Per- and Poly-fluorinated Alkyl Substances (PFAS):
Summary and Introductory Information
DRAFT

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Overview

The per- and poly-fluorinated alkyl substances (PFAS) constitute a large category of chemicals, all of which share certain characteristics of concern. The SAB has reviewed the science on PFAS of several chain lengths. This document provides a brief overview of PFAS, including information on the scientific information reviewed by the SAB to date. This document is an introduction, and is not exhaustive.

PFAS have been studied in detail by a number of authoritative bodies, including the Organisation for Economic Co-operation and Development (OECD). Therefore, the TURA program will make use of existing documentation on the topic wherever possible.

Category description

The following is a description of the broad chemical category of PFAS. This is an approach to organizing chemicals that have similar chemical features, not a description of a proposed regulatory category.

An OECD study identified over 4,700 PFAS-related CAS numbers. OECD has developed a broad categorization of the PFAS, dividing them into perfluoroalkyl/per- and polyfluoroalkylether acids (PFAAs), PFAA precursors, and other PFASs. For convenience and clarity within the present document, TURI uses the following broad terms for subcategories of PFAAs: "carboxylic and sulfonic acids," "phosphonic and phosphinic acids," and "ethers."

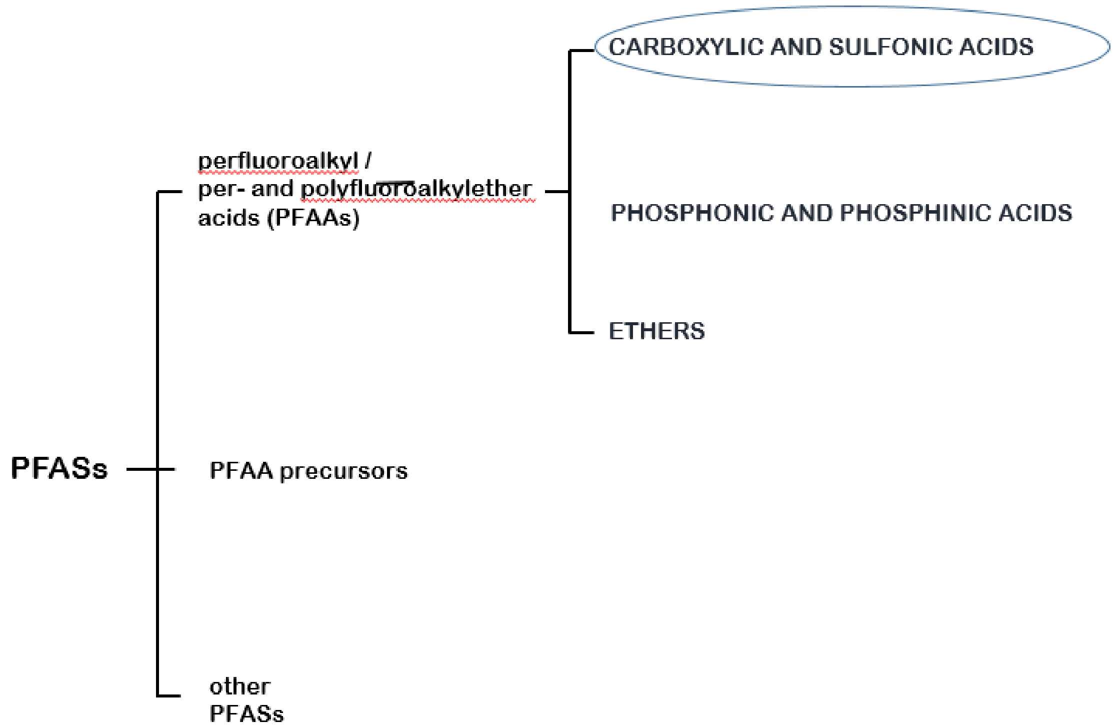
- **PFAAs.** The PFAAs are further separated into sub-groups: the carboxylic and sulfonic acids (perfluoroalkyl carboxylic acids [PFCAs], perfluoroalkane sulfonic acids [PFSAs]) the phosphonic and phosphinic acids (perfluoroalkyl phosphonic acids [PFPAs], perfluoroalkyl phosphinic acids [PFPiAs]), and the ethers (per- and polyfluoroether carboxylic and sulfonic acids [PFECAs and PFESAs]). This grouping is shown below in simplified form in Figure 1, and with additional detail in Appendix A.
- **PFAA Precursors.** The PFAA precursors are chemicals that break down into the PFAAs.
- **Other PFAS.** The category of "other PFASs" includes fluoropolymers. These can be used as solid resins as well as emulsions of low molecular weight polymers.

