serum PFOA concentrations are available for New Hampshire. Across adults and children (n=219) in Southern New Hampshire, the average and 95th percentile for PFOA serum concentrations were 4.4 ng/mL and 26.6 ng/mL, respectively (NH HEALTH WISDOM, accessed December, 2018). Based on the 95th percentile for New Hampshire-specific data, the chemical-specific RSC for PFOA was determined to be 40%.

RSC = (43.5 ng/mL – 26.6 ng/mL) ÷ 43.5 ng/mL = 0.38, rounded to 0.40 or 40%

NHDES calculated the exposure using the water ingestion rate of a lactating woman (0.055 L/kg d). This was based on the 95th percentile consumers estimate for combined direct and indirect community water ingestion for lactating women (EPA, 2011). The water ingestion rate of lactating women is greater than that of non-lactating women, pregnant women or men, and is therefore more protective as it over-estimates an individual's chronic exposure via drinking water.

MCL for PFOA: 38 ppt (ng/L)

The RfD is converted to an equivalent dose in drinking water by selecting a sensitive human receptor and using their drinking water ingestion rate to calculate a drinking water equivalency level (DWEL). The DWEL is 100% of a dose not expected to cause any toxic effects.

DWEL = RfD ÷ Water Ingestion Rate

DWEL = 5.2 ng/kg/d ÷ 0.055 L/kg d = 94.5 ng/L

Taken together with the RSC to account for background sources of exposure, the MCL is derived as follows:

MCL = (DWEL x RSC)

MCL = (94.5 ng/L x 0.40) = 38 ng/L

NHDES is currently reviewing emerging information for the impact the proposed MCL will have on serum concentrations relative to background sources of PFOA.

Appendix 5: PFOS Derivation

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Toxicity Endpoint: **Developmental Delays**

After PFOA, PFOS is one of the most studied PFAS in the toxicological literature. Epidemiology studies associate PFOS with similar effects as PFOA, with some emphasis on developmental delays and immunotoxicity (as reviewed by NTP 2016; Rappazzo et al. 2017; ATSDR 2018; Liew et al. 2018), although it is noted that these latter effects in humans have been disputed (Chang et al. 2016; Negri et al. 2017). Based on more controlled rodent studies, PFOS has been shown to affect the liver, thyroid function, immune system and early development. Developmental delays were determined to be a sensitive and consistent critical effect for reference dose derivation, and concern for immunotoxic effects warranted a UF of 3, discussed below.

As with most PFAS outcomes, the epidemiological studies do not present a clear understanding for the relationship of PFOS and fetal growth and early life development. Most PFAS have been shown to readily cross the placenta, resulting in exposure levels reflecting the mother's blood concentration of PFAS. Of the studies identified by ATSDR (2018), three identified a significant negative association between maternal PFAS levels and low birth weight in infants (Washino et al. 2009; Chen et al. 2012; Maisonet et al. 2012). The 2018 ATSDR draft MRL found that other epidemiology studies have not detected significant effects on birth weight and early growth in infants, but meta-analyses across studies indicate a negative association between PFOS and other PFAS with growth and development (Koustas et al. 2014; Verner et al. 2015). Interpreting these associations in humans is difficult, in part, due to physiological changes in pregnant women that affect how the body clears chemicals like PFOS. To address this, Verner et al. (2015) conducted a meta-analysis of birth weight studies and adjusted for the kidney physiology (glomerular filtration rate) of pregnant women. Physiologically-adjusted analysis revealed that a 1 ng/mL increase in PFOS was associated with a 2.72 g reduction in birth weight. Although some individual studies currently present mixed observations for an effect of PFOS on growth, additional lines of evidence from animal studies support the observation of delayed growth and development following gestational exposure to PFOS.

Several toxicological studies have reported delayed development across different strains of mice and rats following pre- and post-natal exposure to PFOS (Yahia et al. 2008; Butenhoff et al. 2009; Rogers et al. 2014; Wan et al. 2014). In the study ATSDR used for evaluating PFOS, Onishchenko et al. (2011) observed decreased locomotor activity and coordination in adult mice with early-life exposure to PFOS. However, the limitations of this study are similar to those discussed for PFOA in Appendix 4. A comparative study between rats and mice found delayed growth in rat pups following gestational exposure, and the induction of several birth defects in both rodents and mice at higher doses (10-20 mg/kg/d; Thibodeaux et al. 2003; Lau et al. 2003). As concluded by the EPA (2016b), these and other studies support the selection of delayed development as a critical health effect for PFOS.

The reference study selected for deriving the MCL/AGQS was Luebker et al (2005ab), consistent with the EPA (2016) and ATSDR draft MRL for PFOS (2018). This two-generational study evaluated the long-term and reproductive impacts of PFOS on rats and their progeny (Luebker et al. 2005a). Female rats were treated prior to and throughout pregnancy and lactation, and pups birthed to these dams were continuously exposed throughout life. Some of these treated pups were switched with control pups to evaluate the specific role of exposure via gestation and lactation on early growth and development. Pups born to PFOS exposed dams displayed impaired growth, developmental delays and reduced survival. The LOAEL for the

developmental delays was 0.1 mg/kg/d based on transient delays in growth and delayed onset of eye opening. Maternal exposure was a major driver of the observed effects, as determined by cross-fostering of exposed and control animals and evaluation of serum concentration of PFOS in dams and pups (Luebker et al. 2005b). The transient effect on growth is argued to be of questionable significance. From a risk assessment perspective, given the protracted human half-life of PFOS when compared to rats, there is valid concern for what effect modest delays may have on developmental trajectories following in utero exposure.

Experiments using transgenic knock-out mice (PPARα) found the developmental effects of PFOS in rodents are likely PPARα-independent (Abbott et al. 2009). The study exposed mice during the late-stages of gestation and noted decreased survival in both types of mice. Similar to Luebker et al. (2005a), there was a delay in the time to eye opening in both wild-type and the PPARα knock-out mice. There was no transient delay in growth, which may be due to the differences in the start of maternal exposure (Abbott et al. 2009). Such evidence that developmental delays are a PPAR-independent effect further supports the selection of this critical endpoint.

Aside from developmental delays, PFOS is an immunotoxicant in rodent models. Evidence for this was reviewed and summarized by the National Toxicology Program in an assessment of PFOS and PFOA (NTP 2016). NTP found moderate evidence that PFOS was immunotoxic in humans, but had high confidence it was immunotoxic in rodents (NTP 2016). The difference in conclusion is not unexpected, as epidemiological studies in humans and toxicological studies in rodents provide different lines of evidence. The strength of the animal models for studying immunotoxicity is the amount of control the experimenter has for factors that may affect the high-sensitive responses of the immune system. For studies of PFOS and PFOA, the disadvantage of animal models has been the considerable species- and strain-specific differences in immunological responses. For a more thorough review on the effects of PFOS and other PFAS in animal models and their relation to human health outcomes, see DeWitt et al. (2012).

Epidemiology studies have identified varying associations for PFOS with immunomodulation (reviewed NTP 2016; ATSDR 2018), although these associations have been disputed for a variety of criteria (Chang et al. 2016). These effects include hyper-sensitivity, autoimmunity and immunosuppression. Of particular concern for public health is the association between PFOS, and other PFAS, with reduced vaccine response. The primary evidence for suppressed vaccine responses associated with PFOS has come from studies of a highly-exposed population in the Faroe Islands and evidence from the Norwegian birth cohort study (Grandjean et al. 2012; Granum et al. 2013; Kielsen et al. 2015; Looker et al. 2014). In the Faroese, PFOS has been specifically associated with decreases in diphtheria antibodies in children by the age of seven (Grandjean et al. 2012; Mogensen et al. 2015). In surveys of the U.S. population (NHANES), Stein et al. (2016) reported reduction in rubella and mumps antibodies associated with each doubling of serum PFOS concentrations. Re-analysis of similar data from the U.S. population using methods that account for biological differences between men and women found that PFOA was associated with reduced vaccine titers in adults, but there was no association between PFOS and vaccine titers in youths or adults (Pilkerton et al. 2018).

Currently, there is no known mechanism for the associated immunological effects observed in humans. This is a major challenge for scientifically demonstrating causality between PFOS, and other PFAS, with the associated immunomodulatory effects. The growing number of studies is highly suggestive that PFAS act as an immunomodulatory; however, the current evidence is not conclusive.

