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Regulating PFAS as a Chemical Class under the California Safer Consumer Products Program

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Background: Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are a group of manmade chemicals containing at least one fully fluorinated carbon atom. The widespread use, large number, and diverse chemical structures of PFAS pose challenges to any sufficiently protective regulation, emissions reduction, and remediation at contaminated sites. Regulating only a subset of PFAS has led to their replacement with other members of the class with similar hazards, that is, regrettable substitutions. Regulations that focus solely on perfluoroalkyl acids (PFAAs) are ineffective, given that nearly all other PFAS can generate PFAAs in the environment.

Objectives: In this commentary, we present the rationale adopted by the State of California's Department of Toxic Substances Control (DTSC) for regulating PFAS as a class in certain consumer products.

Discussion: We at the California DTSC propose regulating certain consumer products if they contain any member of the class of PFAS because: *a*) all PFAS, or their degradation, reaction, or metabolism products, display at least one common hazard trait according to the California Code of Regulations, namely environmental persistence; and *b*) certain key PFAS that are the degradation, reaction or metabolism products, or impurities of nearly all other PFAS display additional hazard traits, including toxicity; are widespread in the environment, humans, and biota; and will continue to cause adverse impacts for as long as any PFAS continue to be used. Regulating PFAS as a class is thus logical, necessary, and forward-thinking. This technical position may be helpful to other regulatory agencies in comprehensively addressing this large class of chemicals with common hazard traits. https://doi.org/10.1289/EHP7431

Introduction

The PFAS Class

The term perfluoroalkyl and polyfluoroalkyl substances (PFASs) was first introduced by Buck et al. (2011) to describe certain manmade chemicals containing at least one fully fluorinated carbon atom (i.e., a carbon atom surrounded by fluorine instead of hydrogen). Subsequently, the U.S. Environmental Protection Agency (EPA) and others have dropped the extra "s" at the end of the class name, which has now become the standard in the United States. Determining where to draw the line between PFAS and highly fluorinated non-PFAS compounds remains an ongoing challenge. Buck et al. (2011) limited the scope of PFAS to aliphatic substances that contain at least one C_nF_{2n+1} moiety. The OECD (2018) expanded the definition to include substances with the C_nF_{2n} moiety, and are currently considering further revisions to the definition.

Since the late 1940s, PFAS have been used in a wide range of industrial and consumer product applications as oil, grease, soil, and water repellents and as surfactants (OECD 2013; Cousins et al. 2019a). Applications span many sectors of the economy, including aerospace, apparel, automotive, building and construction, chemicals and pharmaceuticals, electronics and semiconductors, energy, oil and gas exploration, first responder safety, and health care (American Chemistry Council 2021).

In 2015, the Swedish Chemicals Agency (KEMI) identified over 3,000 PFAS on the global market (KEMI 2015). A more recent study identified approximately 4,700 Chemical Abstract Services (CAS) Registry Numbers associated with individual PFAS or PFAS mixtures (OECD 2018). In 2019, the U.S. EPA assembled a master list of 6,330 PFAS that combines information from several existing lists into one (U.S. EPA 2020b). The total number of PFAS may be even larger, given that some PFAS class members lack CAS numbers and many are not intentionally manufactured but are metabolites or degradants of other PFAS.

The widespread use, large number, and diverse chemical structures of PFAS pose challenges to any sufficiently protective regulation, emissions reduction, and remediation at contaminated sites. Specific members of the PFAS class have been regulated by several authoritative bodies. For instance, perfluorooctane sulfonic acid (PFOS) and its salts, and perfluorooctane sulfonil fluoride are listed as persistent organic pollutants (POPs) in Annex B of the Stockholm Convention, whereas perfluorooctanoic acid (PFOA), its salts, and related compounds are listed in Annex A (UNEP 2020). Perfluorohexane sulfonic acid (PFHxS), its salts, and related compounds are currently under review for listing (POPRC 2020). Several PFAS are included in the European Chemicals Agency's (ECHA) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Candidate List of Substances of Very High Concern (SVHC) (ECHA 2020). From 2006 to 2015, the U.S. EPA worked with eight major chemical manufacturers to voluntarily phase out production and use of so-called long-chain PFAS and their precursors (U.S. EPA 2020c) and set a nonenforceable lifetime health advisory level for PFOA and PFOS, individually or combined, of 70 ppt in drinking water (U.S. EPA 2020a). Several U.S. states have also set their own drinking water guideline levels for PFOA and PFOS (Cordner et al. 2019).

The approach of regulating only individual PFAS or a limited subset of PFAS has led to the replacement of those PFAS with other members of the class that have less well-characterized hazard profiles. These alternatives may even be worse, in some respects, than the PFAS being replaced, thus constituting a "regrettable substitution" (Scheringer et al. 2014; Blum et al. 2015; Brendel et al. 2018). For instance, since the voluntary phaseout of the longer-chain PFAS in some regions, manufacturers have shifted to PFAS with six or fewer carbons, such as perfluorohexanoic acid (PFHxA) and other shorter-chain PFAS chemistries (OECD 2013; Brendel et al. 2018), which are less studied but have also been documented to display multiple hazard traits (Danish Environmental Protection Agency 2015; Gomis et al. 2018; Brendel et al. 2018; Rice et al. 2020).

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Because all PFAS show high persistence (P) or degrade to other class members that are highly persistent, several recent papers argue that regulators should take a "P-sufficient" approach and regulate all PFAS as a class (Cousins et al. 2019b, 2020a). However, the authors point out that there is no legal precedent in any jurisdiction for this approach (Cousins et al. 2020a). In this commentary, we present the first example of a regulatory agency using the P-sufficient approach as the rationale for regulating PFAS as a chemical class, under the Safer Consumer Products (SCP) framework adopted by the State of California's Department of Toxic Substances Control (DTSC).

The Safer Consumer Products Regulations

California's 2008 SCP law directed the DTSC to "establish a process by which chemicals of concern in products, and their potential alternatives, are evaluated to determine how best to limit exposure or to reduce the level of hazard posed by a Chemical of Concern" (Feuer 2008). The DTSC adopted this process in Article 3 of the SCP regulations (DTSC 2013). The SCP regulatory framework authorizes the DTSC to designate specific consumer products (excluding pesticides, food, and pharmaceuticals) that contain one or more specific Candidate Chemicals as "Priority Products." Any chemical that appears on one or more of 23 established authoritative lists referenced in the DTSC's framework regulations is a Candidate Chemical under this regulatory framework.

Once the DTSC designates a Priority Product, responsible entities (typically the product manufacturers) must either conduct an Alternatives Analysis, remove the Chemical(s) of Concern, or withdraw the product from the California market. In the Alternatives Analysis, each manufacturer identifies one or more potential alternatives to the Chemical of Concern and compares their life cycle impacts to determine whether the alternative is safer. If the DTSC determines that the Alternatives Analysis is deficient in terms of the options it considers, the quality of its research, or its characterization of the tradeoffs between the Priority Product and the alternative or alternatives under consideration, the DTSC can issue a notice of deficiency requesting additional information. If a potentially safer alternative proposed by a manufacturer lacks adequate data, the DTSC can issue a preregulatory response requiring the manufacturer to generate new data to address the data gaps. The DTSC issues a Regulatory Response based on the findings of the Alternatives Analysis. The goal of the Regulatory Response is to minimize the adverse impacts identified for the Priority Product using one or more of the following approaches: restrictions or prohibitions on the sale of the product, product labeling on safe handling procedures to prevent exposure, engineering or administrative controls to reduce exposure, end-of-life product management to reduce environmental releases, and investment in green chemistry and engineering to develop safer alternatives (DTSC 2013).

Identifying Priority Products does not require a formal risk assessment nor setting minimum threshold values. It only requires a finding that exposure to a Chemical of Concern in the product has the potential to "contribute to or cause significant or widespread adverse impacts" to human health or the environment (DTSC 2013). Thus, we believe the SCP regulations enable the DTSC to take a precautionary approach to protecting California's most vulnerable human populations, as well as its threatened and endangered species, sensitive habitats, and impaired environments.

PFAS initially rose to the attention of the DTSC staff due to their endocrine disruption potential (White et al. 2011; C8 Science Panel 2012b) and well-established, unequivocal environmental and biological persistence (OECD 2013). The DTSC's Candidate Chemicals list contains the entire class of PFAS as defined on one of the 23 constituent authoritative lists, namely, the Biomonitoring California Priority Chemicals list. In 2015, Biomonitoring California designated all PFAS, as defined by Buck et al. (2011), as Priority Chemicals (Biomonitoring California 2015, 2019). This PFAS class definition includes all fluorinated aliphatic substances that contain the moiety C_nF_{2n+1}. Between 2016 and 2019, we refined our approach to regulating PFAS as a class in consumer products by researching the publicly available literature, engaging with our stakeholders, and submitting our findings to an external scientific peer review process mandated by California law. The resulting technical position described here may be helpful to other regulatory agencies in comprehensively addressing potential PFAS impacts.

Discussion

Why Regulating Individual PFAS is Ineffective

Other authors have also recently made the case for managing PFAS as a chemical class (Cousins et al. 2020a; Kwiatkowski et al. 2020). To understand why this makes sense, it is important to consider that virtually all the thousands of PFAS, as defined by Buck et al. (2011), can be roughly subdivided into four interrelated categories: perfluoroalkyl acids (PFAAs), PFAA precursors, perfluoropolyethers (PFPEs), and fluoropolymers (Buck et al. 2011; Wang et al. 2017). PFAAs are the most studied PFAS subgroup. They are recalcitrant to degradation and extremely persistent in the environment (Bentel et al. 2019). Examples of PFAAs include perfluoroalkyl carboxylic acids (PFCAs) such as PFOA, perfluoroalkyl sulfonic acids (PFSAs) such as PFOS, perfluoroalkyl sulfinic acids (PFSiAs), perfluoroalkyl phosphonic acids (PFPAs), perfluoroalkyl phosphinic acids (PFPiAs), perfluoroether carboxylic acids (PFECAs) such as GenX, and perfluoroether sulfonic acids (PFESAs) such as 4,8-dioxa-3H-perfluorononanoate (ADONA). PFAAs and their precursors are further subdivided according to their chain length, which is viewed as a proxy for their bioaccumulation potential. By convention, the longer-chain PFSAs are those with six or more perfluorinated carbons; longer-chain PFCAs, PFPAs, and PFPiAs are those with seven or more perfluorinated carbons (Buck et al. 2011). The definition of longer- vs. shorter-chain PFAS is less clear for perfluoroethers.

