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conservation law foundation

For a thriving New England

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Via Electronic Mail

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MassDEP
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Re: Comments on Proposed Changes to the Massachusetts Contingency Plan (MCP) Cleanup Standards for PFAS in Groundwater and on MassDEP's Office of Research & Standards and the Drinking Water Program's Consideration of PFAS

Dear Ms. Callahan:

Conservation Law Foundation (CLF), along with Toxics Action Center (TAC), Clean Water Action (CWA), and Natural Resources Defense Council (NRDC), appreciates the opportunity to comment on the above-referenced proposed rules pertaining to perfluorochemicals as related to drinking water, groundwater, and discharges of wastewater into groundwater. Founded in 1966, CLF is a non-profit, member-supported environmental advocacy organization with offices located in Massachusetts, New Hampshire, Vermont, Maine, and Rhode Island. CLF uses the law, science, and the market to create solutions that protect public health, preserve natural resources, build healthy communities, and sustain a vibrant economy. CLF has been a leading advocate for clean, safe drinking water in Massachusetts and throughout New England, and has engaged in numerous efforts to address the threat of Per- and Polyfluoroalkyl Substances (PFAS) pollution in Massachusetts, including addressing contamination in Devens, advocating for more protective PFAS standards to protect the public health and the environment, and advocating for the regulation of PFAS as a class.[1]

Toxics Action Center was founded in 1987 out of the Woburn contamination crisis. TAC believes that everyone has the right to breathe clean air, drink clean water, and live in a healthy community with a government that operates responsively and democratically. We work to make those rights a reality by working side-by-side community groups fighting pollution threats in

[1] On October 25, 2018 CLF and TAC petitioned MassDEP to establish a drinking water standard for the class of PFAS. That petition is provided as **Attachment A**.

their neighborhoods and by training long-term leadership for the environmental and social change movements. TAC has worked with community groups fighting PFAS drinking water contamination since February 2016 and facilitates the National PFAS Contamination Coalition, a network of nearly 30 community groups fighting PFAS contamination from 17 states and Guam.

Clean Water Action's mission is to protect our environment, health, economic well-being and community quality of life. CWA has over 500,000 members nationally and 37,000 members in Massachusetts.

The Natural Resources Defense Council is an international nonprofit environmental organization with more than 3 million members and online activists across the nation. Since 1970, NRDC has been a leading advocate for drinking water protection. NRDC led efforts to strengthen the Safe Drinking Water Act in the 1986 and 1996 Amendments, spearheaded national campaigns for more protective EPA drinking water rules for microbial contaminants and toxic chemicals, and sued to improve EPA's lead in drinking water standards.

The proposed Massachusetts Contingency Plan (MCP) cleanup standards for PFAS, and the Massachusetts Department of Environmental Protection's (MassDEP) commitment to establish a maximum contaminant level (MCL) for Perfluorodecanoic Acid (PFDA), Perfluoroheptanoic Acid (PFHpA), Perfluorohexanesulfonic Acid (PFHxS), Perfluorooctanoic Acid (PFOA), Perfluorooctanesulfonic Acid (PFOS), and Perfluorononanoic Acid (PFNA) is an important step forward in protecting Massachusetts communities from dangerous PFAS pollution. The proposed cleanup standards, however, do not adequately protect public health from these highly persistent, accumulative, toxic chemicals, and do not account for the potential cumulative and synergistic effects of these six PFAS as well as the thousands of other PFAS that may be present in the environment.

As further discussed below, it is essential that MassDEP's proposed standards protect the health of our most vulnerable sub-populations (developing fetuses and infants) and apply the most protective assumptions at each stage of its risk assessment analysis. Applying this approach, and because it cannot be demonstrated that there is any safe level of exposure to PFAS, MassDEP should establish (1) a maximum contaminant level goal (MCLG) of zero for the PFAS class of chemicals; (2) 1 ppt combined GW-1 standard and drinking water standard for quantifiable PFAS; and (3) a treatment technique drinking water standard for the PFAS class of chemicals.[2] In addition, there is insufficient information in the materials provided by MassDEP for the public to evaluate whether the Method 1 soil standards and GW-3 standards for PFAS are protective of public health and the environment.

[2] MassDEP has stated that it will develop drinking water standards for these six PFAS compounds consistent with the proposed groundwater standards. For this reason and due to the close relationship between the GW-1 standard and drinking water rules, the organizations are also filing preliminary comments on the anticipated drinking water rules.

Note that the organizations' position is that, while MassDEP should establish a treatment technique standard for the PFAS class, this should not delay adoption of drinking water standards for quantifiable PFAS.

I. Introduction

It is essential that Massachusetts residents be protected from the health threat of PFAS in the environment. PFAS are persistent in the environment, bioaccumulative, highly mobile in water, found in hundreds of different products, and are toxic in very small concentrations. As MassDEP itself acknowledged in its online materials related to PFAS chemicals in drinking water:

> PFAS in drinking water is an important emerging issue nationwide. Because PFAS are water soluble, over time PFAS from some firefighting foam, manufacturing sites, landfills, spills, air deposition from factories and other releases can seep into surface soils. From there, PFAS can leach into groundwater or surface water and can contaminate drinking water. PFAS have also been found in rivers, lakes, fish, and wildlife.

See Per- and Polyfluoroalkyl Substances (PFAS), MASSDEP, https://www.mass.gov/info-details/per-and-polyfluoroalkyl-substances-pfas#what-are-pfas-and-why-are-they-a-problem?-.

PFAS have been found at unsafe levels in drinking water in Massachusetts, as well as in groundwater and surface waters. Drinking water contaminated with PFAS is a significant source of exposure.[3] According to MassDEP:

> Studies indicate that exposure to sufficiently elevated levels of certain PFAS may cause a variety of health effects including developmental effects in fetuses and infants, effects on the thyroid, liver, kidneys, certain hormones and the immune system. Some studies suggest a cancer risk may also exist in people exposed to higher levels of some PFAS.

Id.

DuPont, 3M, and other chemical manufacturers recklessly produced these dangerous chemicals for decades despite being aware of the significant health risks associated with PFAS. Furthermore, in 1981, 3M and DuPont were aware that ingestion of PFOA caused birth defects in rats.[4] After receiving this information, DuPont tested seven children of pregnant workers—two had birth defects.[5] DuPont was also aware that at least one facility had contaminated local drinking water supplies with unsafe levels of PFOA by 1991, but it failed to warn anyone.[6]

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[3] *See* Press Release, Vt. Dep't of Health, Health Department Releases PFOA Blood Test and Exposure Assessment Results (Jan. 26, 2017), http://www.healthvermont.gov/sites/default/files/documents/2017/01/NEWS_PFOA%20Blood%20Test%20%26%20Exposure%20Assessment%20Results.pdf (noting that "PFOA levels in blood were strongly correlated with PFOA levels in well water.").

[4] Nathaniel Rich, *The Lawyer Who Became DuPont's Worst Nightmare*, N.Y. TIMES (Jan. 6, 2016), https://www.nytimes.com/2016/01/10/magazine/the-lawyer-who-became-duponts-worst-nightmare.html.

[5] *Id.*

[6] *Id.*

DuPont hid this vital health information from the public and the Environmental Protection Agency (EPA) while making billions of dollars in profits from continued production of PFOA.[7] Ultimately, DuPont was fined a mere $16.5 million dollars in 2005 for failing to disclose information about toxicity and health risks caused by PFOA.[8]

Although PFOA and PFOS have now been phased out of production in the United States,[9] these compounds will remain in our drinking water, groundwater, and surface waters, as well as our bodies, for decades. In addition, manufacturers have rushed to produce thousands of alternative PFAS that are likely to pose similar health risks given the similarities in chemical structure.[10] There are now over 4,000 different kinds of PFAS.

To make matters worse, EPA has failed to take meaningful action to protect the public from exposure to PFAS in drinking water. After becoming aware of contamination of drinking water supplies and the significant health risks posed by these dangerous chemicals, EPA gave manufacturers nearly a decade to phase out production and use of PFOA and PFOS through a voluntary program.[11] Despite learning in 2015 that millions of Americans were, and continue to be, exposed to PFAS-contaminated drinking water, EPA has not taken steps toward requiring public water systems to regularly monitor for PFAS and to treat unsafe water.[12] EPA even suppressed a scientific study suggesting that EPA's current health advisory for PFOA and PFOS does not protect public health.[13] After widespread public outcry, EPA announced the possibility of setting drinking water standards for just two PFAS, yet no enforceable regulatory standard has been proposed to date.[14]

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[7] *See id*.

[8] Memorandum from Grant Y. Nakayama, Assistant Administrator, to Environmental Appeals Board Re Consent Agreement and Final Order to Resolve DuPont's Alleged Failure to Submit Substantial Risk Information Under the Toxic Substances Control Act (TSCA) and Failure to Submit Data Requested Under the Resource Conservation and Recovery Act (RCRA) (Dec. 14, 2005), https://www.epa.gov/sites/production/files/2013-08/documents/eabmemodupontpfoasettlement121405.pdf.

[9] *Assessing and Managing Chemicals under TSCA, Fact Sheet: 2010/2015 PFOA Stewardship Program*, U. S. ENVTL. PROTECTION AGENCY, https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/fact-sheet-20102015-pfoa-stewardship-program#what.

[10] *See, e.g.*, Stephen Brendel et al., *Short-chain perfluoroalkyl acids: environmental concerns and a regulatory strategy under REACH,* 30 ENVTL. SCI. EUR. 1, 3–4 (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5834591/pdf/12302_2018_Article_134.pdf.

[11] *See, e.g.*, Consent Order, *In the matter of: Dupont Company,* (Nos. P-08-508 and P-08-509, U.S. E.P.A. Office of Pollution Prevention and Toxics, April 9, 2009), available at https://assets.documentcloud.org/documents/2746607/Sanitized-Consent-Order-P08-0508-and-P08-0509.pdf; Premanufacture Notification Exemption for Polymers; Amendment of Polymer Exemption Rule to Exclude Certain Perfluorinated Polymers, 75 Fed. Reg. 4295, 4296 (Jan. 27, 2010).

[12] David Andrews, *Report: Up to 110 Million Americans Could Have PFAS-Contaminated Drinking Water*, ENVTL. WORKING GROUP (May 22, 2018), https://www.ewg.org/research/report-110-million-americans-could-have-pfas-contaminated-drinking-water#.W6_7a2hKg2w.

[13] Abraham Lustgarten et al., *Suppressed Study: The EPA Underestimated Dangers of Widespread Chemicals*, PROPUBLICA (June 20, 2018, 4:54 PM), https://www.propublica.org/article/suppressed-study-the-epa-underestimated-dangers-of-widespread-chemicals.

[14] *See The Federal Role in the Toxic PFAS Chemical Crisis, Hearing on SD-342 Before the Subcomittee. on Homeland Security & Governmental Affairs*, 115th Cong. (2018) (statement of Chairman Rand Paul and Ranking Member Gary C. Peters), https://www.hsgac.senate.gov/hearings/the-federal-role-in-the-toxic-pfas-chemical-crisis.

Fortunately, in response to a 2018 "Petition for Rulemaking to Establish a Treatment Technique Drinking Water Standard for Per- and Polyfluoroalkyl Substances" ("Petition") filed by CLF and TAC, MassDEP initiated a process to develop a drinking water MCL for a group of PFAS identified as posing a significant threat to human health and for which both analytical methods exist for their detection and appropriate treatment technologies are available. The development of the MCL for PFAS is informed by these comments as part of MassDEP's process regarding groundwater cleanup standards under the MCP. Importantly, MassDEP's proposed changes to drinking water standards and groundwater cleanup standards reflect MassDEP's determination that current federal MCLs and health advisories are insufficient to protect public health.

II. PFAS are harmful to human health.

PFAS are a public health crisis "perfect storm" because PFAS compounds are extremely persistent in the environment, highly mobile in water, bioaccumulative, toxic in very small quantities, and found in hundreds of products. PFAS compounds are human-made substances that do not occur naturally. They have been used in non-stick cookware, water-repellent clothing, stain resistant fabrics and carpets, cosmetics, firefighting foams, and other products that resist grease, water, and oil.[15] These chemicals are extremely strong and highly resistant to degradation.[16]

PFAS "have been detected in all environmental media including air, surface water, groundwater (including drinking water), soil, and food."[17] A study by the Centers for Disease Control and Prevention (CDC) found four PFAS (PFOS, PFOA, PFNA, and PFHxS) in the serum of nearly all of the people tested, indicating widespread exposure in the U.S. population.[18] PFOA and PFOS were found in up to 99 percent of the U.S. general population between 1999 and 2012.[19] PFAS are found in human breast milk and umbilical cord blood.[20]

[15] Seth Kerschner & Zachary Griefen, *Next Round of Water Contamination Suits May Involve CWA*, LAW 360, (Oct. 5, 2017), https://www.law360.com/articles/970995/next-round-of-water-contamination-suits-may-involve-cwa.

[16] NEW JERSEY DEP'T OF ENVTL. PROTECTION DIVISION OF SCIENCE, RESEARCH, AND ENVTL. HEALTH, INVESTIGATION OF LEVELS OF PERFLUORINATED COMPOUNDS IN NEW JERSEY FISH, SURFACE WATER, AND SEDIMENT 2 (2018), https://www.nj.gov/dep/dsr/publications/Investigation%20of%20Levels%20of%20Perfluorinated%20Compounds%20in%20New%20Jersey%20Fish,%20Surface%20Water,%20and%20Sediment.pdf.

[17] AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, TOXICOLOGICAL PROFILE FOR PERFLUOROALKYLS 2 (2018), https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf [hereinafter "TOXICOLOGICAL PROFILE FOR PERFLUOROALKYLS"].

[18] *Per- and Polyfluorinated Substances (PFAS) Factsheet*, CTR. FOR DISEASE CONTROL AND PREVENTION (last updated Apr. 7, 2017), https://www.cdc.gov/biomonitoring/PFAS_FactSheet.html.

[19] U.S. ENVTL. PROTECTION AGENCY, DRINKING WATER HEALTH ADVISORY FOR PERFLUOROOCTANOIC ACID (PFOA) 10 (2016), https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final_508.pdf [hereinafter DRINKING WATER HEALTH ADVISORY FOR PERFLUOROOCTANOIC ACID (PFOA)].

[20] TOXICOLOGICAL PROFILE FOR PERFLUOROALKYLS, *supra* note 17, at 3.

PFAS are toxic to humans in concentrations as small as *parts per trillion* (ppt).[21] PFAS are suspected carcinogens and have been linked to growth, learning, and behavioral problems in infants and children; fertility and pregnancy problems, including pre-eclampsia; interference with natural human hormones; increased cholesterol; immune system problems; and, interference with liver, thyroid, and pancreatic function.[22] PFAS have been linked to increases in testicular and kidney cancer in human adults.[23]

Developing fetuses and newborn babies are particularly sensitive to some PFAS.[24] As described in a recent report prepared by the Natural Resources Defense Council (NRDC) [hereinafter "NRDC Report" and provided as **Attachment B**] addressing MCLs in Michigan for four of the six PFAS at issue here:[25]

> Developing infants and children are particularly susceptible to the impacts of exposure to toxic chemicals. The impacts of PFAS exposure on fetal development and the young have been studied in both humans and animals. These studies find similar and profound adverse health effects.
>
> Since infants and children consume more water per body weight than adults, their exposures may be higher than adults in communities with PFAS in drinking water. In addition, the young may also be more sensitive to the effects of PFAS due to their immature developing immune system, and rapid body growth during development. Exposure to PFAS before birth or in early childhood may result in decreased birth weight, decreased immune responses, and hormonal effects later in life.[26]

The recently published article by Helen M. Goeden et al. [hereinafter "Goeden" and provided as **Attachment C**] makes clear that PFAS exposure occurs *in utero* as a result of placental transfer of PFAS, and that there is a significant, additive PFAS exposure that occurs in infants through breast-feeding. [27] Goeden notes "the importance of considering placental transfer, as early life serum levels are predicted to be approximately 40% higher than adult steady-state levels," and that "[w]hen both placental and breastmilk transfer are taken into account. . . early life serum levels were predicted to be sixfold higher than adult steady-state levels."[28]

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[21] *See Per- and Polyfluoroalkyl Substances (PFAS) and Your Health*, AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, https://www.atsdr.cdc.gov/pfas/health-effects.html; *see also* TOXICOLOGICAL PROFILE FOR PERFLUOROALKYLS, *supra* note 17, at 5–6.

[22] TOXICOLOGICAL PROFILE FOR PERFLUOROALKYLS, *supra* note 17, at 5–6.

[23] *Id.* at 6; Vaughn Barry et al., *Perfluorooctanoic Acid (PFOA) Exposures and Incident Cancers among Adults Living Near a Chemical Plant*, 121 ENVTL. HEALTH PERSPECTIVES 1313, 1313 (Nov.–Dec. 2013), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3855514/pdf/ehp.1306615.pdf.

[24] *See* DRINKING WATER HEALTH ADVISORY FOR PERFLUOROOCTANOIC ACID (PFOA), *supra* note 19, at 9.

[25] ANNA READE ET AL., NRDC, SCIENTIFIC AND POLICY ASSESSMENT FOR ADDRESSING PER- AND POLYFLUORINATED SUBSTANCES (PFAS) IN DRINKING WATER 23 (2019) [hereinafter "NRDC Report"].

[26] *Id*.

[27] Helen M. Goeden et al., *A transgenerational toxicokinetic model and its use in derivation of Minnesota PFOA water guidance*, 29 J. OF EXPOSURE SCI. & ENVTL. EPIDEMIOLOGY 183 (2019).

[28] *Id*.

Alarmingly, epidemiological studies identify the immune system as a target of PFAS toxicity. Some studies have found decreased antibody response to vaccines, and associations between blood serum PFAS levels and both immune system hypersensitivity (asthma) and autoimmune disorders (ulcerative colitis).[29] Of particular note, research published in 2013 by Phillippe Grandjean and Esben Budtz-Jorgensen [hereinafter "Grandjean and Budtz-Jorgensen" and provided as **Attachment D**] observed a strong dose-response between exposure to perfluorinated chemicals (as measured in children at the age of five) and reduced antibody concentrations against tetanus and diptheria toxoids in serum (as measured in those children at the age of seven). [30] Grandjean and Budtz-Jorgensen considered these reduced antibodies as "clinically relevant measures of immune functions" and concluded:

> BMDL [benchmark dose level] results were about 1.3 ng/mL serum for PFOS and 0.3 ng/mL serum for PFOA at a benchmark response of 5%. Lower values were obtained with the logarithmic curve, and higher results with a larger benchmark response. The BMDL results are in accordance with recent data on toxicity in experimental models. When converted to approximate exposure limits for drinking water, current limits appear to be several hundred fold too high. Current drinking water limits therefore need to be reconsidered in the light of the observed immunotoxicity associated with PFC exposure.[31]

Stating that "an approximate BMDL of 1 ug/L would seem an appropriate order of magnitude for calculation of exposure limits for the PFCs," Grandjean and Budtz-Jorgensen applied an uncertainty factor of 10 to the above serum levels to account for human variability, finding that "[a] concentration of about 0.1 ng/mL could then be used as the serum-based RfD for the PFCs (somewhat higher for PFOS and lower for PFOA)."[32] They then translated those serum-based reference doses (based on a 1:100 ratio of PFOA concentration in drinking water as compared to serum concentrations of long-term residents studied in Ohio and West Virginia) "to a water concentration of 1 ng/L, or .001 ug/L (assuming that no other sources contributed to the PFOA exposure)."[33] Applying this methodology to the 1.3 ng/mL serum for PFOS and 0.3 ng/mL serum for PFOA translates to water concentrations of .0013 ug/L (1.3 ppt) for PFOS and .0003 ug/mL (.3 ppt) for PFOA.[34]

Just last month, prominent PFAS expert Linda Birnbaum told attendees at a conference that a study conducted by the National Toxicology Program, a division of the National Institute of

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[29] *See* DRINKING WATER HEALTH ADVISORY FOR PERFLUOROOCTANOIC ACID (PFOA), *supra* note 19, at 39.
[30] Phillippe Grandjean and Esben Budtz-Jorgensen, *Immunotoxicity of perfluorinated alkylates: calculation of benchmark doses based on serum concentrations in children*, 12 ENVTL. HEALTH 1 (2013).
[31] *Id*. at 6.
[32] *Id.* at 5.
[33] *Id.* at 6. Note that this very low limit assumes no additional exposure to PFAS from other sources, such that the limit could actually be half this or less. *See generally* David Trudel et al., *Estimating consumer exposure to PFOS and PFOA*, 28 RISK ANALYSIS, 251 (2008).
[34] *See* Grandjean & Jorgensen, *supra* note 30, at 5–6.

