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Early life exposure to per- and polyfluoroalkyl substances (PFAS) and latent health outcomes: A review including the placenta as a target tissue and possible driver of peri- and postnatal effects

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Abstract

Per- and polyfluoroalkyl substances (PFAS) are ubiquitous drinking water contaminants of concern due to mounting evidence implicating adverse health outcomes associated with exposure, including reduced kidney function, metabolic syndrome, thyroid disruption, and adverse pregnancy outcomes. PFAS have been produced in the U.S. since the 1940s and now encompass a growing chemical family comprised of diverse chemical moieties, yet the toxicological effects have been studied for relatively few compounds. Critically, exposures to some PFAS *in utero* are associated with adverse outcomes for both mother and offspring, such as hypertensive disorders of pregnancy (HDP), including preeclampsia, and low birth weight. Given the relationship between HDP, placental dysfunction, adverse health outcomes, and increased risk for chronic diseases in adulthood, the role of both developmental and lifelong exposure to PFAS likely contributes to disease risk in complex ways. Here, evidence for the role of some PFAS in disrupted thyroid function, kidney disease, and metabolic syndrome is synthesized with an emphasis on the placenta as a critical yet understudied target of PFAS and programming agent of adult disease. Future research efforts must continue to fill the knowledge gap between placental susceptibility to environmental exposures like PFAS, subsequent perinatal health risks for both mother and child, and latent health effects in adult offspring.

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Declaration of interests

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1. Introduction

Per- and polyfluoroalkyl substances (PFAS) comprise a diverse family of compounds used in a wide variety of industrial processes and the production of consumer goods (ITRC 2020). Since their genesis in the 1940s, PFAS have been detected in the ambient environment, wildlife, and human serum around the globe (Calafat et al. 2007; Domingo and Nadal 2019; Hanssen et al. 2013; Olsen et al. 2017). The environmentally and biologically persistent qualities of PFAS have raised concerns, further heightened by mounting scientific and clinical evidence associating PFAS exposure to multiple adverse health outcomes across all life stages.

1.1 Physicochemical Properties and Characterization of PFAS

Naming conventions for PFAS have evolved over time due in part to the increasing complexity and number of unique congeners, leading to inconsistencies across the scientific literature. For example, the term perfluorinated chemical, or PFC, has been widely used in the scientific literature, but it is inaccurate as it does not describe polyfluorinated substances, which are an important component of the PFAS family (ITRC 2020). Additionally, many PFAS exist in multiple ionic states (e.g. acids, cations, anions), with different names (e.g. perfluorooctane sulfonic acid and perfluorooctane sulfonate), and different physicochemical properties. Consistent and unified naming conventions for PFAS would provide clarity, consistency, and improved scientific communication.

PFAS contain 1 or more carbon atoms with fluorine atoms in place of hydrogen atoms, such that the compound contains the moiety C_nF_{2n+1}-R, where R represents additional functional groups (e.g. sulfonate, carboxylic acid; Figure 1) (ITRC 2020). The per- or polyfluoroalkyl moiety is highly chemically and thermally stable with extremely strong carbon-fluorine bonds, and it exhibits both lipophilic and hydrophilic properties (ITRC 2020). Together, these physical and chemical properties make PFAS ideal as surfactants and surface protection products.

PFAS can be broadly divided into polymers and non-polymers. PFAS polymers are thought to pose less of a risk to human and ecological health than some non-polymers and include fluoropolymers, polymeric perfluoropolyethers, and side-chain fluorinated polymers (ITRC 2020). However, the production of PFAS polymers contributes to the presence of non-polymers in the environment through: (1) release of non-polymers as waste byproducts in the production of polymers, (2) degradation of polymers into non-polymers (e.g. PTFE forms PFOA and *N*-methyl perfluorooctane sulfonamide; ITRC 2020). Non-polymer PFAS can be further separated into perfluorinated (fully fluorinated) and polyfluorinated (partially fluorinated) chemicals.

PFAS are individually characterized by carbon chain length and side group structure as well as their history of use. “Legacy” PFAS include compounds with a longstanding history of use and/or long biologic/environmental persistence, whereas replacement and alternative chemistry PFAS are generally referred to as “alternative PFAS” or “replacement PFAS”. However, certain short-chain legacy PFAS are now substituted in place of longer chain compounds to comply with government-derived standards, hence such PFAS could be

considered both a legacy and a replacement compound. For example, PFBS has been utilized as a substitute for PFOS in some manufacturing processes (Table 1 & Figure 2).

1.2 History of PFAS Usage in the U.S.

The earliest known PFAS compound in the U.S. was first synthesized as a fluoropolymer, called polytetrafluoroethylene (PTFE). Roy J. Plunkett is credited with the accidental discovery of PTFE in 1938 while employed by DuPont de Nemours, Inc. (Plunkett 1986). DuPont patented the discovery under the company Kinetic Chemicals in 1941 (Plunkett 1941) and registered the trademarked name, Teflon, in 1945 (Plunkett 1986). By 1948, DuPont was producing over 900 tons of PTFE per year at their facility in Parkersburg, West Virginia and another company, 3M, had begun production of their signature PFAS at their plant in Minnesota (Funderburg 2010).

Between the 1940s and 1950s, the 8-carbon perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) started to be used in the manufacturing of PTFE-based non-stick coatings. From the 1950s to the 1960s, PFOS and PFOA were also used to manufacture stain- and water-resistant products as well as protective coatings. By 1961, PTFE was applied to commercial cookware. From the 1960s to the 1970s, PFOS-based fire-fighting foam was manufactured, although it was later voluntarily phased out of Class A fire-fighting foams beginning in 2000 (US DOD 2000; 3M 2000).

Since their genesis in the mid-1900s, PFAS have since been incorporated into numerous other industrial and consumer products due to their excellent grease/water repellant properties, including: grease-resistant papers (e.g., fast food containers/wrappers, microwave popcorn bags, pizza boxes, candy wrappers); stain resistance either incorporated into or as spray-on coating applied to carpets and upholstery in home and vehicle products; water-resistant clothing and footwear, cleaning products, personal care products (e.g., shampoo, dental floss, cosmetics such as nail polish and eye makeup); paints, varnishes, ski wax and sealants; and Class B aqueous film forming foams (AFFF), which are used at airports and military facilities for firefighting and training exercises; and likely others (ATSDR 2019).

Now, in the 21st century, many consumer products and drinking water sources contain a mixture of PFAS. The specific mixture and volume of PFAS emitted into the environment varies based on the point source (Guelfo et al. 2019; Guelfo and Adamson 2018; Xu et al. 2016). For example, a water system near a military training area would likely have multiple species derived from AFFF present whereas a water system near a textile manufacturing plant would likely have a blend of PFAS precursor and legacy compounds present (e.g. both PFOSA, a PFOS precursor, and PFOS). Over time, the region-specific magnitudes and compositions of environmental contamination by PFAS has resulted in numerous U.S. states and communities with high levels of PFAS in their water, including states impacted by less well-studied alternative compounds [e.g. GenX and ADONA; for detailed reports see Hopkins et al. (2018) and Wang et al. (2013)].

1.4 Sources of PFAS Exposure—PFAS exposure is considered ubiquitous in the U.S., with PFOA and PFOS detectable in >90% of the population (Kato et al. 2011). Humans are exposed to PFAS through a variety of pathways, including through drinking water, air (both

indoor and outdoor), diet, dust, through maternal to fetal transfer *in utero*, and through breastfeeding as neonates (Figure 3; Sunderland et al. 2019). For adults, diet and drinking water are the main sources of exposure, however this may vary depending on lifestyle, diet, proximity to point and nonpoint sources, and local drinking water contamination levels. Formula-fed infants are thought to be the most highly exposed members of the human population due to their high water intake to body weight ratio (Goeden et al. 2019; Goeden 2018). Drinking water may be the largest source of PFAS exposure for communities impacted by high levels of PFAS contamination.

2. Adverse Health Effects Associated with PFAS

The desirable chemical properties of many PFAS paradoxically impart environmentally and biologically undesirable properties, including indefinite environmental persistence and long half lives in many living organisms, including humans. Unlike other common environmental pollutants, such as organochlorine pesticides, PFAS do not bioaccumulate in adipose tissue (Pérez et al. 2013). Some PFAS are structurally similar to natural fatty acids (Vanden Heuvel et al. 2006). Among the tissues evaluated, PFAS primarily accumulate in the serum, lungs, kidney, liver, and brain (Pérez et al. 2013). Human exposure to PFAS has been associated with adverse effects on the immune (NTP 2016), endocrine, metabolic, and reproductive systems (including fertility and pregnancy outcomes), and increased risk for cancer (ATSDR 2020). However, the weight of evidence supporting these associations varies by both outcome and specific PFAS examined.

2.1 History of PFAS-Related Human Health Concerns

Industrial usage of PFAS began in the 1940s, but exposure-related human health effects were not identified for another twenty years and were specific to occupationally exposed workers. These early concerns were largely contained within the industrial sphere for an additional forty years. Nearly six decades after PFAS began to be produced on an industrial scale, PFAS-related health concerns were raised by private citizens after the general public learned of connections between ecological observations and pollution potentially stemming from a nearby PFOA production site.