The majority ($\sim 85\%$) of PFAS are PFAA precursors, that is, they can degrade or metabolize into PFAAs in the environment or in living organisms (D'eon and Mabury 2007; Butt et al. 2014; OECD 2018). Some of the intermediate metabolites of PFAA precursors may be more toxic than the final PFAA degradation products (Rand and Mabury 2012a, 2012b, 2013, 2014, 2017; Rice et al. 2020). In particular, most PFAS currently used in consumer products are side-chain fluorinated polymers, in which the fluorinated side-chains are attached to a polymeric backbone and can cleave off, leading to PFCA terminal degradation products (Washington et al. 2015, 2019). U.S. EPA scientists have estimated environmental half-lives for these polymers of between 9 and 60 y (Washington et al. 2019). Thus, the side-chain fluorinated polymers found in discarded consumer products in landfills and other waste stocks may continue releasing PFAAs and intermediate degradation products to the environment for decades, or even centuries (Lang et al. 2017; Li et al. 2017; Washington et al. 2019).

PFPEs are fluorinated polymers with ether linkages (Wang et al. 2020). They are less likely to degrade to PFAAs, except perhaps during combustion (Huber et al. 2009; Wang et al. 2020). Fluoropolymers are characterized by large molecular sizes and do not degrade to PFAAs under typical environmental conditions, although they have been observed to release PFCAs, including PFOA, when heated to temperatures between 180°C and 800°C (Schlummer et al. 2015; Feng et al. 2015). PFAAs are used in the manufacture of fluoropolymers and can occur as impurities in the final product. In fact, fluoropolymer manufacturing is the biggest contributor to historical PFCA emissions, accounting for an estimated 55–83% of all emissions between 1951 and 2002 (Wang et al. 2014a).

Although PFAAs constitute only approximately 1% of PFAS, we find that the hazard traits of PFAAs are relevant to the entire class because they are the terminal degradation, metabolism, or combustion products, manufacturing aids, feedstocks, or impurities of nearly all other PFAS class members (OECD 2018; Kwiatkowski et al. 2020). It is, therefore, our opinion that environmental releases of and exposures to PFAAs cannot be regulated without regulating the manufacture, use, and end-of-life fate of the other PFAS.

Criteria for Regulating PFAS under the California Code of Regulations

The California Green Chemistry Hazard Traits Regulations define a series of hazard traits, which are subdivided into toxicological, environmental, exposure potential, and physical hazard traits (OEHHA 2012b), discussed in more detail below. These hazard traits are not weighted. Reliable evidence for any one of these hazard traits can suffice to indicate that a chemical's potential adverse impacts warrant regulatory action.

Exposure potential hazard traits. At the DTSC, we have found that PFAS display one or more of the following exposure potential hazard traits listed in the California Code of Regulations: environmental persistence, mobility in environmental media, bioaccumulation, lactational or transplacental transfer, and global warming potential. Environmental persistence is the most widely recognized hazard trait of the class of PFAS. The carbon–fluorine bond shared by all members of the class is one of the strongest in organic chemistry, and the strongest single bond to carbon (Kiplinger et al. 1994). This makes PFAAs, the terminal degradation products of most PFAS, extremely recalcitrant in the environment (D'eon and Mabury 2011; Buck et al. 2011; Washington et al. 2015; Krafft and Riess 2015)—so much so that they have been called the "forever chemicals" (Pelch et al. 2019). Persistence is arguably "the most important single criterion affecting chemical exposure and risk via the environment" (Mackay et al. 2014). Some have even proposed that high persistence alone should be a sufficient basis for chemical regulation because if adverse impacts are identified, contamination cannot be reversed at scale within a reasonable time frame (Cousins et al. 2019b). According to the Statement of Reasons for the California Green Chemistry Hazard Traits Regulations, "Persistence of a chemical in the environment promotes sustained exposure and contributes to accumulation in the environment. Because persistence is an inherent property of a chemical in the environment that results in increased exposure to the chemical and consequently potential for health risks, it can appropriately be identified as a hazard trait. Legacy chemicals such as dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs) remain public health concerns decades after their production was banned because of their ability to persist in the environment" (OEHHA 2012a).

PFAAs and some of their precursors are known to bioaccumulate in animals or plants. Unlike other persistent organic pollutants, PFAAs are proteinophilic and tend to accumulate not in fat but in protein-rich tissues such as blood (Jones et al. 2003; Chen and Guo 2009; Hebert and MacManus-Spencer 2010; Greaves et al. 2012; Hurley et al. 2018), liver (Greaves et al. 2012; Pérez et al. 2013; Gebbink et al. 2016), brain (Greaves et al. 2012; Pérez et al. 2013), kidney and lung (Pérez et al. 2013), and muscle (Greaves et al. 2012). Human serum elimination half-lives of longer-chain PFAAs range from years (Bartell et al. 2010; Olsen et al. 2007a; Seals et al. 2011) to decades (Shi et al. 2016). For shorter-chain PFAAs, human serum elimination half-lives are on the order of days (Chang et al. 2008; Nilsson et al. 2010; Olsen et al. 2007a). However, recent studies have indicated that some of the intermediate short-chain PFAS metabolites, such as 5:3 fluorotelomer carboxylic acid (FTCA), may biopersist and bioaccumulate (Kabadi et al. 2018, 2020). Shorter-chain PFAAs also tend to accumulate in plants (Blaine et al. 2013, 2014; Gobelius et al. 2017; Lechner and Knapp 2011; Scher et al. 2018; Stahl et al. 2009; Yoo et al. 2011), allowing them to enter terrestrial and aquatic food chains.

PFAAs and several of their nonpolymeric precursors have high mobility in environmental media and can be transported long distances in the atmosphere or hydrosphere (Wang et al. 2014b; Xie et al. 2015; Dreyer et al. 2015). Shorter-chain PFAS are known to be more mobile and difficult to remove from water (Brendel et al. 2018; Ateia et al. 2019), readily contaminating groundwater (McLachlan et al. 2019) and escaping from waste stocks such as landfills and dumps (L Li et al. 2017; F Li et al. 2020). Because they tend to be more volatile, they are more likely to be released from consumer products.

Several PFAS are known to undergo transplacental (Midasch et al. 2007; Zhang et al. 2013; Yang et al. 2016; F Chen et al. 2017; Zhao et al. 2017; Mamsen et al. 2019; Eryasa et al. 2019; Cai et al. 2020) and lactational (Kärrman et al. 2007; Llorca et al. 2010; Mogensen et al. 2015; Mondal et al. 2014; Tao et al. 2008b; Kim et al. 2014; Fromme et al. 2010; Kang et al. 2016; Nyberg et al. 2018; Lee et al. 2018) transfer in humans. Up to 30.3% of the PFAS found to undergo transplacental transfer using nontarget screening were novel PFAS whose impacts on the developing fetus are yet unknown (Y Li et al. 2020).

Toxicological and environmental hazard traits. PFAAs, which are relevant to the entire class as manufacturing aids, degradants, or impurities, collectively also display several toxicological and environmental hazard traits. Potential adverse human health effects and risk factors from longer-chain PFAA exposure include increased serum cholesterol (Skuladottir et al. 2015; Winquist and Steenland 2014), thyroid disease (Winquist and Steenland 2014), immune dysregulation (Grandjean and Clapp 2014; Grandjean et al. 2017a, 2017b), pregnancy-induced hypertension (C8 Science Panel 2011), and kidney and testicular cancers (C8 Science Panel 2012a). Other studies have found positive correlations between long-chain PFAA exposure and low birth weight in humans (Malits et al. 2018), as well as suppressed immune system response, dyslipidemia, impaired kidney function, and delayed first occurrence of menstruation (Rappazzo et al. 2017).

Due to their shorter observed biological half-lives, shorter-chain PFAS have been assumed to be less toxic compared with the longer-chain PFAS (DeWitt 2015; Stahl et al. 2011; Wolf et al. 2008). However, more and more studies are questioning this assumption. A toxicokinetic study found that the potency of shorter-chain PFAAs to induce increased liver weight is similar to that of the longer-chain PFOA, and even greater for the PFECA GenX (Gomis et al. 2018). Limited animal data on GenX and related perfluorinated ethers indicate potential associations with cancer, body weight gain, changes to the immune system and cholesterol levels, increased kidney and liver weights, and liver cell changes (Caverly Rae et al. 2015; Beekman et al. 2016). Several toxicokinetic studies and receptor binding assays report biological activity from exposure to the shorter-chain PFBA and PFBS (Wolf et al. 2008; Danish Environmental Protection Agency 2015). Studies on zebrafish and rodents have linked PFBA with reproductive and developmental toxicity (Das et al. 2008; Hagenaars et al. 2011) and ocular toxicity (Butenhoff et al. 2012), PFBS with developmental toxicity (Hagenaars et al.

2011) and hematotoxicity (Lieder et al. 2009), and PFHxA with respiratory toxicity (Loveless et al. 2009). Neurodevelopmental toxicity has also been demonstrated *in vitro* for PFBS (Slotkin et al. 2008).

Less is known about the toxicity of most PFAA precursors. Some studies suggest that fluorotelomer-based PFAA precursors, including their intermediate degradation products, are more toxic than the final PFAA metabolites (Phillips et al. 2007; Rand et al. 2014; Rice et al. 2020). Hazard traits reported for these precursors include endocrine toxicity (Ishibashi et al. 2008; Rosenmai et al. 2016; Weiss et al. 2009; Ladics et al. 2008; Winkens et al. 2017; Rice et al. 2020), developmental toxicity (Shi et al. 2017b; Rice et al. 2020), and hepatotoxicity and nephrotoxicity (Ladics et al. 2008; Rice et al. 2020).