Environmental Health Sciences (NIEHS), led her to conclude that a safe dose of PFOA is 0.1 ppt.[35]

While a great deal of public attention has recently been paid to PFOA, PFOS, and other short chain PFAS, EPA and other scientists have raised concerns that other chemicals in the PFAS class of compounds are similar in chemical structure and are likely to pose similar health risks.[36] For example, all PFAS share a strong carbon-flourine bond and "degrade very slowly, if at all, under environmental conditions."[37]

Although we have less information about these newer compounds, the information we do have suggests that they are not safe. In fact, the information we do have suggests that these compounds pose just as great of a health risk as longer-chain PFAS.[38] While some newer fluorinated alternatives seem to be less bioaccumulative, they are still as environmentally persistent as long-chain substances or have persistent degradation products.[39] For example, "[a] recent hazard assessment based on the internal dose of Gen X[, a short-chain PFAS,] suggests that it has a higher toxicity than PFOA after accounting for toxicokinetic differences."[40] Because some of the newer PFAS are less effective, larger quantities may be needed to provide the same performance.[41] In addition, these newer PFAS compounds are more mobile in their environment.[42] Finally, because there are thousands of these chemicals in use and in the environment, there may be cumulative and synergistic impacts for individuals.

"The extreme environmental persistence, bioaccumulation, and potential toxicity of the entire class of PFAS has led some researchers to question the use of any highly fluorinated chemicals and to call for a class approach in managing them."[43] Thus, in establishing MCLs, reportable concentrations, and cleanup standards, it is essential to consider additive and cumulative

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[35] Sharon Lerner, *Teflon Toxin Safety Level Should Be 700 Times Lower Than Current EPA Guideline*, THE INTERCEPT_ (June 18, 2019, 11:54 AM), https://theintercept.com/2019/06/18/pfoa-pfas-teflon-epa-limit/. Note that, after the article's publication, Linda Birnbaum gave the following statement:

> The NIEHS has undertaken an extensive PFAS research program, which involves many studies, hundreds of chemicals, and partnerships across federal government. There are almost 5,000 PFAS chemicals in use today. Right now, we don't know enough about the uses and potential hazards of exposure to PFAS, but if our research results for PFAS are similar to what we've seen with other biologically active chemicals such as lead, arsenic, and asbestos, I would not be surprised if the safe level of PFAS for humans is as low as 1.0-0.1 PPT. That's why this research is so important, and necessary for protecting public health.

[36] *See, e.g.*, Consent Order, *supra* note 11, at vii (stating that, with respect to "GenX" compounds (chemical substances intended to replace long-chain (C8) PFAS used in Teflon), "EPA has concerns that these PMN substances will persist in the environment, could bioaccumulate, and be toxic ("PBT") to people, wild mammals, and birds.").

[37] Arlene Blum et al., *The Madrid Statement on Poly- and Perfluoroalkyl Substances (PFASs)*, 123 ENVTL. HEALTH PERSPECTIVES A 107, A 107 (2015), https://ehp.niehs.nih.gov/doi/pdf/10.1289/ehp.1509934.

[38] Elsie Sunderland et al., *A review of the pathways of human exposure to poly- and perfluoroalkyl substances (PFASs) and present understanding of health effects*, 29 J. OF EXPOSURE SCI. & ENVTL. EPIDEMIOLOGY 131 – 147 (2018), available at https://www.nature.com/articles/s41370-018-0094-1.

[39] Blum, *supra* note 37, at A 107.

[40] Sunderland, *supra* note 38.

[41] *Id.*

[42] *See* Brendel et al., *supra* note 10, at 4.

[43] Sunderland, *supra* note 38.

exposures not only among the six PFAS subject to these rule-makings, but also from the many thousands of PFAS compounds that are not currently under review.

III. There is a significant presence of PFAS in Massachusetts drinking water, groundwater, and surface waters.

Not only are PFAS toxic in very small amounts, they are highly mobile in groundwater and surface water. MassDEP is well aware, from its investigations into PFAS problems and its collection of data from entities across the state, that PFAS have been found in waters throughout Massachusetts.[44]

A. Drinking Water

As MassDEP knows, Massachusetts has experienced significant issues related to the presence of PFAS in drinking water. Communities in Cape Cod have been especially impacted by PFAS contamination:

- Groundwater in Barnstable, Massachusetts has been particularly susceptible to the spread of PFAS because of the town's location in an outwash plain with permeable soil.[45]
- In addition, PFAS have entered the system through a number of sources, including fire training areas, airports, and landfills, which has led to an ongoing threat to the sole source aquifer that provides drinking water for all Cape Cod residents.[46]
- A 2009 sampling of 20 wells and two distribution systems that supply drinking water on Cape Cod found that 75 percent of test sites had detectable levels of chemicals, including PFOA and PFOS.[47] PFOS was one of the top two most frequently detected, and the levels detected were among the highest reported in U.S. drinking water.[48]
- PFOS and PFOA were found at high levels in Hyannis Water System wells downgradient of the Barnstable Municipal Airport. At the time the 2009 study was completed, EPA's Provisional Health Advisory for PFOA and PFOS was higher[49] than the Drinking Water Health Advisory (EPA Health Advisory) levels for PFAS eventually set in 2016. Lowered safety levels for the PFAS contaminants place several of the wells above EPA's new guidelines.

PFAS contamination of public drinking water supplies in Massachusetts is by no means limited

[44] *See generally Per- and Polyfluoroalkyl Substances (PFAS)*, MASSDEP, https://www.mass.gov/info-details/per-and-polyfluoroalkyl-substances-pfas#what-are-pfas-and-why-are-they-a-problem?-.
[45] *Sources, Transport, Exposure & Effects of PFASs: Cape Cod*, THE U. OF R.I., https://web.uri.edu/steep/communities/cape-cod/.
[46] *Id*.
[47] LAUREL SCHAIDER ET AL., SILENT SPRING INSTITUTE, EMERGING CONTAMINANTS IN CAPE COD DRINKING WATER iii (2010), http://www.commwater.com/wp-content/uploads/2014/03/silentspringreport2010.pdf.
[48] *Id*.
[49] *See* U.S. ENVTL. PROTECTION AGENCY, PROVISIONAL HEALTH ADVISORIES FOR PERFLUOROOCTANOIC ACID (PFOA) AND PERFLUOROOCTANE SULFONATE (PFOS) 4–5 (2009), https://www.epa.gov/sites/production/files/2015-09/documents/pfoa-pfos-provisional.pdf.

to Cape Cod. On its website, MassDEP notes: "PFAS was detected [between 2013-2015] at nine Massachusetts drinking water sources above EPA's specified reporting limits."[50] A report from the Environmental Working Group found 21 sites in Massachusetts contaminated with PFAS chemicals, affecting nearly 200,000 residents.[51] For example, drinking water supplied to the Town of Ayer from the Grove Pond Water Treatment Plant exceeded 70 ppt (combined) for five PFAS compounds until one of the three Grove Pond wells was closed in 2018. Drinking water from the Grove Pond Plant still exceeds 20 ppt. In addition, PFAS have already been detected in Danvers, Weymouth, Hudson, Ayer, Harvard, Devens, Shirley, and Westfield.

These are but a few examples of PFAS contamination in drinking water in Massachusetts. The PFAS threat to drinking water is significant and widespread, and communities have already been exposed to unsafe drinking water.

B. Groundwater

Cape Cod is also suffering from groundwater contamination from PFAS linked to several sources, including fire training areas, airports, military bases, landfills, municipal wastewater, and septic systems.[52] In July of 2015, Barnstable Municipal Airport conducted investigations of PFAS in six monitoring wells and PFAS compounds were detected in all of them.[53] PFAS concentrations were above the EPA Health Advisory limits in two of the six wells.[54]

Additional groundwater investigations conducted in response to the Barnstable Municipal Airport findings speculated that the source of the PFAS contamination was the Airport Rescue and Fire Fighting Building, a fire fighting training deployment area. The resulting investigation found that there was heavy use of aqueous film forming foam (AFFF) at the fire training academy.

Also, in Weymouth, Massachusetts, PFAS has been detected in groundwater near the site of the former Naval Air Station.[55] Operational closure of the airfield was effected in September of 1996. However, the area was used as a location for fire fighting training exercises from 1950 until 1990.[56] Likely due to the heavy use of AFFF, a 2010 investigation determined widespread

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[50] *See Per- and Polyfluoroalkyl Substances (PFAS)*, *supra* note 44.
[51] *See* Jason Claffey*, Toxic PFAS Found In 21 Places In Massachusetts*, PATCH (May 8, 2019, 7:32 PM), https://patch.com/massachusetts/danvers/toxic-pfas-found-19-places-massachusetts.
[52] *Sources, Transport, Exposure & Effects of PFASs: Cape Cod*, *supra* note 45.
[53] HORSLEY WITTEN GROUP, INC., IMMEDIATE RESPONSE ACTION PLAN STATUS REPORT 3: BARNSTABLE MUNICIPAL AIRPORT 4 (2017), http://eeaonline.eea.state.ma.us/EEA/fileviewer/Default.aspx?formdataid=0&documentid=445359 (responding to a Notice of Responsibility issued by MassDEP, tasking Barnstable Airport with investigating for PFAS previously detected in groundwater at the airport, and at a monitoring well downgradient of the Airport on the Maher wellfield property).
[54] *Id.*
[55] *South Weymouth Naval Air Station: Cleanup Activities*, U.S. ENVTL. PROTECTION AGENCY, https://cumulis.epa.gov/supercpad/SiteProfiles/index.cfm?fuseaction=second.cleanup&id=0101826.
[56] *Id.*

PFAS contamination in soils, groundwater, and surface water.[57] The investigation revealed the presence of PFAS in groundwater at concentrations exceeding the EPA Health Advisory.[58]

C. Surface Water

A study of the Joint Base in Bourne, Massachusetts includes surface water reports showing PFAS contamination above the EPA Health Advisory level.[59] Contamination was again linked to heavy use of AFFFs.[60] Specifically, contaminated surface water was detected in Ashumet and John's Pond and led to findings of affected residential water wells including those in the Lakeside Estates Community and Mashpee Village.[61]

IV. The proposed GW-1 standards for PFAS do not adequately protect public health.

The proposed GW-1 standards[62] are an important step forward in protecting Massachusetts communities from exposure to PFAS.[63] The standards currently proposed by MassDEP are more protective than those published in the current EPA Drinking Water Health Advisory and the June 2018 MassDEP ORSG. MassDEP states that the revisions are based on "consideration of toxicological studies and analyses that have been published subsequent[ly]" to the publications of those earlier standards.[64] Although this is an important step in the right direction, current studies suggest the need for a far more stringent standard.

Specifically, MassDEP's proposed GW-1 standard of 20 ppt combined for PFDA, PFHpA, PFHxS, PFOA, PFOS, and PFNA ignores a growing body of scientific evidence demonstrating that there is no safe level of PFAS compounds in drinking water and is based on assumptions that do not protect the most vulnerable populations. MassDEP should establish a 1 ppt standard for quantifiable PFAS and a treatment technique drinking water standard for the PFAS class.

A. MassDEP's proposed standard is based on assumptions that do not protect the most vulnerable populations.

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[57] *Id.*
[58] TETRA TECH, EXPLANATION OF SIGNIFICANT DIFFERENCES TO THE RECORD OF DECISION OPERABLE UNIT 25 AREA OF CONCERN HANGAR 1 MAIN HANGAR FLOOR DRAINS 3 (2011), https://semspub.epa.gov/work/01/497699.pdf.
[59] Angela Gallagher, Bureau of Waste Site Cleanup, MassDEP, PFAS in the Northeast: State of Practice & Regulatory Perspectives at the NEWMOA Workshop 34 (May 9, 2019).
[60] *Id*. at 10, 25.
[61] *Id*. at 34.
[62] MassDEP has stated that it will develop drinking water standards for these six PFAS compounds consistent with the proposed groundwater standards. These comments are pertinent to the anticipated drinking water rules. In addition, for the reasons discussed in Section II, MassDEP should establish a Maximum Contaminant Level Goal (MCLG) of zero for the class in order to protect public health from these dangerous chemicals.
[63] DEP's proposed changes to the GW-1 standards and RCGW-1 Reportable Concentrations for PFAS are based on an approach that is also being considered for a revised ORSG used to evaluate public water supplies. To promote consistency, groundwater standards are usually set equal to existing drinking water standards or guidelines.
[64] MASSDEP, PFAS-RELATED REVISIONS TO THE MASSACHUSETTS CONTINGENCY PLAN ("MCP", 310 CMR 40.00) (2019) (65. Note to Reviewers of its PFAS-related revisions to the MCP).

MassDEP relied on several assumptions that are not sufficiently conservative and, therefore, result in standards that will not protect public health, particularly the most vulnerable sub-populations of developing fetuses and infants.

MassDEP's proposed GW-1 standard appears to rely upon:[65]

- A reference dose (ng/kg/day) for PFOA (5) that is higher than the reference dose used by ATSDR (3), NJ DWQI (2), NRDC (0.01), and MI[66] (3.9 ng/kg/d);

- A reference dose (ng/kg/d) for PFOS (5) that is higher than the reference dose used by ATSDR (2), NJ DWQI (1.8), NRDC (0.002), MI (2.9), and NH (3);[67]

- A reference dose (ng/kg/day) for PFNA (5) that is higher than the reference dose used by ATSDR (3), NRDC (0.2), NJ DWQI (approx. 0.5), NH (4.3), and MI (2.2);

- A reference dose (ng/kg/day) for PFHxS (5) that is higher than the reference dose used by NRDC (2) and NH (4);

- The application of an additional uncertainty factor (UF) of 3.3333 resulting in a total uncertainty factor for PFOS (100) that is considerably lower than the uncertainty[68] factor used by ATSDR (300);

A water ingestion rate of 0.054 L/kg/d, based on a water consumption rate of a lactating woman at the 90th percentile, as opposed to the much more protective ingestion rate used by VT, ATSDR and NRDC of .175 L/kg/d for an infant less than 1 year of age or ATSDR of .143 L/kg/d for an infant.

Importantly, MassDEP failed to apply an additional UF of 10 to protect infants, developing fetuses, and children as recommended by the National Academy of Sciences.

In recognition of the significant toxicity of PFAS, the vulnerability of the most sensitive sub-populations to PFAS contamination, and the numerous uncertainties regarding the toxicology of PFAS, MassDEP should use only the most conservative assumptions to protect public health. Specifically, MassDEP should, at a minimum, align its approach to regulating PFAS compounds

[65] The toxicity of these compounds and their impact on public health underscores the importance of public participation in the process. MassDEP has taken many important steps to promote an open and meaningful public process as it undertakes the difficult work of developing PFAS standards. Because the development of these standards is highly technical and complex, it is critical that MassDEP provides adequately accessible, transparent information for review. MassDEP's currently available information regarding its methodology and its assumptions is hard to navigate and not sufficiently clear, which ultimately hampers its ability to solicit well-informed public input.

[66] Referring to Michigan's Science Advisory Workgroup. *See Science Advisory Workgroup*, MICHIGAN.GOV, https://www.michigan.gov/pfasresponse/0,9038,7-365-86513_92296-493943--,00.html (last updated July 8, 2019).

[67] Information about New Hampshire's recently released PFAS regulations can be found at their PFAS Investigation website. *See NH PFAS Investigation*, N.H. DEP'T OF ENVTL. SERV. (Sept. 1, 2017), https://www4.des.state.nh.us/nh-pfas-investigation/.

[68] This is our understanding of how MassDEP relied on UFs to derive these proposed standards, but the information provided to the public was not clear.

with the "more protective choices" set forth in Tables 4, 5, 6, and 7 of the NRDC Report, which compare assumptions used by a variety of regulators, including EPA, ATSDR, and agencies in Minnesota, Vermont, New Jersey, and California.[69]

First, MassDEP should rely on the most sensitive health endpoints when developing reference doses (RfDs). MassDEP must develop an RfD for PFAS compounds based on what will be most protective of the populations that are most vulnerable to harm: children, infants, and developing fetuses. We urge MassDEP to consider the Minnesota approach as well, which accounts for fetal, infant and childhood exposures through the use of the toxicokinetic model. As described above, current and emerging research only underscores the need to apply more protective assumptions and account for uncertainty when developing safety thresholds.

Second, MassDEP should adopt the more protective choice of a 0.175 L/kg/d water ingestion rate for infants less than 1 year of age. Breastfeeding and formula fed infants drink the largest volume per body weight and are the most vulnerable to PFAS contamination.[70] Third, MassDEP should apply the most protective UF when developing these standards. At a minimum they should be applying the additional UF of 10, along with the 3.333 additional UF for database uncertainty, when developing the proposed changes. In developing its health advisory of 70 ppt for PFOS, EPA applied a total UF of 30 (10 for human variability and 3 for animal to human toxicodynamic differences). ATSDR, however, relied on a total combined UF of 300: "10 for concern that immunotoxicity may be a more sensitive endpoint than developmental toxicity, 3 for extrapolation from animals to humans with dosimetry adjustments, and 10 for human variability."[71] "The National Academy of Sciences has recommended the use of an additional uncertainty factor of 10 to ensure protection of fetuses, infants and children who often are not sufficiently protected from toxic chemicals such as pesticides by the traditional intraspecies (human variability) uncertainty factor."[72] For all these reasons, MassDEP did not rely upon conservative assumptions that will protect the most vulnerable sub-populations.

B. MassDEP should establish more protective standards that protect communities from exposure to the PFAS class of chemicals.

Current studies suggest the need for a far more stringent and more comprehensive standard than what MassDEP proposes. The significant toxicity and the unique characteristics of the PFAS class of chemicals, along with the potential cumulative and synergistic effects from exposure to thousands of other PFAS chemicals, demand a conservative approach to regulation of these dangerous chemicals. As documented in CLF and TAC's petition and elsewhere, many scientists have raised concerns about the health effects of the PFAS class of chemicals due to similarities in chemical structure.[73] It simply does not make sense to continue using a "whack-a-mole" approach to regulation in light of the fact that over 4,000 of these chemicals already exist and the

[69] NRDC Report, *supra* note 25, at 31–34.
[70] *Id*. at 35–36.
[71] *Id*. at 41.
[72] *Id*.
[73] *See, e.g.*, Consent Order, *supra* note 11, at vii (stating that, with respect to "GenX" compounds (chemical substances intended to replace long-chain (C8) PFAS used in Teflon), "EPA has concerns that these PMN substances will persist in the environment, could bioaccumulate, and be toxic ("PBT") to people, wild mammals, and birds."); *see also* Blum, *supra* note 37, at A 107.

fact that manufacturers will continue producing new PFAS compounds with little oversight.[74] Massachusetts communities should not be forced to continue to bear the health risks associated with these unsafe chemicals while regulators take decades to chase down these chemicals one by one. In order to protect public health, MassDEP should regulate PFAS chemicals as a class.