The first documented concerns regarding the toxicity of PFAS were mentioned in an internal memo at DuPont by Chief Toxicologist Dorothy Hood in 1961 (EWG 2019). By 1980, PFAS were measured in the serum of occupationally exposed workers and in 1981 concerns were raised internally at DuPont regarding birth defects in children born from occupationally exposed women (EWG 2019). Industrial and occupational exposure studies have since shown increased incidence of cancer including bladder (Alexander et al. 2003), kidney (Consonni et al. 2013), prostate (Gilliland and Mandel 1993; Lundin et al. 2009), and liver (Consonni et al. 2013), leukemia (Consonni et al. 2013), kidney disease (Steenland and Woskie 2012), and elevated cholesterol (Costa et al. 2009; Sakr et al. 2007).

Community-based exposure concerns in the U.S. were first raised in 1998 by Wilbur Tennant, a cattle farmer whose land was downstream from and bordered a landfill used by the DuPont Washington Works plant near Parkersburg, WV (Rich 2016). Tennant enlisted legal counsel from Rob Bilott after documenting unusual phenomenon, such as foamy,

discolored water in the creek from which Tennant's cattle drank, atypical behavior of the cattle, and a wide array of physical abnormalities in the cattle including black teeth, skin lesions and tumors, discolored organs, malformed hooves, and calves born with profound birth defects (Rich 2016). One hundred and fifty-three of Tennant's original herd of two hundred cattle died, and Tennant believed the pollution dumped by DuPont into the landfill upstream of his cattle farm was the cause (Rich 2016). What began as a legal case on behalf of a private citizen ultimately led to a larger class-action lawsuit filed by Bilott on behalf of over 70,000 citizens in the Mid-Ohio Valley whose drinking water sources were affected by the contamination stemming from DuPont's plant (Rich 2016).

The class-action lawsuit resulted in a settlement that funded a biomonitoring effort of unprecedented size and scale, called the C8 Health Study (Frisbee et al. 2009). The results of the C8 Health Study identified a probable link between exposure to PFOA and increased cholesterol, kidney cancer, testicular cancer, ulcerative colitis, thyroid disease, and pregnancy-induced hypertension (C8 Science Panel). Since the genesis of the C8 Health Study, numerous epidemiological studies of the adverse health effects associated with PFAS exposure have been conducted across the globe, including many other regions in the U.S., Europe, and China.

Multiple organizations and regulatory agencies in the U.S. have also generated statements based on systematic reviews of the available literature regarding the most well-supported human health effects associated with PFAS. The Center for Disease Control (CDC)/Agency for Toxic Substances and Disease Registry (ATSDR) states that PFAS might increase the risk of cancer, affect the immune system, increase cholesterol levels, act as endocrine disruptors, reduce female fertility, and adversely impact infant/early childhood growth and development (ATSDR 2019). The U.S. Environmental Protection Agency (EPA) states that elevated cholesterol in adults is the most consistent health effect associated with PFAS, but less consistent data suggest PFAS might be associated with low infant birth weight (Johnson et al. 2014; Koustas et al. 2014; Lam et al. 2014), effects on the immune system, increased risk for cancer (specific to PFOA), and disrupted thyroid hormones (specific to PFOS) (822-R-16-005 US EPA). The World Health Organization (WHO)/International Agency for Research on Cancer (IARC) states that PFOA is possibly carcinogenic to humans (IARC 2016). The National Toxicology Program (NTP) states that PFAS might have effects on metabolism, pregnancy, neurodevelopment, and the immune system, with both PFOA and PFOS presumed to be immune hazards (NTP 2016). Such statements only address the possible health effects associated with legacy PFAS as there are little to no data on health outcomes associated with replacement PFAS.

Although many biological systems are adversely impacted by PFAS, this review focuses primarily on PFAS-associated, placenta-based adverse pregnancy outcomes and how they may increase susceptibility for latent health effects including metabolic dyshomeostasis, thyroid disruption, and kidney effects (Figure 4).

2.2 Challenges of Studying PFAS-Related Human Health Effects

There are many challenges in studying PFAS-related human health effects, including ones specific to studying PFAS exposure and effects in the human population as well as those that are specific to the study of PFAS toxicology in animal models.

First, humans are exposed to PFAS as complex mixtures that differ based on the source of exposure (e.g. near a military base or an industrial site, consumer product use) and differ temporally within the same geographic location (e.g. an industrial site phasing out PFOA and PFOS and utilizing alternative PFAS instead; seasonal patterns in rainfall/drought affecting the extent to which PFAS in water systems are diluted or concentrated). States have authority to develop statewide regulations on consumer product labels and contents, which also influences the extent to which individuals are potentially exposed to PFAS (e.g. consumers can choose to avoid PFAS-containing products under regulations such as Proposition 65). Thus, different individuals and populations are exposed to different levels and mixtures of PFAS. Little is known regarding the potential synergistic effects of PFAS mixtures. Human exposure to PFAS also varies by demographic factors, and they likely differ by individual PFAS congener within a given population. Lifelong exposure, combined with variable exposure to temporally stochastic mixtures and congener-specific demographic factors, presents a complex set of challenges to understanding the relationship between PFAS exposure and adverse health outcomes.

A second challenge in epidemiologic studies of PFAS-related health effects is the lack of an unexposed control population. All humans born after the year 1950, when PFAS were first introduced at the industrial scale, have potentially been exposed to PFAS their entire lives, including *in utero.* This precludes the ability to design and conduct cohort studies with a no-exposure comparison group. Instead, such cohort studies of PFAS must make comparisons between low and high exposure groups to estimate disease risk based on exposure status.

Third, it is possible that PFAS-related adverse health outcomes observed in adulthood are latent manifestations of perturbations during sensitive periods of development (Barker 2004). It is also possible that some PFAS-related adverse health outcomes observed in adulthood are due to chronic, lifelong exposure. In order to address these hypotheses, a population of humans without PFAS exposure during early development would be required. However, such a population only existed prior to 1950, making such a study extremely difficult if not impossible.

Fourth, while experimental toxicology studies provide invaluable information, the elimination kinetics, sensitive endpoints, and biological mechanisms of action in target tissue(s) demonstrate interspecies variation between experimental models (rats vs mice) as well as compared to humans (e.g. serum half-life elimination of PFHxS in mice is ~25-30 days, ~2-7 days in rats, and 5-8 years in humans; Fenton et al. 2020). Many of the interspecies differences regarding toxicological effects and toxicokinetics of PFAS are not fully understood and are further complicated by sex differences in elimination rates (e.g. the human serum half-life of GenX has yet to be fully characterized but it is 3 hours in male rats, 8 hours in female rats, and 18-20 hours in male or female mice; Fenton et al. 2020).

2.3 The Placenta as a Target of PFAS and Critical Driver of Adverse Pregnancy Outcomes

The placenta is a critical organ that exists exclusively during pregnancy and serves as a conduit between mother and developing offspring, mediating the maternal-fetal transfer of nutrients, oxygen, blood, waste, and xenobiotics. The healthy development and function of the placenta is paramount to not only the healthy development of the fetus, but also the health of the mother. Indeed, many adverse pregnancy outcomes are due to placental insufficiency (PI), a condition in which the functional capacity of the placenta is limited or deteriorates, resulting in reduced transplacental transfer of oxygen and nutrients to the fetus (Gagnon 2003). Previous studies have demonstrated that the placenta is vulnerable to environmental insults (Laine et al. 2015; Leclerc et al. 2014; Pedersen et al. 2014).

Adverse pregnancy outcomes associated with PFAS exposure in humans include increased time to pregnancy (Bach et al. 2016; Lum et al. 2017), hypertensive disorders of pregnancy (which includes pregnancy induced hypertension [PIH] (Huang et al. 2019; Savitz et al. 2012b), and preeclampsia [PE] (Stein et al. 2009; Wikström et al. 2019)), gestational diabetes (GD) (Matilla-Santander et al. 2017; Zhang et al. 2015), excess gestational weight gain (Ashley-Martin et al. 2016), and low birth weight of the infant (Johnson et al. 2014; Li et al. 2017; Marks et al. 2019; Meng et al. 2018; Sagiv et al. 2018; Starling et al. 2017; Wikstrom et al. 2019; Xu et al. 2019). Independent of PFAS exposure, deficiencies in placental development and/or function are involved in the etiology of many of these adverse pregnancy outcomes (Hutcheon et al. 2012; Risnes et al. 2009; Thornburg et al. 2010). Thus, it is possible the placenta is a target of PFAS such that PFAS-induced reductions in placental function significantly contribute to adverse pregnancy and birth outcomes.

The placenta is a plausible target of PFAS as it is exposed to PFAS via maternal circulation, shares biologic features in common with other known target tissues of PFAS, such as kidney and liver, and plays a role in the etiology of pregnancy disorders related to PFAS exposure. It is well documented in humans and animal models that PFAS readily pass from maternal serum to the developing embryo via the placenta (Chen et al. 2017a; Chen et al. 2017b; Wang et al. 2019; Yang et al. 2016a; Yang et al. 2016b) and that PFOA transplacentally transfers to the mouse offspring (Fenton et al. 2009). During early stages of development, the placenta functions as the liver, lungs, and kidneys for the embryo; the placenta is responsible for xenobiotic metabolism, supplying oxygen to the fetus, and eliminating waste from embryonic/fetal circulation. Placental trophoblasts express multiple types of ATP-binding cassette (ABC) and organic anion transporter (OAT) proteins in order to shuttle nutrients, xenobiotics, and waste between the maternal and fetal compartments. Many of the transporter proteins expressed in placental trophoblasts are also expressed in liver or kidney, where they excrete substrates into the bile or urine, respectively (Joshi et al. 2016). An *ex vivo* study of human placenta showed the involvement of OAT4 in the placental transport of PFOA and PFOS (Kummu et al. 2015).