Available data also link PFAAs and some of their precursors with several of the environmental hazard traits identified in California's Green Chemistry Hazard Traits Regulations: phytotoxicity (Latała et al. 2009), wildlife developmental impairment (Hagenaars et al. 2011; Ulhaq et al. 2013; Shi et al. 2017a), wildlife reproductive impairment (Liu et al. 2009), and wildlife survival impairment (O'Connor et al. 2014; Klaunig et al. 2015; Eggers Pedersen et al. 2015; Shi et al. 2017a).

Widespread human and ecological exposures. In addition to the hazard traits discussed above, the SCP regulations consider the potential for exposures to the Candidate Chemical in a product and the aggregate effects of exposures to the Candidate Chemical from multiple exposure sources and media (DTSC 2013).

PFAAs and some of their precursors are widespread in the environment, including in air (Kim and Kannan 2007; Muir et al. 2019; Wang et al. 2019), dust (Haug et al. 2011; Eriksson and Kärrman 2015; Yao et al. 2018; Shin et al. 2020), wastewater treatment plant effluent (Hamid and Li 2016; Wang et al. 2016; Houtz et al. 2016; H Chen et al. 2017), biosolids (Letcher et al. 2020; Kim Lazcano et al. 2020), soil (Rankin et al. 2016; Dalahmeh et al. 2018; Muir et al. 2019; Washington et al. 2019), snow (Kim and Kannan 2007; Kirchgeorg et al. 2016), inland and ocean waters (Prevedouros et al. 2006; Zhao et al. 2012; Wang et al. 2016; Muir et al. 2019), drinking water (Gellrich et al. 2013; Wang et al. 2016; Boone et al. 2019), and human foods (Pérez et al. 2014; Gebbink et al. 2015; Domingo and Nadal 2017; Christensen et al. 2017; EFSA CONTAM Panel et al. 2018). As a result, human (Cariou et al. 2015; Calafat et al. 2007; Chang et al. 2014; Fraser et al. 2013; Kang et al. 2016; Monroy et al. 2008; OECD 2013; Olsen et al. 2007b; Tao et al. 2008a, 2008b) and ecological (Giesy and Kannan 2001; Liu et al. 2011; OECD 2013) exposures to PFAS mixtures are widely documented. Shorter-chain PFAAs are often not detectable in human serum and plasma but can be found at concentrations comparable to or higher than those of longer-chain PFAS in human whole blood (Poothong et al. 2017), hair (Alves et al. 2015; Ruan et al. 2019; Martín et al. 2019), urine (Hartmann et al. 2017; Kim et al. 2014; Pérez et al. 2012), and certain organs, including the kidney, lung, liver, and brain (Pérez et al. 2013). Given that PFAS are highly persistent and capable of long-range transport, we expect that environmental contamination and exposures will continue for as long as PFAS are manufactured or used anywhere in the world.

Thus, human and ecological receptors are exposed to mixtures of PFAS whose environmental fate and hazard traits are interlinked. Despite recent analytical advancements, most of the PFAS observed in the environment, wildlife, and human tissues remain unidentified (Xiao 2017). Only a small fraction (sometimes $<5\%$) of the organofluorine present in these media have been targeted for analysis. Until analytical methods are developed and validated for more members of the class, the full extent of PFAS contamination, despite extensive research, will remain poorly understood.

Regulatory Implications

Based on the currently available science, we have concluded that it is both ineffective and impractical to regulate this complex class of chemicals with a piecemeal approach and have, therefore, initiated regulatory action to list certain consumer products containing any PFAS as Priority Products under the SCP regulations. The available information demonstrates that all PFAS or their degradation, reaction, or metabolism products have at least one hazard trait of concern to the State of California: environmental persistence. As others have argued, high persistence alone can be a sufficient criterion for regulatory action (Cousins et al. 2019b, 2020b). In the case of PFAS, we believe that all members of the class have a potential for significant and widespread adverse impacts due to their extremely high environmental persistence, coupled with growing evidence for human and ecological health hazards for the impurities, metabolites, and degradation products of the subset commonly used in consumer products. The concerns identified in this commentary reflect our best understanding of the current PFAS in production and use. However, significant data gaps remain, and we cannot exclude the possibility that new PFAS may be developed in the future following green chemistry principles.

Because individual PFAS never occur in isolation, we believe they cannot be effectively regulated in isolation. The potential for widespread exposures will remain for as long as PFAS continue to be used and concerns over their fate and transport remain inadequately addressed. However, although virtually all PFAS studied show at least suggestive evidence of toxicity, the observed effects are variable. This means that PFAS cannot be regulated as a class based on a common mode of action or toxicity. At the DTSC, we were able to take a class approach to regulating PFAS because *a*) persistence is codified as a hazard trait in the California code of regulations; *b*) the entire class is on the DTSC's list of Candidate Chemicals, after being designated as priority chemicals for biomonitoring in California; and *c*) the SCP regulatory framework is based on an inherently precautionary approach, to protect the most vulnerable human and ecological (sub)populations.

Thus, the California Green Chemistry Hazard Traits and SCP regulations (OEHHA 2012b; DTSC 2013) offer a more comprehensive, precautionary approach to assessing potential adverse impacts of PFAS and can serve as a model for other regulatory agencies aiming to address potential PFAS impacts comprehensively. Taking a class approach to regulating PFAS in consumer products could also encourage innovation in developing safer alternatives and reducing the risk of regrettable substitutions. Indeed, under California's regulatory framework, our identification of the entire PFAS class as a Chemical of Concern will compel manufacturers to identify, and rigorously evaluate, the relative safety of non-PFAS alternatives throughout a product's life cycle.

This precautionary regulatory approach may be applicable to other chemical classes in consumer products where class members share life cycle fates or hazard traits, limited toxicological and exposure data are publicly available, and regrettable substitutions are likely. For example, we are also proposing to regulate nonylphenol ethoxylates in laundry detergents as a class (DTSC 2018). We also recommend consideration of this approach for regulating nontraditional complex classes of compounds that are of concern but lack a common mode of action or toxicity, such as microplastics.

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References

American Chemistry Council. 2021. Fluorotechnology makes important products for vital industries possible. https://www.americanchemistry.com/Fluorotechnology-Starburst-Uses-Graphic.pdf [accessed 28 January 2021].

Alves A, Jacobs G, Vanermen G, Covaci A, Voorspoels S. 2015. New approach for assessing human perfluoroalkyl exposure via hair. Talanta 144:574–583, PMID: 26452864, https://doi.org/10.1016/j.talanta.2015.07.009.

Ateia M, Maroli A, Tharayil N, Karanfil T. 2019. The overlooked short- and ultrashort-chain poly- and perfluorinated substances: a review. Chemosphere 220:866–882, PMID: 33395808, https://doi.org/10.1016/j.chemosphere.2018.12.186.

Bartell SM, Calafat AM, Lyu C, Kato K, Ryan PB, Steenland K, et al. 2010. Rate of decline in serum PFOA concentrations after granular activated carbon filtration at two public water systems in Ohio and West Virginia. Environ Health Perspect 118(2):222–228, PMID: 20123620, https://doi.org/10.1289/ehp.0901252.

Beekman M, Zweers P, Muller A, de Vries W, Janssen P, Zeilmaker M. 2016. *Evaluation of Substances Used in the GenX Technology by Chemours, Dordrecht*. RIVM Letter Report 2015-0174. Bilthoven, Netherlands: National Institute for Public Health and the Environment. https://www.rivm.nl/bibliotheek/rapporten/2016-0174.pdf [accessed 19 January 2021].

Bentel MJ, Yu Y, Xu L, Li Z, Wong BM, Men Y, et al. 2019. Defluorination of per- and polyfluoroalkyl substances (PFASs) with hydrated electrons: structural dependence and implications to PFAS remediation and management. Environ Sci Technol 53(7):3718–3728, PMID: 30874441, https://doi.org/10.1021/acs.est.8b06648.

Biomonitoring California. 2015. Potential Priority Chemicals: Perfluoroalkyl and Polyfluoroalkyl Substances (PFASs). 18 November 2015. Sacramento, CA: California Environmental Contaminant Biomonitoring Program. https://biomonitoring.ca.gov/sites/default/files/downloads/PotentialPriority_PFASs_111815.pdf [accessed 19 January 2021].

Biomonitoring California. 2019. Priority Chemicals. February 2019. Sacramento, CA: California Environmental Contaminant Biomonitoring Program. https://biomonitoring.ca.gov/sites/default/files/downloads/PriorityChemicalsList_February2019.pdf [accessed 19 January 2021].

Blaine AC, Rich CD, Hundal LS, Lau C, Mills MA, Harris KM, et al. 2013. Uptake of perfluoroalkyl acids into edible crops via land applied biosolids: field and greenhouse studies. Environ Sci Technol 47(24):14062–14069, PMID: 24206563, https://doi.org/10.1021/es403094q.

Blaine AC, Rich CD, Sedlacko EM, Hundal LS, Kumar K, Lau C, et al. 2014. Perfluoroalkyl acid distribution in various plant compartments of edible crops grown in biosolids-amended soils. Environ Sci Technol 48(14):7858–7865, PMID: 24918303, https://doi.org/10.1021/es500016s.

Blum A, Balan SA, Scheringer M, Trier X, Goldenman G, Cousins IT, et al. 2015. The Madrid statement on poly- and perfluoroalkyl substances (PFASs). Environ Health Perspect 123(5):A107–A111, PMID: 25932614, https://doi.org/10.1289/ehp.1509934.

Boone JS, Vigo C, Boone T, Byrne C, Ferrario J, Benson R, et al. 2019. Per- and polyfluoroalkyl substances in source and treated drinking waters of the United States. Sci Total Environ 653:359–369, PMID: 30412881, https://doi.org/10.1016/j.scitotenv.2018.10.245.

Brendel S, Fetter É, Staude C, Vierke L, Biegel-Engler A. 2018. Short-chain perfluoroalkyl acids: environmental concerns and a regulatory strategy under REACH. Environ Sci Eur 30(1):9, PMID: 29527446, https://doi.org/10.1186/s12302-018-0134-4.

Buck RC, Franklin J, Berger U, Conder JM, Cousins IT, de Voogt P, et al. 2011. Perfluoroalkyl and polyfluoroalkyl substances in the environment: terminology, classification, and origins. Integr Environ Assess Manag 7(4):513–541, PMID: 21793199, https://doi.org/10.1002/ieam.258.