1. MassDEP should establish a 1 ppt standard for quantifiable PFAS chemicals.

MassDEP should, at a minimum, establish a 1 ppt combined GW-1—and maximum contaminant level—standard for PFDA, PFHpA, PFHxS, PFNA, PFOA, and PFOS.[75] As discussed in Section II, a 1 ppt standard is far more consistent with the most current research regarding the significant adverse human health effects from exposure to PFAS chemicals. EPA Method 537.1 and other analytical methods are able to detect many quantifiable PFAS to 1 ppt.[76] Similarly, treatment technologies exist to remove long chain and newer PFAS to concentrations below 2 ppt.[77] To the extent that MassDEP determines that the detection limits for regulated PFAS are above 1 ppt or that treatment technologies are not able to remove these PFAS to concentrations at or below 2 ppt, MassDEP should establish a combined standard at the detection limit or the treatment's removal efficiency.

MassDEP should also, at a minimum, expand the number of PFAS proposed for regulation under the groundwater and drinking water standards. For example, EPA has finalized an analytical methodology for drinking water that quantifies 18 different PFAS.[78] In addition, EPA expects to finalize a methodology for analyzing PFAS in sample types other than groundwater this summer that is "anticipated to include a total of 25 PFAS (14 of the 18 PFAS in Method 537.1 plus an additional 11 "short chain" PFAS)".[79] Commercial laboratories are able to quantify between approximately 30-45 different PFAS compounds using modified methods. Thus, current laboratory methods exist to quantify a broader group of PFAS than those 6 PFAS proposed for regulation here. At a minimum, MassDEP should include quantifiable PFAS within the scope of the groundwater and drinking water standards. The standard should require regular review and a requirement to include additional PFAS compounds as they become quantifiable.

2. MassDEP should establish a treatment technique standard for the PFAS class of chemicals.

MassDEP should establish a treatment technique drinking water standard for the PFAS class of chemicals. As discussed in Section II, there is no reason to believe that the thousands of other PFAS chemicals are safe. In fact, research regarding the health effects from exposure to newer

[74] *See* NRDC Report, *supra* note 25, at 9.
[75] NRDC notes that, while its attached report recommended a 2 ppt standard for several of the PFAS listed based on current reporting limits at specific levels, a 1 ppt standard based on detection limits is also well-justified based on the confirmed presence of PFAS, and therefore NRDC supports the stronger standard.
[76] *See, e.g.*, *id*. at 49–51.
[77] *Id.* at 53–54.
[78] EPA, TECHNICAL BRIEF: PERFLUOROALKYL AND POLYFLUOROALKYL SUBSTANCES (PFAS) METHODS AND GUIDANCE FOR SAMPLING AND ANALYZING WATER AND OTHER ENVIRONMENTAL MEDIA 1 (2019), https://www.epa.gov/sites/production/files/2019-02/documents/pfas_methods_tech_brief_28feb19_update.pdf.
[79] *Id.*

compounds suggest that these compounds pose serious health risks. As stated in CLF and TAC's October 25, 2018 petition, a treatment technique is both authorized by law and is technically feasible.[80] Further, establishing a treatment technique standard for PFAS that are not quantifiable using standard laboratory methods is an effective approach to protecting communities against PFAS contamination in drinking water.[81]

As discussed in CLF and TAC's petition, existing treatment technologies are able to remove long and short chain PFAS to concentrations below 2 ppt, including granular activated carbon, ion exchange, and reverse osmosis.[82] For the reasons articulated by NRDC experts, reverse osmosis appears to be the most robust technology for preventing exposure to PFAS and other unidentified contaminants.[83]

For all these reasons, MassDEP should protect Massachusetts communities from these dangerous chemicals by establishing a 1 ppt GW-1 combined standard and an MCL for quantifiable PFAS, as well as a treatment technique drinking water standard for the PFAS class.

V. <u>There is insufficient information to evaluate whether the Method 1 Soil Standards and the GW-3 standards protect public health and the environment.</u>

For the reasons discussed above, MassDEP should establish these standards for the class of PFAS chemicals or, at a minimum, for all quantifiable PFAS.

In addition, there is insufficient information in the materials provided by MassDEP for the public to evaluate whether the Method 1 soil standards and the GW-3 standards protect public health and the environment. Although there is a limited amount of explanation in the Summary of Proposed MCL Method 1 Standards Revisions document with respect to these standards, much of the information is contained in spreadsheets that are challenging for the public to decipher or based on guidelines that don't appear to be provided to the public. In addition, MassDEP appears to rely upon a survey of laboratory reporting limits to establish the soil standards for GW-1 areas.[84] However, that survey does not appear in the materials on the MassDEP website related to the rulemaking.

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[80] Petition from Heather Govern, Director, Conservation Law Foundation and Sylvia Broude, Executive Director, Toxics Action Center to Martin Suuberg, Commissioner, Massachusetts Department of Environmental Protection (October 25, 2018) [hereinafter "Petition"].

[81] CLF's petition lays out clear, evidence-based arguments for the adoption of a treatment technique standard, citing the legal basis for MassDEP's authority to adopt a treatment technique, the basis and precedent for such an approach, the economic and technical feasibility for a treatment technique, and the cost-benefit basis for a treatment technique standard. *See id*. at 9–15.

[82] NRDC Report, *supra* note 25, at 53–54; Petition, *supra* note 79, at 14–15; SCOTT BARTEL ET AL., MICHIGAN PFAS SCIENCE ADVISORY PANEL, SCIENTIFIC EVIDENCE AND RECOMMENDATIONS FOR MANAGING PFAS CONTAMINATION IN MICHIGAN 60–63 (Dec. 7, 2018), https://www.michigan.gov/documents/pfasresponse/Science_Advisory_Board_Report_641294_7.pdf.

[83] NRDC Report, *supra* note 25 at 66–67.

[84] MASSDEP, SUMMARY OF PROPOSED MCP METHOD-1 STANDARDS REVISIONS 12 (2019), https://www.mass.gov/files/documents/2019/04/02/2019%20Documentation%20of%20Proposed%20Method%201%20Standards_0.pdf.

VI. The State and public water systems have options to address the financial costs associated with the clean-up of PFAS contamination.

There will no doubt be costs associated with the necessary monitoring, clean-up, and treatment to remove PFAS from drinking water. However, this is not a justification for continuing to expose Massachusetts communities to these dangerous chemicals. In fulfilling their obligations to provide safe drinking water and protect public health, the State, public water systems, and other impacted entities have funding assistance options they can pursue, including funding through the Drinking Water State Revolving Loan Fund and from the State "Superfund," which can be accessed to help fund the cleanup of contaminated sites.[85]

In addition, as in New Hampshire and Vermont, the State, through its Attorney General, should hold chemical manufacturers and polluters that have contributed and are contributing to the PFAS pollution crisis accountable for the harm they have caused. Such an action could and should generate substantial resource support to compensate the State and public entities for incurring costs to clean up PFAS contamination.

VII. Conclusion

Thank you for the opportunity to provide these comments. We appreciate MassDEP's attention to the significant public health and environmental problem posed by PFAS pollution. We urge MassDEP to revise the proposed rules consistent with our recommendations to ensure all Massachusetts communities have access to safe drinking water free of toxic PFAS chemicals.

Respectfully submitted,

/s/ Alyssa Rayman-Read

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[85] *The Waste Site Cleanup Program*, MASSDEP, https://www.mass.gov/guides/the-waste-site-cleanup-program.

Attachments:

A. Petition from Heather Govern, Director, Conservation Law Foundation and Sylvia Broude, Executive Director, Toxics Action Center to Martin Suuberg, Commissioner, Massachusetts Department of Environmental Protection (October 25, 2018).

B. ANNA READE ET AL., NRDC, SCIENTIFIC AND POLICY ASSESSMENT FOR ADDRESSING PER- AND POLYFLUORINATED SUBSTANCES (PFAS) IN DRINKING WATER 23 (2019).

C. Helen M. Goeden et al., *A transgenerational toxicokinetic model and its use in derivation of Minnesota PFOA water guidance*, 29 J. OF EXPOSURE SCI. & ENVTL. EPIDEMIOLOGY 183 (2019).

D. Phillippe Grandjean and Esben Budtz-Jorgensen, *Immunotoxicity of perfluorinated alkylates: calculation of benchmark doses based on serum concentrations in children*, 12 ENVTL. HEALTH 1 (2018).

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October 25, 2018

The Honorable Martin Suuberg
Commissioner
Massachusetts Department of Environmental Protection
One Winter Street, 2nd Floor
Boston, MA 02108

Subject: Petition for Rulemaking to Establish a Treatment Technique Drinking Water Standard for Per- and Polyfluoroalkyl Substances

Dear Commissioner Suuberg:

Conservation Law Foundation (CLF) and Toxics Action Center hereby petition the Massachusetts Department of Environmental Protection (MassDEP) to establish a drinking water standard for Per- and Polyfluoroalkyl Substances (PFAS) that is protective of public health.[1] Specifically, CLF and Toxics Action Center petition MassDEP to adopt a treatment technique drinking water standard for the PFAS class of chemicals in lieu of setting a maximum contaminant level (MCL) for specific PFAS.[2] At a bare minimum, if MassDEP does not promulgate a treatment technique standard, MassDEP should adopt an MCL for the PFAS class or MCLs for each PFAS chemical that poses a risk to public water systems in Massachusetts. As an interim step to protect public health, MassDEP should immediately adopt the Vermont Department of Public Health's Health Advisory for PFAS (PFAS Health Advisory) of 20 parts per trillion (ppt) for the PFAS Class as an MCL.[3]

PFAS have been found in drinking water sources across Massachusetts and numerous studies have linked PFAS to significant health risks, including cancer. Although the Commonwealth of

[1] Pursuant to Massachusetts' Administrative Procedure Act, codified at Mass. Gen. Laws Ch. 30A, § 4, "[a]ny interested person may petition an agency requesting the adoption, amendment or repeal of any regulation, and may accompany his petition with such data, views and arguments as he [or she] thinks pertinent." MassDEP has prescribed the procedure for such a petition in 310 Mass. Code Regs. 2.00-2.09.

[2] We are aware that MassDEP is considering setting MCLs for some PFAS but still recommend the approach outlined in this petition.

[3] Although this petition has prioritized a drinking water standard for the PFAS class, there is also an urgent need to develop comprehensive standards for PFAS compounds, including but not limited to, surface water quality standards, pre-treatment standards for industrial users, and limits for land application of sludges.

Massachusetts has taken preliminary steps to limit exposure to this dangerous class of chemicals, MassDEP must take additional affirmative steps to protect Massachusetts residents from PFAS.

CLF protects New England's environment for the benefit of all people. Founded in 1966, CLF is a non-profit, member-supported organization with offices located in Massachusetts, Vermont, Rhode Island, Maine, and New Hampshire. CLF uses the law, science, and the market to create solutions that protect public health, preserve natural resources, build healthy communities, and sustain a vibrant economy. CLF has been a leading advocate for clean water and safe drinking water in Massachusetts and throughout New England, and is engaged in numerous efforts to address the threat of emerging contaminants like PFAS throughout New England.

Founded in 1987, Toxics Action Center works side-by-side with communities across New England to clean up and prevent pollution at the local level.

Introduction

MassDEP must immediately adopt a drinking water standard that protects the residents of Massachusetts from exposure to all PFAS compounds. PFAS are persistent in the environment; bioaccumulative; highly mobile in water; found in hundreds of different products; and are toxic in very small concentrations. PFAS have been found at unsafe levels in drinking water in Massachusetts, as well as in ground- and surface waters. Drinking water contaminated with PFAS is a significant source of exposure.[4] Without a drinking water standard, public water systems in Massachusetts are not required to regularly monitor for PFAS compounds or to treat water with unsafe levels of PFAS.

DuPont, 3M, and other chemical manufacturers recklessly produced these dangerous chemicals for decades despite being aware of the significant health risks associated with PFAS. Furthermore, in 1981, 3M and DuPont were aware that ingestion of perfluorooctanoic acid (PFOA) caused birth defects in rats.[5] After receiving this information, DuPont tested seven children of pregnant workers: two had birth defects.[6] DuPont was also aware that at least one facility had contaminated local drinking water supplies with unsafe levels of PFOA by 1987, but failed to warn anyone.[7]

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[4] *See* Mass. Dep't of Envtl Prot., *Office of Research and Standards Final Recommendation for Interim Toxicity and Drinking Water Guidance Values for Perfluorinated Alkyl Substances Included in the Unregulated Chemical Monitoring Rule 3*, June 8, 2018, https://www.mass.gov/files/documents/2018/06/11/pfas-ors-ucmr3-recs_0.pdf (noting that "All of the UCMR 3 PFAS have been detected in one or more MA water supplies, as well as in some groundwater and surface water samples.").

[5] Nathaniel Rich, *The Lawyer Who Became DuPont's Worst Nightmare*, N.Y. TIMES, Jan. 6, 2016, https://www.nytimes.com/2016/01/10/magazine/the-lawyer-who-became-duponts-worst-nightmare.html.

[6] *Id.*

[7] *Id.*

DuPont hid this vital health information from the public and the U.S. Environmental Protection Agency (EPA) while making billions of dollars in profits from continued production of PFOA.[8] Ultimately, DuPont was fined $16.5 million dollars in 2005 for failing to disclose information about toxicity and health risks cause by PFOA.[9] Although PFOA and perfluoro-octane sulfonic acid (PFOS) have now been phased out of production in the U.S.,[10] these compounds will remain in our drinking water, ground- and surface waters, as well as our bodies, for decades. In addition, manufacturers have rushed to produce thousands of alternative PFAS that are likely to pose similar health risks given the similarities in chemical structure.[11] There are now over 3,000 different kinds of PFAS.

To make matters worse, EPA has failed to take meaningful action to protect the public from exposure to PFAS in drinking water. After becoming aware of contamination of drinking water supplies and the significant health risks posed by these dangerous chemicals, EPA gave manufacturers almost a decade to phase out production and use of PFOA and PFOS through a voluntary program.[12] Despite learning in 2015 that millions of Americans were, and continue to be, exposed to PFAS contaminated drinking water, EPA has not taken steps toward requiring public water systems to regularly monitor for PFAS and to treat unsafe water.[13] EPA even suppressed a scientific study suggesting that EPA's current health advisory for PFOA and PFOS does not protect public health. After

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[8] *Id.*

[9] Memorandum from Grant Y. Nakayama, Assistant Administrator, to Environmental Appeals Board Re Consent Agreement and Final Order to Resolve DuPont's Alleged Failure to Submit Substantial Risk Information Under the Toxic Substances Control Act (TSCA) and Failure to Submit Data Requested Under the Resource Conservation and Recovery Act (RCRA) 3 (Dec. 14, 2005), https://www.epa.gov/sites/production/files/2013-08/documents/eabmemodupontpfoasettlement121405.pdf.

[10] U.S. Envtl. Prot. Agency, *Assessing and Managing Chemicals Under TSCA, Fact Sheet: 2010/2015 PFOA Stewardship Program*, https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/fact-sheet-20102015-pfoa-stewardship-program#what.

[11] *See, e.g.*, Stephen Brendel et al., *Short-Chain Perfluoroalkyl Acids: Environmental Concerns and a Regulatory Strategy under REACH*, 30 ENVTL. SCI. EUR. 9, (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5834591/pdf/12302_2018_Article_134.pdf.

[12] *See, e.g.*, U.S. Env't Prot. Agency, *In the matter of: Premanufacture Notice Numbers: Dupont Company* (April 9, 2009), https://assets.documentcloud.org/documents/2746607/Sanitized-Consent-Order-P08-0508-and-P08-0509.pdf.; Premanufacture Notification Exemption for Polymers; Amendment of Polymer Exemption Rule to Exclude Certain Perfluorinated Polymers, 75 Fed. Reg. 4295, 4296 (Jan. 27, 2010).

[13] David Andrews, *Report: Up to 110 Million Americans Could Have PFAS-Contaminated Drinking Water*, ENVTL WORKING GROUP, May 22, 2018, https://www.ewg.org/research/report-110-million-americans-could-have-pfas-contaminated-drinking-water#.W6_7a2hKg2w.

widespread public outcry, EPA announced the possibility of setting drinking water standards for just two out of more than 3,000 PFAS, but no enforceable regulatory standard has been proposed to date, and even this limited action will take years.[14]

In addition, the federal government's capacity to set a standard protective health has been compromised by the staggering liabilities of the United States for releases of PFAS at federal facilities nationwide, including release from federal facilities in Massachusetts.

Massachusetts can—and must—take the lead in the absence of federal safeguards. We will never be able to reverse the damage caused by chemical manufacturers and EPA's inaction, but MassDEP has broad authority to promulgate rules that limit additional exposure to unsafe levels of PFAS in drinking water.[15] In the absence of such rules, the public will remain at risk, and the most vulnerable among us – nursing infants and children generally, who consume higher volumes of water for their body weight and have greater developmental susceptibility – will be at the greatest risk.

Moreover, in the absence of such rules, homeowners on well-water and municipalities and other drinking water system operators will be stymied in their efforts to recover the costs of adopting filtration and other safeguards from responsible polluters.

For all these reasons, MassDEP should stop putting public health at risk and adopt a treatment technique drinking water standard that will protect Massachusetts residents from the class of PFAS. As an interim step, MassDEP should immediately adopt Vermont's PFAS Health Advisory as a drinking water standard for public water systems.

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[14] *The Federal Role in the Toxic PFAS Chemical Crisis, Hearing on SD-342 Before the Subcommittee on Homeland Security & Governmental Affairs*, 115th Cong. (2018) (statement of Chairman Rand Paul and Ranking Member Gary C. Peters) https://www.hsgac.senate.gov/hearings/the-federal-role-in-the-toxic-pfas-chemical-crisis.

[15] *See* Mass. Gen. Laws ch. 111, § 160 ("[MassDEP] may make rules and regulations and issue such orders as in its opinion may be necessary to prevent the pollution and to secure the sanitary protection of all such waters used as sources of water supply and to ensure the delivery of a fit and pure water supply to all consumers."); *see also* 310 Mass. Code Regs. 22.03 (stating that in the event MassDEP "finds on the basis of a health assessment . . . that the level of any contaminant found in water collected within a Distribution System and/or at a Sampling Point at the entry to a Distribution System, poses an unacceptable health risk to consumers . . . the Supplier of Water shall take appropriate actions to reduce the level of contaminant concentrations to levels [MassDEP] deems safe or remove the source of supply from service by the deadline specified by [MassDEP].").

I. BACKGROUND

A. PFAS are harmful to human health.

PFAS are a public health crisis "perfect storm" because PFAS compounds are extremely persistent in the environment, highly mobile in water, bioaccumulative, toxic in very small quantities, and found in hundreds of products. PFAS compounds are man-made substances that do not occur naturally, and they have been used in non-stick cookware, water-repellent clothing, stain resistant fabrics and carpets, cosmetics, firefighting foams, and other products that resist grease, water, and oil.[16] These chemicals are extremely strong and highly resistant to degradation.[17]

PFAS are toxic to humans in very small concentrations—in the *parts per trillion*.[18] PFAS are suspected carcinogens and have been linked to growth, learning and behavioral problems in infants and children; fertility and pregnancy problems, including pre-eclampsia; interference with natural human hormones; increased cholesterol; immune system problems; and interference with liver, thyroid, and pancreatic function.[19] PFAS have been linked to increases in testicular and kidney cancer in human adults.[20] The developing fetus and newborn babies are particularly sensitive to some PFAS.[21]

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[16] Seth Kerschner and Zachary Griefen *Next Round of Water Contamination Suits May Involve CWA*, LAW 360 (October 5, 2017), https://www.law360.com/articles/970995/next-round-of-water-contamination-suits-may-involve-cwa.