Despite there being a limited number of studies, there is evidence that PFOS is immunosuppressive in rodents. At low doses, B6C3F1 mice showed a suppressed response to sheep's red blood cells (sRBCs) (1.66

µg/kg/d for 28 days; Peden-Adams et al. 2008) and lower resistance to viral infection by influenza (25 µg/kg/d for 21 days; Guruge et al. 2009). Dong et al. (2009; 2011) evaluated immunosuppression in a different strain of mice following a 60-day exposure to PFOS. The NOAELs for suppressed antibody response from these two studies were 8.3 µg/kg/d (Dong et al. 2009) and 16.7 µg/kg/d (Dong et al. 2011), but these were determined using different assays with different low doses. While there is some evidence for suppressed antibody production, there are technical inconsistencies that limit its use for reference dose derivation and therefore justified an UF of 3.

In light of this evidence, an additional UF of 3 was applied to PFOS to address the potential for immunotoxicity observed in rodents at the NOAEL serum concentrations reported in Dong et al. (2011).

Animal Serum Dose: **6,260 ng/mL**

The animal serum dose used for deriving the MCL for PFOS was the same as that estimated by EPA (2016b) and Minnesota Department of Health (2017), which is based on the NOAEL for reduced pup body weight in the two-generation study in rats (Luebker et al. 2005a). In the 2016 Health Advisory for PFOS, EPA (2016b) summarizes the consistency of this serum dose with NOAEL and LOAEL values from other developmental delays associated with PFOS exposure. NHDES noted that the estimated serum concentration is based on an EPA model that utilized the data reported in Luebker et al. (2005ab).

Uncertainty Factors (UF): **Total UF of 100**

A full UF of 10 was applied to account for differences in sensitivity and kinetics across the human population. Given the uncertainty surrounding the exact mechanism(s) of action for PFOS, a partial UF of 3 was applied for rodent-to-human differences in toxicodynamics to account for unknown differences in sensitivity between humans and rodents toward PPARα-independent effects. In practice, an additional UF can be applied to account for suspected differences in toxicokinetics between rodents and humans (i.e., half-life); however, the use of a dosimetric adjustment factor can replace this UF of 3. An UF of 3 was applied due to concern for PFOS' effects on other physiological processes including the immune system (NTP 2016; and lipid metabolism (ATSDR 2018).; Perkins et al. 2018).

UF 10 (Human-to-Human) x UF 3 (Animal-to-Human) x UF 3 (Other Toxicities) = Total UF 100

Note that an UF of 3 is a simplification of a half-log unit ($10^{0.5} = 3.16$), thus $10^{0.5} \times 10^{0.5} = 10$.

Dividing the Animal Serum Dose by the Total Uncertain gives the Target Serum Level in humans.

Target Serum Level = Animal Serum Dose ÷ Total uncertainty Factor

62.6 ng/mL = 6,260 ng/mL ÷ 100

Dosimetric Adjustment: **1.28E-04 L/kg/d, assuming 3.4-year half-life**

The dosimetric adjustment factor (DAF) estimates an externally administered (ingested) dose corresponding to the internal serum dose of concern (i.e., the Human Equivalent Dose). This is necessary since the half-lives

of PFAS in rodents are profoundly shorter than their half-lives in humans. The NHDES approach is similar to the EPA method used for deriving the reference dose for PFOS (EPA 2016). This approach requires a volume of distribution (V_d; 0.23 L/kg, Thompson et al. 2010) and the chemical's half-life ($t_{½}$) in humans.

$$DAF = V_d \times (Ln(2) \div t_{½})$$

$$DAF = 0.17\ L/kg \times (Ln(2) \div (3.4\ y * 365\ d/y)) = 1.2844E^{-04}\ L/kg/d$$

The half-life for PFOS was assumed to be 3.4 years based on the same study selected for the half-life of PFOA (Li et al. 2018). The strengths of this study included its sample size, relevance to drinking water exposure, inclusion of a broad age range (15-50) and balanced representation of both sexes. The average (±SD) serum concentration of PFOS was 387 ± 259 ng/mL amongst 106 participants. Unlike PFOA, there were sex-specific differences in the half-life of PFOS where the half-life in men was 4.6 years (95% CI 3.7-6.1 years) and for women was 3.1 years (95% CI 2.7-3.7 years). The average across both sexes was 3.4 years. NHDES used the reported average across both sexes as a more protective half-life for a lactating women.

Reference Dose (RfD): 8.0 ng/kg/d

The RfD is calculated as:

$$RfD = (Animal\ Serum\ Dose / Total\ UF) \times DAF$$

$$RfD = (6{,}260\ ng/mL \div 100) \times 1.28E^{-04}\ L/kg/d = 8.0\ ng/kg/d$$

This RfD is lower than EPA's current RfD for PFOS (20 ng/kg/d) and greater than the ATSDR's draft MRL for intermediate PFOS (2.0 ng/kg/d). The NHDES assessment utilized the same study as both agencies for the basis of the PFOS RfD development; however, there were differences in the application of Total Uncertainty Factors (EPA applied 30 and ATSDR applied 300) and a shorter half-life for PFOS based on a non-occupational exposure.

It should be noted that in the RfD calculation there is no term that adjusts for the proportion of PFOS actually absorbed following ingestion. This is because NHDES assumed that 100% of the PFOS ingested from environmental sources is absorbed within the gastrointestinal tract. Although ingestion is the primary route of exposure to PFAS, the mechanisms and efficiency of uptake is poorly understood. This is a health-protective assumption as the actual uptake efficiency is currently unknown in humans (summarized by ATSDR 2018), and may be less than 100% as indicated by animal studies following exposure through food or water.

Exposure Assumptions: **Relative Source Contribution of 50%, Water consumption rate of a lactating woman**

Similar to PFOA, the chemical-specific RSC for PFOS was derived using the subtraction method in conjunction with the EPA decision tree for RSC determination (EPA 2000). The subtraction method derives a RSC from the background level of exposure and the target serum level, where:

RSC = (Target Serum Level – Background exposure level) ÷ Target Serum Level

When population specific data for background exposure is not available, it is recommended to utilize the average from datasets such as NHANES. The 2013-2014 NHANES report shows an average PFOS serum concentration of 5.0 ng/mL for all ages, with a high end estimate for the NHANES data shows a 95th percentile of 18.5 ng/mL for those age 12 years or older (NH HEALTH WISDOM, accessed December 2018; ATSDR 2018). Utilizing either the average or the 95th percentile for exposure from the 2013-2014 NHANES data would result in an RSC >80%. However, more recent and population specific data for serum PFOS concentrations is available for New Hampshire, specifically the Pease community. Across those in the 2016 Pease group (n=242), the average and 95th percentile for PFOS serum concentrations were 10.2 ng/mL and 31.7 ng/mL, respectively (NH HEALTH WISDOM accessed December 2018). Based on the 95th percentile for New Hampshire-specific data, the chemical-specific RSC for PFOS was determined to be 50%.

RSC = (62.2 ng/mL – 31.7 ng/mL) ÷ 62.2 ng/mL = 0.49, rounded to 0.50 or 50%

NHDES calculated the exposure using the water ingestion rate of a lactating woman (0.055 L/kg d). This was based on the 95th percentile consumers estimate for combined direct and indirect community water ingestion for lactating women (EPA 2011). The water ingestion rate of lactating women is greater than that of non-lactating women or men, and is therefore more protective as it over-estimates an individual's chronic exposure via drinking water.

MCL for PFOS: **70 ppt (ng/L)**

The RfD is converted to an equivalent dose in drinking water by selecting a sensitive human receptor and using their drinking water ingestion rate to calculate a drinking water equivalency level (DWEL). The DWEL is 100% of a dose not expected to cause any toxic effects.

DWEL = RfD ÷ Water Ingestion Rate

DWEL = 8.0 ng/kg/d ÷ 0.055 L/kg d = 145.5 ng/L

Taken together with the RSC to account for background sources of exposure, the MCL is derived as follows:

MCL = (DWEL x RSC)

MCL = (145.5 ng/L x 0.50) = 73 ng/L, rounded down to 70 ng/L

This was rounded down to 70 ppt to comply with the existing EPA Health Advisory for PFOS.

NHDES is currently reviewing emerging information for the impact the proposed MCL will have on serum concentrations relative to background sources of PFOS.

Appendix 6: PFNA Derivation

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Toxicity Endpoint: **Altered Liver Weight and Function**

Significantly less peer-reviewed literature is available for PFNA than PFOA and PFOS, with only slightly more studies than PFHxS. Relative to human epidemiological studies, PFNA has been studied in the context of exposure to multiple PFAS and is loosely associated with altered liver enzyme activity and potential effects on the immune system (as reviewed by ATSDR). However, PFNA-specific effects on human health are unknown as there remains insufficient information to draw conclusions about the human health effects from the observed associations (summarized by ATSDR 2018 and NJ DWQI 2018). Based on more controlled rodent studies, PFNA seems to have similar biological properties as PFOA as seen through effects on the liver, immune system and early development; although the degree to which these two are similar is poorly quantified. Limited data on PFNA results in greater uncertainty regarding PFNA-specific health effects and its relative potency when compared with similar PFAS.