There is growing evidence of the mechanisms of PFAS toxicity towards the placenta. A study in mice showed dose-dependent necrotic changes in placenta after gestational exposure to 10 mg/kg/day and 25 mg/kg/day PFOA (Suh et al. 2011). In rats, gestational exposure to 20 mg/kg/day PFOS reduced fetal and placental weight, inhibited placental 11β-hydroxysteroid dehydrogenase 2 activity, and down-regulated 45 gene corresponding to

growth factors and hormones, transporters, and signal transduces, among others (Li et al. 2016). More recently, it was demonstrated that gestational exposure to either PFOA or GenX induced placental lesions in CD-1 mice, with disrupted placental weights and fetal:placental weight ratios and histopathological changes in the placental labyrinth, including congestion and atrophy (Blake et al. 2020).

A study of *ex vivo* term placental cytotrophoblasts exposed to PFOS demonstrated concentration-dependent suppression of estradiol, human chorionic gonadotropin, and progesterone, reduced cell viability, and dysregulation of apoptotic proteins in favor of proapoptosis (Zhang et al. 2015). *In vitro* studies of JEG-3 human placental trophoblasts showed PFOS, PFOA, and PFBS inhibit aromatase (CYP19) activity and an exposure to a mixture of eight different PFAS caused an increase in certain lipid classes (Gorrochategui et al. 2014). In the JEG-3 human placental trophoblast line, exposure to PFOA, PFOS, or GenX altered gene expression profiles towards an anti-proliferative and pro-apoptotic state after exposure to 10 μg/mL in cell culture media (Bangma et al. 2020). However, JEG-3 internal cellular accumulation of GenX was far lower than that of PFOS or PFOA, which suggests a higher sensitivity of placental cells towards GenX as compared to PFOS or PFOA (Bangma et al. 2020). These findings suggest GenX, PFOA, and PFOS may adversely affect placental development and function via disrupted balance of apoptosis and proliferation of the trophoblasts.

Human-derived first trimester trophoblast HTR-8/SV_{neo} cells have been used to demonstrate that PFOS, PFOA, and GenX disrupt inflammatory signaling, decrease trophoblast migration, and decrease trophoblast invasion (GenX only), which indicates a potential mechanism through which PFAS exposure could disrupt placental development and function (Szilagyi et al. 2020). Another study utilizing HTR-8/SV_{neo} trophoblasts similarly showed concentration-dependent decreased migration and invasion after exposure to PFBS, in addition to altered expression of genes implicated in PE (Marinello et al. in press). Additionally, PFOS exposure in HTR-8/SV_{neo} trophoblasts increased levels of miR29-b, a microRNA associated with PE, altered downstream epigenetic processes including global DNA hypomethylation and hyperacetylation of protein, and increased reactive oxidative species production, suggesting a mechanism for increased placental oxidative stress due to PFAS exposure which could ultimately lead to preeclampsia (Sonkar et al. 2019).

Taken together, these studies suggest PFAS induce adverse outcomes in the placenta via mechanisms involving endocrine/lipid/sterol disruption, oxidative stress, disrupted balance of pro- and anti-apoptotic signaling, impaired trophoblast function, and epigenetic alterations. It is possible that mechanisms of PFAS toxicity towards the placenta are compound-specific and may involve numerous overlapping aspects of biology. Improper development or function of the placenta is associated with an array of adverse pregnancy outcomes (including hypertensive disorders of pregnancy), many of which are also associated with maternal exposure to PFAS. It is possible that adverse pregnancy outcomes associated with PFAS exposure are mediated in part by the negative impact of PFAS on the development and function of the placenta. Understanding the risk of environmental insults on the health and development of the placenta is critical for protecting both short and long-

term maternal and offspring health outcomes because the placenta is a driver of latent disease risk for both postpartum women and their offspring.

2.3.1 PFAS Exposure, Hypertensive Disorders of Pregnancy, and the Placenta—Hypertensive disorders of pregnancy (HDP) are a family of disorders that include PE, eclampsia, HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome, and PIH, all of which are related to deficiencies in placental development and/or function (Pijnenborg et al. 1991). This family of disorders not only endangers the health of both the mother and developing fetus during pregnancy, but also increases the risk of post-pregnancy hypertension, heart disease, and stroke in affected women as well as increased risk for adverse cardiometabolic outcomes in adult offspring (Pinheiro et al. 2016).

During normal pregnancy, at 13 weeks gestation the placental cytotrophoblasts begin to invade the maternal uterine wall and remodel the maternal spiral arteries to establish blood flow to the growing embryo (Shah 2020). This process of vasculogenesis and angiogenesis by placental cytotrophoblasts remodels the maternal spiral arteries to become low-resistance, low-capacitance vessels so that blood flow and sufficient nutrients and oxygen are supplied to the growing embryo (Shah 2020). This carefully coordinated process requires an appropriate balance of proangiogenic and antiangiogenic signals (Shah 2020). Disruption of this process can lead to abnormal placental vascularization, resulting in suboptimal pregnancy hemodynamics which can give rise to HDP as well as impaired fetal growth (Shah 2020).

There is growing evidence from human studies implicating maternal PFAS exposure in the development of HDP. Multiple epidemiologic studies have found positive associations between maternal exposure to PFAS and PE (Huang et al. 2019; Savitz et al. 2012a; Savitz et al. 2012b; Stein et al. 2009; Wikström et al. 2019a) as well as PFAS and PIH (C8 Science Panel; Darrow et al. 2013; Holtcamp 2012). It is possible that reduced or impaired placental function as a consequence of PFAS exposure results in or significantly contributes to the development of HDP. Indeed, a recent study in mice showed increased placenta weight, reduced fetal:placental weight ratios, and placental lesions following gestational exposure to PFOA or GenX, suggesting a role for placental toxicity by PFAS (Blake et al. 2020).

Furthermore, it is well documented that the placenta itself is strongly associated with cardiometabolic disease risk in adults. Indeed, the size of the placenta is strongly associated with both perinatal and adult outcomes. In a study of 87,600 Canadian singleton births, fetuses with abnormally small placentas were at increased risk for stillbirth (OR 2.0, 95% CI 1.4-2.6) while fetuses with abnormally large placentas were at increased risk for adverse neonatal outcomes, including seizures, respiratory morbidity, and low Apgar score (odds ratio [OR] 1.4, 95% confidence interval [CI] 1.2-1.7) (Hutcheon et al. 2012). Bigger is not necessarily better; it has been hypothesized that an enlarged placenta is a biomarker for impaired nutrient supply to the fetus. This reduced capacity could be explained by restricted or impaired blood flow through the placenta. It is possible that impaired blood flow, which would in turn disrupt the normal flow of nutrients, oxygen, and waste between maternal and fetal compartments, during critical windows of *in utero* development may result in long-term adverse function of the cardiometabolic system. A U.S. cohort study of nearly 30,000 births

showed that large placenta relative to birth weight, but not birth weight itself, is associated with high blood pressure in childhood (Hemachandra et al. 2006). In a study of 31,307 Norwegian adults, disproportionately large placentas at birth were associated with increased risk of death associated with cardiovascular disease (CVD), and this association remained positive when considering placenta weight alone (Risnes et al 2009).

While mounting epidemiologic evidence suggests PFAS exposure as a risk factor for the development of HDP, a specific mechanism has yet to be validated in experimental settings. Such experimental systems are critical in addressing the hypothesis that maternal exposure to PFAS increases the risk of developing HDP via disruption of the placenta. Due to the complex and multifactorial nature of HDPs, and interspecies differences in maternal spiral artery structure and formation, current animal models are unable to adequately recapitulate the multiple manifestations of this complex group of disorders (Cushen and Goulopoulou 2017; Marshall et al. 2017). Indeed, there is no “standard” or preferred animal model of HDP, and it is unlikely that such an animal model will ever exist (Cushen and Goulopoulou 2017; Marshall et al. 2017). Thus, the development of sensitive laboratory tools for assessing clinically relevant biomarkers of HDPs in animal models is a necessary next step towards determining mechanisms of PFAS toxicity.

2.3.2 PFAS Exposure and Low Birth Weight—Low birth weight is the most consistently reported adverse pregnancy outcome associated with gestational exposure to PFAS in human epidemiologic and animal studies. It is also well established in the literature that placental insufficiency contributes to the etiology of low birth weight (Audette and Kingdom 2018; Cuffe et al. 2017; Henriksen and Clausen 2002). What remains unaddressed by the current body of literature is the relationship between gestational exposure to PFAS, placental function, and birth weight.

In 2014, a three-paper series performed systematic reviews of the existing human and animal literature on the relationship between *in utero* exposure to PFOA and low birth weight (Johnson et al. 2014; Koustas et al. 2014; Lam et al. 2014). After gathering primary data sets and detailed descriptions of study designs from numerous research teams, the authors were able to calculate estimates corresponding to the predicted reduction in birth weight in humans [−18.9 g birth weight per 1 ng PFOA/mL maternal serum, 95% CI: −29.8, −7.9; (Johnson et al. 2014)] and in mice [−23.0 mg birth weight per 1 mg PFOA/kg maternal body weight/day, 95% CI: −29.0, −16.0; (Koustas et al. 2014)]. The authors concluded from their systematic analyses of the literature that PFOA is indeed associated with reduced birth weight in both humans and mice. The effect estimate corresponding to birth weight in mice after gestational exposure to 1 mg PFOA/kg maternal body weight/day generated by Koustas et al. (2014) was consistent with findings in a recent study that measured near-term fetal body weights after gestational exposure to 1 mg PFOA/kg maternal body weight/day (−28 mg fetal weight at embryonic day 17.5, 95% CI: −114, 59; Blake et al. 2020).