[17] New Jersey Dep't of Envtl Prot. Division of Science, Research, and Envtl Health, *Investigation of Levels of Perfluorinated Compounds in New Jersey Fish, Surface Water, and Sediment*, June 18, 2018, https://www.nj.gov/dep/dsr/publications/Investigation%20of%20Levels%20of%20Perfluorinated%20Compounds%20in%20New%20Jersey%20Fish,%20Surface%20Water,%20and%20Sediment.pdf.

[18] Agency for Toxic Substances and Disease Registry, *Per- and Polyfluoroalkyl Substances (PFAS) and Your Health*, https://www.atsdr.cdc.gov/pfas/health-effects.html; Agency for Toxic Substances and Disease Registry, *Toxicological Profile for Perfluoroalkyls*, https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf, at 5–6.

[19] *Id.*

[20] *Id.* at 6; Vaughn Barry et al., *Perfluorooctanoic Acid (PFOA) Exposures and Incident Cancers among Adults Living Near a Chemical Plant*, 121 ENVTL. HEALTH PERSPECTIVES 11-12, 1313-18 (Nov.-Dec. 2013), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3855514/pdf/ehp.1306615.pdf.

[21] U.S. Envtl. Prot. Agency, *Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS)*, (May 2016) https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final_508.pdf at 10.

Alarmingly, epidemiological studies identify the immune system as a target of PFAS toxicity. Some studies have found decreased antibody response to vaccines, and associations between blood serum PFAS levels and immune system hypersensitivity (asthma) and autoimmune disorders (ulcerative colitis).[22] There are no medical interventions that will remove PFAS from the body.[23]

PFAS are very resistant to breakdown, bioaccumulate, and easily migrate. "As a result, they may be found throughout the environment in groundwater, surface water, soil, and air, as well as in food, breast milk, and human blood serums."[24] A study by the Centers for Disease Control and Prevention (CDC) found four PFAS (PFOS, PFOA, perfluorohexane sulfonic acid (PFHxS), and perfluorononanoic acid (PFNA)) in the serum of nearly all of the people tested, indicating widespread exposure in the U.S. population.[25] PFOA and PFOS were found in up to 99 percent of the U.S. general population between 1999 and 2012.[26] PFAS are found in human breast milk and umbilical cord blood.[27]

While a great deal of public attention has recently been paid to PFOA and PFOS, and MassDEP recently issued Office of Research and Standards Guidelines (ORSGs) of 70ppt for five PFAS compounds (PFOA, PFOS, perfluoroheptanoic acid (PFHpA), PFNA, PFHxS), when all or some of these occur together in drinking water,[28] EPA and other scientists have raised concerns that other chemicals in the PFAS class of compounds are similar in chemical structure and are likely to pose similar health risks.[29] For example, all PFAS share a strong carbon-flourine bond and

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[22] *Id.* at 39.
[23] Vermont Dep't of Health, *Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS) in Drinking Water*, July 9, 2018, http://www.healthvermont.gov/sites/default/files/documents/pdf/ENV_DW_PFAS.pdf.
[24] Agency for Toxic Substances and Disease Registry, *Toxicological Profile for Perfluoroalkyls*, *supra* note 18, at 2.
[25] Ctr. for Disease Control and Prevention, *Per- and Polyfluorinated Substances (PFAS) Factsheet* (Apr. 7, 2017), https://www.cdc.gov/biomonitoring/PFAS_FactSheet.html.
[26] U.S. Envtl. Prot. Agency, *Drinking Water Health Advisory for Perflourooctanoic Acid (PFOA)* (May 2016) at 9, https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final_508.pdf.
[27] Agency for Toxic Substances and Disease Registry, *Toxicological Profile for Perfluoroalkyls*, *supra* note 18, at 3.
[28] MassDEP, Office of Research and Standards Guideline for Per- and Polyfluoroalkyl Substances (PFAS), including the US EPA UCMR3 analytes, June 8, 2018, https://www.mass.gov/files/documents/2018/06/11/orsg-pfas-20180608.pdf.
[29] *See, e.g.*, U.S. Envtl. Prot. Agency, *supra* note 11 (stating that, with respect to "GenX" compounds (chemical substances intended to replace long-chain (C8) PFAS used in Teflon), "EPA has concerns that these PMN substances will persist in the environment, could bioaccumulate, and be toxic ("PBT") to people, wild mammals, and birds.").

"degrade very slowly, if at all, under environmental conditions."[30] Although some of the long-chain PFASs are being regulated or phased out, the most common replacements are short-chain PFASs with similar structures, or compounds with fluorinated segments joined by ether linkages. While some shorter-chain fluorinated alternatives seem to be less bioaccumulative, they are still as environmentally persistent as long-chain substances or have persistent degradation products.[31] In addition, because some of the shorter-chain PFASs are less effective, larger quantities may be needed to provide the same performance.[32] Thus, drinking water rules must protect the public health from unsafe exposure to all compounds in the PFAS class.

B. PFAS have been found in Massachusetts drinking water, groundwater, and surface waters.

Not only are PFAS toxic in very small amounts (in the nanograms per liter or parts per trillion), they are highly mobile in groundwater and surface water, and have been found in waters throughout Massachusetts.

1. Drinking Water

Groundwater in Barnstable, Massachusetts has been particularly susceptible to the spread of PFAS because of the town's location in an outwash plain with permeable soil.[33] In addition, there have been multiple sources of PFAS entering the system, including fire training areas, airports, and landfills, which have led to an ongoing threat to the sole source aquifer that provides drinking water for all Cape Cod residents.[34]

A 2009 sampling of 20 wells and two distribution systems that supply drinking water on Cape Cod found that 75 percent of test sites had detectable levels of chemicals, including PFOA and PFOS.[35] PFOS was one of the top two most frequently detected, and the levels detected were among the highest reported in U.S. drinking water.[36] PFOS and PFOA were found at high levels in Hyannis Water System wells downgradient of the Barnstable Municipal Airport. At the time the 2009 study was completed EPA's Provisional Health Advisory for PFOA and PFOS was

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[30] Arlene Blum et al., *The Madrid Statement on Poly- and Perfluoroalkyl Substances (PFASs)*, ENVTL HEALTH PERSPECTIVES, May 2015, https://ehp.niehs.nih.gov/doi/pdf/10.1289/ehp.1509934.
[31] *Id.*
[32] *Id.*
[33] Sources, Transport, Exposure & Effects of PFASs, Cape Cod, THE UNIV. OF RHODE ISLAND, https://web.uri.edu/steep/communities/cape-cod/.
[34] *Id.*
[35] *Tests find new contaminants in Cape Cod's drinking water supply, septic systems are likely the main source of pollution*, SILENT SPRING INSTITUTE (May 10, 2010), https://silentspring.org/research-update/tests-find-new-contaminants-cape-cod's-drinking-water-supply-septic-systems-are
[36] *Id.*

higher[37] than the Drinking Water Health Advisory (EPA Health Advisory) levels for PFAS eventually set in 2016. Lowered safety levels for the PFAS contaminants place a number of the wells above EPA's new guidelines.

PFAS contamination of public drinking water supplies in Massachusetts is by no means limited to Cape Cod. For example, drinking water supplied to the Town of Ayer from the Grove Pond Water Treatment Plant exceeded 70 ppt (combined) for five PFAS compounds until one of the three Grove Pond wells was closed in 2018. Drinking water from the Grove Pond Plant still exceeds 20 ppt.

2. Groundwater

In Cape Cod, groundwater contamination from PFAS has been linked to several sources, including fire training areas, airports, military bases, landfills, municipal wastewater, and septic systems.[38] In July of 2015, Barnstable Airport conducted investigations of PFAS in six monitoring wells and PFAS compounds were detected in all of them.[39] PFAS concentrations were above the EPA Health Advisory limits in two of the six wells.[40]

Additional groundwater investigations conducted in response to the Barnstable Airport findings speculated that the source of the PFAS contamination was the Airport Rescue and Fire Fighting Building, a fire fighting training deployment area. The resulting investigation found that there was heavy use of aqueous film forming foam (AFFF) at the fire training academy.

Also, in Weymouth, Massachusetts, PFAS has been detected in groundwater near the site of the former Naval Air Station.[41] Operational closure of the airfield was effected in September of 1996, however the area was used as a location for fire-fighting training exercises from 1950 until 1990.[42] Likely due to the heavy use of AFFF, a 2010 investigation determined widespread PFAS

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[37] U.S. Envtl Prot. Agency, *Provisional Health Advisories for Perfluorooctanoic Acid (PFOA) and Perfluorooctane Sulfonate (PFOS)*, January 8, 2009, https://www.epa.gov/sites/production/files/2015-09/documents/pfoa-pfos-provisional.pdf.

[38] *Sources, Transport, Exposure & Effects of PFASs*, *supra* note 35.

[39] Immediate Response Action Plan Status Report 3: Barnstable Municipal Airport, prepared by Horsley Witten Group, Inc. (April 18, 2017), http://eeaonline.eea.state.ma.us/EEA/fileviewer/Default.aspx?formdataid=0&documentid=445359 (Responding to a Notice of Responsibility issued by MassDEP, tasking Barnstable Airport with investigating for PFAS previously detected in groundwater at the airport, and at a monitoring well downgradient of the Airport on the Maher wellfield property).

[40] *Id.*

[41] U.S. Envtl Prot. Agency, *South Weymouth Naval Air Station: Cleanup Activities*, https://cumulis.epa.gov/supercpad/SiteProfiles/index.cfm?fuseaction=second.cleanup&id=0101826

[42] *Id.*

contamination in soils, groundwater, and surface water.[43] The investigation revealed the presence of PFAS in groundwater at concentrations exceeding the EPA Health Advisory.[44]

3. Surface Water

A study of the Joint Base in Bourne, Massachusetts includes surface water reports showing PFAS contamination above the EPA Health Advisory level.[45] Contamination was again linked to heavy use of AFFFs.[46] Specifically, contaminated surface water was detected in Ashumet and John's Pond and led to findings of affected residential water wells including those in the Lakeside Estates Community and Mashpee Village.[47]

II. MassDEP should establish a treatment technique drinking water standard for the PFAS class that is protective of human health.

In the absence of federal safeguards, Massachusetts must act to protect drinking water and limit Massachusetts residents' exposure to PFAS. As described below, setting MCLs on a chemical-by-chemical basis does not adequately protect the public from PFAS health impacts. Instead, a treatment technique drinking water standard for the class of PFAS is needed. This regulatory approach is authorized by law and technically feasible.

A. The chemical-by-chemical, MCL approach to regulating toxic chemicals is not protective of public health and the environment.

The current chemical-by-chemical regulatory framework for toxic chemicals is so inefficient it puts public health at risk. For example, even after the 2016 amendment to the Toxic Substances Control Act (TSCA), "it could take decades to evaluate the 80,000 chemicals already in commerce that have yet to be tested, let alone the 2,000 new chemicals introduced each year."[48] The EPA "still treats each chemical individually, continuing the saga in which similar, but slightly different, chemicals can be regrettably substituted."[49]

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[43] *Id.*
[44] Tetra Tech, *Signed Explanation of Significant Differences Re: Area of Concern Hangar 1, Former Naval Air Station South Weymouth*, December 15, 2011, https://www3.epa.gov/region1/superfund/sites/sweymouth/497699.pdf
[45] Mass. Dept. of Envtl. Prot., *supra* note 12.
[46] *Id.*
[47] *Id.*
[48] Joseph Allen, *Stop playing whack-a-mole with hazardous chemicals*, WASH. POST (December 15, 2016), https://www.washingtonpost.com/opinions/stop-playing-whack-a-mole-with-hazardous-chemicals/2016/12/15/9a357090-bb36-11e6-91ee-1adddfe36cbestory.html?utm_term=.52a9c9f5b23c
[49] *Id.*

The "whack-a-mole" approach is especially troublesome when it comes to setting drinking water standards for emerging contaminants like PFAS, because it is time consuming and expensive to assess them, it is "technically and financially challenging to identify and reverse environmental and human exposure to PFASs[,]" and both of these issues are exacerbated by the continual introduction of new PFAS compounds.[50] There are at least 3,000 PFAS compounds in use currently[51] and regulators don't know the names of all PFAS compounds, much less where they are located in their state. Recently developed PFAS are regarded as trade secrets and closely-guarded confidential business information, so manufacturers often do not apply for patents or supply regulators with information about molecular structure or usage.[52]

In light of the thousands of PFAS that have been introduced into commerce, and more introduced each year, establishing MCLs for each PFAS compound is simply not sustainable. The regulators fall farther behind every year, putting our citizens in harm's way. Thus, Massachusetts should adopt a treatment technique drinking water standard that protects Massachusetts residents from exposure to unsafe levels of all chemicals in the PFAS class.

B. The current ORSG for PFAS does not protect Massachusetts residents.

Massachusetts's current ORSG for PFAS does not protect the Massachusetts residents from exposure to unsafe PFAS levels in public water systems. Even though Massachusetts has issued these ORSGs, public water systems in Massachusetts are not required to test for and treat unsafe concentrations of PFAS because there is no federal or state drinking water standard for any of the PFAS compounds. In June of 2018, the MassDEP's Office of Research and Standards issued the guideline for five PFAS compounds (PFOA, PFOS, PFHpA, PFNA, PFHxS).[53] MassDEP also adopted an interim guidance on sampling and analysis for PFAS at disposal sites regulated under the Massachusetts Contingency Plan.[54] However, MassDEP has yet to adopt an MCL or establish an alternative drinking water standard for PFAS, which means that public water

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[50] Zhanyun Wang et al., *A Never-Ending story of Per- and Polyfluoroalkyl Substances (PFASs)*?, ENVTL SCIENCE & TECH., (February 22, 2017), at 2511, https://pubs.acs.org/doi/pdf/10.1021/acs.est.6b04806.
[51] KEMI Swedish Chemicals Agency, *Occurrence and use of highly fluorinated substances and alternatives; Report from a government assignment*, 6-78, 26 (August 9, 2009), https://www.kemi.se/en/global/rapporter/2015/report-7-15-occurrence-and-use-of-highly-fluorinated-substances-and-alternatives.pdf.
[52] Zhanyun Wang et al., *supra* note 50.
[53] Mass. Dept. of Envtl Prot., *supra* note 4.
[54] Mass. Dept. of Envtl Prot., *Interim Guidance on Sampling and Analysis for PFAS at Disposal Sites Regulated under the Massachusetts Contingency Plan*, June 19, 2018, https://www.mass.gov/files/documents/2018/06/19/2018-06-19%20-%20MassDEP%20BWSC%20PFAS%20Sampling%20Guidance.pdf.

systems in Massachusetts are not required to monitor for or treat unsafe concentrations of PFAS. Even if the ORSG for PFAS were adopted as an MCL, it would not be protective of public health because it does not address the thousands of PFAS chemicals in the PFAS class.

C. A treatment technique drinking water standard is appropriate for PFAS.

MassDEP has broad authority to regulate unsafe chemicals in drinking water.[55] In this case, the unique nature of PFAS demands an alternative approach to chemical-by-chemical regulation through MCLs. Regulation of PFAS as a class and through a treatment technique standard is necessary. There are well-established drinking water treatment technologies that public water systems can install to remove unsafe levels of PFAS from drinking water. There is simply no excuse for MassDEP to delay the promulgation of a drinking water standard for the PFAS class to address this public health crisis "perfect storm."

1. MassDEP has the authority to adopt a treatment technique drinking water standard.

MassDEP has authority to adopt a treatment technique drinking water standard for PFAS. Pursuant to Mass. Gen. Laws ch. 111, § 310, MassDEP "may make rules and regulations and issue such orders as in its opinion may be necessary to prevent the pollution and to secure the sanitary protection of all such waters used as sources of water supply and to ensure the delivery of a fit and pure water supply to all consumers."[56] The Massachusetts Drinking Water Regulations do not expressly provide for how MassDEP should establish water standards but it recognizes MassDEP's authority, after it has made a finding that a level of a contaminant poses an unacceptable health risk, to require a public water system to take actions to "reduce the level of contaminant concentrations to levels [MassDEP] deems safe or remove the source of supply from service." 310 CMR 22(8). MassDEP made such a finding for at least five PFAS compounds (PFOA, PFOS, PFHpA, PFNA, PFHxS) when it issued the ORSG for PFAS.

"A treatment technique is an enforceable procedure or level of technological performance which public water systems must follow to ensure control of a contaminant."[57] Where a treatment technique is selected in lieu of an MCL, the treatment technique must "prevent known or anticipated adverse effects on the health of persons to the extent feasible."[58] EPA has adopted

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[55] Mass. Gen. Laws Ch. 111, § 160; 310 Mass. Code Regs. 22.03.
[56] Mass. Gen. Laws Ch. 111, § 310. The Commonwealth of Massachusetts has primacy for the Safe Drinking Water Act in Massachusetts and has adopted the authority of the Safe Drinking Water Act via rulemaking. Mass. Dep't of Envtl. Protection, *Massachusetts Drinking Water Regulations*, 310 CMR 22.
[57] U.S. Envtl. Prot. Agency, *How EPA Regulates Drinking Water Contaminants*, https://www.epa.gov/dwregdev/how-epa-regulates-drinking-water-contaminants.
[58] 42 U.S.C. § 300g-1(b)(7)(A).

several treatment technique drinking water standards in lieu of an MCL where EPA has determined that it is "not om technologically feasible to ascertain the level of [a] contaminant."[59] For example, the Lead and Copper Rule requires the use of a treatment technique.[60] This rule requires public water systems to test drinking water in the homes of consumers and undertake additional treatment measures to control lead if 10% of the samples exceed 15 ppb.[61] The Surface Water Treatment Rule also requires the use of a treatment technique. Under this rule, most public water systems that obtain water from surface water or groundwater under the direct influence of surface water must use filters and disinfectants to reduce pathogens.[62] In both cases, EPA had to establish a unique procedure to address the risks posed by a specific contaminant because an MCL would not have been practical or protective of public health due to the unique characteristics of the contaminants.

Similarly, the unique characteristics of the PFAS class pose a public health threat that cannot be adequately addressed with the establishment of an MCL for one or a few PFAS chemicals. MassDEP has the authority to develop a procedure that would require installation of specific drinking water treatment technologies under certain circumstances. MassDEP has multiple options to protect Massachusetts residents from exposure to the PFAS class. For example, MassDEP could promulgate a rule that requires public water systems to install appropriate treatment technologies where (1) the sum of all measurable PFAS exceeds a conservative threshold level that is protective of public health and takes into account the cumulative impacts of all PFAS chemicals or (2) the presence of PFAS compounds is detected using "non-targeted" laboratory analysis.[63] Non-targeted analysis allows "researchers [to] rapidly characterize thousands of never studied chemical compounds in a wide variety of environmental, residential, and biological media.[64] An alternative option would be to require: 1) a robust source water assessment for PFAS and 2) treatment where PFAS may be present in the source water. MassDEP should determine a specific procedure for the drinking water standard through a robust stakeholder process as part of the rulemaking process.