Note: PFAS are often identified by the length of the fluorinated carbon chain. For example, C8 refers to an 8-carbon alkyl chain. OECD and EPA have also developed an approach to categorizing PFAS into "long chain" and "short chain."[1]

[1] For details on naming conventions, see ITRC. "Naming Conventions and Physical and Chemical Properties of Per- and Polyfluoroalkyl Substances (PFAS), available at https://pfas-1.itrcweb.org/wp-content/uploads/2018/03/pfas_fact_sheet_naming_conventions__3_16_18.pdf.

The SAB's work to date has focused on the PFAAs. Within this category, the science described in this document refers to the carboxylic and sulfonic acids, which have been widely identified as contaminants in the environment. The SAB plans to examine one or more of the ethers (PFECAs and PFESAs) and the phosphonic/phosphinic acids next.

Figure 1: Overview of PFAS



Note: The SAB's work to date has focused on the carboxylic and sulfonic acids, circled in this diagram.

Summary of Scientific Information: PFAAs

The present summary focuses only on the PFAAs as this has been the SAB's focus to date. More specifically, the SAB has to date only focused on the carboxylic and sulfonic acids (circled in Figure 1, above).

Summary. In general, the chemicals that the SAB has reviewed are characterized by very high persistence in the environment; they do not break down under normal environmental conditions. In addition, all of these chemicals pose some degree of bioaccumulation concern, especially in air breathing organisms. The longer-chain chemicals are the most bioaccumulative, but the shorter-chain chemicals also bioaccumulate, at least in plants. Key health endpoints of concern include effects on the endocrine system, including liver and thyroid, as well as metabolic effects, developmental effects, neurotoxicity, and immunotoxicity. Some of these health endpoints have been documented for multiple chemicals that the SAB reviewed. Other health effects have been documented for only one or two chemicals, but are highlighted here because they have been found in a large number of studies.

SAB approach. In order to understand the characteristics of a range of PFAAs, the SAB examined eight substances of varying chain lengths: PFNA (C9); PFOS and PFOA (C8); PFHpA (C7); PFHxA and PFHxSs (C6)[2]; and PFBA and PFBS (C4).

TURI conducted a literature review for all of these chemicals. The SAB reviewed this literature for all except PFOS and PFOA. It was not necessary to review the literature on PFOS and PFOA as their hazards are well understood and they have been studied by authoritative bodies. PFOS and PFOA were recommended for listing due to authoritative PBT data, so the literature on these substances was used for context in evaluating other substances. In addition to considering primary research publications, the SAB was able to draw upon analyses conducted by other states, including Minnesota and New Jersey, among others.

PFAAs are highly persistent and do not break down under environmentally relevant conditions. Longer-chain substances (in particular the C8 substances, PFOS and PFOA) have been studied in greater depth than shorter-chain substances.

C8 substances: In its examination of the C8 substances, the SAB found evidence of persistence, bioaccumulation, and acute toxicity. These findings were sufficient for the SAB to recommend listing these substances. In addition, the SAB was able to review the results of the C8 Health Project.[1] This project resulted from a settlement agreement related to PFOA contamination in two states. It documented a wide range of chronic human health endpoints associated with exposure to PFOA. Hazards that were documented within the C8 Health Project include carcinogenicity (probable links to kidney and testicular cancer), pregnancy-induced hypertension (PIH), ulcerative colitis, thyroid disease, and hematological effects including effects on blood cholesterol levels, among others. In addition, a report by the National Toxicology Program (NTP) notes that PFOS and PFOA are "presumed to be an immune hazard to humans." [2] This information added important additional context for understanding the range of health impacts of PFAS of other lengths as well.