Butenhoff JL, Bjork JA, Chang SC, Ehresman DJ, Parker GA, Das K, et al. 2012. Toxicological evaluation of ammonium perfluorobutyrate in rats: twenty-eight-day and ninety-day oral gavage studies. Reprod Toxicol 33(4):513–530, PMID: 21878386, https://doi.org/10.1016/j.reprotox.2011.08.004.

Butt CM, Muir DCG, Mabury SA. 2014. Biotransformation pathways of fluorotelomer-based polyfluoroalkyl substances: a review. Environ Toxicol Chem 33(2):243–267, PMID: 24114778, https://doi.org/10.1002/etc.2407.

C8 Science Panel. 2011. Probable link evaluation of pregnancy induced hypertension and preeclampsia. 5 December 2011. http://www.c8sciencepanel.org/pdfs/Probable_Link_C8_PIH_5Dec2011.pdf [accessed 11 May 2020].

C8 Science Panel. 2012a. Probable link evaluation of cancer. 15 April 2012. http://www.c8sciencepanel.org/pdfs/Probable_Link_C8_Cancer_16April2012_v2.pdf [accessed 11 May 2020].

C8 Science Panel. 2012b. Probable link evaluation of thyroid disease. 30 July 2012. http://www.c8sciencepanel.org/pdfs/Probable_Link_C8_Thyroid_30Jul2012.pdf [accessed 14 September 2020].

Cai D, Li QQ, Chu C, Wang SZ, Tang YT, Appleton AA, et al. 2020. High trans-placental transfer of perfluoroalkyl substances alternatives in the matched maternal-cord blood serum: evidence from a birth cohort study. Sci Total Environ 705:135885, PMID: 31841927, https://doi.org/10.1016/j.scitotenv.2019.135885.

Calafat AM, Kuklenyik Z, Reidy JA, Caudill SP, Tully JS, Needham LL, et al. 2007. Serum concentrations of 11 polyfluoroalkyl compounds in the U.S. population: data from the National Health and Nutrition Examination Survey (NHANES). Environ Sci Technol 41(7):2237–2242, PMID: 17438769, https://doi.org/10.1021/es062686m.

Cariou R, Veyrand B, Yamada A, Berrebi A, Zalko D, Durand S, et al. 2015. Perfluoroalkyl acid (PFAA) levels and profiles in breast milk, maternal and cord serum of French women and their newborns. Environ Int 84:71–81, PMID: 26232143, https://doi.org/10.1016/j.envint.2015.07.014.

Caverly Rae JM, Craig L, Slone TW, Frame SR, Buxton LW, Kennedy GL, et al. 2015. Evaluation of chronic toxicity and carcinogenicity of ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)-propanoate in Sprague–Dawley rats. Toxicol Rep 2:939–949, PMID: 28962433, https://doi.org/10.1016/j.toxrep.2015.06.001.

Chang ET, Adami HO, Boffetta P, Cole P, Starr TB, Mandel JS, et al. 2014. A critical review of perfluorooctanoate and perfluorooctanesulfonate exposure and cancer risk in humans. Crit Rev Toxicol 44(suppl 1):1–81, PMID: 24793953, https://doi.org/10.3109/10408444.2014.905767.

Chang SC, Das K, Ehresman DJ, Ellefson ME, Gorman GS, Hart JA, et al. 2008. Comparative pharmacokinetics of perfluorobutyrate in rats, mice, monkeys, and humans and relevance to human exposure via drinking water. Toxicol Sci 104(1):40–53, PMID: 18353799, https://doi.org/10.1093/toxsci/kfn057.

Chen F, Yin S, Kelly BC, Liu W. 2017. Chlorinated polyfluoroalkyl ether sulfonic acids in matched maternal, cord, and placenta samples: a study of transplacental transfer. Environ Sci Technol 51(11):6387–6394, PMID: 28482666, https://doi.org/10.1021/acs.est.6b06049.

Chen H, Peng H, Yang M, Hu J, Zhang Y. 2017. Detection, occurrence, and fate of fluorotelomer alcohols in municipal wastewater treatment plants. Environ Sci Technol 51(16):8953–8961, PMID: 28728413, https://doi.org/10.1021/acs.est.7b00315.

Chen YM, Guo LH. 2009. Fluorescence study on site-specific binding of perfluoroalkyl acids to human serum albumin. Arch Toxicol 83(3):255–261, PMID: 18854981, https://doi.org/10.1007/s00204-008-0359-x.

Christensen KY, Raymond M, Blackowicz M, Liu Y, Thompson BA, Anderson HA, et al. 2017. Perfluoroalkyl substances and fish consumption. Environ Res 154:145–151, PMID: 28073048, https://doi.org/10.1016/j.envres.2016.12.032.

Cordner A, De La Rosa VY, Schaider LA, Rudel RA, Richter L, Brown P, et al. 2019. Guideline levels for PFOA and PFOS in drinking water: the role of scientific uncertainty, risk assessment decisions, and social factors. J Expo Sci Environ Epidemiol 29(2):157–171, PMID: 30622333, https://doi.org/10.1038/s41370-018-0099-9.

Cousins IT, DeWitt JC, Glüge J, Goldenman G, Herzke D, Lohmann R, et al. 2020a. Strategies for grouping per- and polyfluoroalkyl substances (PFAS) to protect human and environmental health. Environ Sci Process Impacts 22(7):1444–1460, PMID: 32495786, https://doi.org/10.1039/d0em00147c.

Cousins IT, DeWitt JC, Glüge J, Goldenman G, Herzke D, Lohmann R, et al. 2020b. The high persistence of PFAS is sufficient for their management as a chemical class. Environ Sci Process Impacts 22(12):2307–2312, PMID: 33230514, https://doi.org/10.1039/D0EM00355G.

Cousins IT, Goldenman G, Herzke D, Lohmann R, Miller M, Ng CA, et al. 2019a. The concept of essential use for determining when uses of PFASs can be phased out. Environ Sci Process Impacts 21(11):1803–1815, PMID: 31204421, https://doi.org/10.1039/c9em00163h.

Cousins IT, Ng CA, Wang Z, Scheringer M. 2019b. Why is high persistence alone a major cause of concern? Environ Sci Process Impacts 21(5):781–792, PMID: 30973570, https://doi.org/10.1039/C8EM00515J.

D'eon JC, Mabury SA. 2007. Production of perfluorinated carboxylic acids (PFCAs) from the biotransformation of polyfluoroalkyl phosphate surfactants (PAPS): exploring routes of human contamination. Environ Sci Technol 41(13):4799–4805, PMID: 17695932, https://doi.org/10.1021/es070126x.

D'eon JC, Mabury SA. 2011. Exploring indirect sources of human exposure to perfluoroalkyl carboxylates (PFCAs): evaluating uptake, elimination, and biotransformation of polyfluoroalkyl phosphate esters (PAPs) in the rat. Environ Health Perspect 119(3):344–350, PMID: 21059488, https://doi.org/10.1289/ehp.1002409.

Dalahmeh S, Tirgani S, Komakech AJ, Niwagaba CB, Ahrens L. 2018. Per- and polyfluoroalkyl substances (PFASs) in water, soil and plants in wetlands and agricultural areas in Kampala, Uganda. Sci Total Environ 631–632:660–667, PMID: 29539594, https://doi.org/10.1016/j.scitotenv.2018.03.024.

Danish Environmental Protection Agency. 2015. *Short-Chain Polyfluoroalkyl Substances (PFAS). A Literature Review of Information on Human Health Effects and Environmental Fate and Effect Aspects of Short-Chain PFAS*. Environmental Project No. 1707. Copenhagen, Denmark: Danish Environmental

Protection Agency. https://www2.mst.dk/Udgiv/publications/2015/05/978-87-93352-15-5.pdf [accessed 19 January 2021].

Das KP, Grey BE, Zehr RD, Wood CR, Butenhoff JL, Chang SC, et al. 2008. Effects of perfluorobutyrate exposure during pregnancy in the mouse. Toxicol Sci 105(1):173–181, PMID: 18511431, https://doi.org/10.1093/toxsci/kfn099.

DeWitt JC. 2015. *Toxicological Effects of Perfluoroalkyl and Polyfluoroalkyl Substances*. Cham, Switzerland: Springer.

Domingo JL, Nadal M. 2017. Per- and polyfluoroalkyl substances (PFASs) in food and human dietary intake: a review of the recent scientific literature. J Agric Food Chem 65(3):533–543, PMID: 28052194, https://doi.org/10.1021/acs.jafc.6b04683.

Dreyer A, Kirchgeorg T, Weinberg I, Matthias V. 2015. Particle-size distribution of airborne poly- and perfluorinated alkyl substances. Chemosphere 129:142–149, PMID: 25027782, https://doi.org/10.1016/j.chemosphere.2014.06.069.

DTSC (Department of Toxic Substances Control). 2013. Safer Consumer Product Regulations. https://dtsc.ca.gov/regs/safer-consumer-product-regulations/ [accessed 12 December 2019].

DTSC. 2018. *Product-Chemical Profile for Nonylphenol Ethoxylates in Laundry Detergents*. May 2018, Discussion Draft. https://dtsc.ca.gov/wp-content/uploads/sites/31/2019/03/Internal_Profile_for-NPEs_Laundry_Detergent.pdf [accessed 4 December 2020].

ECHA (European Chemicals Agency). 2020. Candidate list of substances of very high concern for authorisation. https://echa.europa.eu/web/guest/candidate-list-table [accessed 11 May 2020].

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), Knutsen HK, Alexander J, Barregård L, Bignami M, Brüschweiler B, et al. 2018. Risk to human health related to the presence of perfluorooctane sulfonic acid and perfluorooctanoic acid in food. EFSA J 16(12):5194, PMID: 32625773, https://doi.org/10.2903/j.efsa.2018.5194.

Eggers Pedersen K, Basu N, Letcher R, Greaves AK, Sonne C, Dietz R, et al. 2015. Brain region-specific perfluoroalkylated sulfonate (PFSA) and carboxylic acid (PFCA) accumulation and neurochemical biomarker responses in east Greenland polar bears (*Ursus maritimus*). Environ Res 138:22–31, PMID: 25682255, https://doi.org/10.1016/j.envres.2015.01.015.