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[59] *Id.*
[60] U.S. Envtl. Prot. Agency, *How EPA Regulates Drinking Water Contaminants, supra* note 57.
[61] U.S. Envtl. Prot. Agency, *Lead and Copper Rule*, https://www.epa.gov/dwreginfo/lead-and-copper-rule.
[62] U.S. Envtl. Prot. Agency, *Surface Water Treatment Rules, https://www.epa.gov/dwreginfo/surface-water-treatment-rules*.
[63] U.S. Envtl. Prot. Agency, *EPA Researchers Use Innovative Approach to Find PFAS in the Environment*, https://www.epa.gov/sciencematters/epa-researchers-use-innovative-approach-find-pfas-environment.; Karl Leif Bates, *Duke Expert Helps Spearhead State's New Water-Testing Program*, DUKE TODAY, Aug. 8, 2018, https://today.duke.edu/2018/08/duke-expert-helps-spearhead-states-new-water-testing-program.
[64] *Id.*

2. Due to the unique characteristics of the PFAS class of compounds, a treatment technique is necessary to protect public health.

i. Regulation of PFAS chemicals as a class is necessary.

Even if MassDEP were to adopt the current ORSG (or a lower ppt value) as an MCL, a combined limit for five PFAS would not protect Massachusetts residents from the 3,000 or more other PFAS.[65]

First, in addition to PFOA, PFOS, PFHxS, PFHpA, and PFNA, other PFAS have been found or are being investigated in Massachusetts, including, for example, PFBS.[66] There are likely many other PFAS in Massachusetts that the Commonwealth is simply not aware of yet given the speed and secrecy with which chemical manufacturers have introduced these dangerous chemicals into commerce.[67]

Second, as discussed above, PFAS are similar in chemical structure and some PFAS break down into each other. While long-chain PFAS compounds may be decreasing in the environment due to voluntary phase-outs by manufacturers, "the most common replacements are short-chain PFAS with similar structures."[68] Third, these PFAS chemicals are often found together, and fourth, they are likely to have similar health effects as discussed in Section I.A.

EPA has applied similar concepts to establish an MCL for a group of chemicals.[69] For example, EPA established an MCL for five haloacetic acid disinfection byproducts (HAA5) because it did not have sufficient information regarding (1) the occurrence of individual haloacetic acids; (2) how water quality parameters affect the formation of haloacetic acids; (3) how "treatment technologies control the formation of individual . . . [haloacetic acids]; and (4) toxicity information for some of the individual haloacetic acids.[70] In light of the unique challenges associated with regulation of these chemicals, EPA promulgated a group MCL even in the absence of complete information about each individual haloacetic acid in order to better protect public health.[71] For all these reasons, it is appropriate to regulate PFAS chemicals as a class.

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[65] KEMI Swedish Chemicals Agency, *supra* note 51, at 6.
[66] Massachusetts Dept. of Envtl Prot., *supra* note 4.
[67] Environmental Working Group Comments on the Agency for Toxic Substances and Disease Registry (ATSDR) Draft Toxicological Profile for Perfluoroalkyls, ENVTL WORKING GROUP (August 20, 2018), https://cdn.ewg.org/sites/default/files/testimony/EWG%20Comments%20for%20ATSDR_Aug20..pdf?_ga=2.236461961.949885036.1539136763-1789323056.1527870942.
[68] Blum, *supra* note 31.
[69] *Drinking Water Guidance, Grouping Process for Drinking Water Health Advisories*, *supra* note 87.
[70] 63 Fed. Reg. 69390, 69409 (Dec. 16, 1998), https://www.gpo.gov/fdsys/pkg/FR-1998-12-16/pdf/98-32887.pdf#page=1.
[71] *Id.*

ii. A treatment technique in lieu of an MCL is necessary.

A treatment technique in lieu of an MCL for specific PFAS chemicals or small groups of PFAS chemicals is necessary. As discussed previously, scientists suspect that PFAS chemicals in the class may have similar adverse health effects as the handful of PFAS compounds that have been studied more extensively.[72] EPA has only developed targeted test methods for 14 PFAS chemicals out of more than 3,000 compounds.[73] Thus, it is simply not economically or technically feasible to ascertain the level of each specific PFAS chemicals in the PFAS class that pose a risk to Massachusetts residents.

As MassDEP is well aware, establishing an MCL for one compound is resource intensive and time consuming. Adopting a treatment technique drinking water standard for the PFAS class in lieu of establishing MCLs for thousands of PFAS chemicals will require far fewer resources and will provide protection from exposure to unsafe levels of PFAS on a much shorter timeline. For these reasons, a treatment technique drinking water standard is necessary to protect Massachusetts residents.

3. Treatment technologies are available to remove long- and short-chain PFAS.

There are both established and novel methods to remove and destroy PFAS. While long- and short-chain PFAS may be difficult to treat with any one traditional technology—some new technologies are in development—, a "treatment train" of several technologies combining adsorption, separation, and destruction in sequence, for example, would be effective in treating drinking water and protecting public health.

Adsorption technologies such as GAC and ion exchange "are currently the most commonly encountered interim response measures to achieve immediate compliance with drinking water standards and serve as the benchmark of practicality and effectiveness for other treatment technologies."[74]

While new adsorption technologies like organically modified silica adsorbents show promise,[75] GAC has long been used for adsorption of chemical pollutants, consistently removes PFOS with an efficiency of more than 90 percent, and is the treatment technique specified in Safe Drinking Water Act (SDWA) for the control of synthetic organic chemicals:

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[72] KEMI Swedish Chemicals Agency, *supra* note 51.
[73] Mass. Dept. of Envtl Prot., *supra* note 60, at 10-12.
[74] J. Horst et al., *Water Treatment Technologies for PFAS: The Next Generation, 38,* Groundwater Monitoring & Remediation (Spring 2018), at 15.
[75] *Id.* at 15–16.

> granular activated carbon is feasible for the control of synthetic organic chemicals, and any technology, treatment technique, or other means found to be the best available for the control of synthetic organic chemicals must be at least as effective in controlling synthetic organic chemicals as granular activated carbon.[76]

Separation technologies, including reverse osmosis, microfiltration, ultrafiltration and nanofiltration, are highly effective for PFAS removal and can remove PFAS at more than 99% effectiveness.[77] "Membrane filtration has several benefits including: achieving continuous separation, low energy consumption, ease of combination with other existing techniques, easy up-scaling, and low chemical costs."[78] Ozofractionation (a patented process by the company EVOCRA and available commercially as Ozofractionative Catalyzed Reagent Addition (OCRA) (Dickson 2013, 2014)) is a novel separation technology that shows high (>99.99 percent reduction) effectiveness for PFAS.[79]

Finally, novel destructive treatment technologies for PFAS are becoming available. Destructive technologies include sonochemical decomposition, chemical/advanced photochemical oxidation, and AECOM's DE-FLUOROTM technology.

This treatment train solution will also confer significant co-benefits for public health, because the same technologies that are effective in PFAS treatment are effective in removing a host of other dangerous chemicals. Granular activated carbon (GAC) adsorption filters alone, for example, are effective in removing dozens of harmful contaminants in addition to PFAS (including, but not limited to: RDX, arsenic, benzene, cryptosporidium, MTBE, mercury, perchlorate, tetrachloroethylene (Perc), and trichloroethylene (TCE)).[80] Other technologies that should be considered as components of the treatment train confer similar co-benefits; for example, membrane separation technologies like reverse osmosis not only treat PFAS but, without limitation, also treat 1,4-dioxane, alachlor, chromium, malathion, and nitrates.[81]

For all these reasons, CLF and Toxics Action Center urge MassDEP to initiate a rulemaking for a treatment technique drinking water standard for the PFAS class.

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[76] 42 U.S.C. § 300g-1(b)(4)(D).
[77] Kucharzyk et al, *supra* note 103, at 759–60; Horst, supra note 101.
[78] V.A. Arias Espana et al., *Treatment technologies for aqueous perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA): A critical review with an emphasis on field testing*, 4 ENVIRONMENTAL TECHNOLOGY & INNOVATION (2015) 168, 177.
[79] Horst et al., at 17.
[80] U.S. Envtl. Prot. Agency, *Welcome to the Drinking Water Treatability Database, Granular Activated Carbon*, https://oaspub.epa.gov/tdb/pages/treatment/treatmentContaminant.do.
[81] *Id.*

III. In the alternative, MassDEP should either adopt an MCL for the PFAS class or for each individual PFAS chemical.

MassDEP must take action to establish drinking water standards for PFAS in the absence of federal safeguards even if MassDEP does not establish a treatment technique standard. As discussed in Section II.C, MassDEP has the authority to regulate PFAS as a class or on a chemical-by-chemical basis. PFAS are present in Massachusetts waters and are known to cause adverse health effects. Thus, at a bare minimum, MassDEP should either 1) adopt an MCL for the PFAS class, or 2) set a schedule for the adoption of an MCL for each individual PFAS chemical that has been identified and begin establishing MCLs immediately. Of course, as new PFAS chemicals are identified the schedule of MCL adoption will need to be modified.

IV. MassDEP should immediately adopt Vermont's PFAS Health Advisory as a maximum contaminant level.

In the interim and until MassDEP establishes a treatment technique drinking water standard for PFAS, MassDEP should immediately adopt Vermont's PFAS Health Advisory of 20 ppt for the PFAS Class as an MCL.

CONCLUSION

For all the forgoing reasons, CLF and Toxics Action Center petition MassDEP to establish a drinking water standard for PFAS that is protective of public health. Specifically, MassDEP should adopt a treatment technique drinking water standard for the PFAS class. In the alternative, MassDEP should establish an MCL for the PFAS class or individual MCLs for each PFAS chemical that poses a risk to public water systems in Massachusetts. As an interim step, MassDEP should immediately adopt Vermont's PFAS Health Advisory of 20 ppt for the PFAS Class as an MCL.

The significant threats posed to human health and the environment by the PFAS class of compounds are clear. These compounds have been found in Massachusetts drinking water, groundwater, and surface waters. The dangers this class of chemicals pose to Massachusetts residents demand immediate action to limit further exposure. Thank you for your consideration.

Sincerely,

Heather A. Govern, Director
Conservation Law Foundation

Sylvia Broude, Executive Director
Toxics Action Center

CC:

The Honorable Monica Bharel, MD, MPH
Commissioner
Massachusetts Department of Public Health

Maura Healey
Massachusetts Attorney General
Office of the Attorney General

Melissa Hoffer
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ARTICLE

A transgenerational toxicokinetic model and its use in derivation of Minnesota PFOA water guidance

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Abstract

Minnesota has been grappling with extensive per- and polyfluoroalkyl substances (PFASs) groundwater contamination since 2002, in a major metropolitan setting. As toxicological information has accumulated for these substances, the public health community has become increasingly aware of critically sensitive populations. The accumulation of some PFAS in women of childbearing age, and the placental and breastmilk transfer to their offspring, require new risk assessment methods to protect public health. The traditional water guidance paradigm is inadequate to address maternal-to-infant transfer of accumulated levels of perfluorooctanoate (PFOA), in particular. Even short exposures during infancy have dramatic impacts on serum levels for many years. In addition, developmental effects are the critical effects anchoring recent risk assessments. In response, the Minnesota Department of Health created an Excel-based model that incorporates chemical-specific properties and exposure parameters for early life stages. Serum levels were assessed in both formula-fed and breastfed infants, with placental transfer in both scenarios. Peak breastfed infant serum levels were 4.4-fold higher than in formula-fed infants, with both of these scenarios producing serum levels in excess of the adult steady-state level. The development and application of this model to PFOA are described.

Introduction

Per- and polyfluoroalkyl substances (PFASs) are a group of fluorinated organic pollutants with over 60 years of widespread industrial and commercial use. These water contaminants are highly problematic due to their water solubility, high persistence, and bioaccumulation, especially in humans. The increasing detection of these contaminants, as well as increasing concerns regarding potential adverse health effects, have resulted in their emergence as drinking water contaminants of global concern.

In Minnesota, since 2002, the Minnesota Department of Health (MDH), in partnership with the Minnesota Pollution Control Agency (MPCA), has been involved in investigating PFAS contamination. This work began when MDH received a request to develop health-based guidance values (HBGVs) for two PFAS chemicals, perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA), to assist in evaluating human health risks associated with groundwater contamination at the 3M Corporation's Cottage Grove manufacturing plant (see Fig. 1).

In 2004, PFOS and PFOA contamination was detected in the drinking water supplies of several eastern Twin Cities suburbs (East Metro). These contaminants originate from three sites used by the 3M Corporation over several decades for disposal of PFAS manufacturing wastes. In response, MDH and MPCA began extensive testing of public and private wells in the area for PFOS and PFOA. In 2006, the MDH Public Health Laboratory developed new analytical methods, expanding the list of chemicals to include five more PFAS: perfluorobutanoic acid (PFBA), perfluoropentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), perfluorobutane sulfonate (PFBS), and perfluorohexane sulfonate (PFHxS). To date, multiple public water supplies and over 2600 private wells have been sampled. The East Metro PFAS groundwater contamination plume currently covers over 150 square miles, affecting the drinking water supplies of over 140,000 Minnesotans.

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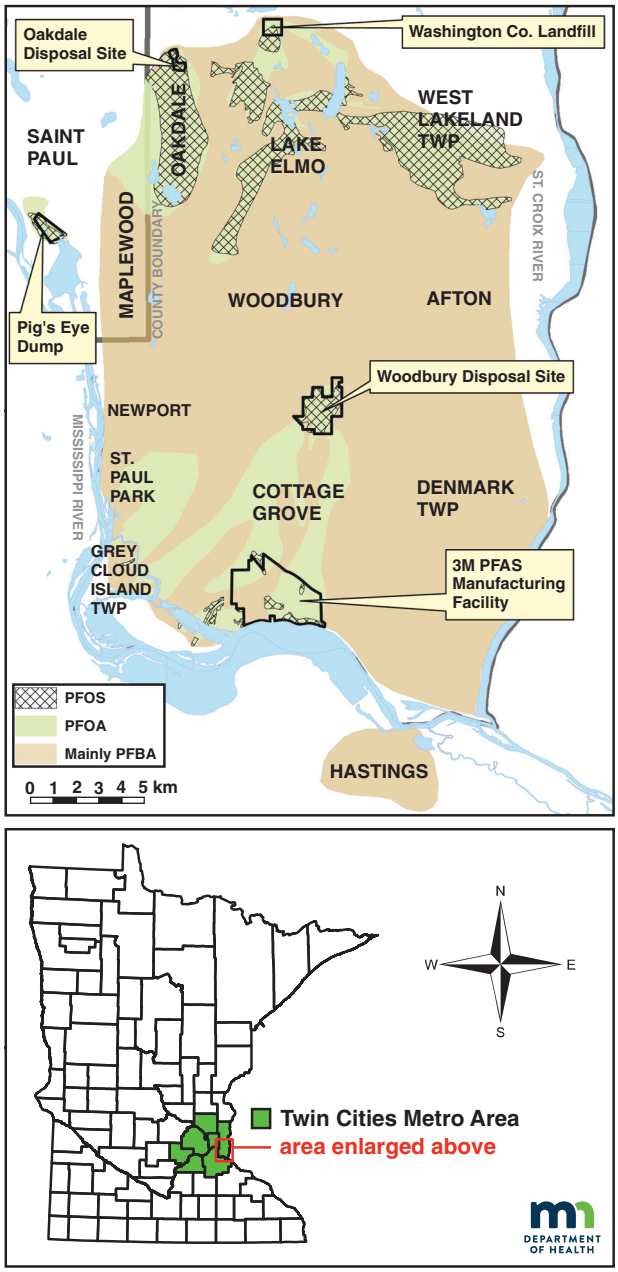

Fig. 1 Map of PFAS-impacted area east of St. Paul, Minnesota metropolitan area

PFBA is the most widely detected PFAS, whereas PFOA, PFOS, and other PFAS are present over a smaller area (Fig. 1). Statewide, MDH and MPCA have evaluated other potential sources of PFAS contamination, including fire-training facilities, chrome plating operations, wastewater treatment plants, and landfills. Low concentrations of PFAS were detected at many of these locations, often below the threshold of human health concern, although these thresholds continue to decline as more information becomes available.

MDH derives HBGVs to assist risk managers in identifying water sources with contaminants at levels of potential human health concern. An HBGV represents a concentration in drinking water of a chemical or mixture of chemicals that is likely to pose little or no health risk to humans, including vulnerable subpopulations. To protect the majority of the general population, MDH uses a reasonable maximum exposed (RME) individual scenario, which uses central tendency values for some parameters coupled with upper-end values for others (e.g., 95th percentile water intake rate) [1]. Following the 2016 issuance of lifetime health advisories (HAs) of 0.07 μg/L for PFOS and PFOA by the US Environmental Protection Agency (USEPA) [2, 3], MDH initiated an expedited reassessment of Minnesota's PFOS and PFOA HBGVs.

In its reassessment, MDH found that its standard approach for deriving HBGVs was inadequate when applied to PFOS and PFOA for several reasons. PFOS and PFOA are bioaccumulative chemicals, resulting in higher serum concentrations than the concentrations in environmental media (e.g., water). Recent studies have demonstrated significant maternal transfer across the placental barrier, resulting in measurable neonatal serum concentrations at birth [4–7], and partitioning into breastmilk [7–10]. Empirical data from these populations clearly demonstrate higher serum levels of PFOS and PFOA in nursing infants compared with their mother. Kinetic models of infant serum levels also predict several fold higher serum levels following breastfeeding [11, 12]. Therefore, in addition to being born with a transgenerational body burden from placental transfer based on maternal accumulation, infants may also experience subsequent higher exposures, especially from breastfeeding. Developmental effects have been identified as sensitive health effects; therefore, consideration of these exposure pathways is relevant and likely even critical to protection of all sensitive subpopulations. For these reasons, MDH developed a new approach to derive HBGVs, accounting for bioaccumulation and transgenerational exposure.

This publication presents the development and application of a flexible and transparent Excel-based toxicokinetic (TK) model, as applied to water guidance derivation for PFOA. The model incorporates body burden at birth (placental transfer), ingestion of breastmilk, and age-specific water intake rates in order to derive sufficiently protective HBGVs.

Materials and methods

MDH's TK maternal/infant model approach for deriving HBGVs

MDH developed an Excel-based TK model to predict serum levels from birth through adulthood. MDH chose to develop its model in Excel to maximize the transparency and accessibility of the model. In addition, the relationship between intake (dose) and serum concentration can

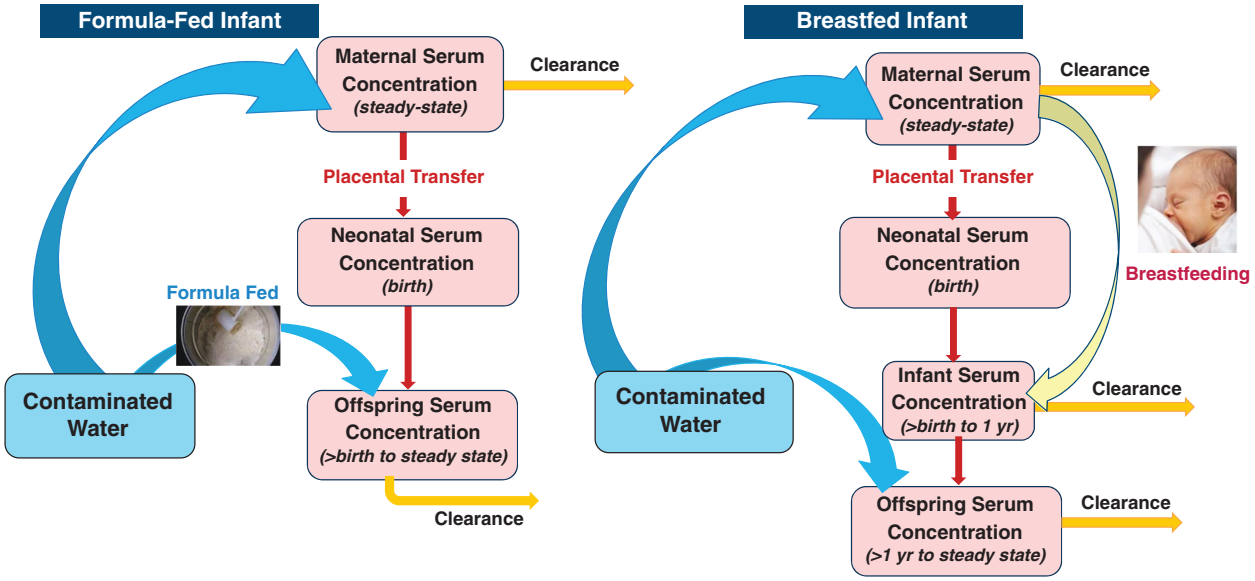

Fig. 2 Conceptual representation of the toxicokinetic model for the two exposure scenarios evaluated

adequately be described by a single-compartment model [13]. This type of model has been used by others to describe the relationship between dose and serum levels [14]. Two exposure scenarios were evaluated (Fig. 2): (1) an infant fed with formula reconstituted with contaminated water starting at birth, followed by a lifetime of drinking contaminated water; and (2) an infant breastfed for 12 months, followed by a lifetime of drinking contaminated water. In both scenarios, infants began life with a transgenerational body burden calculated from the mother's serum concentration using a placental transfer factor. Exposure was simulated through consumption of breastmilk or formula reconstituted with contaminated water. Daily intake, elimination, and serum concentrations were calculated over a simulated period of 20,000 days (about 55 years) to ensure attainment of steady state (See Table 1).