Relatively fewer epidemiological studies have characterized the associations of PFNA with health outcomes. As with most PFAS, the existing literature is focused on changes with clinical measures of enzymes, hormones and blood chemistry with far fewer evaluating specific disease diagnoses. Many of the findings are conflicting, emphasizing the need for additional research to understand the effects, if any, PFNA has on human health (reviewed by ATSDR 2018). An example for how little is known about PFNA is the fact that there is no reported serum half-life for this compound. In developing the 2018 draft MRL for PFNA, ATSDR (2018) relied on estimated half-lives based on urine measurements (Zhang et al. 2013) which are less accurate than serum-derived half-lives. No associations have been found between PFNA and cancer.

Similar to PFOA, the most consistent effect observed in animal studies has been increased relative liver weight and altered lipid metabolism (Wolf et al. 2012; Das et al. 2015, 2017; Wang et al. 2015; Rosen et al. 2017). Wolf et al. (2012) showed that PFNA is a stronger activator of PPARα than PFOA using *in vitro* assays. As discussed in Appendix 3, a PPARα-dependent mechanism of toxicity may not be relevant to human health. Gene expression profiles show that PFNA does activate PPARα, but can also act on the liver via other nuclear receptors including PPARγ and the estrogen receptor (Rosen et al. 2017). In addition to liver toxicity, PFNA has been associated with immunotoxic effects in rodents following acute exposures (Fang et al. 2009), but these studies provide limited information for understanding chronic exposures or PFNA-related effects during early development.

The reference study used to derive the MCL/AGQS was Das et al. (2015) which characterized the toxicity of PFNA in pregnant CD-1 mice and their pups. This study was a follow-up to another toxicity study of PFNA that showed some of the adverse developmental impacts of PFNA were dependent on PPARα activation (Wolf et al. 2010). Similar to gestational exposure to PFOA (Lau et al. 2006), relative liver weights of pregnant and non-pregnant mice displayed dose-dependent increases with PFNA treatment. Fetal effects included increased fetal liver weight, reduced pup weight and delays in developmental milestones (Das et al. 2015). In PPARα-null mice (genetic knockouts), the developmental effects of PFNA are absent, but the effects on maternal liver weight are retained at slightly higher doses (Wolf et al. 2010). As noted by Das et al. (2015), benchmark dose analysis found that increased relative liver weight was more sensitive than many of the developmental outcomes.

The similarity in hepatic effects observed with PFOA and evidence for potential relevance to human health based on the available, but limited, human evidence was the basis for selecting increased relative liver

weight as a precursor for altered liver function. The developmental toxicity in rodents appears to be highly dependent on PPARα, which may translate into limited relevance for human health. If the observed developmental outcomes seen in rodents are relevant to human health, liver toxicity is the more sensitive and therefore protective health endpoint. Given the lack of a robust database on the effects of PFNA, additional studies that quantify the serum half-life in humans and the basis for developmental impacts seen in animals would merit re-evaluation of this critical health effect and its derived RfD.

Animal Serum Dose: **4,900 ng/mL**

Das et al. (2015) reported serum concentrations for PFNA at both the LOAEL and NOAEL. When feasible, it is recommended to utilize benchmark dose (BMD) modeling to address technical uncertainties related to the use of NOAELs for determining a point of departure from animal studies (EPA 2002). Given the time required for *de novo* development and appropriate validation of BMD models, NHDES deferred to the BMD model previously derived by NJ DWQI for the same study by Das et al. (2015) (detailed methodology is summarized in NJ DWQI 2018). Briefly, BMD analysis estimated the serum concentration for a 10% increase in relative liver weight from exposure to PFNA. The serum concentration for the lower 95% confidence limit (the BMDL) from the best fit model was found to be 4,900 ng/mL (NJ DWQI 2018).

Uncertainty Factors (UF): **Total UF of 300**

A full UF of 10 was applied to account for differences in sensitivity and toxicokinetics (e.g., half-lives and elimination rates) across the human population. Given the uncertainty surrounding the exact mechanism(s) of action for PFNA, a partial UF of 3 was applied for rodent-to-human differences in toxicodynamics to account for unknown differences in sensitivity between humans and rodents toward PPARα-independent effects. In practice, an additional UF can be applied to account for suspected differences in toxicokinetics between rodents and humans (i.e, half-life); however, the use of a dosimetric adjustment factor can replace this UF of 3. A UF of 10 was applied due to the limited number of studies on PFNA, specifically the lack of information for a serum half-life in humans, as well as uncertainty for associated effects on other physiological processes including the immune system (summarized by ATSDR 2018).

UF 10 (Human-to-Human) x UF 3 (Animal-to-Human) x MF 10 (Limited Database and Other Toxicities) = Total UF 300

Note that an UF of 3 is a simplification of a half-log unit ($10^{0.5}$ = 3.16), thus $10^{0.5}$ x $10^{0.5}$ = 10. In the case of 300, this is rounded down from 316.

Dividing the Animal Serum Dose by the Total Uncertainty Factor gives the Target Serum Level in humans.

Target Serum Level = Animal Serum Dose ÷ Total Uncertainty Factor

16.3 ng/mL = 4,900 ng/mL ÷ 300

Dosimetric Adjustment: **$1.52E^{-04}$ L/kg/d, assuming 2.5-year half-life**

The dosimetric adjustment factor (DAF) estimates an externally administered (ingested) dose corresponding to the internal serum dose of concern (i.e., the Human Equivalent Dose). This is necessary since the half-lives of PFAS in rodents are profoundly shorter than their half-lives in humans. The NHDES approach is similar to the EPA method used for deriving the reference dose for PFOA and PFOS (EPA 2016ab). This approach requires a volume of distribution (V_d; 0.20 L/kg, ATSDR 2018) and the chemical's half-life ($t_{½}$) in humans.

$$DAF = V_d \times (Ln(2) \div t_{½})$$

$$DAF = 0.20\ L/kg \times (Ln(2) \div (2.5\ y * 365\ d/y)) = 1.5189E^{-04}\ L/kg/d$$

The half-life for PFNA was assumed to be 2.5 years. Unlike PFOA, PFOS and PFHxS, Li et al. (2018) did not quantify serum PFNA or its half-life in the community exposed via drinking water. A single study has estimated half-lives of PFNA in a Chinese population by measuring urinary concentrations of PFNA (Zhang et al. 2013). It should be noted that serum derived half-lives are preferable to those derived from urine concentrations of PFAS. Consistent with ATSDR (2018), we applied an assumed half-life of 2.5 years for women under the age of 50. The uncertainty for a potentially longer half-life is addressed by the previously discussed MF of 3.

Reference Dose (RfD): **2.5 ng/kg/d**

The RfD is calculated as:

$$RfD = (Animal\ Serum\ Dose / Total\ UF) \times DAF$$

$$RfD = (4{,}900\ ng/mL \div 300) \times 1.52E^{-04}\ L/kg/d = 2.5\ ng/kg/d$$

This RfD is slightly lower than the ATSDR's draft MRL for intermediate exposure to PFNA (3.0 ng/kg/d). The US EPA has not developed an RfD for PFNA. The NHDES assessment utilized the same study as the basis for RfD development; however, there was a difference in selection of critical effects and application of uncertainty/modifying factors.

It should be noted that in the RfD calculation there is no term that adjusts for the proportion of PFNA actually absorbed following ingestion. This is because NHDES assumed that 100% of the PFNA ingested from environmental sources is absorbed within the gastrointestinal tract. Although ingestion is the primary route of exposure to PFAS, the mechanisms and efficiency of uptake is poorly understood. This is a health-protective assumption as the actual uptake efficiency is currently unknown in humans (summarized by ATSDR 2018), and may be less than 100% as indicated by animal studies following exposure through food or water.