Eriksson U, Kärrman A. 2015. World-wide indoor exposure to polyfluoroalkyl phosphate esters (PAPs) and other PFASs in household dust. Environ Sci Technol 49(24):14503–14511, PMID: 26000882, https://doi.org/10.1021/acs.est.5b00679.

Eryasa B, Grandjean P, Nielsen F, Valvi D, Zmirou-Navier D, Sunderland E, et al. 2019. Physico-chemical properties and gestational diabetes predict transplacental transfer and partitioning of perfluoroalkyl substances. Environ Int 130:104874, PMID: 31200157, https://doi.org/10.1016/j.envint.2019.05.068.

Feng M, Qu R, Wei Z, Wang L, Sun P, Wang Z, et al. 2015. Characterization of the thermolysis products of Nafion membrane: a potential source of perfluorinated compounds in the environment. Sci Rep 5:9859, PMID: 25947254, https://doi.org/10.1038/srep09859.

Feuer M. 2008. Assembly Bill No. 1879. Chapter 559. Hazardous materials: toxic substances. https://dtsc.ca.gov/wp-content/uploads/sites/31/2018/01/ab_1879_GCI.pdf [accessed 19 January 2021].

Fraser AJ, Webster TF, Watkins DJ, Strynar MJ, Kato K, Calafat AM, et al. 2013. Polyfluorinated compounds in dust from homes, offices, and vehicles as predictors of concentrations in office workers' serum. Environ Int 60:128–136, PMID: 24041736, https://doi.org/10.1016/j.envint.2013.08.012.

Fromme H, Mosch C, Morovitz M, Alba-Alejandre I, Boehmer S, Kiranoglu M, et al. 2010. Pre- and postnatal exposure to perfluorinated compounds (PFCs). Environ Sci Technol 44(18):7123–7129, PMID: 20722423, https://doi.org/10.1021/es101184f.

Gebbink WA, Bossi R, Rigét FF, Rosing-Asvid A, Sonne C, Dietz R. 2016. Observation of emerging per- and polyfluoroalkyl substances (PFASs) in Greenland marine mammals. Chemosphere 144:2384–2391, PMID: 26610298, https://doi.org/10.1016/j.chemosphere.2015.10.116.

Gebbink WA, Glynn A, Darnerud PO, Berger U. 2015. Perfluoroalkyl acids and their precursors in Swedish food: the relative importance of direct and indirect dietary exposure. Environ Pollut 198:108–115, PMID: 25590128, https://doi.org/10.1016/j.envpol.2014.12.022.

Gellrich V, Brunn H, Stahl T. 2013. Perfluoroalkyl and polyfluoroalkyl substances (PFASs) in mineral water and tap water. J Environ Sci Health A Tox Hazard Subst Environ Eng 48(2):129–135, PMID: 23043333, https://doi.org/10.1080/10934529.2013.719431.

Giesy JP, Kannan K. 2001. Global distribution of perfluorooctane sulfonate in wildlife. Environ Sci Technol 35(7):1339–1342, PMID: 11348064, https://doi.org/10.1021/es001834k.

Gobelius L, Lewis J, Ahrens L. 2017. Plant uptake of per- and polyfluoroalkyl substances at a contaminated fire training facility to evaluate the phytoremediation potential of various plant species. Environ Sci Technol 51(21):12602–12610, PMID: 28972370, https://doi.org/10.1021/acs.est.7b02926.

Gomis MI, Vestergren R, Borg D, Cousins IT. 2018. Comparing the toxic potency in vivo of long-chain perfluoroalkyl acids and fluorinated alternatives. Environ Int 113:1–9, PMID: 29421396, https://doi.org/10.1016/j.envint.2018.01.011.

Grandjean P, Clapp R. 2014. Changing interpretation of human health risks from perfluorinated compounds. Public Health Rep 129(6):482–485, PMID: 25364048, https://doi.org/10.1177/003335491412900605.

Grandjean P, Heilmann C, Weihe P, Nielsen F, Mogensen UB, Budtz-Jørgensen E, et al. 2017a. Serum vaccine antibody concentrations in adolescents exposed to perfluorinated compounds. Environ Health Perspect 125(7):077018, PMID: 28749778, https://doi.org/10.1289/EHP275.

Grandjean P, Heilmann C, Weihe P, Nielsen F, Mogensen UB, Timmermann A, et al. 2017b. Estimated exposures to perfluorinated compounds in infancy predict attenuated vaccine antibody concentrations at age 5-years. J Immunotoxicol 14(1):188–195, PMID: 28805477, https://doi.org/10.1080/1547691X.2017.1360968.

Greaves AK, Letcher RJ, Sonne C, Dietz R, Born EW. 2012. Tissue-specific concentrations and patterns of perfluoroalkyl carboxylates and sulfonates in East Greenland polar bears. Environ Sci Technol 46(21):11575–11583, PMID: 23057644, https://doi.org/10.1021/es303400f.

Hagenaars A, Vergauwen L, De Coen W, Knapen D. 2011. Structure–activity relationship assessment of four perfluorinated chemicals using a prolonged zebrafish early life stage test. Chemosphere 82(5):764–772, PMID: 21111445, https://doi.org/10.1016/j.chemosphere.2010.10.076.

Hamid H, Li L. 2016. Role of wastewater treatment plant in environmental cycling of poly- and perfluoroalkyl substances. Ecocycles 2(2):43–53, https://doi.org/10.19040/ecocycles.v2i2.62.

Hartmann C, Raffesberg W, Scharf S, Uhl M. 2017. Perfluoroalkylated substances in human urine: results of a biomonitoring pilot study. Biomonitoring 4(1):1–10, https://doi.org/10.1515/bimo-2017-0001.

Haug LS, Huber S, Schlabach M, Becher G, Thomsen C. 2011. Investigation on per- and polyfluorinated compounds in paired samples of house dust and indoor air from Norwegian homes. Environ Sci Technol 45(19):7991–7998, PMID: 21417377, https://doi.org/10.1021/es103456h.

Hebert PC, MacManus-Spencer LA. 2010. Development of a fluorescence model for the binding of medium- to long-chain perfluoroalkyl acids to human serum albumin through a mechanistic evaluation of spectroscopic evidence. Anal Chem 82(15):6463–6471, PMID: 20590160, https://doi.org/10.1021/ac100721e.

Houtz EF, Sutton R, Park JS, Sedlak M. 2016. Poly- and perfluoroalkyl substances in wastewater: significance of unknown precursors, manufacturing shifts, and likely AFFF impacts. Water Res 95:142–149, PMID: 26990839, https://doi.org/10.1016/j.watres.2016.02.055.

Huber S, Moe MK, Schmidbauer N, et al. 2009. *Emissions from Incineration of Fluoropolymer Materials: A literature Survey*. Report Number OR112/2009. Kjeller, Norway: Norwegian Institute for Air Research.

Hurley S, Goldberg D, Wang M, Park JS, Petreas M, Bernstein L, et al. 2018. Time trends in per- and polyfluoroalkyl substances (PFASs) in California women: declining serum levels, 2011–2015. Environ Sci Technol 52(1):277–287, PMID: 29198103, https://doi.org/10.1021/acs.est.7b04650.

Ishibashi H, Yamauchi R, Matsuoka M, Kim JW, Hirano M, Yamaguchi A, et al. 2008. Fluorotelomer alcohols induce hepatic vitellogenin through activation of the estrogen receptor in male medaka (*Oryzias latipes*). Chemosphere 71(10):1853–1859, PMID: 18334264, https://doi.org/10.1016/j.chemosphere.2008.01.065.

Jones PD, Hu W, De Coen W, Newsted JL, Giesy JP. 2003. Binding of perfluorinated fatty acids to serum proteins. Environ Toxicol Chem 22(11):2639–2649, PMID: 14587903, https://doi.org/10.1897/02-553.

Kabadi SV, Fisher J, Aungst J, Rice P. 2018. Internal exposure-based pharmacokinetic evaluation of potential for biopersistence of 6:2 fluorotelomer alcohol (FTOH) and its metabolites. Food Chem Toxicol 112:375–382, PMID: 29331735, https://doi.org/10.1016/j.fct.2018.01.012.

Kabadi SV, Fisher JW, Doerge DR, Mehta D, Aungst J, Rice P. 2020. Characterizing biopersistence potential of the metabolite 5:3 fluorotelomer carboxylic acid after repeated oral exposure to the 6:2 fluorotelomer alcohol. Toxicol Appl Pharmacol 388:114878, PMID: 31923437, https://doi.org/10.1016/j.taap.2020.114878.

Kang H, Choi K, Lee HS, Kim DH, Park NY, Kim S, et al. 2016. Elevated levels of short carbon-chain PFCAs in breast milk among Korean women: current status and potential challenges. Environ Res 148:351–359, PMID: 27111244, https://doi.org/10.1016/j.envres.2016.04.017.

Kärrman A, Ericson I, van Bavel B, Darnerud PO, Aune M, Glynn A, et al. 2007. Exposure of perfluorinated chemicals through lactation: levels of matched human milk and serum and a temporal trend, 1996–2004, in Sweden. Environ Health Perspect 115(2):226–230, PMID: 17384769, https://doi.org/10.1289/ehp.9491.

KEMI (Swedish Chemicals Agency). 2015. Occurrence and use of highly fluorinated substances and alternatives. Report from a government assignment. Swedish Chemicals Agency (KEMI). Stockholm, Sweden. 2021. https://www.kemi.se/download/18.6df1d3df171c243fb23a98ea/1591454109137/report-7-15-occurrence-and-use-of-highly-fluorinated-substances-and-alternatives.pdf [accessed 29 January 2021].

Kim DH, Lee MY, Oh JE. 2014. Perfluorinated compounds in serum and urine samples from children aged 5–13 years in South Korea. Environ Pollut 192:171–178, PMID: 24952613, https://doi.org/10.1016/j.envpol.2014.05.024.