Because PFOA is well absorbed and not metabolized, the dynamic relationship between serum concentrations and intake (dose) can be calculated using Eq. 1:

$$\text{Serum concentration}\left(\frac{\text{mg}}{\text{L}}\right) = \frac{\text{Dose}\left(\frac{\text{mg}}{\text{kg·day}}\right)}{\text{Clearance rate}\left(\frac{\text{L}}{\text{kg·day}}\right)} \quad (1)$$

Where:

for water ingestion—

$$\text{Dose}\left(\frac{\text{mg}}{\text{kg·day}}\right) = \text{Water intake rate}\left(\frac{\text{L}}{\text{kg·day}}\right) \times \text{Water concentration}\left(\frac{\text{mg}}{\text{L}}\right)$$

for breastmilk—

$$\text{Dose}\left(\frac{\text{mg}}{\text{kg·day}}\right) = \text{Breastmilk intake rate}\left(\frac{\text{L}}{\text{kg·day}}\right) \times \text{Breastmilk concentration}\left(\frac{\text{mg}}{\text{L}}\right)$$

and

$$\text{Clearance rate}\left(\frac{\text{L}}{\text{kg·day}}\right) = V_\text{d} \times k$$

$$V_\text{d} = \text{Volume of distribution}\left(\frac{\text{L}}{\text{kg}}\right)$$

$$k = \frac{\ln(2)}{\text{half} - \text{life (d)}}$$

An annotated list of model exposure and chemical parameter values is presented in Table 1.

The model assumes that maternal exposure began prior to pregnancy, so that steady-state serum concentration was achieved by the time of delivery. The infant's serum concentration at birth was calculated using Eq. 2:

$$\text{Serum conc.}\left(\frac{\text{mg}}{\text{L}}\right) = \text{Maternal serum conc.}\left(\frac{\text{mg}}{\text{L}}\right) \times \text{Placental transfer factor} \quad (2)$$

For all subsequent days, the infant's final daily post-elimination serum concentration was calculated using Eq. 3:

$$\text{Serum conc.}\left(\frac{\text{mg}}{\text{L}}\right) = \left[\text{Prev.day serum conc.}\left(\frac{\text{mg}}{\text{L}}\right) + \frac{\text{Today's intake(mg)}}{V_\text{d}\left(\frac{\text{L}}{\text{kg}}\right) \times \text{BW(kg)}}\right] \times e^{-k} \quad (3)$$

The V_d parameter, assumed to be extracellular water, is both chemical specific and age specific. In order to account for age-specific differences in extracellular water volume during early childhood, V_d was multiplied by an adjustment factor (AF) starting at 2.1 at birth and declining to 1.0 by 10 years of age [15].

To maintain mass balance, daily maternal serum concentrations incorporated loss of chemical via transfer to the

Table 1 Exposure and chemical-specific toxicokinetic parameters used in modeling PFOA serum concentrations

Parameter	Central tendency value (e.g. mean)	Upper percentile value (e.g., 95th percentile)	Source and comment
Half-life ($t_{½}$)	**840 days [2.3 years]**	1679 days [4.6 years]	Bartell et al. [37]. Similar mean values have been reported in several publications. Wide variability within the general population has been noted. Life-stage-specific information is not available. Therefore, the same half-life was used across all life stages. See Supplemental Table S1 for more information.
Placental (infant:maternal) transfer	**0.87**	1.69	Mean paired ratios ranging from 0.68 [38] to 1.26 [4] have been reported. A more comprehensive literature review has been conducted since MDH selected 0.87 during its expedited review [16]. See Supplemental Table S2. Preference was given to paired ratios over ratios based on summary statistics. Maximum ratios for individual mother–infant pairs range from 1.52 [7] to 2.16 [6]. 95th percentile values (mean + 2SD) were calculated from author-reported mean and SD values, and range from 1.11 [7] to 1.69 [4].
Breastmilk (milk:maternal) transfer	**0.052**	0.12	Mean paired ratios ranging from 0.025 [39] to 0.12 [40] have been reported. A more comprehensive literature review has been conducted since MDH selected 0.052 during its expedited review [16]. See Supplemental Table S3. Maximum individual pair ratios were not reported by study authors. In the absence of maximum individual values, the maximum mean value of 0.12 is used to represent an upper percentile value.
Breastmilk intake rate (mL/kg per day)			Values for exclusively[a] breastfed infants (Table 15-1 [36]). Body weight at birth was set at **3.38** kg, the mean birth weight for singleton births at 37–41 weeks of gestation [41]. Body weights (kg) were calculated from data presented in Table 15-1 for each age group (i.e., mL/day ÷ mL/kg per day): The midpoint in time for each age group was set equal to age group value. Daily intake rates and body weights between one midpoint and the next were calculated by linear interpolation to avoid abrupt changes in values.
Age group			Mean based (kg) / Upper percentile-based (kg)
Birth to <1 month	150	**220**	3.4 / **4.3**
1 to <3 months	140	**190**	4.9 / **5.2**
3 to <6 months	110	**150**	7.0 / **6.7**
6 to <12 months	83	**130**	7.5 / **7.7**
Duration (months) of breastfeeding	6 months, then phased out to zero by 12 months	**12 months**	American Academy of Pediatrics [42] recommends exclusively breastfeeding for the first 6 months, with continued breastfeeding

Table 1 (continued)

Parameter	Central tendency value (e.g. mean)	Upper percentile value (e.g., 95th percentile)	Source and comment	
			alongside introduction of complementary food for at least 12 months. The Center for Disease Control (CDC) Breastfeeding Report Card for 2016 [43] reports nearly 66% of mothers in Minnesota report breastfeeding at 6 months, with 31.4% exclusively breastfeeding. At 12 months, 41% of mothers reported breastfeeding.	
Water intake rate (mL/kg per day)			Central tendency: exclusively[a] breastfed intake rates used from birth to 6 months of age. From 6 to 12 months, breastfeeding is phased out and water intake is phased in. **Upper percentile: exclusively breastfed intake rates used from birth to 12 months of age. At 12 months, breastfeeding ends and water intake begins**. Values for consumers only. (Table 3-1 [36]). Body weights (kg) were calculated from data presented in Table 3-1 for each age group (i.e., mL/day ÷ mL/kg per day): The midpoint in time for each age group was set equal to age group value. Daily intake rates and body weights between one midpoint and the next were calculated by linear interpolation to avoid abrupt changes in values. **For calculation of maternal serum concentration at time of delivery, a time-weighted average water intake rate was calculated from birth to 30–35 years of age**, resulting in a mean and **95th percentile water intake rate** of 18 and **47 mL/kg per day**, respectively.	
Age group			Mean based (kg)	Upper percentile based (kg)
<1 month	137	**238**	3.4	**3.6**
1 to <3 months	119	**285**	4.6	**3.7**
3 to <6 months	80	**173**	7.0	**6.8**
6 to <12 months	53	**129**	8.8	**8.9**
1 to <2 years	27	**75**	11. 4	**11.9**
2 to <3 years	26	**62**	13. 7	**14.7**
3 to <6 years	21	**52**	18. 2	**19.2**
6 to <11 years	17	**47**	30. 1	**29.9**
11 to <16 years	12	**35**	53. 1	**56.5**
16 to <18 years	10	**30**	70. 2	**62.8**
18 to <21 years	11	**36**	74. 2	**78.3**
>21 years	16	**42**	76.7	**73.6**
Volume of distribution (L/kg)	**0.17**			

Table 1 (continued)

Parameter	Central tendency value (e.g., mean)	Upper percentile value (e.g., 95th percentile)	Source and comment
			USEPA and Han et al. [14, 44]. Consistent with extracellular fluid as volume of distribution. Friis-Hansen [15] (and consistent with Felter et al. [45]). Early life stages have higher body water content per unit weight than adults. Adjustment factor is designed to account for this difference. This is an area of uncertainty since the precise nature of the V_d is not known. Use of the V_d AF reduces serum concentration estimates, and increases model accuracy compared with empirical data. The midpoint in time for each age group was set equal to age group value. Daily V_d AF between one midpoint and the next were calculated by linear interpolation to avoid abrupt changes in values.
V_d age adjustment factor (V_d AF)			
0–1 day	**2.4**		
1–30 days	**2.1**		
1–3 months	**1.7**		
3–6 months	**1.6**		
6–12 months	**1.5**		
1–3 years	**1.4**		
3–5 years	**1.1**		
5–10 years	**1.2**		
>10 years	**1.0**		

Final model parameters for calculation of the PFOA HBGVs shown in **bold**

[a]Exclusively breastfed as defined by USEPA [36] refers to infants whose sole source of milk is breastmilk and not formula. Exclusively breastfed infants in the studies underlying these USEPA estimates were not excluded from other foods, typically after six months. This definition differs from other sources, which may define exclusive breastfeeding as the only source of nourishment (solid or liquid) as breastmilk

infant during breastfeeding, as well as excretion represented by the clearance rate. The infant's daily intake (and thus the mother's loss) was calculated from the breastmilk intake rate and the breastmilk concentration, derived using Eq. 4:

$$\text{Breastmilk conc.}\left(\frac{\text{mg}}{\text{L}}\right) = \text{Maternal serum conc.}\left(\frac{\text{mg}}{\text{L}}\right) \times \text{Breastmilk transfer factor} \quad (4)$$

Model evaluation

Model results were compared with empirical data from published studies to ensure that the model was fit-for-purpose, i.e., capable of generating representative upper percentile serum concentration estimates over a lifetime for a population of concern, in particular, infants breastfed by chronically exposed mothers. MDH also solicited input from six external experts for advice on how to improve the model predictions and for feedback regarding the suitability of the model for the intended purpose [16].

Reference dose (RfD) calculation and relative source contribution (RSC) selection

Derivation of HBGVs typically requires determination of an RfD (mg/kg per day) and an appropriate RSC. However, serum concentration, a measure of internal exposure, was identified as the best dose metric for assessing PFOA's health effects. The point of departure was a serum concentration of 38 mg/L from a developmental study in mice [17]. The application of a total uncertainty factor of 300 ($10^{0.5}$ for potential interspecies toxicodynamic differences, 10 for intraspecies variability, $10^{0.5}$ for use of a lowest observable adverse effect level (LOAEL), and $10^{0.5}$ for database insufficiencies) produced a 'reference' serum concentration of 0.13 mg/mL. A traditional RfD of 0.000018 mg/kg per day can be derived by multiplying the 'reference' serum concentration of 0.13 mg/L by a clearance rate of 0.00014 L/kg per day [18].

Total exposure from all sources, including potential ingestion of contaminated drinking water, should not result in higher serum concentrations than those associated with the RfD (hereto referred to as 'reference' serum concentration). Exposures contributed by non-water sources are addressed through the application of an RSC, which allocates a fraction of the RfD to drinking water exposure. National and local biomonitoring data were used to identify an appropriate RSC for PFOA (see details in Results section).

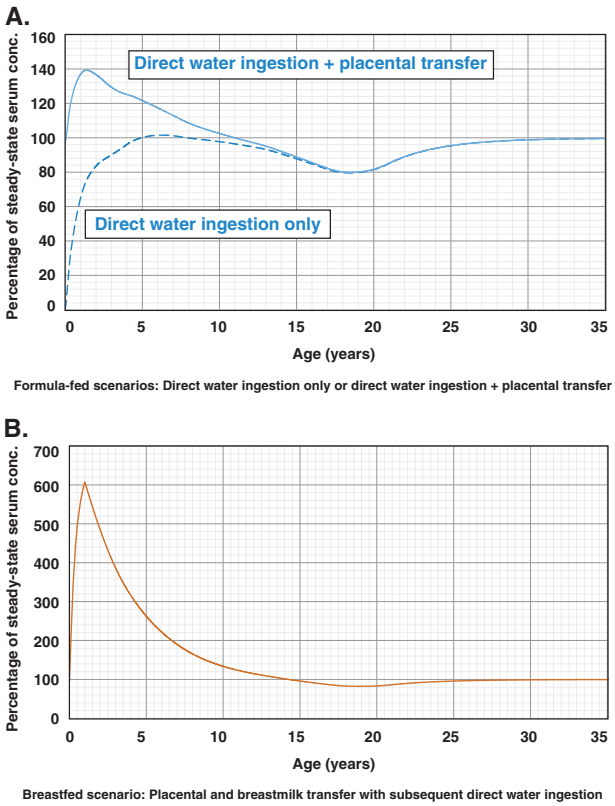

Fig. 3 Offspring serum concentration as a percentage of steady-state serum concentration (**a**) formula-fed scenarios—direct water ingestion exposure only or placental transfer (from chronically exposed mother at steady state) and direct water ingestion exposure, and (**b**) breastfed scenario—placental and breastmilk transfer (from chronically exposed mother at steady state) and direct water ingestion exposure. Note different scales are used for percentage of steady-state concentration in **a** (0–160) than in **b** (0–700). (Horizontal scale truncated at 35 years to enhance detail)

Results

Comparison of breastmilk versus formula-fed exposure pathways

MDH developed a preliminary model to evaluate whether placental and breastmilk transfer, as well as high fluid intake rates could result in serum concentrations that exceeded steady-state serum concentrations. Two formula-fed scenarios and one breastfed scenario were evaluated: a formula-fed infant exposed to contaminated water with or without placental transfer (Fig. 3a) and a breastfed infant with both placental and breastmilk transfer (Fig. 3b). Figure 3a demonstrates the importance of considering placental transfer, as early life serum levels are predicted to be approximately 40% higher than adult steady-state levels. When both placental and breastmilk transfer are taken into account (Fig. 3b), early life serum levels were predicted to be sixfold higher than adult steady-state levels. Given the impact of exposure via placental and breastmilk transfer, MDH pursued the development of a model that incorporated these pathways into the derivation of an HBGV for PFOA.

Model evaluation

Empirical infant serum data [8, 19] were used to ascertain whether the Excel-based model produces reasonable estimates of serum concentration, keeping in mind that the model parameter selections assume an RME scenario. For each model comparison, the mother's serum concentration at delivery was assumed to be at steady state. Individual maternal:child paired numeric data were preferred, but was not included in the publications or available by request.

Fromme and colleagues [8] investigated maternal and infant PFOA body burden during the 6 months following birth. Breastfeeding status was reported for 50 of the 53 participants; 37 infants drank only breastmilk, 6 predominantly drank breastmilk, 6 partially drank breastmilk, and 1 infant received no breastmilk. Two comparisons were conducted: (1) a population-based evaluation, and (2) modeling of individual infant serum levels after 6 months of breastfeeding. For the population-based evaluation, the overall maternal mean (2.3 µg/L) and 95th percentile (5.2 µg/L) PFOA serum concentrations at delivery (Table 1 in Fromme et al. [8]) was input into the model. Maternal exposure during lactation was assumed to be the same as prior to delivery and was estimated by multiplying the maternal serum concentration by a PFOA clearance rate of 0.00014 L/kg per day, which is based on a 0.17 L/kg volume of distribution and a half-life of 840 days. Placental and breastmilk transfer rates of 0.87 and 0.052, respectively, were used to estimate infant serum concentrations at birth and breastmilk concentration from maternal serum concentrations over the course of lactation. Predicted serum concentrations, following 6 months of breastfeeding, aligned closely with the reported mean and 95th percentile infant serum concentrations at 6 months of age (Fromme Table 1 [8]). The reported overall mean and 95th percentile infant PFOA serum concentrations at 6 months were 8.0 and 19.5 µg/L, respectively, and the predicted values were 7.9 and 21.2 µg/L, respectively, based on mean (dashed line) and upper percentile (solid line) breastmilk intake rates (Fig. 4).

For modeling of individual serum concentrations, WebPlotDigitizer (Austin, Texas, USA) [20] was used to approximate the serum concentration at birth (cord blood) and at 6 months of age from Figure S6 [8] for each of the 14 infants and compared these values with the MDH model results. The reported birth serum concentration was used as the input to the model for each infant. An upper percentile breastmilk intake rate was used for the entire 6-month period. Maternal serum concentration at delivery was back

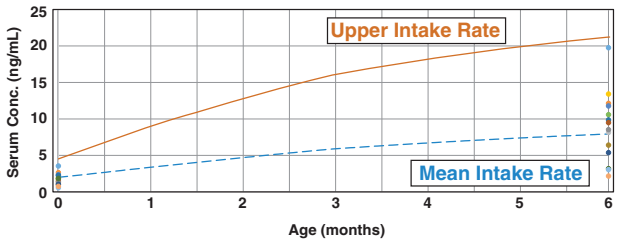

Fig. 4 Mean and 95th percentile infant PFOA serum concentrations predicted by MDH's model for breastfed infants in comparison with measured infant PFOA serum levels presented in Fromme (Table 1 [8]). Upper and mean intake rates derived from USEPA [36] (see Table 1)

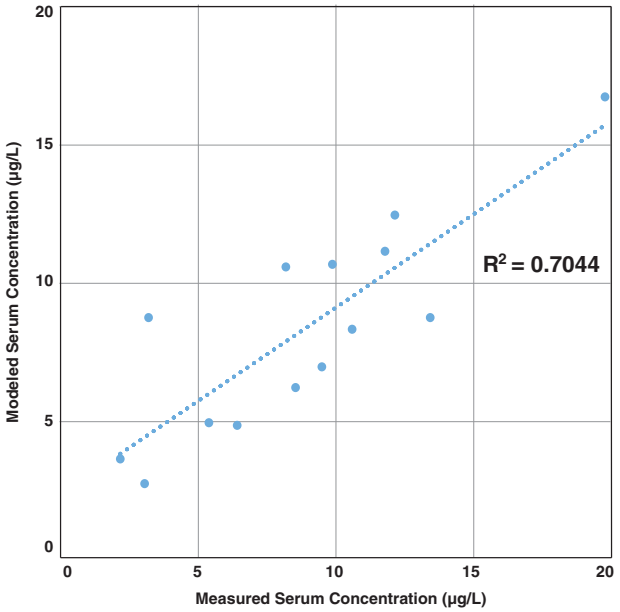

Fig. 5 Modeled individual infant PFOA serum concentration at 6 months of age versus measured levels estimated from Fromme et al. (Figure S6 [8])

calculated using the infant birth serum concentration and a placental transfer rate of 0.87. Initial breastmilk concentration was calculated using the estimated maternal serum concentration at delivery and a breastmilk transfer factor of 0.052. Total maternal exposure during lactation was assumed to be the same as prior to delivery and was calculated by multiplying the maternal serum concentration by a clearance rate of 0.00014 L/kg per day. Model performance was evaluated using the coefficient of determination (R^2) from linear regression of predicted versus measured infant serum levels. A comparison of predicted to the estimated measured infant serum concentrations at 6 months of age produced an R^2 of 0.7044 (Fig. 5). On average, model predictions slightly (<10%) overestimated PFOA levels.