C7 and lower. For the substances with fewer than eight carbons, less information was available. They are all highly persistent in the environment and have long half-lives in the human body. These substances also show some evidence of bioaccumulation and they are very mobile, creating the potential for global transport. They have been found in serum and breastmilk, and their presence in the environment creates the potential for on-going exposures. They are less acutely toxic than the C8 substances. However, the SAB's literature review found evidence of a range of chronic health effects, including immunotoxicity, thyroid, liver/metabolic effects, endocrine effects, hematological effects, neurodevelopmental effects, reproductive effects, asthma, and neurotoxicity. These substances are strong acids and are very corrosive in their concentrated form.

It is also worth noting that while the shorter-chain substances are not as bioaccumulative in air-breathing organisms as the longer-chain substances, they do bioaccumulate in plants.[34]

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[2] Note regarding the C6 molecules: EPA classifies PFHxS along with PFOS and PFOA as a long-chain PFAS, while PFHxA is classified with the shorter-chain PFAS.

It is also helpful to understand that while bioaccumulation is often assessed through studies of fish, in the case of PFAS, this approach is less relevant. PFAS bind to proteins, not to lipids, so they accumulate in blood serum, rather than in fatty tissue. In addition, gill-breathing organisms are more able to eliminate PFAS due to their water solubility, while air-breathing organisms are more vulnerable to bioaccumulation.[5]

Table 1 shows the information reviewed by the SAB regarding chronic health effects. For additional information, see Appendix B. Note that for PFNA and PFHpA, at the time of drafting this document, the SAB has not yet finished its examination of these substances.

Table 1: Chronic health effects

	PFNA*	PFOA	PFOS	PFHpA*	PFHxA	PFHxS	PFBA	PFBS
Cancer		Kidney, testicular						
Immunotoxicity		Ulcerative colitis	X					X
Thyroid		X			X	X	X	X
Endocrine (other than thyroid)					X	X	X	X
Hematological		Cholesterol				X	X	X
Liver/metabolic				X	X	X	X	X
Reproductive		PIH						
Developmental	X			X	X		X	X
Neurodevelopmental						X		
Neurotoxicity	X				X	X		X
Asthma						X		X
Other	Mutagenicity				Kidney			Kidney

Note: The SAB did not conduct a literature review for PFOS and PFOA due to the volume of information available through authoritative bodies and large scale epidemiological studies. Therefore, the endpoints shown for PFOA are not identical to those shown for the other chemicals. For PFOS, the SAB was able to use information from NTP so literature review of additional studies was not necessary.
* SAB examination of data still in process.

Table 2 shows the information reviewed by the SAB regarding the presence of PFAS in the environment, including presence in groundwater and surface water, as well as their potential for persistence and bioaccumulation. Again, note that for PFNA and PFHpA, the SAB's work has not yet been completed.

Table 2: Persistence, presence in the environment, and bioaccumulation

	PFNA*	PFOA	PFOS	PFHpA*	PFHxA	PFHxS	PFBA	PFBS
Persistence	X	X	X	X	X	X	X	X
Bioaccumulation	X	X	X	X	X	X	X	X
Presence in the environment	X	X	X	X	X	X	X	X
Presence in biota, including humans	X	X	X	X	X	X	X	X

Information on these chemical properties is drawn from peer reviewed studies and from US or EU government documents. PFOS and its salts and perfluorooctanyl sulfonyl fluoride are designated as Persistent Organic Pollutants under the Stockholm Convention; PFOA, its salts, and PFOA-related compounds as well as PFHxS, its salts and PFXxS-related compounds are currently under review for possible addition to the Convention as well. PFHxS and its salts are listed as vPvB, and PFNA and its salts, APFO, and PFOA are listed as PBT, by the European Chemicals Agency (ECHA, Candidate List of Substances of Very High Concern for Authorization, https://echa.europa.eu/candidate-list-table).
* SAB work still in progress.