Exposure Assumptions: **Relative Source Contribution of 50%,**
Water consumption rate of a lactating woman

Similar to PFOA and PFOS, the chemical-specific RSC for PFNA was derived using the subtraction method in conjunction with the EPA decision tree for RSC determination (EPA 2000). The subtraction method derives a RSC from the background level of exposure and the target serum level, where:

RSC = (Target Serum Level – Background exposure level) ÷ Target Serum Level

When population specific data for background exposure is not available, it is recommended to utilize the average from datasets such as NHANES. The 2013-2014 NHANES report shows an average PFNA serum concentration of 0.68 ng/mL for all ages, with a high end estimate (95th percentile) of 2.00 ng/mL for those age 12 years or older (ATSDR 2018). Utilizing either the average or the 95th percentile for exposure from the 2013-2014 NHANES data would result in an RSC >80%. Additionally, more recent and population specific data for serum PFNA concentrations is available for New Hampshire. Across adults and children (n=219) in Southern New Hampshire the average and 95th percentile for PFNA serum concentrations were 0.66 ng/mL and 1.70 ng/mL, respectively (provided by NHDHHS Environmental Public Health Tracking program). Based on the 95th percentile for New Hampshire-specific data, the chemical-specific RSC for PFNA was determined to be 90%.

RSC = (16.3 ng/mL – 1.70 ng/mL) ÷ 16.3 ng/mL = 0.90, or 90%

However, uncertainty about uncharacterized sources of PFNA in the environment resulted in the decision to limit the RSC to 50% (EPA 2000).

NHDES calculated the exposure using the water ingestion rate of a lactating woman (0.055 L/kg d). This was based on the 95th percentile consumers estimate for combined direct and indirect community water ingestion for lactating women (EPA 2011). The water ingestion rate of lactating women is greater than that of non-lactating women or men, and is therefore more protective as it over-estimates an individual's chronic exposure via drinking water.

MCL for PFNA: 23 ppt (ng/L)

The RfD is converted to an equivalent dose in drinking water by selecting a sensitive human receptor and using their drinking water ingestion rate to calculate a drinking water equivalency level (DWEL). The DWEL is 100% of a dose not expected to cause any toxic effects.

DWEL = RfD ÷ Water Ingestion Rate

DWEL = 2.5 ng/kg/d ÷ 0.055 L/kg d = 45.5 ng/L

Taken together with the RSC to account for background sources of exposure, the MCL is derived as follows:

MCL = (DWEL x RSC)

MCL = (45.5 ng/L x 0.50) = 23 ng/L

NHDES is currently reviewing emerging information for the impact the proposed MCL will have on serum concentrations relative to background sources of PFNA.

Appendix 7: PFHxS Derivation

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Toxicity Endpoint: **Impaired Reproduction (Reduced Litter Size)**

Significantly less peer-reviewed literature is available for PFHxS than PFOA and PFOS. NHDES identified six animal studies on PFHxS (Butenhoff et al. 2008; Bijland et al. 2011; Viberg et al. 2013; Das et al. 2017; Chang et al. 2018; Ramhøj et al. 2018), where only four evaluated more than one dose level of PFHxS. Relative to human epidemiological studies, PFHxS has been evaluated in the context of exposure to multiple PFAS. This makes it challenging to discern PFHxS-specific effects on human health from those of other PFAS typically detected at higher concentrations in human serum. A result of this paucity of data is greater uncertainty regarding specific health effects and relative potency of PFHxS when compared with similar PFAS.

Based on the small number of animal studies, there appears to be limited evidence that PFHxS affects the thyroid gland and liver, with subtle effects on growth and development. Butenhoff et al. (2008) reported thyroid hypertrophy and altered clinical chemistry in male rats following exposure to PFHxS. This same study served as the basis of the 2018 ATSDR draft MRL for PFHxS (20 ng/kg/d), although it was noted that the thyroid effects may be related to enzyme activity that, at present, is not clearly relevant to human health. Ramhøj et al. (2018) reported altered thyroid hormone levels in rats and their pups following gestational exposure to PFHxS, where the effects were potentiated by the presence of other endocrine disrupting compounds. As reviewed and summarized by ATSDR (2018), very few associations have been found between PFHxS and clinical markers of thyroid function in humans, with no associations to clinical thyroid disease. Most of these associations were found in women, not men, which is the opposite of what is seen in rodent models. Similar to other PFAS, PFHxS can elicit hepatic hypertrophy and altered lipid metabolism at higher doses (Butenhoff et al. 2008; Bijland et al. 2011; Das et al. 2017) and are also associated with mixed responses of clinical markers of hepatic function in humans (reviewed by ATSDR 2018).

The most recent study, and basis for the NHDES derivation of a reference dose for PFHxS, was conducted on mice to evaluate reproductive and developmental impacts associated with PFHxS (Chang et al. 2018). In this study, male and female mice were treated with PFHxS by oral gavage and evaluated for a battery of clinical and reproductive outcomes. Male mice were exposed for 42 days, whereas females were exposed for 14-days prior to pregnancy and through gestation and lactation. PFHxS exposure was found to affect liver weight and cholesterol in males, with no alterations in other clinical markers including thyroid function (Chang et al. 2018). Of key interest was a reduction in litter size of female mice starting at the administered dose of 1.0 mg/kg/d, with a NOAEL of 0.3 mg/kg/d. In male mice, there was no relationship between PFHxS exposure and sperm quality, suggesting the reduction in litter size was the result of a female-specific effect. Unlike PFOS in rats (Luebker et al. 2005a), there was no sign of in utero loss of fetal pups, as determined by the pup-born-to-implant ratio, suggesting an effect prior to implantation.

It is acknowledged that the authors of Chang et al. (2018) regard the observed reduction in litter size as toxicologically insignificant. This is based on the contention that this effect is inconsistent with two other studies showing no reduction in the litter size of rats that were exposed to PFHxS (Butenhoff et al. 2008; Ramhøj et al. 2018). However, these comparisons are complicated by the issues of exposure dose and timing. It is true that Butenhoff et al. (2008) did not see reduced litter size from female rats that were administered higher doses of PFHxS than those used in Chang et al. (2018). However, the highest internal dose observed in female rats prior to breeding (42,000 ng/mL; Butenhoff et al. 2008) was approximately half

of the lowest internal dose observed in female mice with reduced litters (89,000 ng/mL; Chang et al. 2018). Thus, the dose that elicited reduced litter size in mice was not achieved in rats. This difference is likely due to the shorter half-life of PFHxS in rats compared to mice. Ramhøj et al. (2018) also reported that higher administered doses than those used by Chang et al. (2018) did not reduce litter size at birth. This does not address the issue of exposure timing as Ramhøj et al. (2018) initiated PFHxS treatment *after* female rats were confirmed to be pregnant, unlike Chang et al. (2018) that had initiated treatment prior to pregnancy. Taken together, the evidence from Butenhoff et al. (2008) and Ramhøj et al. (2018) does not support the contention that the reduction in litter size observed by Chang et al. (2018) is an inconsistent effect.

To date, there are two studies that have evaluated associations between PFHxS and reproductive outcomes in women. Vélez et al. (2015) evaluated a cohort of 1,743 women from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, all of which were recruited before 14 weeks of gestation from ten Canadian cities between 2008 and 2011. They found significant associations for PFHxS with reduced fecundability and increased infertility (Vélez et al. 2015). This observation is contrasted with the lack of association with fertility reported in a comparably sized population with lower median PFHxS levels (Bach et al. 2015). It should be noted that these studies do not prove or disprove a relationship between PFHxS and human fertility due to several factors addressed by the authors, including limitations of experimental design, statistical analyses and evaluation of male reproductive effects. However, the limited number of human epidemiology studies, and limitations of data therein, preclude them as the basis of RfD determination. Thus, the Chang et al. (2018) was deemed sufficient for identifying the RfD required for MCL/AGQS derivation. Additional epidemiological studies are needed to determine if there is a causal relationship between PFHxS and human reproduction.

Given the lack of a robust database on the effects of PFHxS, additional studies that further assess reproductive impacts, changes in thyroid function and other health outcomes would merit re-evaluation of this critical health effect and its derived RfD.

Animal Serum Dose: **27,200 ng/mL**

The animal study selected for PFHxS was a mouse study conducted by Chang et al. (2018). In the study, male and female mice were administered PFHxS by oral gavage at doses of 0, 0.3, 1.0 and 3.0 mg/kg/d. Female mice showed a statistically significant reduction in litter size with a LOAEL of 1.0 mg/kg/d, and a NOAEL of 0.3 mg/kg/d. Additionally, the study reported an increase in the anogenital distance in male pups born to females across all doses. As noted by the authors of the study, the biological implications of an increased anogenital distance are unclear as this would suggest masculinization by androgens, and this effect was not observed in female pups. Given some evidence for associated impacts on fertility and limited database on the effects of PFHxS in animals, reduced litter size was selected as the critical health effect. Instead of benchmark dose modeling to determine a dose from a specified threshold, the serum concentration at the NOAEL before pregnancy was selected as the animal serum dose (0.3mg/kg/d, 14-d exposure, 27.2µg/mL). Due to current feasibility, and as recommended by the EPA guidance (2002; 2012), the NOAEL was used in place of BMD modeling.