Since the publication of these systematic reviews in 2014, the human epidemiologic literature on the relationship between PFAS and birth weight has expanded to include understudied PFAS (e.g. PFNA, PFDA, PFHxS). In a recent report, an analysis of 3,535 mother-infant pairs in the Danish National Birth Cohort examined six different PFAS and

reported increased risk for preterm birth associated with maternal serum levels of PFOA, PFOS, PFNA, PFDA, and perfluoroheptane sulfonate (Meng et al. 2018). Low birth weight risk was also elevated, but estimates were less precise in this analysis (Meng et al. 2018). In a study of 1,533 Swedish mother-infant pairs, increased maternal exposure to PFOS, PFOA, PFNA, PFDA, and perfluorooundecanoic acid were associated with lower birth weight and size, but associations were only significant in girls (Wikstrom et al. 2019). Conversely, a study of 457 British motherson dyads showed inverse associations between maternal PFOS and measures of both birth weight and size (Marks et al. 2019), which had previously been shown in mother-daughter dyads in the same cohort (Maisonet et al. 2012). A study of 1,645 mother-infant pairs in Massachusetts showed that PFOS and PFNA were weakly inversely associated with birth weight and positively associated with higher odds of preterm birth (Sagiv et al. 2018). In another U.S. cohort, maternal serum PFOA and PFNA was inversely associated with birth weight in an analysis of 628 mother-infant pairs (Starling et al. 2017). A smaller study of 98 Chinese mother-infant pairs also found PFOS was negatively associated with birth weight, and that both PFOS and PFHxS were negatively associated with birth size (small for gestational age, SGA) (Xu et al. 2019). Taken together, these epidemiological studies further underscore the potential for PFAS other than PFOA to adversely affect fetal growth *in utero*.

There are limited animal studies supporting the association between PFAS, other than PFOA and PFOS, and reduced birth weight. Studies of both mice (Chang et al. 2018) and rats (Ramhoj et al. 2018) have shown reduced offspring body weight after developmental exposure to PFHxS. In rats, developmental exposure to perfluoroundecanoic acid has been shown to reduce offspring weight (Takahashi et al. 2014). Previous animal studies of the developmental effects of PFNA have reported adverse neonatal outcomes but did not report effects on birth weight (Das et al. 2015; Wolf et al. 2010). Similarly, a previous study of the developmental toxicity of PFDA in mice found no reductions in birth weight (Harris and Birnbaum 1989). Studies in mice have demonstrated a modest effect of prenatal exposure to GenX on near-term (Blake et al. 2020) and early postnatal offspring body weights, with effects becoming more significant throughout lactation (DuPont-18405-1037).

The association between PFAS exposure and low birth weight is well supported in humans, as is the causal link between placental insufficiency and low birth weight. This, in combination with the biologically plausible proposed mechanisms of PFAS toxicity towards the placenta, further underscores the need to test the hypothesis that the PFAS-mediated placental effects are a critical driver of adverse pregnancy and birth outcomes.

2.4 PFAS Exposure and Metabolic Effects

Metabolic syndrome (also referred to as cardiometabolic syndrome) describes a group of disorders that affects approximately one third of the U.S. adult population and includes obesity, dyslipidemia, elevated blood pressure, and impaired glucose tolerance (Eckel et al. 2005; Ervin 2009). The liver is a central hub in the regulation of pathways controlling systemic metabolic homeostasis, and liver dysfunction is a major component of metabolic syndrome **(**D'Amore et al. 2014). While the liver regulates metabolic homeostasis, lifelong metabolic health is influenced by placental health and function during critical periods of *in*

utero fetal programming (Nugent & Blake, 2016; Rinaudo & Wang, 2012). Therefore, environmental exposures impacting placental health and function, such as PFAS, may prime the system for increased susceptibility to metabolic syndrome, which could be further exacerbated by continued PFAS exposure across the lifespan.

A recent review of the literature examined 69 epidemiological studies evaluating the association between PFAS exposure and a variety of metabolic outcomes, including lipid homeostasis, diabetes, overweight/obesity, and cardiovascular disease (Sunderland et al. 2019). Across the human literature, Sunderland et al. (2019) reported relatively consistent and modest positive associations between PFAS exposure and serum lipids, such as total cholesterol and triglycerides. Although associations were less consistent across studies, Sunderland et al. (2019) also reviewed epidemiologic studies examining the adverse effect of PFAS exposure on insulin resistance, diabetes, hypertension, vascular disease, and stroke. Across these health outcomes, adverse effects were most consistently reported in association with exposure to PFOA (Sunderland et al. 2019). The effects of PFAS on metabolism of developmentally exposed offspring is the topic covered more in depth by Cope et al. (*this issue*).

More recently, additional studies of humans have explored the association between PFAS exposure and metabolic syndrome. Christensen et al. (2019) leveraged National Health and Nutrition Examination Survey (NHANES) data sets to investigate the relationship between PFAS exposure and metabolic syndrome in the general U.S. population between years 2007-2014 and found PFNA was consistently associated with increased risk of metabolic syndrome, while the highest levels of PFHxS exposure were associated with elevated triglycerides (Christensen et al. 2019). This study suggests that PFAS other than PFOA and PFOS may contribute to adverse metabolic health outcomes in humans.

Most animal studies investigating the effect of PFAS exposure on metabolic syndrome have focused on PFOA. Previous work in mice has shown that developmental exposure to PFOA disrupts weight gain, serum leptin, and insulin sensitivity later in life (Abbott et al. 2012; Hines et al. 2009). While data from adult-dosed animals initially suggested that peroxisome proliferator-activated receptor alpha (PPARα) was the mechanism through which PFOA exerted deleterious effects on the liver and metabolic system (Elcombe et al. 2012; Kennedy et al. 2004; Klaunig et al. 2003; Rosen et al. 2007), later work using mice null for PPARα revealed adverse liver effects persisted or worsened following perinatal exposures, suggesting PFOA can induce toxicity (e.g. tumor development) in the liver via PPARα-independent mechanisms such as glycogen depletion and mitochondrial dysfunction (Filgo et al. 2015; Mashayekhi et al. 2015; Quist et al 2015) and that effects may have been mediated *in utero* (Filgo et al 2015; Quist et al 2015). However, more recently PFOA, PFOS, PFNA, and PFHxS were evaluated in mice and found to induce expression of hepatic genes involved in fatty acid and triglyceride synthesis, potentially causing steatosis through disruption of the balance between fatty acid accumulation and oxidation (Das et al. 2017). Similarly, in primary human and rat hepatocytes, PFOA and PFOS were shown to activate multiple nuclear receptors and the metabolic response shifted from carbohydrate metabolism to fatty acid accumulation and oxidation (Bjork et al. 2011). In an *in vitro* 3D spheroid model of mouse liver AML12 cells, PFOA, GenX, and another PFOA alternative, 3,5,7,9-

tetraoxadecanoic perfluoro acid (PF04DA), were shown to induce PPARα targets, oxidative stress, and lactate dehydrogenase (LDH) leakage, suggesting PFOA alternatives have the potential to induce liver injury (Sun et al. 2019). Across the human, animal, and *in vitro* literature, there is consistent evidence to suggest PFAS disrupt metabolic homeostasis through damaging the liver. Whether PFAS-mediated effects on the placenta may have a role in programming latent liver and metabolism-related outcomes is the focus of on-going work.

2.5 PFAS Exposure and Thyroid Effects

PFAS are hypothesized to target the thyroid by influencing multiple biological mechanisms involved in thyroid homeostasis, including thyroid hormone biosynthesis, transport, metabolism, and interference with thyroid receptors in target tissues (Boas et al. 2009). Proposed mechanisms of action of thyroid disruption by PFAS include reduced circulating levels of thyroxine (T4) due to competitive binding to thyroid hormone transporter (THT) proteins (Weiss et al. 2009), increased T4 metabolism in the thyroid and liver (Chang et al. 2009; Yu et al. 2009; Yu et al. 2011), reduced thyroid production of T4 (Webster et al. 2014), or reduced thyroid peroxidase (TPO) activity (Coperchini et al. 2015). During pregnancy, the placenta regulates the exchange of thyroid hormone (TH) from the maternal to fetal compartments and must maintain appropriate TH levels in the fetal circulation throughout gestation to ensure healthy development (Chan et al. 2009). Fetal TH levels are modulated by the placenta through plasma membrane THTs, metabolism, and binding to proteins in trophoblast cells (Chan et al. 2009). Thus, any PFAS implicated as TH disrupters may perturb the ability of the placenta to appropriately modulate fetal thyroid hormone balance during development.