Regulatory context: preliminary overview

Due to the emerging nature of scientific knowledge about health and environmental impacts of the PFAS, as well as revelations about water supply contamination in an increasing number of geographic areas, a number of regulatory processes are on-going. Sample regulatory actions are described here. The TURA program will examine additional regulatory actions going forward.

At the international level, PFOS as well as its salts and perfluorooctanyl sulfonyl fluoride have been placed on Annex B of the Stockholm Convention on Persistent Organic Pollutants and are targeted for phaseout globally, with some exemptions.[6] In addition, PFOA, its salts, and PFOA-related compounds as well as PFHxS, its salts and PFXxS-related compounds are currently under review for possible addition to the Convention.[7]

PFOS and PFOA are no longer manufactured within the US, although they are present in some products imported into the US. EPA has issued a significant new use rule (SNUR) for these and other substances.

PFOA, PFHxS and its salts, PFNA and its salts, and APFO are listed on the Candidate List of Substances of Very High Concern for Authorization under EU's REACH regulation.[8] In addition, a number of other PFAS have been added to ECHA's Registry of Intentions for SVHC designation. These include nonadecafluorodecanoic acid (PFDA), henicosafluoroundecanoic acid (PFUnDA), tricosafluorododecanoic acid (PFDoDA) and several others.[9]

EPA is working to address selected PFAS under its Unregulated Contaminant Monitoring Rule 3 (UCMR 3) (77 FR 26072, 2012). UCMR allows EPA "to collect data for contaminants that are suspected to be present in drinking water and do not have health-based standards set under the Safe Drinking Water Act (SDWA)."[10] Under UCMR 3, EPA has required testing for PFOS, PFOA, PFHxS, PFNA, PFHpA, and PFBS in all larger drinking water systems.[11]

For PFOS and PFOA, EPA has developed a health advisory of 70 ppt (equivalent to ng/L) for the sum of PFOS and PFOA in public drinking water. "EPA's health advisories are non-enforceable and non-regulatory" and are designed to provide technical information to states and other public health officials.[12]

Because PFAS have been found as widespread contaminants in many public water supplies, many state level regulatory authorities are working to develop maximum contaminant levels (MCLs) or other regulatory standards. Most or all of these regulatory efforts address chemicals in the carboxylic and sulfonic acids category. Some states have relied primarily on EPA's health advisory, while others have evaluated the science and proposed more protective standards and/or have undertaken to address a larger number of PFAS.

For example, in September 2018, New Jersey adopted a statewide drinking water standard for PFNA with a Maximum Contaminant Level (MCL) of 13 parts per trillion (ppt). Public water systems in New Jersey will be required to start testing for PFNA in 2019.[13] A ground water quality standard for PFNA of 0.01 µg/L (equivalent to 10 ppt) was adopted under amendments to New Jersey's Ground Water Quality Standards Rules in January 2018. PFNA was also added to

NJ's List of Hazardous Substances.[14] NJ has also established a drinking water guidance value for PFOA of 14 ppt, and the NJ Drinking Water Quality Institute has published a draft health based recommendation of 13 ppt for PFOS.[15]