Mogensen and colleagues estimated or measured serum concentrations of PFOA in a Faroese birth cohort at delivery and 11, 18, and 60 months of age to determine the impact of breastfeeding [19]. This set of data is less optimal than Fromme for evaluating model performance for a variety of reasons, including the time interval between cessation of breastfeeding and serum sampling (see Supplemental Information). WebPlotDigitizer allowed estimation of serum concentrations for PFOA at birth and at 11 months of age from curves for 11 children, who were at least partially breastfed (as presented in Mogensen's Fig. 1 [19]). Two comparisons were conducted: (1) magnitude of relative change in infant serum concentrations from birth to 11 months of age and (2) modeling of individual infant serum concentrations after 11 months of breastfeeding. The magnitude of relative change predicted by the MDH model aligned well with the middle to upper range of the relative changes in measured serum concentrations from birth to 11 months of age for the 11 children (Figure S1). The mean and 95th percentile of predicted serum concentrations at 11 months of age aligned well with the reported values, differing by <10% (see Supplemental Information).

Transfer of PFOA to infants via breastmilk decreases maternal serum concentrations while increasing infant serum concentrations. Consequently, the concentration of PFOA in breastmilk also decreases over the course of lactation as a portion of the mother's body burden is transferred to the infant. Based on empirical data, Thomsen and colleagues studied the impact of breastfeeding on PFOA breastmilk concentrations in 10 Norwegian mothers [21]. This study estimated a decrease of 7.7% in breastmilk concentration per month of breastfeeding, which corresponds to a decrease of approximately 47% over 6 months. Empirical data from other sources [8, 22] support Thomsen's observations, as well as results from MDH's model that indicates a 40 or 52% decrease over 6 months of breastfeeding using a mean or upper percentile breastmilk intake rate, respectively.

Use of model to derive HBGV

The model developed by MDH predicts serum concentrations over a person's lifetime arising directly and/or indirectly (e.g., breastmilk) from water intake. Exposure sources other than ingestion of water are taken into account through the use of an RSC, which allocates a fraction of the RfD to water exposures and the remaining portion to other sources. In the case of PFOA, selection of the appropriate RSC must recognize PFOA's long elimination half-life. This extended half-life means that past exposures, even ones of short duration, impact contemporary serum concentrations. In addition, the transgenerational transfer from mother to child is also an important factor when selecting the appropriate RSC.

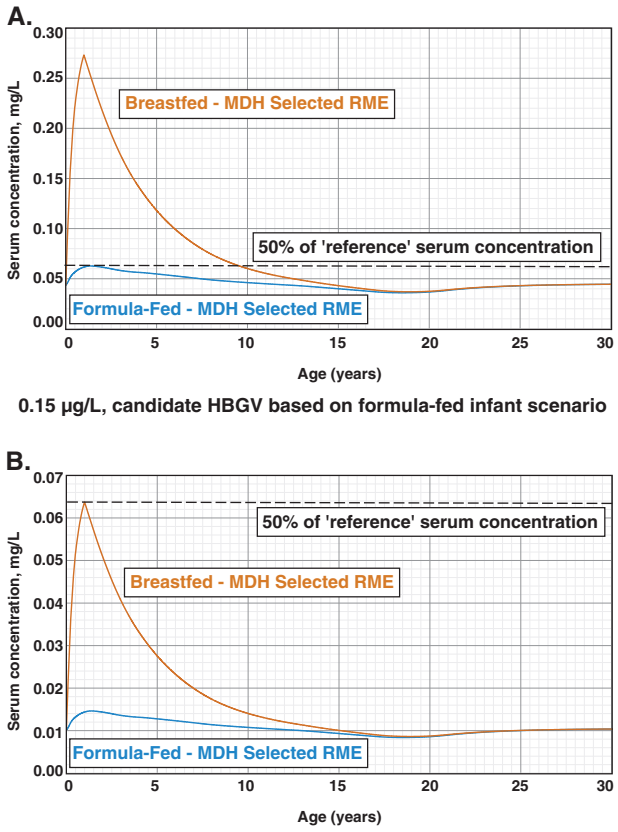

Fig. 6 Candidate HBGVs based on PFOA serum concentrations for (**a**) 0.15 µg/L, formula-fed or (**b**) 0.035 µg/L, breastfed scenarios. Note different scale is used for serum concentration in **a** (0–0.3 mg/L) than **b** (0–0.07 mg/L). (Horizontal scale truncated at 30 years to enhance detail)

Biomonitoring data from the National Health and Nutrition Examination Survey (NHANES) [23] and the Minnesota East Metro PFC Biomonitoring projects [24], provide high-quality data on PFOA serum concentrations in two relevant populations. Given the long half-life of PFOA, these results can be compared with the 'reference' serum concentration of 0.13 mg/L to provide insight into the magnitude of non-water exposures. It should be noted that the 'reference' serum concentration is based on population-based parameters and should not be used for clinical assessment or for interpreting serum levels in individuals.

The most recent NHANES biomonitoring data (2013–2014) provides an estimate of serum levels in the US general population of individuals over 12 years of age [23]. NHANES reported a 95th percentile serum concentration of 0.00557 mg/L. Biomonitoring data (2014) for a group of East Metro adult residents who moved into the affected area after a treatment system was installed on the public water supply (i.e., newer residents to the area), show a similar 95th percentile serum value (0.005 mg/L) [24]. Although data for infants are very limited, there are publications regarding serum levels in young children [25–27]. These publications indicate that the 95th percentile values in young children are similar to adult levels. Therefore, available data support the use of 95th percentile values from NHANES and the East Metro newer residents as conservative estimates of non-water ingestion routes of exposure.

MDH uses USEPA's Exposure Decision Tree methodology [28] to identify an appropriate RSC by subtracting the serum level associated with non-water exposures from the 80% ceiling level ([0.13 mg/L × 0.8] – 0.00557 mg/L = 0.0984 mg/L). This value is approximately 75% of the 'reference' serum concentration and represents a residual or maximum serum level that can be apportioned to exposure via ingestion of water. Therefore, an appropriate RSC would be >50% but <80%. Given the limited information regarding non-water exposures in the population of concern (i.e., infants), MDH selected an RSC of 50% for PFOA water ingestion. The resulting serum concentration allocated or 'allowed' to result from ingestion of water was 0.065 mg/L ('reference' serum concentration of 0.13 mg/L × 0.5). MDH used the model iteratively to identify the water concentration that resulted in a stable or steady-state serum concentration at or below 50% of the 'reference' serum concentration (0.065 mg/L) for each of the two RME scenarios shown in Fig. 2.

The water concentration that maintained a PFOA serum concentration at or below 0.065 mg/L throughout life for the formula-fed infant MDH RME scenario was 0.15 µg/L (Fig. 6a). This water concentration, when used in the breastfed infant MDH RME scenario, exceeded the 'reference' serum concentration (0.13 mg/L) for >4 years and exceeded 50% of the 'reference' serum concentration for >9 years. In order to maintain a PFOA serum concentration at or below 0.065 mg/L, the water concentration had to be lowered to 0.035 µg/L (Fig. 6b). Model simulations using various breastfeeding scenarios that combined different central tendency and upper percentile values for the most sensitive parameters were also assessed (see Table 2) using a water concentration of 0.035 µg/L to ensure that the RME scenario selected by MDH was sufficiently protective.

The peak serum concentrations for the alternative scenarios ranged from 68% to 96% of the peak serum concentration predicted using the RME scenario selected by MDH (Fig. 7). Based on these results, MDH set final the HBGV for PFOA at 0.035 µg/L, to ensure protection of all segments of the population.

Discussion

MDH derives HBGVs that are protective of the general population, including sensitive and more highly exposed

Table 2 Selection of different central (e.g., mean) and upper (e.g., 95th percentile) parameter values for alternative scenario evaluation

Scenario	Intake rate	Breastfeeding duration	Half-life	Transfer rates	Volume of distribution (V_d)	V_d adjustment factor
MDH RME	Upper	Upper	Central	Central	Central	Central
Alternative 1	Central	Central	Upper	Upper	Central	Central
Alternative 2	Upper	Central	Upper	Central	Central	Central
Alternative 3	Central	Upper	Upper	Central	Central	Central

See Table 1 for actual numerical values used for each parameter

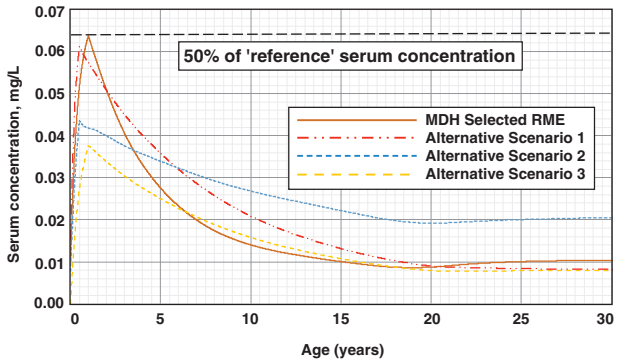

Fig. 7 Comparison of MDH selected RME breastfeeding scenario with alternative parameter selection scenarios

populations. Addressing higher water intake rates during early life has been integrated into MDH's current methodology for deriving HBGVs since 2008 [1]. This peer reviewed and promulgated methodology, however, does not address the significant placental and breastmilk transfer and bioaccumulation potential of PFOA. Recent studies have reported compelling evidence that breastfeeding has a significant impact on PFOA serum levels in both nursing infants and their mothers. Empirical data have demonstrated that infant PFOA serum concentrations are higher than those of older individuals exposed to the same contaminated drinking water source [29] and that breastfeeding results in lower PFOA serum concentrations in women and higher concentrations in infants and young children [30]. Despite these observations, PFOA drinking water guidance values derived by other government agencies are typically based on attainment of steady-state serum concentrations from constant exposure over a duration sufficient to achieve steady state (e.g., approximately five half-lives). If this traditional approach were to be used with MDH's 2017 RfD (0.000018 mg/kg day), RSC (0.5) and a 95th percentile time-weighted average intake rate of 0.064 L/kg per day from birth to 11.5 years of age (half-life of 2.3 years × 5 half-lives to attain steady state), it would result in an HBGV of 0.14 µg/L. This value would be sufficiently protective for formula-fed infants but would be fourfold higher than the water concentration predicted to be protective for breastfed infants. To our knowledge, MDH is the first agency to develop PFOA water guidelines that directly incorporate early life exposure via placental transfer and via breastfeeding.

MDH model parameters have been carefully selected based on the best available science, external peer review comments, and departmental policy. A formal sensitivity analysis of the model was not conducted, however, the limited number of parameters and single-compartment nature of the model lends itself to straightforward decision-making based on the fit-for-purpose concept. Empirical data and modeling studies suggest that half-life, transfer factors, breastfeeding duration, and intake rate are among the most important (impactful) parameters [12]. The current MDH model was evaluated by direct comparison with limited empirical data, which found good agreement. Published pharmacokinetic models also exist and have noted similar dynamics of breastfeeding being a significant source of exposure and early life predicted as having a higher potential for greater serum concentrations of PFOA [11, 12]. Additionally, MDH sought informal input from six external experts regarding the adequacy (e.g., fit-for-purpose) of the model prior to deriving PFOS and PFOA HBGVs in 2017 [16]. Reviewers were not explicitly asked to endorse or approve of the final model. The reviewers' consensus was that the model was fit-for-purpose, but subject to uncertainties and data gaps that are common to models of this type.

Although PFOA, PFHxS, and PFOS can be excreted through breastmilk, MDH recognizes the important short- and long-term health benefits of breastfeeding for both mother and infant. MDH used an RME scenario to generate HBGVs. An RME scenario depicts a data-driven, realistic, but high-end exposure situation to ensure that even the most heavily exposed individuals within the population will be protected. MDH recommends that women currently breastfeeding, and pregnant women who plan to breastfeed, continue to do so. Exclusive breastfeeding is recommended by doctors and other health professionals for the first 6 months. It is unlikely that potential health concerns from infant PFOA exposure exceed the known benefits of breastfeeding. Application of MDH's revised HBGVs will ultimately result in lower body burdens and breastmilk concentrations of PFOA so that infants can receive the optimal benefits from breastfeeding.

Among PFAS, PFOA has the largest epidemiological database and, as indicated by serum levels, has been associated with multiple health endpoints, including elevated cholesterol and other serum lipid parameters, as well as liver enzymes, changes in thyroid serum levels and increased incidence of thyroid disease, increased risk of preeclampsia, reduced antibody response, and reduced birth weight [31, 32]. MDH's 'reference' serum concentration is based on laboratory studies where the animals were exposed only to PFOA. These studies found PFOA exposure to cause a variety of health effects, including developmental effects, hepatic toxicity (e.g., effects on lipid metabolism), changes in thyroid hormone levels, and immune system effects. For the human population, where serum is known to contain multiple PFAS, causality has not been established in epidemiological studies. However, consistency of findings across epidemiological studies and concordance with laboratory animal studies raises the level of concern.

PFAS commonly co-occur in drinking water and may have additive health effects. When multiple substances are present, MDH recommends evaluating the potential risk from the combined exposure. Evaluating a mixture of chemicals, based solely on individual HBGVs, may not provide an adequate margin of safety. MDH uses an additive approach, in which chemicals that share a common health endpoint (e.g., liver, developmental) are evaluated together [33]. For each chemical sharing a health endpoint, a ratio of the water concentration of the chemical and the corresponding HBGV is calculated. The ratios are then summed to calculate a health risk index, with any health risk index greater than one receiving further scrutiny.

MDH first released HBGVs for PFOS and PFOA in 2002, PFBA in 2008, and PFBS in 2009. The science regarding PFAS continues to evolve at a rapid pace and MDH has revised their HBGVs several times, most recently in 2017. Currently, six community public water supplies in Minnesota have individual wells above the 2017 revised values. Over 800 homes with private wells have received drinking water well advisories, resulting in either connection to city water or whole-house granular activated carbon filters, which are maintained by the state of Minnesota. Biomonitoring of exposed residents has also been conducted and has demonstrated the effectiveness of treatment systems in reducing or eliminating drinking water exposures to PFAS [34].

Recent estimates conclude that at least 16.5 million people in 36 U.S. states and territories are exposed to PFAS contaminated drinking water, based on USEPA UCMR3 (Unregulated Contaminant Monitoring Rule 3) [32]. It is highly likely that the number of people exposed is higher since this estimate is based on testing of all large (serving > 10,000 people) public water supplies, a limited number of small water supplies, no private drinking water wells, and only six PFAS chemicals. The Minnesota experience with PFAS reinforces a critical need to examine private drinking water wells, while the Organization for Economic Cooperation and Development (OECD) has recently published an updated comprehensive list of over 4700 PFAS-related CAS numbers on the global market [35]. Drinking water surveillance activities are expanding beyond the six PFAS chemicals included in USEPA UCMR3 (PFBS, PFHxS, PFOS, PFOA, perfluorononanoic acid, and perfluoroheptanoic acid), and analytical detection limits continue to improve. Although the national spotlight has only recently been cast upon PFAS in drinking water, based on Minnesota's decade and a half of experience, concerns regarding these chemicals as groundwater contaminants are likely to persist and grow in prominence.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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ENVIRONMENTAL HEALTH

RESEARCH Open Access

Immunotoxicity of perfluorinated alkylates: calculation of benchmark doses based on serum concentrations in children

Philippe Grandjean[1,2*] and Esben Budtz-Jørgensen[3]

Abstract

Background: Immune suppression may be a critical effect associated with exposure to perfluorinated compounds (PFCs), as indicated by recent data on vaccine antibody responses in children. Therefore, this information may be crucial when deciding on exposure limits.

Methods: Results obtained from follow-up of a Faroese birth cohort were used. Serum-PFC concentrations were measured at age 5 years, and serum antibody concentrations against tetanus and diphtheria toxoids were obtained at age 7 years. Benchmark dose results were calculated in terms of serum concentrations for 431 children with complete data using linear and logarithmic curves, and sensitivity analyses were included to explore the impact of the low-dose curve shape.

Results: Under different linear assumptions regarding dose-dependence of the effects, benchmark dose levels were about 1.3 ng/mL serum for perfluorooctane sulfonic acid and 0.3 ng/mL serum for perfluorooctanoic acid at a benchmark response of 5%. These results are below average serum concentrations reported in recent population studies. Even lower results were obtained using logarithmic dose–response curves. Assumption of no effect below the lowest observed dose resulted in higher benchmark dose results, as did a benchmark response of 10%.

Conclusions: The benchmark dose results obtained are in accordance with recent data on toxicity in experimental models. When the results are converted to approximate exposure limits for drinking water, current limits appear to be several hundred fold too high. Current drinking water limits therefore need to be reconsidered.

Keywords: Benchmark dose, Developmental exposure, Immunotoxicity, Perfluorinated compounds, Risk assessment

Background

Perfluorinated compounds (PFCs) have been in use for over 60 years in a wide array of applications. PFCs were first manufactured in the US from about 1947, with perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) as primary products [1]. PFC was later found to contaminate ground and surface water, and PFOS was found to accumulate in freshwater fish [2]. These compounds possess a strong carbon-fluorine bond, which leads to persistence of the PFCs in the environment and the human body [2]. Thus, the high thermal, chemical and biological inertness that make the PFCs useful for many industrial purposes at the same time also generates an environmental hazard.

Serum-PFC analyses conducted by the Centers for Disease Control and Prevention (CDC) show that PFOS and PFOA are detectable in virtually all Americans [3], with children often showing higher serum concentrations than adults [4]. Analyses of paired samples of maternal serum and cord serum show that PFCs are transferred through the human placenta [5,6]. Due to global dissemination of PFCs, their serum concentrations in children and pregnant women even in the remote locations, such as the Faroe Islands [7], are similar to US levels. Exposures to some PFCs in the Faroes may occur primarily through marine diets [8]. Despite the extensive use of these compounds for many decades, and the persistence and

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cumulative properties of the PFCs, the toxicology data base is still incomplete and has allowed only preliminary risk assessments so far.

Using animal toxicity data, calculations of benchmark dose levels (BMDLs) have been carried out for a 10% deviation relative to control values (i.e., a Benchmark Response or BMR of 10%); they resulted in serum concentrations of 23 mg/L and 35 mg/L for PFOA and PFOS, respectively [9-11]. Toxicokinetic modeling and standard assumptions about water intake then allow derivation of acceptable drinking water levels [11,12]. So far, the U.S. Environmental Protection Agency (EPA) has issued a draft risk assessment of PFOA in 2005, but no final version has yet been published, nor has a Reference Dose (RfD) been defined. However, the EPA has issued provisional health advisories of 0.4 μg/L (400 ng/L) for PFOA and 0.2 μg/L (200 ng/L) for PFOS in drinking water [13]. Similarly, the Agency for Toxic Substances and Disease Registry concluded in its draft toxicological profile in 2009 that there was insufficient evidence at the time to develop a minimal risk level [1]. For chronic exposure, state authorities have issued limits for PFC concentrations in drinking the water, e.g., in Minnesota [14], where the limit for both PFOS and PFOA is 0.3 μg/L (300 ng/L). The limits were based on PFOS effects on the liver and thyroid, and PFOA effects on the liver, fetal development, reduction in red blood cell numbers, and immune system changes in experimental studies [11]. A lower guidance limit of 0.04 μg/L (40 ng/L) has been determined for PFOA by the state of New Jersey [15]. Other agencies, such as the European Food Safety Authority [16] have recommended similar exposure limits that relied on the same toxicology data while using different default assumptions.