Kim SK, Kannan K. 2007. Perfluorinated acids in air, rain, snow, surface runoff, and lakes: relative importance of pathways to contamination of urban lakes. Environ Sci Technol 41(24):8328–8334, PMID: 18200859, https://doi.org/10.1021/es072107t.

Kim Lazcano R, Choi YJ, Mashtare ML, Lee LS. 2020. Characterizing and comparing per- and polyfluoroalkyl substances in commercially available biosolid and organic non-biosolid-based products. Environ Sci Technol 54(14):8640–8648, PMID: 32567309, https://doi.org/10.1021/acs.est.9b07281.

Kiplinger JL, Richmond TG, Osterberg CE. 1994. Activation of carbon-fluorine bonds by metal complexes. Chem Rev 94(2):373–431, https://doi.org/10.1021/cr00026a005.

Kirchgeorg T, Dreyer A, Gabrieli P, Gabrieli J, Thompson LG, Barbante C, et al. 2016. Seasonal accumulation of persistent organic pollutants on a high altitude glacier in the Eastern Alps. Environ Pollut 218:804–812, PMID: 27554981, https://doi.org/10.1016/j.envpol.2016.08.004.

Klaunig JE, Shinohara M, Iwai H, Chengelis CP, Kirkpatrick JB, Wang Z, et al. 2015. Evaluation of the chronic toxicity and carcinogenicity of perfluorohexanoic acid (PFHxA) in Sprague-Dawley rats. Toxicol Pathol 43(2):209–220, PMID: 25377447, https://doi.org/10.1177/0192623314530532.

Krafft MP, Riess JG. 2015. Selected physicochemical aspects of poly- and perfluoroalkylated substances relevant to performance, environment and sustainability—part one. Chemosphere 129:4–19, PMID: 25245564, https://doi.org/10.1016/j.chemosphere.2014.08.039.

Kwiatkowski CF, Andrews DQ, Birnbaum LS, Bruton TA, DeWitt JC, Knappe DRU, et al. 2020. Scientific basis for managing PFAS as a chemical class. Environ Sci Technol Lett 7(8):532–543, https://doi.org/10.1021/acs.estlett.0c00255.

Ladics GS, Kennedy GL, O'Connor J, Everds N, Malley LA, Frame SR, et al. 2008. 90-day oral gavage toxicity study of 8-2 fluorotelomer alcohol in rats. Drug Chem Toxicol 31(2):189–216, PMID: 18330782, https://doi.org/10.1080/01480540701873103.

Lang JR, Allred BM, Field JA, Levis JW, Barlaz MA. 2017. National estimate of per- and polyfluoroalkyl substance (PFAS) release to U.S. municipal landfill leachate. Environ Sci Technol 51(4):2197–2205, PMID: 28103667, https://doi.org/10.1021/acs.est.6b05005.

Latała A, Nędzi M, Stepnowski P. 2009. Acute toxicity assessment of perfluorinated carboxylic acids towards the Baltic microalgae. Environ Toxicol Pharmacol 28(2):167–171, PMID: 21783999, https://doi.org/10.1016/j.etap.2009.03.010.

Lechner M, Knapp H. 2011. Carryover of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) from soil to plant and distribution to the different plant compartments studied in cultures of carrots (*Daucus carota* ssp. *sativus*), potatoes (*Solanum tuberosum*), and cucumbers (*Cucumis sativus*). J Agric Food Chem 59(20):11011–11018, PMID: 21905714, https://doi.org/10.1021/jf201355y.

Lee S, Kim S, Park J, Kim HJ, Choi G, Choi S, et al. 2018. Perfluoroalkyl substances (PFASs) in breast milk from Korea: time-course trends, influencing factors, and infant exposure. Sci Total Environ 612:286–292, PMID: 28865262, https://doi.org/10.1016/j.scitotenv.2017.08.094.

Letcher RJ, Chu S, Smyth SA. 2020. Side-chain fluorinated polymer surfactants in biosolids from wastewater treatment plants. J Hazard Mater 388:122044, PMID: 31955025, https://doi.org/10.1016/j.jhazmat.2020.122044.

Li F, Duan J, Tian S, Ji H, Zhu Y, Wei Z, et al. 2020. Short-chain per- and polyfluoroalkyl substances in aquatic systems: occurrence, impacts and treatment. Chem Eng J 380:122506, https://doi.org/10.1016/j.cej.2019.122506.

Li L, Liu J, Hu J, Wania F. 2017. Degradation of fluorotelomer-based polymers contributes to the global occurrence of fluorotelomer alcohol and perfluoroalkyl carboxylates: a combined dynamic substance flow and environmental fate modeling analysis. Environ Sci Technol 51(8):4461–4470, PMID: 28301932, https://doi.org/10.1021/acs.est.6b04021.

Li Y, Yu N, Du L, Shi W, Yu H, Song M, et al. 2020. Transplacental transfer of per- and polyfluoroalkyl substances identified in paired maternal and cord sera using suspect and nontarget screening. Environ Sci Technol 54(6):3407–3416, PMID: 32013415, https://doi.org/10.1021/acs.est.9b06505.

Lieder PH, Chang SH, York RG, Butenhoff JL. 2009. Toxicological evaluation of potassium perfluorobutanesulfonate in a 90-day oral gavage study with Sprague–Dawley rats. Toxicology 255(1–2):45–52, PMID: 18992301, https://doi.org/10.1016/j.tox.2008.10.002.

Liu C, Gin KYH, Chang VWC, Goh BPL, Reinhard M. 2011. Novel perspectives on the bioaccumulation of PFCs—the concentration dependency. Environ Sci Technol 45(22):9758–9764, PMID: 21988464, https://doi.org/10.1021/es202078n.

Liu C, Yu L, Deng J, Lam PKS, Wu RSS, Zhou B, et al. 2009. Waterborne exposure to fluorotelomer alcohol 6:2 FTOH alters plasma sex hormone and gene transcription in the hypothalamic–pituitary–gonadal (HPG) axis of zebrafish. Aquat Toxicol 93(2–3):131–137, PMID: 19443055, https://doi.org/10.1016/j.aquatox.2009.04.005.

Llorca M, Farré M, Picó Y, Teijón ML, Alvarez JG, Barceló D, et al. 2010. Infant exposure of perfluorinated compounds: levels in breast milk and commercial baby food. Environ Int 36(6):584–592, PMID: 20494442, https://doi.org/10.1016/j.envint.2010.04.016.

Loveless SE, Slezak B, Serex T, Lewis J, Mukerji P, O'Connor JC, et al. 2009. Toxicological evaluation of sodium perfluorohexanoate. Toxicology 264(1–2):32–44, PMID: 19632293, https://doi.org/10.1016/j.tox.2009.07.011.

Mackay D, Hughes DM, Romano ML, Bonnell M. 2014. The role of persistence in chemical evaluations. Integr Environ Assess Manag 10(4):588–594, PMID: 24753402, https://doi.org/10.1002/ieam.1545.

Malits J, Blustein J, Trasande L, Attina TM. 2018. Perfluorooctanoic acid and low birth weight: estimates of US attributable burden and economic costs from 2003 through 2014. Int J Hyg Environ Health 221(2):269–275, PMID: 29175300, https://doi.org/10.1016/j.ijheh.2017.11.004.

Mamsen LS, Björvang RD, Mucs D, Vinnars MT, Papadogiannakis N, Lindh CH, et al. 2019. Concentrations of perfluoroalkyl substances (PFASs) in human embryonic and fetal organs from first, second, and third trimester pregnancies. Environ Int 124:482–492, PMID: 30684806, https://doi.org/10.1016/j.envint.2019.01.010.

Martín J, Santos JL, Aparicio I, Alonso E. 2019. Exposure assessment to parabens, bisphenol A and perfluoroalkyl compounds in children, women and men by hair analysis. Sci Total Environ 695:133864, PMID: 31421338, https://doi.org/10.1016/j.scitotenv.2019.133864.

McLachlan MS, Felizeter S, Klein M, Kotthoff M, De Voogt P. 2019. Fate of a perfluoroalkyl acid mixture in an agricultural soil studied in lysimeters. Chemosphere 223:180–187, PMID: 30776763, https://doi.org/10.1016/j.chemosphere.2019.02.012.

Midasch O, Drexler H, Hart N, Beckmann MW, Angerer J. 2007. Transplacental exposure of neonates to perfluorooctanesulfonate and perfluorooctanoate: a pilot study. Int Arch Occup Environ Health 80(7):643–648, PMID: 17219182, https://doi.org/10.1007/s00420-006-0165-9.

Mogensen UB, Grandjean P, Nielsen F, Weihe P, Budtz-Jørgensen E. 2015. Breastfeeding as an exposure pathway for perfluorinated alkylates. Environ Sci Technol 49(17):10466–10473, PMID: 26291735, https://doi.org/10.1021/acs.est.5b02237.

Mondal D, Weldon RH, Armstrong BG, Gibson LJ, Lopez-Espinosa MJ, Shin HM, et al. 2014. Breastfeeding: a potential excretion route for mothers and implications for infant exposure to perfluoroalkyl acids. Environ Health Perspect 122(2):187–192, PMID: 24280536, https://doi.org/10.1289/ehp.1306613.

Monroy R, Morrison K, Teo K, Atkinson S, Kubwabo C, Stewart B, et al. 2008. Serum levels of perfluoroalkyl compounds in human maternal and umbilical cord blood samples. Environ Res 108(1):56–62, PMID: 18649879, https://doi.org/10.1016/j.envres.2008.06.001.

Muir D, Bossi R, Carlsson P, Evans M, De Silva A, Halsall C, et al. 2019. Levels and trends of poly- and perfluoroalkyl substances in the Arctic environment—an update. Emerg Contam 5:240–271, https://doi.org/10.1016/j.emcon.2019.06.002.

Nilsson H, Kärrman A, Rotander A, van Bavel B, Lindström G, Westberg H, et al. 2010. Inhalation exposure to fluorotelomer alcohols yield perfluorocarboxylates in human blood? Environ Sci Technol 44(19):7717–7722, PMID: 20828202, https://doi.org/10.1021/es101951t.