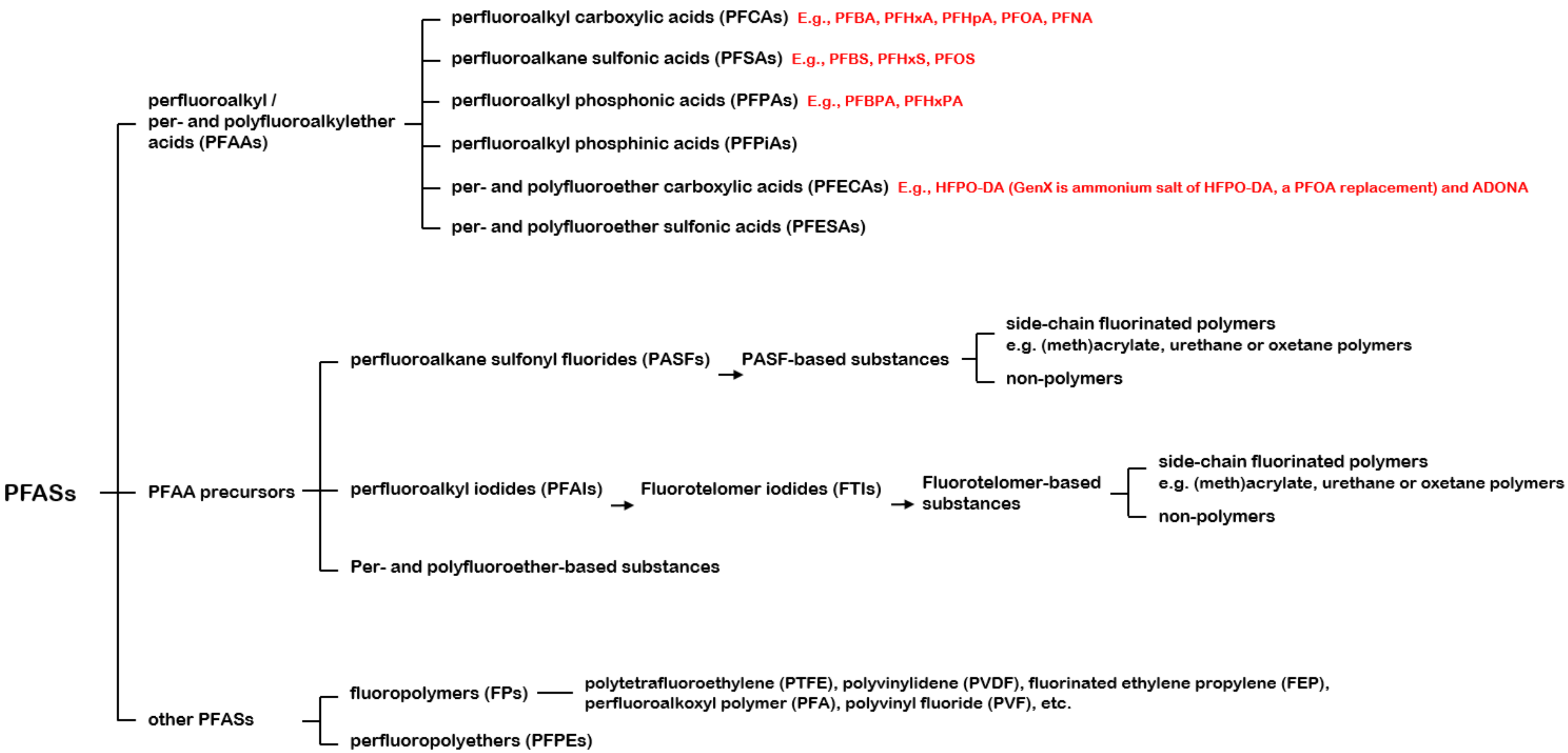
In other examples, the Connecticut Department of Public Health has developed a Drinking Water Action Level for private wells in CT "in which the sum of five PFAS chemicals (PFOA and PFOS, plus perfluorononanoic acid, PFNA, perfluorohexane sulfonate, PFHxS, and perfluoroheptanoic acid, PFHpA) should not exceed the limit of 70 ppt."[16] Minnesota has developed Health Risk Limit values for PFOS, PFOA, PFBA and PFBS. Minnesota has also examined information on PFHxS but has not developed a Human Risk Limit value for this chemical.[17]

In Massachusetts, MassDEP's Office of Research and Standards (ORS) has developed a set of recommendations regarding an approach to regulating PFAS in drinking water.[18] The recommendations, published in June 2018, note that all of the PFAS for which EPA has conducted testing under UCMR 3 have been found in Massachusetts water supplies. ORS has recommended that EPA's Health Advisories (HAs) and Reference Doses (RfDs) for PFOS and PFOA be applied to three other PFAS (PFNA, PFHxS, and PFHpA), and that "an additive toxicity approach be used for these compounds when they occur together," because they have similar effects. For PFBS, ORS has recommended an interim approach of using the Minnesota standard.

