Ms. Sarah Pillsbury
NHDES Drinking Water and Groundwater Bureau
New Hampshire Department of Environmental Services
P. O. Box 95
Concord, NH 03302

SUBJECT: Recommendations Addressing Studies, Data and Methodology for the Derivation of NH Drinking Water and Groundwater Standards

Dear Ms. Pillsbury,

By way of background, I am a board-certified toxicologist. I have 30 years of experience providing consulting services in the field of environmental risk assessment and have evaluated the adverse effects of hundreds of different compounds, including emerging contaminants (e.g. dioxins/furans, perchlorate, 1,4-dioxane, BPA, etc.) on both humans and ecological receptors. For the past two years I have served as a co-author on ITRC's "PFAS Factsheet Team" and am currently continuing with that effort, producing a more comprehensive document that expands on the seven fact sheets, which will be released in the Spring of 2019.

I recently attended one of the "Stakeholder and Technical Work Sessions" that NHDES held between October 16th – 19th 2018. This is a short letter that presents my view the current scientific and regulatory atmosphere surrounding the many different issues on PFAS.

I anticipate that the new toxicologists that NHDES recently hired will be limited to the existing data that has been published to date, principally the USEPA drinking water health advisory (DWHA) documents on PFOA/PFOS as well as the recent Minimal Risk Levels derived by ATSDRs "Draft Toxicological Profile on Perfluoroalkyls". As you are aware, there is a large degree of variability in the drinking water standards being derived by many of the States and this is confusing many in the public who are essentially asking "Why is there such a large difference in drinking water advisories/standards?". For example, although most States have adopted USEPA's DWHA of 70 parts per trillion (ppt), Minnesota, Vermont and New Jersey have respective health-based standards of 35, 20 and 14 ppt. The reason for these differences is generally due to a) the selection of a different animal species and/or study b) the selection of a different "point-of-departure" within a study c) the selection and/or use of inter- and intraspecies safety/uncertainty factors and d) the selection/use of assumptions in the final derivation of the reference dose (e.g. child vs. adult body weight, drinking water intake, relative source contribution, etc.).

I would like to take this opportunity to urge newly hired NHDES toxicologists to consider all of the scientific work and decisions that went into the derivation of the 70 ppt DWHA for PFOA and PFOS. It is my strong opinion that the derivation of the "safe" RfDs for these two compounds err on the conservative for the following reasons:

- **These RfDs represent the most sensitive effect, for the most sensitive life stage, in the most sensitive species**. The USEPA drinking water health advisories for both PFOA and PFOS pulled

together every available scientific study that was available in the peer-reviewed literature at the time. They put aside human epidemiological data as well as toxicity study on primates (which are genetically closer to humans) to focus on rodents which appeared to have the most uniform responses within a similar dose range. Although this species may not be the best choice as an animal model, the science to date is fairly solid and the RfD's for both PFOA and PFOS are virtually identical.

- **The derivation of the RfDs for both PFOA and PFOS are the same.** The estimation of the Human Equivalent Doses (HEDs) and the subsequent RfD's for both PFOA and PFOS (USEPA, 2016a,b; Table 5-2) are remarkably uniform, so much so that several reviewers of the DWHA documents thought the selection of uncertainty factors were purposely biased so that all the RfD values came out close together. In any event, the fact that two separate comprehensive toxicity evaluations for two somewhat similar compounds speaks to the fact that the mechanisms of action may be quite similar for C8 compounds.

- **Humans are less sensitive than rats to PFAS**. Despite all of the available information on the toxicity of PFAS compounds, there is still no know mechanism of toxicity for PFAS. Unlike most toxicants, PFAS are not metabolized and are therefore "metabolically inert". They will not form reactive intermediates, deplete endogenous glutathione, covalently bind to DNA, or compete with cellular ligands that may, in turn, adversely affect normal cell or tissue processes. Additionally, the only known mechanism of toxicity shown to have any scientific merit to date is the induction of the peroxisome proliferator-activate receptor (or PPAR). This receptor active in many test animals but apparently has little relevance to humans since the enzyme system is either weak or nonexistent depending on the tissue.