PFC toxicity in animal models at first suggested the liver as a main target organ, but so far chronic toxicity data only in the rat have been published [1,12,17,18]. However, recent evidence suggests that toxicology outcomes used in derivation of exposure limits may not represent the most sensitive endpoints. Thus, interference with mammary gland development in mice with developmental exposure seems to occur at low exposures; benchmark dose calculations using a variety of models showed that a 10% BMR corresponded to a serum-based BMDL for PFOA of 23–25 μg/L (or ng/mL) [12,17]. This BMDL differs by a factor of 1,000 from the previously mentioned BMDL based on liver toxicity (i.e., 23 mg/L or 23,000 μg/L). Thus, current limits for PFOA in drinking water based on the latter value may not be as protective as intended, despite the use of uncertainty factors.

Likewise, immunotoxicity of PFCs has been demonstrated in rodent models, avian models, reptilian models, and mammalian and nonmammalian wildlife [19]. For example, in a commonly used mouse model, PFOA effects include decreased spleen and thymus weights, decreased thymocyte and splenocyte counts, decreased immunoglobulin response, and changes in specific populations of lymphocytes in the spleen and thymus. Reduced survival after influenza infection has also been reported as an apparent effect of PFOS exposure in mice [20]. Another study found that the lowest observed effect level (LOEL) for males corresponded to an average serum-PFOS concentration of 92 ng/g (about 94 μg/L), though 7-fold higher in females [21]. The LOEL serum concentration in males is similar to typical levels found in serum samples from subjects exposed to contaminated drinking water [22].

Given the concern about immunotoxicity as a possible critical effect [19] and the possibility of developmental toxicity [23], studies in child populations have recently focused on antibody responses to childhood immunizations as a clinically relevant parameter that reflects major immune system functions [24]. The subjects have all received the same doses of vaccine antigens at the same ages and can then be examined at similar ages, i.e., similar intervals after the most recent vaccination [25]. Our studies focused on the fishing community of the Faroe Islands [8], and these prospective population data [7] seem appropriate for calculating benchmark doses as a contribution to future risk assessments.

While benchmark dose calculations from toxicology data are fairly straightforward, using epidemiological studies can be more complicated due to the need for covariate adjustments [26]. In addition, decisions on dose–response models may be crucial, as a null exposure group is usually not available, thus requiring extrapolations beyond the exposure interval observed.

Methods

A birth cohort in the Faroe Islands was recruited and consisted of 656 consecutive singleton births from late 1997 to early 2000. Prospective follow-up included 587 cohort members participated in one or both examinations at ages 5 and 7 years [7], of whom 460 participated on both examinations, and complete data with serum analyses were obtained for 431. As exposure indicator, we used the PFC concentrations in the child's serum obtained at the clinical examination at age 5 years. The outcomes were the specific antibody concentrations against tetanus and diphtheria toxoids in serum at age 7 years. Of the PFCs, PFOS and PFOA showed the highest concentrations (Table 1), similar to levels reported from the US [3]. We also measured maternal pregnancy serum PFC concentrations, which showed strong negative correlations with antibody concentrations at age 5 years. However, we chose to focus on the PFCs in the child's serum at age 5 and their uniformly negative associations with antibody levels at age 7, as these data apparently represented the greatest sensitivity to PFC exposure so far documented and were not confounded by exposures to other environmental chemicals. The dependence of the

Table 1 Characteristics of 431 Faroese birth cohort members with complete data from examinations at ages 5 and 7 years

Variable	Result
Girl, n (%)	223 (48.5)
Birth weight, mean (SD) g	3724 (505)
Birth weight ≤ 2500 g, n (%)	3 (0.7)
Age at 5-year examnination, mean (SD) years	5.0 (0.1)
Age at 7-year examination, mean (SD) years	7.5 (0.1)
Serum-PFOS concentration at age 5, ng/mL[a]	17.3 (14.1; 21.3)
Serum-PFOA concentration at age 5, ng/mL[a]	4.06 (3.33; 4.95)
Anti-tetanus concentration at age 7, IU/mL[a]	1.80 (0.75; 4.60)
Anti-diphtheria concentration at age 7, IU/mL[a]	0.80 (0.40; 1.60)

[a] Median (interquartile range).

antibody concentrations on PFC exposures was determined by generalized additive models [27]. Written maternal consent was obtained, and the protocol was approved by the ethical review committee at the Faroe Islands and by the review board at the US institution.

Benchmark calculations

The data were analyzed as continuous variables in SAS version 9.2. Although a clinical cut-off level exists for antibody concentrations that represent long-term protection, this limit is somewhat arbitrary, and transformation of the continuous data to a dichotomous variable results in a loss of information.

Benchmark calculations were therefore based on regression models with antibody concentrations as dependent variables while PFC-concentrations were included as independent variables along with potential confounders sex, age and booster type at age 5 [7]. To achieve normally distributed residuals, antibody concentrations were log-transformed. Thus, we based models on the formula

$$\log(\text{antibody}) = \alpha_0 + \alpha_1 \times \text{sex} + \alpha_2 \times \text{age} + \alpha_3 \times \text{booster type} + f(d) + \varepsilon,$$

where d is the PFC concentration (PFOS or PFOA) measured at 5 years and f is the dose–response function satisfying $f(0) = 0$. We modeled the PFC-effect using a linear-dose response function [$f(d) = \beta \times d$], a logarithmic model [$f(d) = \beta \times \log(d + 1)$] and the so-called K-power model [$f(d) = \beta \times d^K$, $K > =1$]. As the dose–response relationship at low doses may differ from the one at higher doses, we also used a piecewise linear model, which allowed for a difference in slopes at the median exposure. Calculations were carried out for PFOS and PFOA separately. Given their close correlations, it was not possible to include mutual adjustment in the models.

The BMD is the dose which reduces the outcome by a certain percentage (BMR) compared to unexposed controls [28,29]. Several different BMR values have been used in the past, and lower BMR levels are known to result in decreased BMD results, in part because the uncertainty increases [26]. By convention, a 10% BMR is often used for experimental toxicology data [28,29]. On the other hand, a decreased antibody response to vaccinations must be regarded as an important adverse effect, thus supporting the selection of a lower BMR. Thus, in human studies, a BMR of 5% is often chosen [29]. We therefore calculated BMD results for BMR values of 5% and 10%. An advantage of a log-transformed response is that BMD can be estimated independently of the confounders as the dose where the dose–response function is equal to log(1-BMR), i.e., the BMD, will satisfy the equation f(BMD) = log(1-BMR).

As the main result of the calculations, the benchmark dose level (BMDL) is defined as the lower one-sided 95%-confidence limit of the BMD. In the dose–response models with linear parameters (linear, log and piecewise linear models), the derivation of closed form expressions for the BMDL is straight forward [30]. Based on the estimated uncertainty in the parameter estimates, the lower confidence limit of the dose-effect function [f(d)] can be determined. The BMDL is given as the dose where this confidence limit is equal to log(1-BMR). For non-linear models, the BMDL was calculated using the (iterative) profile likelihood method. The fit of the models was based on minus two times the log-maximum likelihood function (–2 log(L)), where a smaller value indicates a better fit. The low dose fit was measured by calculating -2log(L) based on children with exposures in the lowest quartile.

As a consequence of the relatively steep dose–response relationships, the BMDs were sometimes lower than the minimum observed exposure, and some results therefore depended on a part of the dose–response curve, for which the data does not hold any information. As a sensitivity analysis, we therefore developed a low-dose threshold version of each of the dose–response models used. Each of these models was identical to the original dose–response model within the observed dose range, but with a flat dose–response slope below the lowest dose observed (Figure 1).

Results

Descriptive results are shown in Table 1. Children who participated in one clinical examination, but not the other, did not seem to differ in terms of exposure levels and antibody concentrations from those cohort subjects who participated in both examinations.

Generally, the log model yielded lower BMDs, but only for the PFOS did these results provide a (marginally) better fit than the linear slope (Table 2). The model-dependence was similar for tetanus and diphtheria antibody concentrations as outcome variables. When using the linear slope and a BMR of 5%, the BMDL was about 1.3 ng/mL and

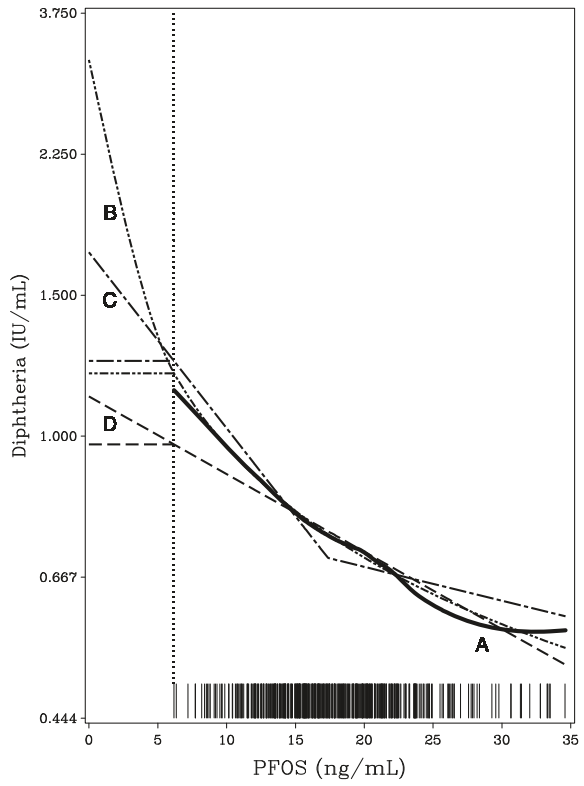

Figure 1 Estimated dose–response functions for the relationship between PFOS and the diphtheria-antibody concentration. Curve A is estimated as a generalized additive model. **Curve B** is the log-function, **C** is piecewise linear, and **D** is linear. The low-dose threshold models (see Table 3) assume a flat curve below the lowest observed dose indicated by the dotted vertical line, i.e., that a threshold exists at the lowest serum-PFOS concentration observed. The bars on the horizontal scale indicate the serum-PFOS concentration of each participating cohort member.

0.3 ng/mL for PFOS and PFOA, respectively. The piecewise linear curve showed BMDL results about half the level of the linear dose–response curve, while the logarithmic curve showed even lower results. In the K-power model, the power parameter was estimated to one, and this model was therefore identical to the linear model. As expected, results were higher at a BMR of 10%.

All dose–response models had normally distributed residuals with a homogeneous scatter. The piecewise linear generally had the closest fit, but it was not significantly better than the alternative models. For the association between PFOS and the diphtheria antibody concentration, Figure 1 illustrates the agreement between the different models within the observed data range. The linear function is less steep at the low doses, which explains why this model yields higher benchmark results.

Using the low-dose threshold models with a flat dose–response below the lowest observed exposure levels, the BMDL results for the linear curve were about 5-fold higher than for the non-threshold curve (Table 3). The low-dose threshold results for both the piecewise and the logarithmic curves approximated those obtained using a linear slope.

Discussion

The present report presents the first benchmark dose results for human PFC exposure. It relies on serum-PFC measurements at age 5, and serum concentrations of specific antibodies two years later as clinically relevant measures of immune functions. The size and homogeneity of the study population and the high participation rate are major strengths [7]. The associations that appeared the strongest were selected for BMD calculations. Although this selection was not based on an *a priori* hypothesis and therefore could result in bias, structural equation model analyses suggest that the overall effects of PFCs on antibodies were stronger than most individual effects [7]. Concomitant exposure to PCBs did not cause any important confounding. We included age and sex as covariates, but they affected the results to a negligible degree only.

However, a weakness is the close correlation between PFOA and PFOS, which makes mutual PFC adjustment difficult. Structural equation models suggest that the joint effects of major PFCs were stronger than those that could be ascribed to single compounds [7], and it is therefore possible that each of the major PFCs contribute to the effects. Given the strong experimental support for immunotoxicity of both PFOA and PFOS [19], the BMD levels would seem to provide approximate levels of concern for human exposures.

The choice of dose–response models is known to result in different BMD results from epidemiological studies, where unexposed controls are often missing [26]. In the absence of prior knowledge regarding the shape of the curve, we used two common curve shapes (linear and logarithmic) to explore the dependence of the data on these two assumptions. The two curves fit the data equally well, and no statistical justification is therefore available for choosing one set of results above the others. The linear curve is often used as a default, and we therefore further examined a model with a piecewise linear shape and one with a flat slope below the lowest observed level of exposure. For each of the two PFCs, these sensitivity analyses showed that the BMDL results remained low. As anticipated, the 5% BMR results in BMDL values somewhat below those for 10%, but differences between the curve shapes were not smaller at an increased BMR.

The vaccine-specific antibody concentrations used in our recent study [7] are thought to represent sensitive immunotoxicity parameters. Other clinical outcome measures may be less sensitive. For example, hospitalization of 363 children up to an average age of 8 years for infectious diseases (such as middle ear infection, pneumonia, and appendicitis) was not associated with PFOS and PFOA

Table 2 Benchmark results for postnatal PFC exposure (in terms of serum concentrations in ng/mL measured at 5 years) with vaccine antibody concentrations at 7 years as the outcomes

			BMR = 5%		BMR = 10%		Fit (−2log(L))	
Outcome	**Exposure**	**Model***	**BMD**	**BMDL**	**BMD**	**BMDL**	**Full scale**	**Low dose**
Tetanus	PFOS	Linear	2.70	1.31	5.55	2.69	1719.81	313.78
		Log	0.13	0.07	0.29	0.14	1719.30	313.75
		Piecewise	1.45	0.56	2.98	1.16	1719.54	313.54
	PFOA	Linear	0.38	0.25	0.77	0.51	1712.43	391.53
		Log	0.07	0.04	0.14	0.09	1712.88	391.63
		Piecewise	0.52	0.16	1.07	0.34	1712.33	391.64
Diphtheria	PFOS	Linear	2.30	1.25	4.72	2.57	1656.86	314.00
		Log	0.11	0.06	0.24	0.13	1655.96	313.38
		Piecewise	0.98	0.49	2.01	1.01	1655.77	313.10
	PFOA	Linear	0.59	0.33	1.21	0.68	1656.15	362.37
		Log	0.10	0.06	0.22	0.12	1656.14	362.39
		Piecewise	0.48	0.17	0.99	0.34	1656.12	362.30

*K-power model was identical to the linear model.

concentrations in serum from pregnant women from the Danish National Birth Cohort [31]. Multiple social, demographic and other factors may have affected these results, and hospitalization does not seem to be a sensitive or appropriate test of the presence of immune system dysfunction. In adults exposed to PFOA through contaminated drinking water, the serum-PFOA concentration was associated with lower serum concentrations of total IgA, IgE (in females only), though not IgG [32]. Although confirmation from other human studies is therefore lacking so far, experimental studies offer support that specific immunoglobulin concentrations may be sensitive indicators of immune system dysfunctions [19].

Interaction with peroxisome proliferator-activated receptors (PPARs) may be involved in the immunotoxic mechanisms [1,19]. While human PPARα expression is significantly less than that of rodents, current evidence suggests that both PPARα-dependent and -independent pathways may be relevant to PFC immunotoxicity [33]. In human white blood cells *in vitro*, mechanistic studies of PFC-induced suppression of cytokine secretion demonstrated that PPARα activation was involved in the PFOA-induced immunotoxicity, while other pathways appeared responsible in regard to the effects of PFOS [34]. White blood cells from human volunteers showed effects at PFOS concentrations in the medium of 0.1 μg/mL (100 ng/mL), which was the lowest concentration tested [35]. This level is similar to concentrations seen both in affected male mice [21] and in subjects exposed to contaminated drinking water [22].

Table 3 Results of sensitivity analyses using low-dose threshold models with no effect below the lowest observed exposures

		BMR = 5%		BMR = 10%	
Outcome/Exposure	**Model**	**BMD**	**BMDL**	**BMD**	**BMDL**
Diphtheria/PFOS	Linear	8.48	7.43	10.90	8.75
	Log	6.96	6.62	7.89	7.11
	Piecewise	7.16	6.67	8.19	7.19
Tetanus/PFOA	Linear	1.70	1.57	2.10	1.83
	Log	1.48	1.43	1.65	1.53
	Piecewise	1.85	1.49	2.40	1.66

Benchmark results for serum concentrations (in ng/mL) measured at 5 years in regard to vaccine antibody concentrations at 7 years. Results are given for the exposures and outcomes showing the lowest results in Table 1.

Based on both experimental and human studies, an approximate BMDL of 1 μg/L would seem to be an appropriate order of magnitude for calculation of exposure limits for the PFCs. As the BMDL assumes equal sensitivity within the population studied, current guidelines [28,29] require that the BMDL be divided by an uncertainty factor of 10 to take into account the existence of subjects with increased vulnerability. A concentration of about 0.1 ng/mL could then be used as the serum-based RfD for the PFCs (somewhat higher for PFOS and lower for PFOA).

Using mammary gland development as a sensitive outcome in experimental studies [17], a BMDL of about 23 ng/mL serum was calculated for PFOA [12]. Taking into account interspecies differences in vulnerability and using a total uncertainty factor of 30, an RfD of 0.8 ng/mL serum would be derived from this BMDL. Thus, although referring to a different endpoint, this calculation is in good accordance with the one estimated from our epidemiological data.

A serum-based RfD less than 1 ng/mL for PFOS and PFOA would be below most concentrations reported in

recent studies [3,7,31]. Importantly, estimated RfD values below 1 ng/mL are at least 100-fold below those used for calculation of current water contamination limits. PFOA concentrations in drinking water are known to correlate with the serum concentrations of long-term residents in Ohio and West Virginia at an approximate ratio of about 1:100 [12,15,36]. Thus, from these data, a serum-based RfD of 0.1 ng/mL can be translated to a water concentration of 1 ng/L, or 0.001 μg/L (assuming that no other sources contributed to the PFOA exposure). The current EPA limit for this PFC is 300-fold higher. Thus, the recent evidence on PFC immunotoxicity in humans and toxicity in animal models suggests that current limits for drinking water contamination are too permissive and must be decreased substantially.

Conclusions

BMDL results were about 1.3 ng/mL serum for PFOS and 0.3 ng/mL serum for PFOA at a benchmark response of 5%. Lower values were obtained with the logarithmic curve, and higher results with a larger benchmark response. The BMDL results are in accordance with recent data on toxicity in experimental models. When converted to approximate exposure limits for drinking water, current limits appear to be several hundred fold too high. Current drinking water limits therefore need to be reconsidered in the light of the observed immunotoxicity associated with PFC exposure.

Abbreviations

BMD: Benchmark dose; BMDL: Benchmark dose level, i.e., the lower 95% confidence limit for the BMD; BMR: Benchmark response; EPA: Environmental Protection Agency; LOEL: Lowest observed effect level; log: Natural logarithm; PFC: Perfluorinated compound; PFOA: Perfluorooctanoic acid; PFOS: Perfluorooctane sulfonic acid; PPAR: Peroxisome proliferator-activated receptor; RfD: Reference Dose.

Competing interests

PG is editor-in-chief of this journal, but was not involved in the editorial handling of this manuscript. The authors declare that they have no competing interests.

Authors' contributions

PG performed the literature review and drafted the manuscript. EBJ carried out the benchmark analyses and commented on the interpretation. Both authors contributed to, read, and approved the final version.

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