Uncertainty Factors (UF): **Total UF of 300**

A full UF of 10 was applied to account for differences in sensitivity and kinetics across the human population. Given the uncertainty surrounding the exact mechanism(s) of action for PFHxS, a partial UF of 3 was applied for rodent-to-human differences in toxicodynamics to account for unknown differences in sensitivity between humans and rodents toward PPARα-independent effects. In practice, an additional UF can be applied to account for suspected differences in toxicokinetics between rodents and humans (i.e, half-life); however, the use of a dosimetric adjustment factor can replace this UF of 3. An UF of 10 was applied due to the limited number of studies on PFHxS, both animal and epidemiological, as well as uncertainty for associated effects on other physiological processes including the thyroid system (ATSDR 2018).

UF 10 (Human-to-Human) x UF 3 (Animal-to-Human) x MF 10 (Limited Database and Other Toxicities) = Total UF 300

Note that an UF of 3 is a simplification of a half-log unit ($10^{0.5}$ = 3.16), thus $10^{0.5}$ x $10^{0.5}$ = 10. In the case of 300, this is rounded down from 316.

Dividing the Animal Serum Dose by the Total Uncertain gives the Target Serum Level in humans.

Target Serum Level = Animal Serum Dose ÷ Total Uncertainty Factor

90.7 ng/mL = 27,200 ng/mL ÷ 300

Dosimetric Adjustment: 1.03E^{-04} L/kg/d, assuming 5.3-year half-life

The dosimetric adjustment factor (DAF) estimates an externally administered (ingested) dose that corresponds to the internal serum dose of concern (i.e., the Human Equivalent Dose). This is necessary since the half-lives of PFAS in rodents are profoundly shorter than their half-lives in humans. The NHDES approach is similar to the EPA method used for deriving the reference dose for PFOA and PFOS (EPA 2016ab). This approach utilizes a volume of distribution (V_d, 0.287 L/kg; ATSDR 2018; Sundström et al. 2012) and the chemical's half-life ($t_{½}$) in humans.

$DAF = V_d$ x (Ln(2) ÷ $t_{½}$)

*$DAF = 0.287$ L/kg x (Ln(2) ÷ (5.3 y * 365 d/y)) = 1.03^{-04} L/kg/d*

The half-life for PFHxS was assumed to be 5.3 years based on the same study selected for the half-lives of PFOA and PFOS (Li et al. 2018). The strengths of this study included its sample size, relevance to drinking water exposure, inclusion of a broad age range (15-50) and balanced representation of both sexes. The average (±SD) serum concentration of PFHxS was 353 ± 260 ng/mL amongst 106 participants. Unlike PFOA, there were sex-specific differences in the half-life of PFHxS where the half-life in men was 7.4 years (95% CI 6.0-9.7 years) and 4.7 years for women (95% CI 3.9-5.9 years). The average across both sexes was 5.3 years.

Reference Dose (RfD): **9.3 ng/kg/d**

The RfD is calculated as:

RfD = (Animal Serum Dose / Total UF) x DAF

RfD = (27,200 ng/mL ÷ 300) x 1.03E^{-04} L/kg/d = 9.3 ng/kg/d

This RfD is lower than the ATSDR's draft MRL for intermediate exposure to PFHxS (20 ng/kg/d). EPA has not developed an RfD for PFHxS. The NHDES assessment utilized an entirely different study and critical health effects than those selected by ATSDR.

It should be noted that in the RfD calculation there is no term that adjusts for the proportion of PFHxS actually absorbed following ingestion. This is because NHDES assumed that 100% of the PFHxS ingested from environmental sources is absorbed within the gastrointestinal tract. Although ingestion is the primary route of exposure to PFAS, the mechanisms and efficiency of uptake are poorly understood. This is a health-protective assumption as the actual uptake efficiency is currently unknown in humans (summarized by ATSDR 2018), and may be less than 100% as indicated by animal studies following exposure through food or water.

Exposure Assumptions: **Relative Source Contribution of 50%,**
Water consumption rate of a lactating woman

Similar to PFOA, PFOS and PFNA, the chemical-specific RSC for PFHxS was derived using the subtraction method in conjunction with the EPA decision tree for RSC determination (EPA 2000). The subtraction method derives a RSC from the background level of exposure and the target serum level, where:

RSC = (Target Serum Level – Background exposure level) ÷ Target Serum Level

When population specific data for background exposure is not available, it is recommended to utilize the average from datasets such as NHANES. The 2013-2014 NHANES report shows an average PFHxS serum concentration of 1.4 ng/mL for ages 12 and older, with a high end estimate (95th percentile) of 5.6 ng/mL for those age 12 years or older (NH HEALTH WISDOM, accessed December 2018; ATSDR 2018). Utilizing either the average or the 95th percentile for exposure from the 2013-2014 NHANES data would result in an RSC >80%. However, more recent and population specific data for serum PFHxS concentrations is available for New Hampshire. Across those 12 and older in the 2016 Pease group (n=242), the average and 95th percentile for PFHxS serum concentrations were 4.5 ng/mL and 26.0 ng/mL, respectively (NH HEALTH WISDOM accessed December 2018). Based on the 95th percentile for New Hampshire-specific data, the chemical-specific RSC for PFHxS was determined to be 70%.

RSC = (90.7 ng/mL – 26.0 ng/mL) ÷ 90.7 ng/mL = 0.71, rounded to 0.70 or 70%

However, uncertainty about uncharacterized sources of PFHxS in the environment resulted in the decision to limit the RSC to 50% (EPA 2000).

NHDES calculated the exposure using the water ingestion rate of a lactating woman (0.055 L/kg d). This was based on the 95th percentile consumers estimate for combined direct and indirect community water ingestion for lactating women (EPA 2011). The water ingestion rate of lactating women is greater than that

of non-lactating women or men, and is therefore more protective as it over-estimates an individual's chronic exposure via drinking water. Additionally, the critical health effect of impaired reproduction was specific to females as no effects were observed in male sperm (Chang et al. 2018).

MCL for PFHxS: 85 ppt (ng/L)

The RfD is converted to an equivalent dose in drinking water by selecting a sensitive human receptor and using their drinking water ingestion rate to calculate a drinking water equivalency level (DWEL). The DWEL is 100% of a dose not expected to cause any toxic effects.

DWEL = RfD ÷ Water Ingestion Rate

DWEL = 9.3 ng/kg/d ÷ 0.055 L/kg d = 169.1 ng/L

Taken together with the RSC to account for background sources of exposure, the MCL is derived as follows:

MCL = (DWEL x RSC)

MCL = (169.1 ng/L x 0.50) = 85 ng/L

NHDES is currently reviewing emerging information for the impact the proposed MCL will have on serum concentrations relative to background sources of PFHxS.

Appendix 8: References

Appendix 8: References

This list includes references for the main summary report and Appendices 3-7. This list is for documents specifically cited within these appendices and does not contain all of the research articles, reviews, technical document and various reports reviewed by NHDES.

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Appendix 9: Analysis of Increased Costs for PWS to comply with Proposed MCLs for PFOA, PFOS, PFNA, PFHxS

Appendix 9: Cost of Compliance with Proposed MCL for PFOA, PFOS, PFNA & PFOA/PFOS Combined for PWS and Private Wells

1.0 PFAS Treatment Costs

Costs to operate and maintain treatment systems to remove PFAS has been prepared assuming treatment is required when

a. PFOS & PFOA combined exceeds 70 parts-per-trillion (ppt);
b. PFOA exceeds 38 ppt;
c. PFNA exceeds 23 ppt; or
d. PFHXS exceeds 85 ppt.

1.1 Occurrence Information

The PFAS sampling results for non-transient PWS were reviewed. Four hundred and two sources of water associated with non-transient PWS were sampled. Two sources of water (0.5% of the sources sampled) equaled or exceeded 70 ppt for PFOA and PFOS combined. Three sources of water (0.75% of the sources sampled) equaled or exceeded 38 ppt for PFOA. Three sources of water exceeded 23 ppt for PFNA, however two of these three sources of water already exceeded the standard for PFOA and PFOA and PFOS combined. None of the results exceeded 85 ppt for PFHxS. Non-transient PWS sources around the Saint Gobain site and the Haven well at Pease Tradeport are not included in the occurrence analysis above, as there are likely not any sources of public drinking water near the type of large scale contamination sources that impacted these wells.