Nyberg E, Awad R, Bignert A, Ek C, Sallsten G, Benskin JP, et al. 2018. Inter-individual, inter-city, and temporal trends of per- and polyfluoroalkyl substances in human milk from Swedish mothers between 1972 and 2016. Environ Sci Process Impacts 20(8):1136–1147, PMID: 29987291, https://doi.org/10.1039/c8em00174j.

O'Connor JC, Munley SM, Serex TL, Buck RC. 2014. Evaluation of the reproductive and developmental toxicity of 6:2 fluorotelomer alcohol in rats. Toxicology 317:6–16, PMID: 24447377, https://doi.org/10.1016/j.tox.2014.01.002.

OECD (Organisation for Economic Co-operation and Development). 2013. *Synthesis Paper on Per- and Polyfluorinated Chemicals (PFCs)*. Paris, France: OECD. http://www.oecd.org/env/ehs/risk-management/pfc_final-web.pdf [accessed 19 January 2021].

OECD. 2018. *Toward a New Comprehensive Global Database of Per- and Polyfluoroalkyl Substances (PFASs): Summary Report on Updating the OECD 2007 List of Per- and Polyfluoroalkyl Substances (PFASs)*. Series on Risk Management No. 39. ENV/JM/MONO(2018)7. Paris, France: OECD. http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-JM-MONO(2018)7&doclanguage=en [accessed 19 January 2021].

OEHHA (Office of Environmental Health Hazard Assessment). 2012a. Amended Final Statement of Reasons, Division 4.5, Title 22, Cal. Code of Regulations, Chapter 54, Green Chemistry Hazard Traits. https://oehha.ca.gov/media/downloads/risk-assessment/gcfsor011912.pdf [accessed 11 May 2020].

OEHHA. 2012b. Division 4.5, Title 22, California Code of Regulations, Chapter 54. Green Chemistry Hazard Traits for California's Toxics Information Clearinghouse. https://oehha.ca.gov/media/downloads/risk-assessment//gcregtext011912.pdf [accessed 12 May 2020].

Olsen GW, Burris JM, Ehresman DJ, Froehlich JW, Seacat AM, Butenhoff JL, et al. 2007a. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environ Health Perspect 115(9):1298–1305, PMID: 17805419, https://doi.org/10.1289/ehp.10009.

Olsen GW, Mair DC, Reagen WK, Ellefson ME, Ehresman DJ, Butenhoff JL, et al. 2007b. Preliminary evidence of a decline in perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations in American Red Cross blood donors. Chemosphere 68(1):105–111, PMID: 17267015, https://doi.org/10.1016/j.chemosphere.2006.12.031.

Pelch KE, Reade A, Wolffe TAM, Kwiatkowski CF. 2019. PFAS health effects database: protocol for a systematic evidence map. Environ Int 130:104851, PMID: 31284092, https://doi.org/10.1016/j.envint.2019.05.045.

Pérez F, Llorca M, Farré M, Barceló D. 2012. Automated analysis of perfluorinated compounds in human hair and urine samples by turbulent flow chromatography coupled to tandem mass spectrometry. Anal Bioanal Chem 402(7):2369–2378, PMID: 22227745, https://doi.org/10.1007/s00216-011-5660-5.

Pérez F, Llorca M, Köck-Schulmeyer M, Škrbić B, Oliveira LS, da Boit Martinello K, et al. 2014. Assessment of perfluoroalkyl substances in food items at global scale. Environ Res 135:181–189, PMID: 25282275, https://doi.org/10.1016/j.envres.2014.08.004.

Pérez F, Nadal M, Navarro-Ortega A, Fàbrega F, Domingo JL, Barceló D, et al. 2013. Accumulation of perfluoroalkyl substances in human tissues. Environ Int 59:354–362, PMID: 23892228, https://doi.org/10.1016/j.envint.2013.06.004.

Phillips MMM, Dinglasan-Panlilio MJA, Mabury SA, Solomon KR, Sibley PK. 2007. Fluorotelomer acids are more toxic than perfluorinated acids. Environ Sci Technol 41(20):7159–7163, PMID: 17993163, https://doi.org/10.1021/es070734c.

Poothong S, Thomsen C, Padilla-Sanchez JA, Papadopoulou E, Haug LS. 2017. Distribution of novel and well-known poly- and perfluoroalkyl substances (PFASs) in human serum, plasma, and whole blood. Environ Sci Technol 51(22):13388–13396, PMID: 29056041, https://doi.org/10.1021/acs.est.7b03299.

POPRC (Persistent Organic Pollutants Review Committee). 2020. POPRC recommendations for listing chemicals. http://chm.pops.int/tabid/243/Default.aspx [accessed 11 May 2020].

Prevedouros K, Cousins IT, Buck RC, Korzeniowski SH. 2006. Sources, fate and transport of perfluorocarboxylates. Environ Sci Technol 40(1):32–44, PMID: 16433330, https://doi.org/10.1021/es0512475.

Rand AA, Mabury SA. 2012a. Assessing the structure–activity relationships of fluorotelomer unsaturated acids and aldehydes with glutathione. Reactivity of glutathione with fluorotelomer unsaturated acids and aldehydes. Cell Biol Toxicol 28(2):115–124, PMID: 22252736, https://doi.org/10.1007/s10565-012-9211-4.

Rand AA, Mabury SA. 2012b. In vitro interactions of biological nucleophiles with fluorotelomer unsaturated acids and aldehydes: fate and consequences. Environ Sci Technol 46(13):7398–7406, PMID: 22582947, https://doi.org/10.1021/es3008485.

Rand AA, Mabury SA. 2013. Covalent binding of fluorotelomer unsaturated aldehydes (FTUALs) and carboxylic acids (FTUCAs) to proteins. Environ Sci Technol 47(3):1655–1663, PMID: 23256684, https://doi.org/10.1021/es303760u.

Rand AA, Mabury SA. 2014. Protein binding associated with exposure to fluorotelomer alcohols (FTOHs) and polyfluoroalkyl phosphate esters (PAPs) in rats. Environ Sci Technol 48(4):2421–2429, PMID: 24460105, https://doi.org/10.1021/es404390x.

Rand AA, Mabury SA. 2017. Is there a human health risk associated with indirect exposure to perfluoroalkyl carboxylates (PFCAs)? Toxicology 375:28–36, PMID: 27876672, https://doi.org/10.1016/j.tox.2016.11.011.

Rand AA, Rooney JP, Butt CM, Meyer JN, Mabury SA. 2014. Cellular toxicity associated with exposure to perfluorinated carboxylates (PFCAs) and their metabolic precursors. Chem Res Toxicol 27(1):42–50, PMID: 24299273, https://doi.org/10.1021/tx400317p.

Rankin K, Mabury SA, Jenkins TM, Washington JW. 2016. A North American and global survey of perfluoroalkyl substances in surface soils: distribution patterns and mode of occurrence. Chemosphere 161:333–341, PMID: 27441993, https://doi.org/10.1016/j.chemosphere.2016.06.109.

Rappazzo KM, Coffman E, Hines EP. 2017. Exposure to perfluorinated alkyl substances and health outcomes in children: a systematic review of the epidemiologic literature. Int J Environ Res Public Health 14(7):691, PMID: 28654008, https://doi.org/10.3390/ijerph14070691.

Rice PA, Aungst J, Cooper J, Bandele O, Kabadi SV. 2020. Comparative analysis of the toxicological databases for 6:2 fluorotelomer alcohol (6:2 FTOH) and perfluorohexanoic acid (PFHxA). Food Chem Toxicol 138:111210, PMID: 32087313, https://doi.org/10.1016/j.fct.2020.111210.

Rosenmai AK, Taxvig C, Svingen T, Trier X, van Vugt-Lussenburg BMA, Pedersen M, et al. 2016. Fluorinated alkyl substances and technical mixtures used in food paper-packaging exhibit endocrine-related activity in vitro. Andrology 4(4):662–672, PMID: 27152447, https://doi.org/10.1111/andr.12190.

Ruan Y, Lalwani D, Kwok KY, Yamazaki E, Taniyasu S, Kumar NJI, et al. 2019. Assessing exposure to legacy and emerging per- and polyfluoroalkyl substances via hair—the first nationwide survey in India. Chemosphere 229:366–373, PMID: 31078894, https://doi.org/10.1016/j.chemosphere.2019.04.195.

Scher DP, Kelly JE, Huset CA, Barry KM, Hoffbeck RW, Yingling VL, et al. 2018. Occurrence of perfluoroalkyl substances (PFAS) in garden produce at homes with a history of PFAS-contaminated drinking water. Chemosphere 196:548–555, PMID: 29329087, https://doi.org/10.1016/j.chemosphere.2017.12.179.

Scheringer M, Trier X, Cousins IT, de Voogt P, Fletcher T, Wang Z, et al. 2014. Helsingør statement on poly- and perfluorinated alkyl substances (PFASs). Chemosphere 114:337–339, PMID: 24938172, https://doi.org/10.1016/j.chemosphere.2014.05.044.

Schlummer M, Sölch C, Meisel T, Still M, Gruber L, Wolz G, et al. 2015. Emission of perfluoroalkyl carboxylic acids (PFCA) from heated surfaces made of polytetrafluoroethylene (PTFE) applied in food contact materials and consumer products. Chemosphere 129:46–53, PMID: 25496745, https://doi.org/10.1016/j.chemosphere.2014.11.036.

Seals R, Bartell SM, Steenland K. 2011. Accumulation and clearance of perfluorooctanoic acid (PFOA) in current and former residents of an exposed community. Environ Health Perspect 119(1):119–124, PMID: 20870569, https://doi.org/10.1289/ehp.1002346.

Shi G, Cui Q, Pan Y, Sheng N, Guo Y, Dai J. 2017a. 6:2 Fluorotelomer carboxylic acid (6:2 FTCA) exposure induces developmental toxicity and inhibits the formation of erythrocytes during zebrafish embryogenesis. Aquat Toxicol 190:53–61, PMID: 28688371, https://doi.org/10.1016/j.aquatox.2017.06.023.

Shi G, Cui Q, Pan Y, Sheng N, Sun S, Guo Y, et al. 2017b. 6:2 Chlorinated polyfluorinated ether sulfonate, a PFOS alternative, induces embryotoxicity and disrupts cardiac development in zebrafish embryos. Aquat Toxicol 185:67–75, PMID: 28187362, https://doi.org/10.1016/j.aquatox.2017.02.002.