Previous epidemiologic studies have examined the association between exposure to PFAS and THs, with inconsistent findings across the literature. Several studies leveraged the NHANES database and showed positive associations between PFOA and total triiodothyronine (T3) (Jain 2013; Webster et al. 2016; Wen et al. 2013), TSH (Jain 2013; Lewis et al. 2015), and self-reports of current thyroid disease (Melzer et al. 2010). PFHxS has been associated with increases in total T4 across the general U.S. population (Jain 2013) as well as with sex-specific positive associations in women (Wen et al. 2013). A recent meta-analysis of twelve epidemiologic studies found that PFAS are generally negatively associated with T4, but certain associations may be non-monotonic (Kim et al. 2018). For example, PFOS was positively associated with T4 and TSH only in the intermediate exposure group (Kim et al. 2018). Positive associations between serum PFOS and TSH were similarly reported in a longitudinal study of adults with serum levels of PFOS within the range of the general U.S. population (Blake et al. 2018), and PFAS were generally found to be positively associated with TSH in pregnant women in a systematic review (Ballesteros et al. 2017). However, it is possible that inconsistencies across the human literature are attributable to differences in the overall range of PFAS exposure across populations studied, which may help explain the non-monotonic dose-response described in Kim et al. (2018).

Pregnant women and their developing offspring are particularly sensitive to disruptions in THs, which are critical endocrine modulators of early neurodevelopment (de Escobar et al. 2004; Porterfield 1994). PFAS have been documented as thyroid disrupters in pregnant

women in some epidemiologic studies (Ballesteros et al. 2017; Berg et al. 2015; Wang et al. 2014; Webster et al. 2014). Generally, maternal PFAS levels during pregnancy are associated with shifts in TH levels consistent with hypothyroidism (e.g. elevated TSH), which is associated with increased risk for low birth weight (Alexander et al. 2017; Belet et al. 2003). In rodent models, gestational exposure to GenX resulted in reduced maternal serum T3 and T4 levels in rats (Conley et al. 2019) and increased placental T4 levels in mice (Blake et al. 2020), demonstrating the potential for this replacement compound to act as a TH disruptor during pregnancy.

A current challenge in studying the effect of PFAS on THs is the inherent negative bias of common analog methods used to measure THs (e.g. radioimmunoassay, chemiluminescent assay), but this artifact is likely specific to rodent studies. Reduction in TH binding protein or displacement of TH via competitive binding, such as displacement of T4 by PFOS in rats, reduces serum binding capacity for TH and analog and result in negatively biased measurements of free THs (for an in-depth explanation, see Chang et al. 2007). In order to avoid such negative bias, equilibrium dialysis or high-performance liquid chromatography-based methods should be employed in animal studies. However, a follow up study conducted using human samples demonstrated no such negative bias for either PFOA or PFOS with respect to free T4 whether assayed using the analog or equilibrium dialysis method (Lopez-Espinosa et al. 2012).

Due to the critical role that THs play in human health and development, disruptions at any life stage warrant further study to understand potential underlying mechanisms. Both hyperthyroidism and hypothyroidism are suboptimal health outcomes and increase risk for adverse effects on the function of TH-responsive tissues, such as kidney and the cardiovascular system. Therefore, continued study of the effects of PFAS on thyroid function are warranted, especially as it pertains to other associated health effects. The role of placenta-specific TH action on fetal development and metabolism needs additional research; how PFAS may affect this target is poorly understood.

2.6 PFAS Exposure and Kidney Effects

The kidney is considered a target tissue of PFAS, evidenced by a growing body of human epidemiologic data further supported by animal studies and *in vitro* models. In humans, PFAS exposure has been associated with adverse kidney outcomes such as reduced kidney function, chronic kidney disease (CKD), and kidney cancer, including mortality from kidney cancer. Human epidemiologic studies have shown an association between low birth weight and adverse kidney outcomes in later life (Dotsch et al. 2011; Hershkovitz et al. 2007). It is possible that placental dysfunction due to PFAS resulting in low birth weight may result in lifelong increased susceptibility and reduced kidney function. However, similar to metabolic syndrome, it is difficult to determine what proportion of disease susceptibility is programmed during development and how much is exclusively a consequence of adult exposures. Due to lifelong PFAS exposure stemming from their ubiquity in the environment, it is likely that increased susceptibility resulting from exposure during critical periods of development and continued exposure through adulthood interact in complex ways to influence disease risk.

The primary elimination route for PFAS is via urinary excretion. Given that the most well-studied PFAS do not undergo biotransformation prior to urinary excretion, one hypothesized mechanism of PFAS-induced kidney injury is via reabsorption of PFAS across the renal tubules which causes localized damage, potentially through oxidative stress (Han et al., 2011). It has been demonstrated in humans that PFAS, once absorbed, distribute primarily to serum, liver, and kidney (Fabrega et al. 2014; Perez et al. 2013). It is yet to be determined if the kidney is a sensitive target of PFAS due to high accumulation of PFAS within the renal tissue, creating a high internal dose in kidney, or if the kidney is particularly sensitive to PFAS-induced effects. The extent to which PFAS distribute and/or accumulate in different tissues likely varies by individual congener. For example, perfluorododecanoic acid (PFDoA), perfluorodecanoic acid (PFDeA), and perfluorobutyrate have been shown to highly accumulate in kidney relative to other tissues (Perez et al. 2013).

Elimination rates also vary widely by individual congener with human serum half-lives spanning from about 24 hours to ~15 years which generally (though not always) corresponds to carbon chain length and functional groups (Fenton et al. 2020). Such differences in elimination rate and serum half-life are hypothesized to result from different rates of secretion and reabsorption by the kidney proximal tubules. This process, driven by renal tubule efflux transporters, actively transports PFAS back into systemic circulation, thus contributing to their long half-lives in the human body (Han et al., 2011). Uptake of PFAS into proximal tubules, both apically and basolaterally, is mediated by solute-carrier protein family transporters such as organic anion transporters (OAT). OAT1 and OAT3 have been shown to transport PFAS basolaterally in proximal tubules with apical transport mediated by OAT4 and urate transporter 1 (URAT1) (Worley et al. 2017; Yang et al. 2010; Zhang et al. 2013).

In a recent scoping review of the effect of PFAS on kidney health, Stanifer et al. (2018) identified 74 studies comprised of epidemiologic, pharmacokinetic, and toxicological studies of humans, animals, and *in vitro* models (Stanifer et al. 2018). Across 21 epidemiologic studies of occupationally and non-occupationally exposed populations, Stanifer et al. (2018) reported consistent associations between PFAS exposure and adverse kidney outcomes, which included reduced kidney function and kidney cancer (Stanifer et al. 2018). Studies published since this scoping review have similarly provided evidence suggesting human exposure to PFAS is detrimental to kidney health (Blake et al. 2018, Jain and Ducatman 2019a).

In addition to concerns over reduced kidney function, compensatory increases in kidney function (e.g. glomerular filtration rate) are associated with increased risk for cardiovascular morbidity and mortality. Such hyperfiltration has been observed in patients with prediabetes and prehypertension (Palatini 2012; Shastri and Sarnak 2011). A positive association between methyl-perfluorosulfonic acid (Me-PFOSA) and increased kidney filtration was reported (Blake et al. 2018). Indeed, the relationship between PFAS exposure and kidney function (glomerular filtration rate) is nonmonotonic (Jain and Ducatman 2019a). It has been hypothesized that altered balance between glomerular secretion of PFAS into the urine for excretion (e.g. via OAT1 and OAT3) and renal reabsorption (e.g. via OAT4) with increasing severity of kidney disease progression may explain the inverse U-shaped relationship. Based

on these findings, Jain and Ducatman (2019a) hypothesized that PFAS reabsorption in renal tubules decreases with advancing stages of renal failure. In a follow up study, Jain and Ducatman (2019b) demonstrated that increased albuminuria may provide further explanation for decreasing serum PFAS concentrations with increasing kidney failure. Excessive albumin proteins in the urine may essentially off-load the body burden of PFAS with high binding affinity to albumin proteins (Jain and Ducatman 2019b). However, these studies were conducted using cross-sectional data from NHANES and the reported findings would be greatly strengthened if validated in longitudinal cohorts.

Animal studies and *in vitro* models have provided further evidence for the adverse effect of PFAS on kidney health (Stanifer et al. 2018). Studies conducted in rats and mice have reported increased kidney weight (Butenhoff et al. 2012; Curran et al. 2008; Ladics et al. 2005), increased blood urea nitrogen (BUN) (Butenhoff et al. 2012; Seacat et al. 2003; Takahashi et al. 2014), renal tubular atrophy (Klaunig et al. 2015) or hypertrophy (Ladics et al. 2005), and tubular epithelial hyperplasia (Kim et al. 2011), among other adverse kidney findings (see Stanifer et al. 2018 for a comprehensive review). *In vitro* systems have provided further evidence to suggest oxidative stress as a mechanism of PFAS-induced kidney damage (Chung 2015; Wen et al. 2016). A recent study by Gong et al. (2019) used rat mesangial cells as an *in vitro* model of diabetic kidney disease to determine the effect of PFAS exposure in the diabetic condition, and similarly reported PFOA or PFOS exposure resulted in increased oxidative stress, fibrosis, and inflammation in this *in vitro* model (Gong et al. 2019). Studies using rats must be interpreted with some caution due to interspecies differences in PFAS elimination rates, with PFAS excretion rates being more rapid in rats (especially female rats) compared to mice (Loccisano et al. 2013; Lou et al. 2007; Pizzurro et al. 2019; Russell et al. 2013).

Overall, there is consistent evidence across human epidemiologic, animal, and *in vitro* studies to support the claim that PFAS are damaging to kidney health, however the relationship between *in utero* exposure to PFAS, placental dysfunction, and latent kidney disease, failure, or cancer is less clear and should be investigated further.