The state actions described above are examples and do not constitute a comprehensive review.

Appendix A

This flow chart is simplified and adapted from a flow chart published by OECD.[19] TURI has added the example notations in red font.



Appendix B

The table below shows key studies that were reviewed by the SAB and on which the SAB has relied in establishing a basis for concern about the health endpoint in question. The SAB's review included many additional studies beyond those noted here, including studies that show effects as well as studies that show no effect. The full set of references consulted by the SAB is shown in the SAB's bibliography.

	PFNA*	PFOA	PFHpA*	PFHxA	PFHxS	PFBA	PFBS
Cancer		C8 Health Study					
Immunotoxicity		C8 Health Study					Corsini 2012
Thyroid		C8 Health Study		Ren 2016	Jain 2013 Weiss 2009	Bjork and Wallace '09 Butenhoff 2012	Feng 2017
Endocrine (other than thyroid)				Wolf 2008 Rosenmai 2016	Das 2017, Rosenmai 2017	Foreman 2009	Gorrochategui 2014
Hematological		C8 Health Study				Butenhoff 2012 Van Otterdijk 2007	
Liver/metabolic			Wolf 2012, ATSDR 2018	Loveless 2009	Butenhoff 2009	Foreman 2009 Bjork and Wallace 2009 Wolf 2008 Rosenmai 2016	
Reproductive		C8 Health Study					
Developmental	Das 2015		Kim 2015	Loveless 2009 Iwai 2014		Das 2008	Feng 2017 Lieder 2009
Neurodevelopmental					Maisonet 2012 Joensen 2009 Viberg 2013 Lee and Viberg 2013 Yang 2016		
Neurotoxicity	Oulhote 2016			Loveless 2009 Klaunig 2015	Zhang 2016 Lee and Yang 2014 Viberg 2013		Slotkin 2008
Asthma					Dong 2013		Dong 2013
Other	Mutagenicity: Yahia 2016			Kidney: Leider 2009			Kidney: NICNAS 2017

* SAB work still in process

[1] The C8 Health Project "was created, authorized, and funded as part of the settlement agreement reached in the case of *Jack W. Leach, et al. v. E.I. du Pont de Nemours & Company* (no. 01-C-608 W.Va., Wood County Circuit Court, filed 10 April 2002). The settlement stemmed from the perfluorooctanoic acid (PFOA, or C8) contamination of drinking water in six water districts in two states near the DuPont Washington Works facility near Parkersburg, West Virginia." Description drawn from: Frisbee SJ et al. 2009. "The C8 Health Project: Design, Methods, and Participants." *Environ Health Perspect* 117:2, 1873-1882. Information on the project is also available on the website of the C8 Science Panel. See: http://www.c8sciencepanel.org/index.html, viewed September 24, 2018.
[2] NTP 2016: NTP Monograph: Immunotoxicity Associated with Exposure to Perfluorooctanoic Acid (PFOA) or Perfluorooctane Sulfonate (PFOS), September 2016. Accessed online at: https://ntp.niehs.nih.gov/ntp/ohat/pfoa_pfos/pfoa_pfosmonograph_508.pdf .

[3] Blaine, et al. Perfluoroalkyl acid uptake in lettuce (*Lactuca sativa*) and strawberry (*Fragaria ananassa*) irrigated with reclaimed water. *Environ Sci Technol*. 2014 Dec 16;48(24):14361-8.
[4] Muller CE, et al. Competing Mechanisms for Perfluoroalkyl Acid Accumulation in Plants Revealed Using an Arabidopsis Model System. *Environmental Toxicology and Chemistry*, 35(5), pp. 1138-1147, 2016.