Shi Y, Vestergren R, Xu L, Zhou Z, Li C, Liang Y, et al. 2016. Human exposure and elimination kinetics of chlorinated polyfluoroalkyl ether sulfonic acids (Cl-PFESAs). Environ Sci Technol 50(5):2396–2404, PMID: 26866980, https://doi.org/10.1021/acs.est.5b05849.

Shin HM, Moschet C, Young TM, Bennett DH. 2020. Measured concentrations of consumer product chemicals in California house dust: implications for sources, exposure, and toxicity potential. Indoor Air 30(1):60–75, PMID: 31587372, https://doi.org/10.1111/ina.12607.

Skuladottir M, Ramel A, Rytter D, Haug LS, Sabaredzovic A, Bech BH, et al. 2015. Examining confounding by diet in the association between perfluoroalkyl acids and serum cholesterol in pregnancy. Environ Res 143(pt A):33–38, PMID: 26432473, https://doi.org/10.1016/j.envres.2015.09.001.

Slotkin TA, MacKillop EA, Melnick RL, Thayer KA, Seidler FJ. 2008. Developmental neurotoxicity of perfluorinated chemicals modeled *in vitro*. Environ Health Perspect 116(6):716–722, PMID: 18560525, https://doi.org/10.1289/ehp.11253.

Stahl T, Heyn J, Thiele H, Hüther J, Failing K, Georgii S, et al. 2009. Carryover of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) from soil to plants. Arch Environ Contam Toxicol 57(2):289–298, PMID: 19112561, https://doi.org/10.1007/s00244-008-9272-9.

Stahl T, Mattern D, Brunn H. 2011. Toxicology of perfluorinated compounds. Environ Sci Eur 23(1):38, https://doi.org/10.1186/2190-4715-23-38.

Tao L, Kannan K, Aldous KM, Mauer MP, Eadon GA. 2008a. Biomonitoring of perfluorochemicals in plasma of New York State personnel responding to the World Trade Center disaster. Environ Sci Technol 42(9):3472–3478, PMID: 18522136, https://doi.org/10.1021/es8000079.

Tao L, Kannan K, Wong CM, Arcaro KF, Butenhoff JL. 2008b. Perfluorinated compounds in human milk from Massachusetts, U.S.A. Environ Sci Technol 42(8):3096–3101, PMID: 18497172, https://doi.org/10.1021/es702789k.

U.S. EPA (U.S. Environmental Protection Agency). 2020a. Drinking water health advisories for PFOA and PFOS. https://www.epa.gov/ground-water-and-drinking-water/drinking-water-health-advisories-pfoa-and-pfos [accessed 11 May 2020].

U.S. EPA. 2020b. PFAS Master List of PFAS Substances (Version 2). https://comptox.epa.gov/dashboard/chemical_lists/pfasmaster [accessed 11 May 2020].

U.S. EPA. 2020c. Risk management for per- and polyfluoroalkyl substances (PFASs) under TSCA. https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-management-and-polyfluoroalkyl-substances-pfass [accessed 11 May 2020].

Ulhaq M, Carlsson G, Örn S, Norrgren L. 2013. Comparison of developmental toxicity of seven perfluoroalkyl acids to zebrafish embryos. Environ Toxicol Pharmacol 36(2):423–426, PMID: 23770452, https://doi.org/10.1016/j.etap.2013.05.004.

UNEP (United Nations Environment Programme). 2020. All POPs listed in the Stockholm Convention. http://chm.pops.int/TheConvention/ThePOPs/AllPOPs/tabid/2509/Default.aspx [accessed 12 May 2020].

Wang C, Lu Y, Li Q, Cao X, Zhang M, Zhou Y, et al. 2019. Assessing the contribution of atmospheric transport and tourism activities to the occurrence of perfluoroalkyl acids (PFAAs) in an Alpine nature reserve. Sci Total Environ 697:133851, PMID: 31479908, https://doi.org/10.1016/j.scitotenv.2019.133851.

Wang Z, Cousins IT, Berger U, Hungerbühler K, Scheringer M. 2016. Comparative assessment of the environmental hazards of and exposure to perfluoroalkyl phosphonic and phosphinic acids (PFPAs and PFPiAs): current knowledge, gaps, challenges and research needs. Environ Int 89–90:235–247, PMID: 26922149, https://doi.org/10.1016/j.envint.2016.01.023.

Wang Z, Cousins IT, Scheringer M, Buck RC, Hungerbühler K. 2014a. Global emission inventories for C4–C14 perfluoroalkyl carboxylic acid (PFCA) homologues from 1951 to 2030, part I: production and emissions from quantifiable sources.

Environ Int 70:62–75, PMID: 24932785, https://doi.org/10.1016/j.envint.2014.04.013.

Wang Z, DeWitt JC, Higgins CP, Cousins IT. 2017. A never-ending story of per- and polyfluoroalkyl substances (PFASs)? Environ Sci Technol 51(5):2508–2518, PMID: 28224793, https://doi.org/10.1021/acs.est.6b04806.

Wang Z, Goldenman G, Tugran T, McNeil A, Jones M. 2020. Per- and polyfluoroalkylether substances: identity, production and use. Working Paper NA2020:901. Copenhagen, Denmark: Nordic Council of Ministers.

Wang Z, Xie Z, Möller A, Mi W, Wolschke H, Ebinghaus R, et al. 2014b. Atmospheric concentrations and gas/particle partitioning of neutral poly- and perfluoroalkyl substances in northern German Coast. Atmos Environ 95:207–213, https://doi.org/10.1016/j.atmosenv.2014.06.036.

Washington JW, Jenkins TM, Rankin K, Naile JE. 2015. Decades-scale degradation of commercial, side-chain, fluorotelomer-based polymers in soils and water. Environ Sci Technol 49(2):915–923, PMID: 25426868, https://doi.org/10.1021/es504347u.

Washington JW, Rankin K, Libelo EL, Lynch DG, Cyterski M. 2019. Determining global background soil PFAS loads and the fluorotelomer-based polymer degradation rates that can account for these loads. Sci Total Environ 651(pt 2):2444–2449, PMID: 30336434, https://doi.org/10.1016/j.scitotenv.2018.10.071.

Weiss JM, Andersson PL, Lamoree MH, Leonards PEG, van Leeuwen SPJ, Hamers T, et al. 2009. Competitive binding of poly- and perfluorinated compounds to the thyroid hormone transport protein transthyretin. Toxicol Sci 109(2):206–216, PMID: 19293372, https://doi.org/10.1093/toxsci/kfp055.

White SS, Fenton SE, Hines EP. 2011. Endocrine disrupting properties of perfluorooctanoic acid. J Steroid Biochem Mol Biol 127(1–2):16–26, PMID: 21397692, https://doi.org/10.1016/j.jsbmb.2011.03.011.

Winkens K, Vestergren R, Berger U, Cousins IT. 2017. Early life exposure to per- and polyfluoroalkyl substances (PFASs): a critical review. Emerg Contam 3(2):55–68, https://doi.org/10.1016/j.emcon.2017.05.001.

Winquist A, Steenland K. 2014. Perfluorooctanoic acid exposure and thyroid disease in community and worker cohorts. Epidemiology 25(2):255–264, PMID: 24407430, https://doi.org/10.1097/EDE.0000000000000040.

Wolf CJ, Takacs ML, Schmid JE, Lau C, Abbott BD. 2008. Activation of mouse and human peroxisome proliferator-activated receptor alpha by perfluoroalkyl acids of different functional groups and chain lengths. Toxicol Sci 106(1):162–171, PMID: 18713766, https://doi.org/10.1093/toxsci/kfn166.

Xiao F. 2017. Emerging poly- and perfluoroalkyl substances in the aquatic environment: a review of current literature. Water Res 124:482–495, PMID: 28800519, https://doi.org/10.1016/j.watres.2017.07.024.

Xie Z, Wang Z, Mi W, Möller A, Wolschke H, Ebinghaus R, et al. 2015. Neutral poly-/perfluoroalkyl substances in air and snow from the Arctic. Sci Rep 5:8912, PMID: 25746440, https://doi.org/10.1038/srep08912.

Yang L, Wang Z, Shi Y, Li J, Wang Y, Zhao Y, et al. 2016. Human placental transfer of perfluoroalkyl acid precursors: levels and profiles in paired maternal and cord serum. Chemosphere 144:1631–1638, PMID: 26517392, https://doi.org/10.1016/j.chemosphere.2015.10.063.

Yao Y, Zhao Y, Sun H, Chang S, Zhu L, Alder AC, et al. 2018. Per- and polyfluoroalkyl substances (PFASs) in indoor air and dust from homes and various microenvironments in China: implications for human exposure. Environ Sci Technol 52(5):3156–3166, PMID: 29415540, https://doi.org/10.1021/acs.est.7b04971.

Yoo H, Washington JW, Jenkins TM, Ellington JJ. 2011. Quantitative determination of perfluorochemicals and fluorotelomer alcohols in plants from biosolid-amended fields using LC/MS/MS and GC/MS. Environ Sci Technol 45(19):7985–7990, PMID: 21247105, https://doi.org/10.1021/es102972m.

Zhang T, Sun H, Lin Y, Qin X, Zhang Y, Geng X, et al. 2013. Distribution of poly- and perfluoroalkyl substances in matched samples from pregnant women and carbon chain length related maternal transfer. Environ Sci Technol 47(14):7974–7981, PMID: 23777259, https://doi.org/10.1021/es400937y.

Zhao L, Zhang Y, Zhu L, Ma X, Wang Y, Sun H, et al. 2017. Isomer-specific transplacental efficiencies of perfluoroalkyl substances in human whole blood. Environ Sci Technol Lett 4(10):391–398, https://doi.org/10.1021/acs.estlett.7b00334.

Zhao Z, Xie Z, Möller A, Sturm R, Tang J, Zhang G, et al. 2012. Distribution and long-range transport of polyfluoroalkyl substances in the Arctic, Atlantic Ocean and Antarctic coast. Environ Pollut 170:71–77, PMID: 22771353, https://doi.org/10.1016/j.envpol.2012.06.004.