2.7 The Interplay Between Biologic Systems Affected by PFAS Exposure

The adverse health effects of PFAS exposure on human metabolic homeostasis, thyroid function, kidney function, and pregnancy outcomes are likely interrelated due to the extensive overlap between these biologic systems and how each of these systems are influenced by placental health in the context of pregnancy. For example, the liver is responsible for thyroid hormone metabolism and transport, both kidney and liver express type 1 deiodinase (an enzyme that converts T4 to T3) (Sanders et al. 1997), and both the liver and placenta express enzymes of the type 3 deiodinase system, which converts active T4 to inactive rT3, and/or active T3 or inactive rT3 to inactive T2 (Bianco et al. 2002; Darras et al. 1999). During pregnancy, the placenta regulates the degree to which maternal thyroid hormones pass to the developing fetus and maintains the optimal balance of thyroid hormones throughout *in utero* development (Chan et al. 2009).

There is human clinical evidence to suggest shared pathogenic mechanisms for non-alcoholic fatty liver disease and chronic kidney disease (Musso et al. 2016), thyroid disease

(both hyperthyroidism and hypothyroidism) and liver injury (Malik and Hodgson 2002), and hypothyroidism and chronic kidney disease (Rhee 2016). The proposed shared pathogenic mechanisms for these overlapping biologic systems also coincide with hypothesized mechanisms of PFAS toxicity, including disruption of lipid metabolism (e.g. cholesterol and triglycerides), nuclear receptor activation (e.g. peroxisome proliferator-activated receptors, retinoid X receptor), and oxidative stress (Malik and Hodgson 2002; Musso et al. 2016; Rhee 2016), among others. In the context of pregnancy, chronic kidney disease increases the risk of PE and low birth weight (Fischer 2007), and non-alcoholic fatty liver disease increases risk of gestational diabetes and pregnancy-induced hypertension (Hershman et al. 2019).

The clinical evidence underscores the careful balance between multiple biologic systems, and the shared pathogenic mechanisms affecting these systems coincides with toxicologic mechanisms through which PFAS affect these same systems. The complex interplay between the placenta, liver, kidney, and thyroid is further complicated by the physiological demands of pregnancy, such as increased metabolic rate, oxygen consumption, blood volume, weight gain and fluid retention. Furthermore, *in utero* exposure to PFAS occurring during critical periods of development may increase susceptibility for latent onset of chronic adult diseases, such as obesity, diabetes, problems in kidney function, and fatty liver disease. Some of these latent effects have been demonstrated in the context other exposures, such as maternal malnutrition, to be directly associated with poor fetal growth and placental abnormalities (Barker 2004), suggesting a potential shared mechanism across different maternal/developmental/placental stressors and latent health outcomes. Given the complex interplay between placenta, PFAS-sensitive organ systems influencing maternal health, and PFAS-sensitive latent health outcomes in adulthood, pregnant women and their developing offspring should continue to be considered the most sensitive populations when conducting PFAS health and risk assessments.

3. Health Effects-Based Risk Evaluations of PFAS in the U.S.

Human health risk assessments of PFAS have been hindered by a paucity of data, which was first remedied by reports and publications resulting from the C8 Health Study. These data provided the foundation for preliminary risk evaluations and subsequent decision-making processes. The first U.S. actions taken to limit the use and emission of PFAS began in 2000 when the company 3M voluntarily phased PFOS out of production and use. Then in 2006, the U.S. EPA invited eight major fluoropolymer and fluorotelomer manufacturing companies to participate in a global stewardship program to commit to a 95% reduction of PFOA emissions and product by the year 2010 and a complete elimination by 2015 (EPA 2006). To meet these program goals, companies ceased manufacturing and importation of long-chain PFAS and/or transitioned to alternative chemicals while some companies exited the PFAS industry altogether. The impact of this phaseout can be appreciated by temporal declines in human serum PFOA and PFOS concentrations in datasets such as the NHANES; between 1999 and 2014, average PFOA and PFOS serum levels in the general U.S. population declined by ~60% and ~80%, respectively (ATSDR 2017).

Despite the reduction in serum burden of PFOA and PFOS since the genesis of the stewardship program, a recent biomonitoring effort (Hu et al. 2016) determined that drinking water sources for as many as six million U.S. citizens exceed the U.S. EPA-derived lifetime drinking water Health Advisory Level (HAL) for PFOA alone or in combination with PFOS of 70 parts per trillion (ppt) (822-R-16-005 US EPA). However, this number likely underestimates the number of U.S. citizens with drinking water exposure above the PFOA/PFOS HAL as the sampling method used by Hu et al. (2016) was conducted under the scope of the third Unregulated Contaminant Monitoring Rule (UCMR3), which limits drinking water PFAS measurements to public systems serving over 10,000 people. The exposure levels for U.S. citizens on private well water or public water systems serving under 10,000 people have yet to characterized.

The PFOA/PFOS HAL represents a non-enforceable exposure level under which no adverse health outcomes would be expected given a lifetime of exposure, based on the U.S. EPA's risk assessment of PFOA, which used a weight of evidence approach to examine existing human epidemiologic and animal toxicity studies. Data from a carefully conducted developmental and reproductive toxicity study was selected to obtain the reference dose (RfD) used in calculation of the lifetime HAL for PFOA, in order to generate the most protective exposure level (822-R-16-005 US EPA; Lau et al. 2006).

The lack of federally enforceable regulations on any PFAS in the U.S., as well as increasing concerns over local contamination levels has led several states to implement their own regulatory actions based on varied health effects (Figure 5). The states of California, Connecticut, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New York, North Carolina, and Vermont have each proposed various drinking water actions to address PFAS contamination (ASDWA 2020). New Hampshire and New Jersey have formally adopted statewide regulations, mandating drinking water levels for PFOA (NH: 12 ppt), PFOS (NH: 15 ppt), PFHxS (NH: 18 ppt), and PFNA (NH: 11 ppt; NJ: 13 ppt) substantially lower than the U.S. EPA HAL of 70 ppt for PFOA alone or combined with PFOS (ASDWA 2020). Other states, such as North Carolina and Michigan, have proposed health advisories or maximum contaminant levels (MCLs) for replacement PFAS, such as GenX (NC: 140 ppt; MI: 370 ppt) (ASDWA 2020) while Ohio and Washington are in the process of developing draft health advisories for various PFAS (OH EPA 2019; WA DOH 2020). In August 2020, Michigan set new limits for several more PFAS: PFNA (6-ppt); PFOA (8-ppt); PFOS (16-ppt); PFHxS (51-ppt); PFBS (420-ppt); PFHxA (400,000-ppt).

Regulation of PFAS as the statewide level has resulted in disparate regulatory standards with regards to both the drinking water limit and extent to which regulations may be enforced. PFAS contamination in the environment and drinking water is driven by point sources of pollution, such as industrial/manufacturing sites, airports, biosolids fields, and military training bases. At each site, different levels of a multitude of PFAS are used in complex mixtures, depending on the application. The heterogeneity of the exposure mixture as well as relative concentrations of individual PFAS adds to the complexity of both studying PFAS effects of human health and setting appropriate standards to adequately protect the most vulnerable members of society. There is little to no toxicity data for the vast majority of

PFAS currently in use, therefore there is great need for efficient methods to evaluate these compounds.

4. Conclusions

The complex family of PFAS compounds presents unique challenges to toxicologists and risk assessors. The effects of PFAS on human health differ based on compound, impact multiple overlapping biological systems, affect health outcomes at all life stages, and exposure levels (and mixtures) differ temporally and geographically. Importantly, early life PFAS insults may in fact disrupt placental growth and function, thereby increasing susceptibility for later life chronic health conditions, which may be further exacerbated by lifelong PFAS exposure. Thus, it is critical to improve our understanding of the developmental and adult health consequences associated with PFAS exposure over time, identify emerging PFAS threats to sensitive subpopulations, and develop tools to efficiently evaluate and characterize PFAS toxicity on sensitive targets such as the placenta. Future research is needed to determine if latent health effects of PFAS exposure are programmed or mediated by the placenta. Going forward, experimental toxicology studies designed to formally assess the placenta are needed to determine the sensitivity of this tissue towards PFAS and explore the molecular mechanisms of placental toxicity.