[5] Swedish Chemicals Agency, (2017). Annex XV report – Proposal for Identification of a Substance of Very High Concern on the Basis of the Criteria set out in REACH article 57, Substance Name(s): Perfluorohexane-1-sulphonic acid and its salts. 2017-03-02. Accessed online 04/20/17, https://echa.europa.eu/documents/10162/40a82ea7-dcd2-5e6f-9bff-6504c7a226c5.

[6] Stockholm Convention. "The New POPs under the Stockholm Convention." Viewed at http://chm.pops.int/TheConvention/ThePOPs/TheNewPOPs/tabid/2511/Default.aspx, September 17, 2018.
[7] Stockholm Convention. "Chemicals Proposed for Listing under the Convention." Viewed at http://chm.pops.int/TheConvention/ThePOPs/ChemicalsProposedforListing/tabid/2510/Default.aspx, September 17, 2018.
[8] European Chemicals Agency. "Candidate List of Substances of Very High Concern for Authorisation." Viewed at https://echa.europa.eu/candidate-list-table, September 20, 2018.
[9] European Chemicals Agency. "Registry of Restriction Intentions." Viewed at https://echa.europa.eu/registry-of-restriction-intentions, September 20, 2018.
[10] US EPA. No date. "Learn About the Unregulated Contaminant Monitoring Rule." Viewed at https://www.epa.gov/dwucmr/learn-about-unregulated-contaminant-monitoring-rule, September 4, 2018.
[11] US EPA. No date. "Third Unregulated Contaminant Monitoring Rule." Viewed at https://www.epa.gov/dwucmr/third-unregulated-contaminant-monitoring-rule, September 4, 2018.
[12] US EPA. July 2018. "Ground Water and Drinking Water: Drinking Water Health Advisories for PFOA and PFOS." Viewed at https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos, September 4, 2018.
[13] New Jersey Department of Environmental Protection. September 4, 2018. "Drinking Water Standards by Constituent." Viewed at https://www.nj.gov/dep/standards/drinking%20water.pdf, September 20, 2018.

[14] New Jersey Department of Environmental Protection. "Contaminants of Emerging Concern." Viewed at https://www.nj.gov/dep/srp/emerging-contaminants/, September 20, 2018.
[15] New Jersey Department of Environmental Protection. "Contaminants of Emerging Concern." Viewed at https://www.nj.gov/dep/srp/emerging-contaminants/, September 20, 2018.
[16] https://portal.ct.gov/DPH/Drinking-Water/DWS/Per--and-Polyfluoroalkyl-Substances
[17] Minnesota Department of Health. "Human Health-Based Water Guidance Table." Viewed at http://www.health.state.mn.us/divs/eh/risk/guidance/gw/table.html, September 20, 2018. Specifically, information is available for the following chemicals: PFOS (http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfos2010.pdf), PFOA (http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfoa.pdf), PFBA (http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfba2summ.pdf), PFBS (http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfbs.pdf), and PFHxS (http://www.health.state.mn.us/divs/eh/risk/guidance/gw/pfhxs.pdf).
[18] Massachusetts Department of Environmental Protection. June 8, 2018. "Massachusetts Department of Environmental Protection Office of Research and Standards Final Recommendations for Interim Toxicity and

Drinking Water Guidance Values for Perfluorinated Alkyl Substances Included in the Unregulated Chemical Monitoring Rule 3." Viewed at https://www.mass.gov/files/documents/2018/06/11/pfas-ors-ucmr3-recs_0.pdf, September 20, 2018.

[19] OECD. 2018. "Toward a New Comprehensive Database of Per- and Polyfluoroalkyl Substances (PFASs): Summary Report Updating the OECD 2007 List of Per- and Polyfluoroalkyl Substances (PFASs). OECD Report. ENV/JM/MONO(2018)7. Series on Risk Management, No. 39. Page 17. Viewed at http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-JM-MONO(2018)7&doclanguage=en, September 6, 2018.