1.2 Costs for Water Treatment for Water Sources Associated with Non-transient PWS With Sampling Results

All sources for PWS that exceed 38 ppt for PFOA and/or 70 ppt for PFOA and PFOS combined already exceed the existing 70 ppt AGQS for PFOA and PFOS combined and costs are already being incurred by these water systems to comply the current AGQS. Therefore, the proposed values of 38 ppt for PFOA and 70 ppt for PFOS and PFOA combined do not require the expenditure of additional funds.

1.3 Costs for Water Treatment for Water Sources Associated with Non-transient Public Water Systems Without Sampling Results

In order to estimate the volume of water that may require treatment for non-transient public water systems that were not sampled, the daily flow volumes for these systems were estimated based on the volume of flow associated with the wellhead protection area for each unsampled source. Generally, this flow volume is the maximum volume that would be used from a particular source.

The cost per gallon to treat water for PFAS can vary broadly. Issues such as the potential for the need to construct a new building, volume of flow, initial PFAS concentrations or pretreatment requirements for constituents such as iron, manganese and radon can cause costs to vary by up to 300% from source to source. The costs per unit of flow used in the estimate were based on the costs associated with treatment at sites in New Hampshire and New York. These are summarized below. The lowest cost per gallon ($2.91 for MVD 4 & 5) and the highest cost per gallons ($8.10 for Pease) were used to develop high and low end estimates.

PFAS Treatment Costs Associated with PWS in New Hampshire and New York:

	Gallons Per Day	Cost	Cost Per Gallon
MVD 4/5	1,152,000	$3,350,000	$2.90
MVD 7/8	1,800,000	$8,000,000	$4.44
Pease	1,728,000	$14,000,000	$8.10
Hooksick Falls	500,000	$3,000,000	$6
Marlow School	1,125	$4,000	$3.56

The treatment costs for sources of water associated with non-transient PWS were estimated. The production volumes associated with the wellhead protection area for the unsampled sources were summed and multiplied by the 0.5% to estimate treated costs associated with sources of water that may exceed 70 ppt PFOA and PFOS combined. Similarly, the production volumes were summed and multiplied by 0.75% to estimate the treatment costs for sources that may exceed 38 ppt for PFOA.

The spreadsheet used to complete the calculations is attached.

The total cost estimates are below:

	Low Estimate	High Estimate
PWS with Sampling Results	$0	$0
Unsampled Public Water Systems	$1,851,354	$5,171,022
Total Cost	$1,851,354	$5,171,022

1.4 Operation and Maintenance Costs for PFAS Water Treatment Systems for Public Water Systems

The operation and maintenance (O&M) cost estimates for PWS were developed using estimated O&M costs associated with the treatment system being constructed for Merrimack Village District's wells 4/5 and the estimated O&M costs associated with the treatment system being constructed at Pease. The estimated annual O&M cost based on the average daily volume that is anticipated to require treatment is $0.18 per gallon to $0.35 per gallon

The annual O&M costs are estimated to be *$114,912 - $223,439* per year.

The cost estimates do not include O&M costs for non-transient public water systems that currently exceed the current AGQS of 70 ppt for PFOA and PFOS combined.

1.5 Chemical Monitoring Costs

Upon the adoption of the proposed MCLs, all non-transient public water systems will be required to sample all sources of their water for four consecutive quarters. After the first year of initial sampling, the average concentration of PFOA, PFOS, PFNA and PFHxS will be calculated for each water source to determine compliance with the MCLs. After the first year of sampling, the frequency of future sampling will be dictated by the results of the first year of sampling. The tables below estimate the cost associated with testing all sources of water on a quarterly basis for the first year and estimated ongoing sampling costs after the first year of sampling.

Assuming Sample Analysis cost of $175 - $450 per sample
1st Year Laboratory Costs - Quarterly Compliance Sampling

Owner	# PWS	# Sites	Initial Cost
State	6	13	$9100 - $23,400
Federal	3	4	$2800 - $7200
Local	274	472	$330,400 - $849,600
Others	907	1086	$760,200 - $1,955,800
TOTAL	1190	1575	$1,102,500 - $2,836,000

Projected Percentage of PWS Sample Sites at Various Contaminant Levels

% of MCL	PFHXS	PFNA	PFOA	PFOS	PFOA + PFOS
ND	86.4%	92.8%	50.3%	79.7%	
<20%	11.4%	3.0%	37.1%	16.4%	38.3%
20 to 75%	2.2%	2.5%	10.7%	3.2%	8.9%
>75% to MCL	0%	1.0%	1.2%	0.5%	1.2%
>=100%	0%	0.7%	0.7%	0.2%	0.5%

Projected Annual Compliance Monitoring Laboratory Costs (years 2 - 9)

Contaminant Range	% of Sites	# of Sites	Sampling Frequency	Cost/Site/Year	Total Sampling Cost/Year
>MCL or Treatment	2%	32	Quarterly	$700 - $1800	$22,400 - $57,600
>75% to MCL	3%	47	Annually	$175 - $450	$8225 - $21,150
20 to 75%	15%	236	Every 3 Years	$60 - $150	$14,160 - $35,400
<20%	19.5%	307	Every 6 Years	$30 - $75	$9210 - $23,025
ND**	60.5%	953	Every 9 Years	$20 - $50	$19,060 - $47,650
				Average Annual Cost	$73,055 - $184,825

**Most sites that have any detection will exceed the threshold value for more than one contaminant. Preliminary study shows 243 out of 402 sites tested as having no detections (60.5%).

1.6 Other Potential Costs that Could Impact Public Water Systems

In southern New Hampshire, several square miles of soil have been contaminated with PFAS due to air emissions. Water utilities completing construction projects in these areas may incur increased costs associated with managing potentially contaminated soils and construction dewatering in these areas.

2.0 Cost Estimates for Private Wells

It is estimated that there are 250,000 private wells in New Hampshire. If it is assumed 0.75% of the private wells in the state will require treatment for PFOA exceeding 38 ppt and 0.5% of the private wells will require treatment for PFOA and PFOS exceeding 70 ppt, the treatment costs will be approximately *$9,375,000 for 3125 private wells*. This assumes there are 250,000 private wells and it will cost $3000 per well to install treatment. [(0.75% x 250,000 wells + 0.5% x 250,000 wells) x $3000/well]

It is estimated that it will cost $900 per year per well to sample and test and maintain treatment systems for PFOS and PFOA. *The total cost annual cost to test and maintain treatment systems for 3125 private wells is estimated to be $2,812,500*.

Appendix 10: Analysis of Increased Costs for Municipal and Private Landfills and Hazardous Waste Sites to comply with Proposed MCLs for PFOA, PFOS, PFNA, PFHxS

Appendix 10: Table 1- Estimated Cost to Hazardous Waste and Landfills Sites for Proposed PFAS MCLs