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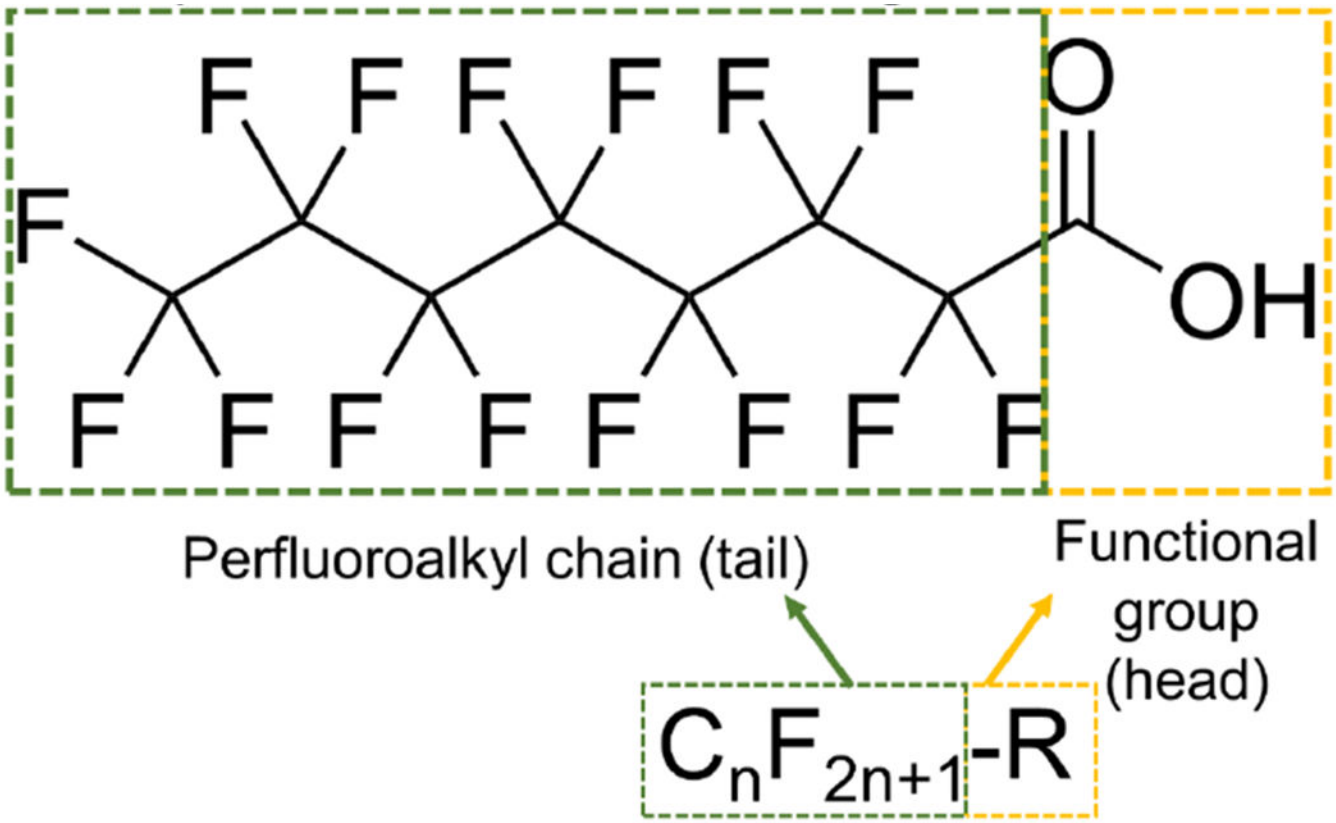

Figure 1. Basic structural features of a perfluoroalkyl substance (PFAS).

The compound perfluorooctanoic acid (PFOA) is shown here as an example. The perfluoroalkyl chain (tail) is indicated by a dashed green outline, while the functional group (head) is indicated by a dashed yellow outline. Legacy PFAS share these structural features while replacement, or "alternative chemistry" PFAS, contain substitutions along the carbon tail.

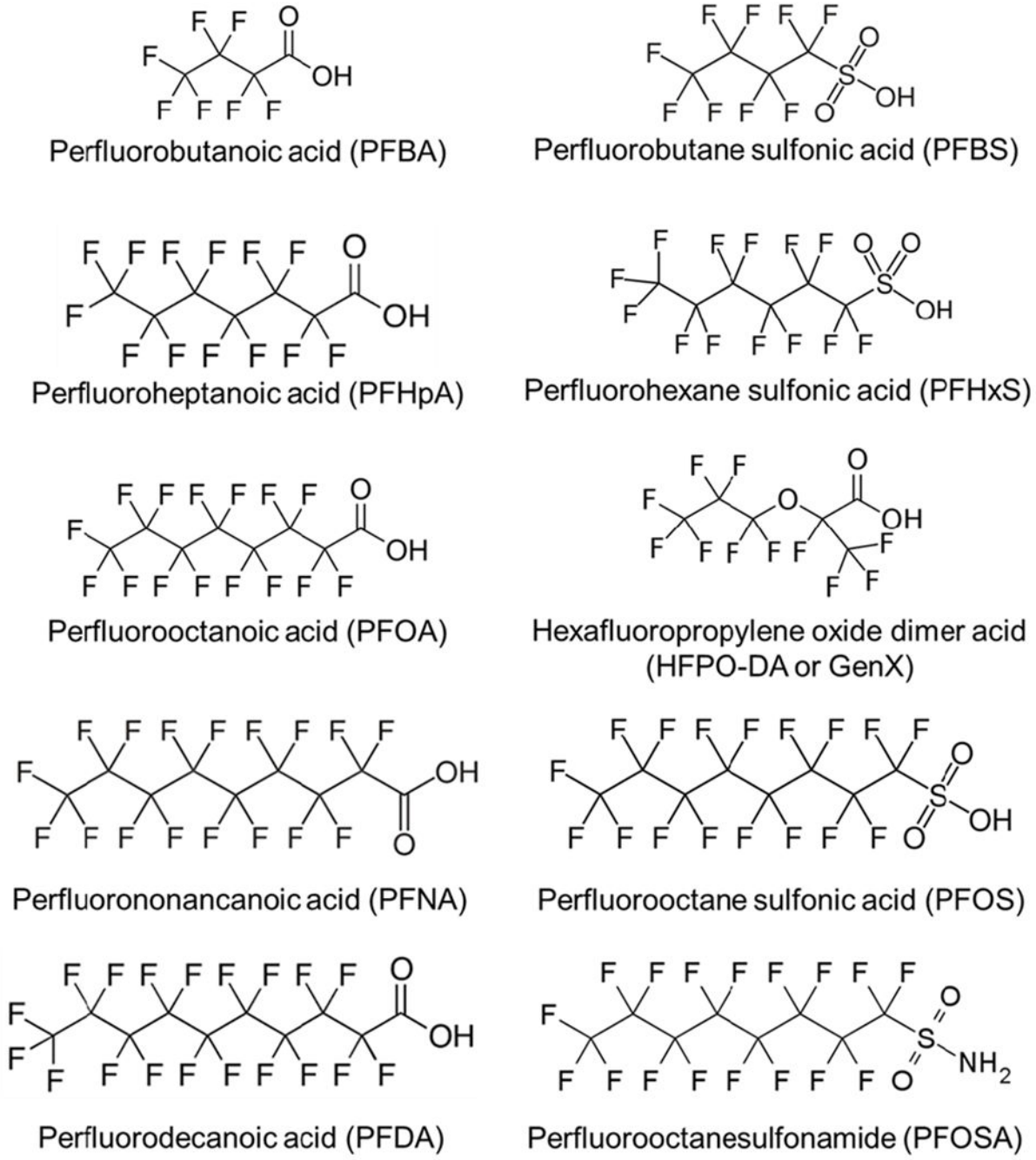

Figure 2. Structures of common legacy perfluoroalkyl substances (PFAS) and replacement PFAS.
The ether substitution in the carbon tail of hexafluoropropylene oxide dimer acid (HFPO-DA, or GenX) is thought to favorably alter the toxicokinetic profile of the compound. Perfluorobutane sulfonic acid (PFBS) has classic structural features but has been selected as a replacement compound for longer-chain PFAS.

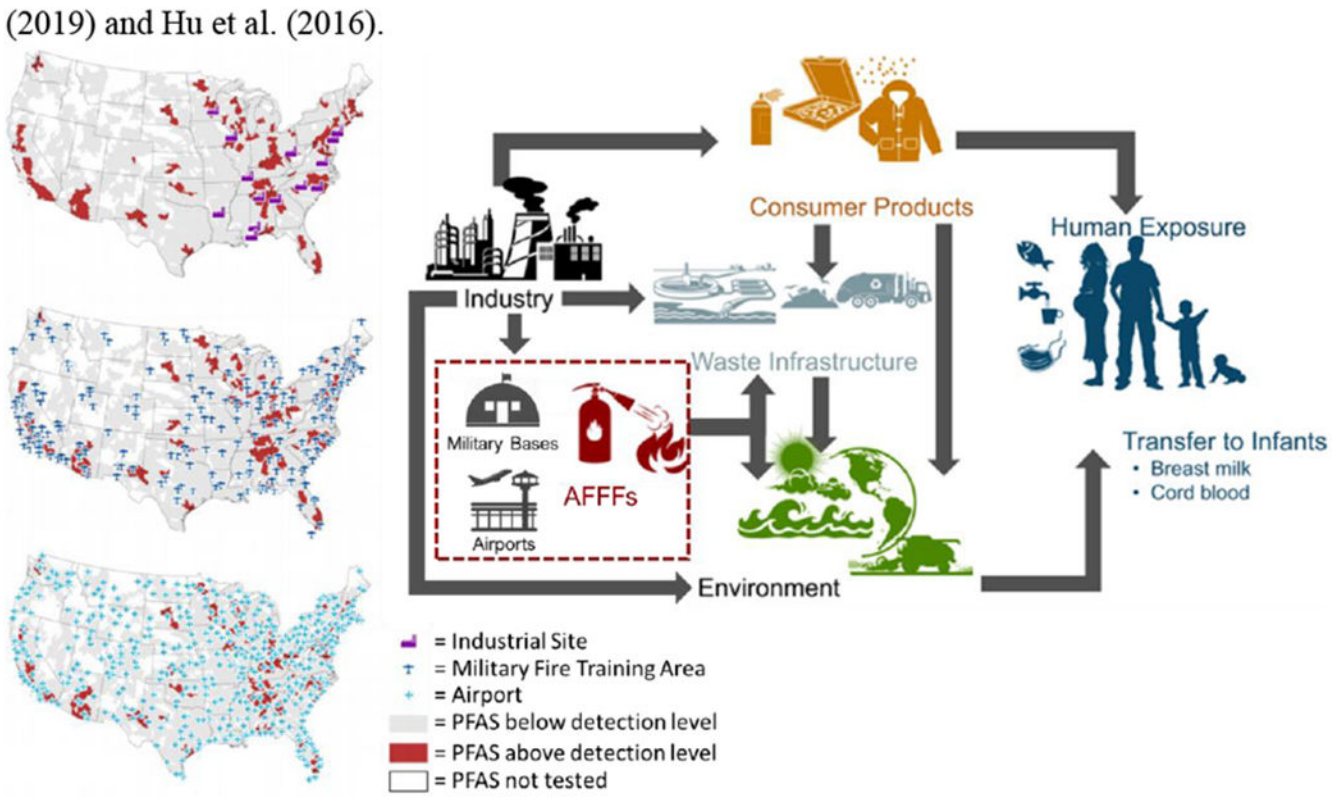

Figure 3. Major sources of human exposure to per- and polyfluoroalkyl substances.