- **The difference between a "safe" dose in the rodent(s) vs. a human is ~50,000**. The "Human Equivalent Dose" (HED) was derived mainly based on the fact that the ½-life in the human body is several orders of magnitude larger than the ½-life in a laboratory test animal (e.g., mice, rats, monkeys). However, from the perspective of internal bioavailability, it is also true that >99% of PFAS are tightly bound to serum albumin for all species (including humans). In other words, what the body "sees" in terms of "free" PFAS would be similar, whether a human or a lab animal. Taken together, when converting from a LOAEL in the mouse to a HED, a factor of about 180 is used. When all of the factors are estimated into the final derivation of the RfD, the difference between a "no effect" dose in the rodent and a "safe" dose for humans is a factor of approximately 50,000. Compare this very large margin-of-safety to the range of engineering safety factors (1.5 to 20) that is required for a civil or mechanical engineer when constructing an engine, aircraft or bridge. The current DWHA's for both PFOA and PFOS clearly err on the side of conservatism.

- **The derivation of the ATSDR Minimal Risk Levels for PFOS and PFOA are not supported by the USEPA's DWHA documents**. Although I have not had much time to review the ATSDR MRLs, it is clear that the methods they used are not supported by what was presented in the USEPA DWHS documentation. First, the ATSDR use a monkey animal model for both PFOA and PFOS. For PFOS, the USEPA rejected the monkey as a test species because of premature deaths in two of the six males at the LOAEL. Additionally, it is my opinion that ATSDR chose one of the least sensitive endpoints (increased liver weight) and there were too few animals per dose level to allow a robust statistical analysis. For PFOA, the number of individuals per dose group (2 per gender) was also small, all the animals in the high dose group and several in the intermediate dose group died, and the LOAELs were based on

animals per dose level to allow a robust statistical analysis. For PFOA, the number of individuals per dose group (2 per gender) was also small, all the animals in the high dose group and several in the intermediate dose group died, and the LOAELs were based on frank effects (decreased heart and brain weight) rather than a more sensitive endpoint like reproduction. It is also my opinion that the use of the BMDL model to derive safe doses in humans is typically reserved for carcinogens which are assumed to have a "no threshold" response. PFAS likely have a threshold below which no adverse effects can be discerned, even in the long run.

- **An Australian Health Study opines that the risks of PFAS to humans is overstated**. An Expert Health Panel was recently convened to advise the Australian Government on the evidence for potential health impacts associated with PFAS exposure. The Panel "focused on identifying and reviewing the *latest* systematic reviews of human epidemiological studies and (inter)national authority/ intergovernmental/governmental reviews and reports on potential human health effects of PFAS exposure". They found the same associations as reported by both NHDES "Draft List of Health Effects" and others in the literature (e.g. increased cholesterol, increased uric acid, reduced kidney function, altered markers of immunological response, levels of thyroid and sex hormone levels, later menarche and earlier menopause, and lower birth weight). However, they also state that "Differences between those with the highest and lowest exposures are generally small, with the highest groups generally still being within the normal ranges for the whole population. There is mostly limited or no evidence for an association with human disease accompanying these observed differences. There is no current evidence that supports a large impact on an individual's health. In particular, there is no current evidence that suggests an increase in overall cancer risk." In other words, despite hundreds of studies on both humans (epidemiological) and animals (laboratory), the evidence associated with an adverse outcome following exposure to PFAS is either weak or unsubstantiated.

In conclusion, I would urge the NHDES toxicologists utilize the best science moving forward, not a "one size fits all" approach that several States are enacting. Each MCL needs to be derived using a weight-of-evidence approach that combines three or more solid lines-of-evidence that share consistent results. I am concerned that communities are now running on emotion rather than logic and we are now at a point where regulators think an MCL of 70 ppt is somehow not low enough. This type of thinking will cross over to other media (such as wastewater and biosolids) which will not only result in exorbitant cost to the taxpayer, but also a reversal of decades of research into best available control technology(s).

Sincerely,

Stephen R. Clough, Ph.D., DABT

USEPA, 2016a. Drinking Water Health Advisory for Perfluorooctanoic Acid (PFOA). Prepared by: U.S. Environmental Protection Agency, Office of Water (4304T), Health and Ecological Criteria Division, Washington, DC. EPA Document Number: 822-R-16-005. May 2016.

USEPA, 2016b. Drinking Water Health Advisory for Perfluorooctanoic Sulfonate (PFOs). Prepared by: U.S. Environmental Protection Agency, Office of Water (4304T), Health and Ecological Criteria Division, Washington, DC. EPA Document Number: 822-R-16-004. May 2016.