Est. No. Hazardous Waste Sites	Est. No. of Landfill Sites		Additional Capital Costs	Hazardous Waste Sites	Landfill Sites		Additional Annual Costs	Hazardous Waste Sites	Landfill Sites
Projected # of existing Sites w/ PFAS			*GMP Expansion of Existing Sites*	*Est. Cost*	*Est. Cost*		*GMP Expansion of Existing Sites*	*Est. Cost*	*Est. Cost*
		A	**Monitoring Network Enhancments**			A	**Annual Sampling and Reporting**		
252	**84**		Monitoring Well Install (assume 3 wells) + Initial Sampling Round	$ 12,000	$ 12,000		Annual Sampling/Lab fee (1 round, 3 wells)	$ 3,000	$ 3,000
			Receptor Survey	$ 1,000	$ 1,000		Annual GMP Reporting	$ 2,400	$ 2,400
			Est. Subtotal Capital Cost	$ 13,000	$ 13,000		Est. Subtotal Annual Cost	$ 5,400	$ 5,400
			Numbers below rounded to the nearest $5,000				Numbers below rounded to the nearest $5,000		
	25%		***Est. Total Capital Costs for GMP Expansion*** *(assumes 25% of all sites require expansion)*	**$ 820,000**	**$ 275,000**		***Est. Total Annual Monitoring/Reporting Costs*** *(assumes 25% of all sites require expansion)*	**$ 340,000**	**$ 115,000**
	50%		***Est. Total Capital Cost for GMP Expansion*** *(assumes 50% of all sites require expansion)*	**$ 1,635,000**	**$ 545,000**		***Est. Total Annual Monitoring/Reporting Costs*** *(assumes 50% of all sites require expansion)*	**$ 680,000**	**$ 225,000**
		B	**Water Supply Well Treatment**			B	**Water Supply Well Treatment**		
			POE Install -assume 3 per site	$ 3,000	$ 3,000		Annual O&M of POE (assume 3 per site)	$ 1,000	$ 600
			Est. Subtotal Cost	$ 9,000	$ 9,000		Est. Subtotal Annual O&M Cost	$ 3,000	$ 1,800
			Numbers below rounded to the nearest $5,000				Numbers below rounded to the nearest $5,000		
	10%		***Est. Total for Expansion of Sites 10% of all sites will have 3 new POEs***	**$ 225,000**	**$ 75,000**		***Est. Total for Expansion of Sites 10% of all sites will have 3 new POEs***	**$ 75,000**	**$ 15,000**
	20%		***Est. Total for Expansion of Sites - 20% of all sites will have 3 new POEs***	**$ 455,000**	**$ 150,000**		***Est. Total for Expansion of Sites 20% of all sites will have 3 new POEs***	**$ 150,000**	**$ 30,000**
						C	**NHDES Staff Time (Assume Annual Salary/benefits for 2 FTE staff will be required at $120,000/yr)**	$ 120,000	$ 120,000
			I. Est. Capital Cost range for GMZ Expansion: Low	**$ 1,045,000**	**$ 350,000**		**I. Est. Annual Cost range for GMZ Expansion: Low**	**$ 535,000**	**$ 250,000**
			High	**$ 2,090,000**	**$ 695,000**		**High**	**$ 950,000**	**$ 375,000**
Projected # of Sites w/ PFAS Exceedances			*Sites that may be required to address PFAS as a new Contaminant of Concern*	*Est. Cost*	*Est. Cost*		*Sites that may be required to address PFAS as a new Contaminant of Concern*	*Est. Cost*	*Est. Cost*
19	**5**	A	**Monitoring Network Enhancments**			A	**Annual Sampling and Reporting**		
			Monitoring Well Install (assume 5 wells) + Initial Sampling Round	$ 18,000	$ 18,000		Annual Sampling/Lab fee (1 round, 5 wells)	$ 3,500	$ 3,500
			Receptor Survey	$ 1,500	$ 1,500		Annual GMP Reporting	$ 2,900	$ 2,900
			Est. Subtotal Cost	$ 19,500	$ 19,500		Est. Subtotal Cost	$ 6,400	$ 6,400
			Numbers below rounded to the nearest $5,000				Numbers below rounded to the nearest $5,000		
	25%		**Est. Total for New Sites - 25%**	**$ 90,000**	**$ 25,000**		***Est. Total Annual Monitoring Costs for New Sites - 25% of all sites***	**$ 30,000**	**$ 10,000**
	50%		**Est. Total for New Sites - 50%**	**$ 185,000**	**$ 50,000**		***Est. Total Annual Monitoring Costs for New Sites - 50% of all sites***	**$ 60,000**	**$ 15,000**
		B	**Water Supply Well Treatment**			B	**Water Supply Well Treatment**		
			POE Install - assume 3 per site	$ 3,000	$ 3,000		Annual O&M of POE (assume 3 per site)	$ 1,000	$ 600
			Est. Subtotal Cost	$ 9,000	$ 9,000		Est. Subtotal Cost	$ 3,000	$ 1,800
			Numbers below rounded to the nearest $5,000				Numbers below rounded to the nearest $5,000		
	10%		***Est. Total for New Sites 10% of all sites will have 3 new POEs***	**$ 15,000**	**$ 5,000**		***Est. Total for New Sites 10% of all sites will have 3 new POEs***	**$ 5,000**	**$ -**
	20%		***Est. Total for New Sites 20% of all sites will have 3 new POEs***	**$ 35,000**	**$ 10,000**		***Est. Total for New Sites 20% of all sites will have 3 new POEs***	**$ 10,000**	**$ -**
			II. Est. Cost range for Sites w/ PFAS as New COC: Low	**$ 105,000**	**$ 30,000**		**I. Est. Annual Cost range for or Sites w/ PFAS as New COC: Low**	**$ 35,000**	**$ 10,000**
			High	**$ 220,000**	**$ 60,000**		**High**	**$ 70,000**	**$ 15,000**
			Est. Total Capital Cost Impacts for Proposed MCLs: Low	**$ 1,150,000**	**$ 380,000**		**Est. Total Annual Operating Budget Impacts for Proposed MCLs: Low**	**$ 570,000**	**$ 260,000**
			High	**$ 2,310,000**	**$ 755,000**		**High**	**$ 1,020,000**	**$ 390,000**

	Hazardous Waste Sites	Landfills	
$1.15M to $2.31M	$380K to $755K	Additional capital cost to expand existing GMZs, establish new sites and treat impacted drinking water supply wells.
$570 to $1.0M	$260K to $390K	Additional annual operating costs (monitoring and reporting), and NHDES permit administration costs

For the Following Standards (PPT):
PFOA = 38
PFOS = 70
PFNA = 23
PFHxS = 85
PFOA+PFOS = 70

Appendix 10: Table 2 Estimated Cost to Hazardous Waste and Landfill Sites for Proposed MCLs

Hazardous Waste Site Projections are based on:	
515	Hazardous Waste Sites
137	Number of sites PFAS Sampling has been completed
27%	Percent of Sites Sampled
Analysis of Existing Data and Current Standard of 70 PPT PFOA + PFOS	
Of the 137	sites sampled:
49%	had exceedances of the current standard
9%	had water supply wells with exceedances of current standards
Estimate of # of Hazardous Waste Sites with Existing PFAS Compliance Issues	
Assumption:	*Apply similar trend of existing data outlined above.*
252	sites may have exceedances of the current standard
25 to 50	estimated number of sites with drinking water impacts[1]
Analysis of Existing Data and Proposed Standards in Parts per Trillion	
PFOA	38
PFOS	70
PFNA	23
PFHxS	85
PFOA+PFOS	70
53%	of sites sampled w/ exceed. of proposed stds of one or more compounds
27 to 54	estimated number of sites with drinking water impacts[1]

Notes:
1. Based on the limited data to estimate this, NHDES used a range of 10-20% of the projected number of sites with exceedances.

Landfill Site Projections are based on:	
201	Landfill Sites
117	Number of sites PFAS Sampling has been completed
58%	Percent of Sites Sampled
Analysis of Existing Data and Current Standard of 70 PPT PFOA + PFOS	
Of the 117	sites sampled:
42%	had exceedances of the current standard
1%	had water supply wells with exceedances of current standards
Estimate of # of Landfill Sites with Existing PFAS Compliance Issues	
Assumption:	*Apply similar trend of existing data outlined above.*
84	sites may have exceedances of the current standard
8 to 17	estimated number of sites with drinking water impacts[1]
Analysis of Existing Data and Proposed Standards in Parts per Trillion	
PFOA	38
PFOS	70
PFNA	23
PFHxS	85
PFOA+PFOS	70
44%	sites sampled w/ exceed. of proposed stds of one or more compounds
9 to 18	estimated number of sites with drinking water impacts[1]

Notes:
1. Based on the limited data to estimate this, NHDES used a range of 10-20% of the projected number of sites with exceedances.

Appendix 10: Table 3-Estimated Cost to Select Southern New Hampshire Hazardous Waste Sites for Proposed MCLs

Additional Capital Costs			Additional Annual Costs		Hazardous Waste Sites
	Additional Private Well Testing [2,3]	***Est. Cost***		***Additional Private Well Testing***	***Est. Cost***
A	**Additional Private Well Testing**		**A**	**Additional Annual Private Well Sampling and Reporting**	
	Initial Sampling Round (assume 500 wells)	$ 500,000		Annual Sampling/Lab fee (2 rounds, 50 wells)	$ 100,000
	Receptor Survey	$ 10,000		Annual GMP Reporting	$ 10,000
	Est. Subtotal Capital Cost	$ 510,000		Est. Subtotal Annual Cost	$ 110,000
	Provision of Alternate Water [5]	***Est. Cost***		***Provision of Alternate Water***	***Est. Cost***
B	**Water Supply Well Treatment** [5]		**B**	**Water Supply Well Treatment**	
	POE installations (assume 180)	$ 3,000		Annual O&M of POE (assume 150)	$ 1,000
	Est. Subtotal Cost	$ 540,000		Est. Subtotal Annual O&M Cost	$ 180,000
C	**Waterline Connections** [6]		**C**	**Waterline Connections**	
	In areas with existing waterlines (assume 65)	$ 15,000		N/A	
	Est. Subtotal Cost	$ 975,000		Est. Subtotal Annual O&M Cost	$ -
	Total Costs (A,B, and C)	$2,025,000		Total Costs (A,B, and C)	$ 290,000
	Est. Total Capital Cost Impacts for Proposed MCLs: Low (75% of Total Costs)	**$1,520,000**		**Est. Total Annual Cost Impacts for Proposed MCLs: Low (75% of Total Costs)**	**$ 220,000**
	High (125% of Total Costs)	**$2,530,000**		**High (125% of Total Costs)**	**$ 365,000**

Notes and Assumptions:

Costs presented in the table above are for two large sites in southern New Hampshire, where groundwater in portions of the communities of Amherst, Bedford, Hollis, Litchfield, Londonderry, Manchester, and Merrimack has been impacted by PFAS.

1. The number of additional potentially impacted properties is unknown. An extrapolation of the sample results from private drinking water wells was completed to provide a general screening-level approximation of the number of additional properties that could potentially be impacted. Note the dataset used in the extrapolation contains data from both overburden and bedrock wells and wells of various depths, and most of the well were only sampled on one occasion. Additional sampling will be required to evaluate actual concentrations in groundwater. In areas where information about water sources for individual properties was not available, it was assumed that properties within a proximity of a waterline were connected to public water; all other properties were assumed to be served by private wells. This information needs to be confirmed.

2. Based on the extrapolation, approximately 500 properties are located in areas where groundwater could be impacted by PFOA at concentrations greater than half of the proposed AGQS. The actual number will likely vary based on further evaluation of sample results.

3. Potential additional site investigation costs are not able to be determined, as plans for off-site investigations have not yet been developed.

4. A determination of sources of alternate water will be made following an evaluation of additional sampling data and feasibility. For this cost estimate, it was assumed that approximately half of the properties sampled would need alternate water.

5. For purposes of this cost estimate, it was assumed that point-of-entry treatment systems (POEs) would be provided in areas where waterlines are currently not present.

6. For purposes of this cost estimate, it was assumed that connections to public water would be provided only in areas where waterlines are already present. These costs assume that no new water main extensions would needed.

Capital costs would be significantly higher if water main extensions would be required to service those properties in Section B that are assumed to be covered by POEs. Costs for additional waterline extensions are not able to be determined at this time and would vary significantly based on the number of properties served, length of water main needed, service connection lengths, water source, and contractor pricing, but could potentially be in the ballpark of $10-45 MM.

Appendix 11: Analysis of Increased Costs for Groundwater Discharge Permittees to comply with Proposed MCLs for PFOA, PFOS, PFNA, PFHxS

Cost Estimates - Reduction in PFAS Standards - Groundwater Discharge Permit (GWDP) Sites

Isolated Sites : Non-Developed Areas, Able to Expand Groundwater Discharge Zones (GDZ), No Private/Public Water Supply Receptors

Small GWDP Sites
Non POTW sites, usually privately owned

Additional Capital Costs				Additional Annual Costs			
Item	Count	Unit Cost	Total	Item	Count	Unit Cost	Total
Mon Well	3	$ 12,000	$ 36,000	Smpl Rnd	6	$ 1,000	$ 6,000
Priv Well Svy	1	$ 1,000	$ 1,000	Rpting	1	$ 2,400	$ 2,400
		Total	*$ 37,000*			*Total*	*$ 8,400*
1X	***Add'l sites***		***$ 37,000***	1X	***Add'l sites***		***$ 8,400***

Large GWDP Sites
POTW sites, usually publicly owned

Additional Capital Costs				Additional Annual Costs			
Item	Count	Unit Cost	Total	Item	Count	Unit Cost	Total
Mon Well	6	$ 12,000	$ 72,000	Smpl Rnd	12	$ 1,000	$ 12,000
Priv Well Svy	1	$ 1,000	$ 1,000	Rpting	1	$ 2,400	$ 2,400
		Total	*$ 73,000*			*Total*	*$ 14,400*
3X	***Add'l sites***		***$ 219,000***	3X	***Add'l sites***		***$ 43,200***

Non-Isolated Sites : Developed Areas, Not (Easily) Able to Expand GDZ, Private/Public Water Supply Receptors Present

Small GWDP Sites
Non POTW sites, usually privately owned

Additional Capital Costs				Additional Annual Costs			
Item	Count	Unit Cost	Total	Item	Count	Unit Cost	Total
Mon Well	2	$ 12,000	$ 24,000	Smpl Rnd	4	$ 1,000	$ 4,000
Priv Well Svy	1	$ 2,500	$ 2,500	Rpting	1	$ 2,400	$ 2,400
POE-PFAS	3	$ 3,000	$ 9,000	O&M	3	$ 900	$ 2,700
		Total	*$ 35,500*			*Total*	*$ 9,100*
Fac Trtmnt	***Range: 10k to 100k***						
2X	***Add'l sites***		***$ 71,000***	2X	***Add'l sites***		***$ 18,200***

Large GWDP Sites
POTW sites, usually publicly owned

Additional Capital Costs				Additional Annual Costs			
Item	Count	Unit Cost	Total	Item	Count	Unit Cost	Total
Mon Well	4	$ 12,000	$ 48,000	Smpl Rnd	8	$ 1,000	$ 8,000
Priv Well Svy	1	$ 5,000	$ 5,000	Rpting	1	$ 2,400	$ 2,400
POE-PFAS	6	$ 3,000	$ 18,000	O&M	6	$ 900	$ 5,400
		Total	*$ 71,000*			*Total*	*$ 15,800*
Fac Trtmnt	***Flows too large***						
1X	***Add'l sites***		***$ 71,000***	1X	***Add'l sites***		***$ 15,800***

	Additional Capital Costs	Additional Annual Costs
Multiplier 2.3	**Add'l at new PFAS st $ 915,400**	**Add'l at new PFAS st $196,880**

4x sites ***Fac Trtmnt Range : $20,000 to $200,000***

*Small Facilities only

New PFAS Standard Evaluated:
PFOA: 38 ppt
PFOS: 70 ppt
PFOA + PFOS: 70 ppt
PFNA: 23 ppt
PFHxS: 85 ppt

SUMMARY

-***For change to lower PFAS standards***:
- Adds ~12 GWDP sites to the list of sites with PFAS compliance issues.
-Adds ~ $900K to capital costs
-Adds ~ $200K to annual costs

Sites with Existing PFAS issues:
-Potential additional costs to sites with existing compliance issues that exceed the current PFAS standard : ~$200K

Cost impact to small (mostly privately owned) GWDP sites could be greater if WW pre-treatment is put in place: estimate ~ $20K to $200K capital costs

Assumption Summary for development of Cost Impacts to Groundwater Discharge Permit (GWDP) sites due to the lowering of the PFAS standards

Breakdown of all Sites in GWDP program: 96 GWDP sites - Four Categories

Geographically Isolated Sites: -Located in non-developed area -Commonly able to easily expand GDZ -No public or private water wells nearby (no receptors)	**Small sites:** -Flows less than 50K per day -Usually privately owned -Contaminant specific treatment may be feasible
	Large sites: -Flows greater than 50K per day -Usually publically owned POTW -Contaminant specific treatment usually NOT feasible
Non-isolated Sites: -Located in developed area -Not easily able to expand GDZ -Public and/or private water wells nearby (receptors)	**Small sites:** -Flows less than 50K per day -Usually privately owned -Contaminant specific treatment may be feasible
	Large sites: -Flows greater than 50K per day -Usually publically owned POTW -Contaminant specific treatment usually NOT feasible

Breakdown of GWDP sites with PFAS in groundwater at or above current AGQS based on sampling:

- 1-Isolated Small sites
- 2-Isolated Large sites
- 0-Non Isolated Small sites
- 1-Non Isolated Large sites

Assumptions related to number of GWDP sites affected by lowering of PFAS standards:

- For new PFAS standard, the number of current sites that would exceed standards at those sites that have sampled would increase from 4 sites to 7 sites.
- Forty two (42) of 96 sites have sampled, therefore number of exceeding sites were scaled up by a factor or 2.3 (96/42) projecting exceedances at approximately 16 groundwater discharge permit sites across the entire population of permit holders.

Response actions at sites that exceed the new standard that impact cost:

- Isolated sites:
  - Conduct Receptor Survey
  - Expand GDZ where feasible
  - Add monitoring wells (3 per small site, 6 per large site)
  - Conduct additional annual sampling
- Non-Isolated sites
  - Conduct Receptor Survey
  - Expand GDZ where feasible
  - Add monitoring wells (less than isolated sites)
  - Conduct additional annual sampling
  - Install POE treatment systems (up to 3 units per small site, up to 6 units per large site)

Private Well Mitigation Considerations: POE only, no public water system extensions or connections
WW Treatment Considerations: Modifications to WW treatment systems are only feasible at Small Sites