Humans are directly exposed to PFAS through the ambient environment (e.g. air), consumer products, house dust, drinking water, and diet. For developing humans, exposure can occur transplacentally *in utero* and through breastmilk. Environmental PFAS contamination is caused by waste and pollution generated by industrial complexes in the manufacturing or use of PFAS, including in the manufacturing of downstream products containing PFAS, such as aqueous filmforming foams (AFFFs). Environmental PFAS contamination is also caused by run-off of PFAS-containing AFFFs at military training bases and airports. Figure adapted from Sunderland et al. (2019) and Hu et al. (2016).

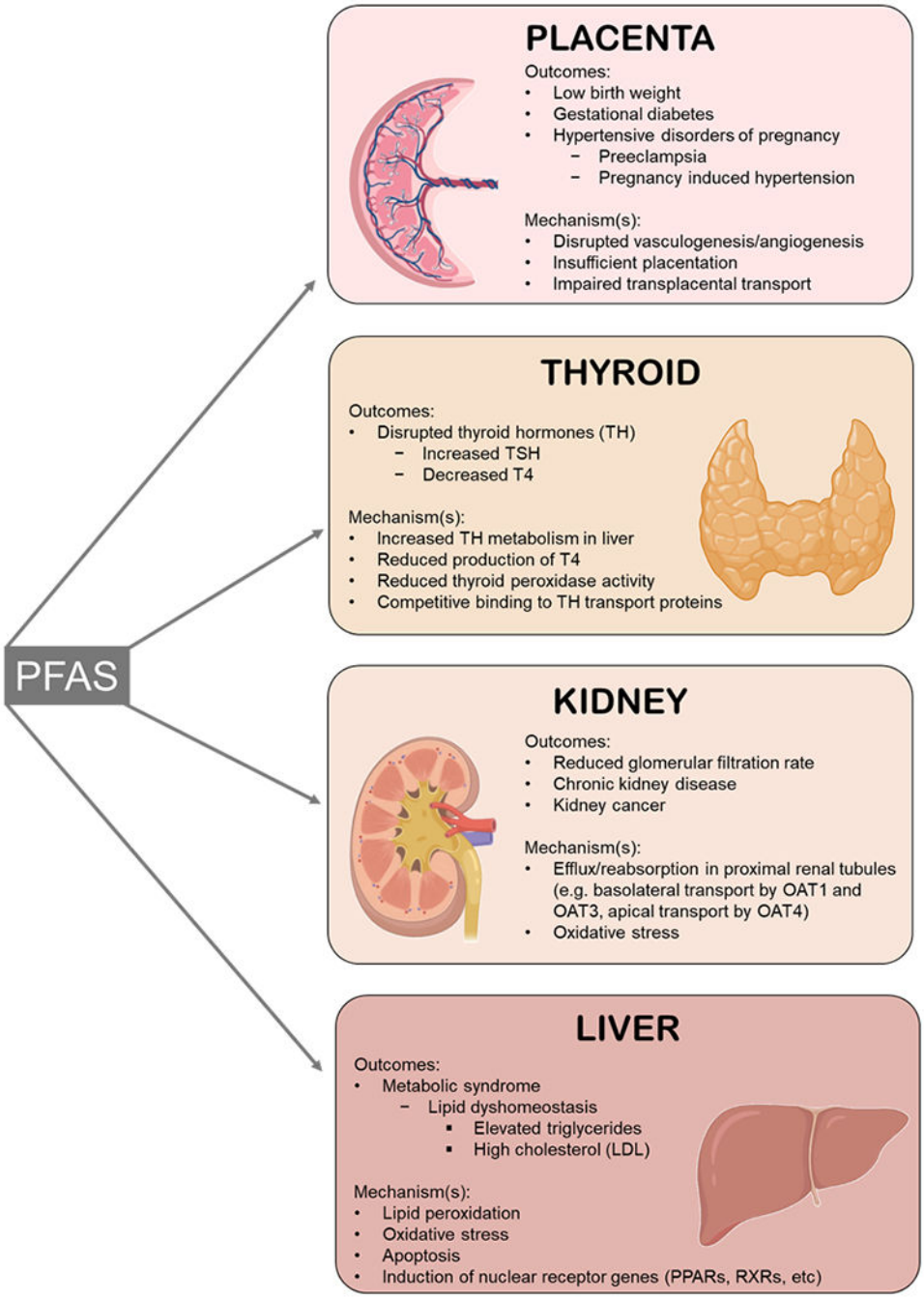

Figure 4. Summary of adverse health outcomes associated with PFAS exposure, the target tissue implicated by the outcomes, and hypothesized mechanism(s) of PFAS toxicity.

Image created using BioRender.

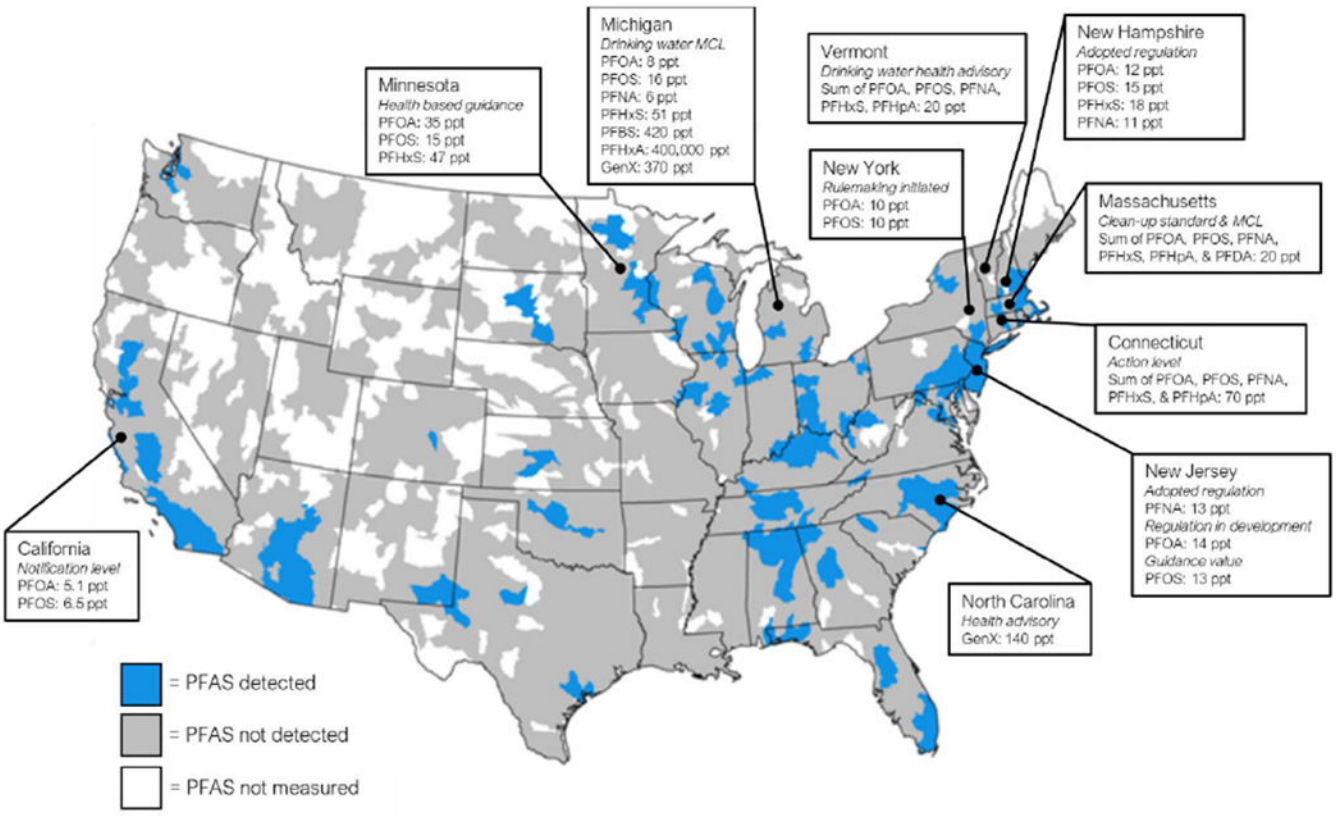

Figure 5. Responses of U.S. states to PFAS contamination compared to nationwide PFAS levels (inset).

Most state actions are non-enforceable and include notification levels, maximum contamination limits (MCLs), health advisories or guidance, and action levels. Several states have adopted enforceable regulation, such as New Hampshire and New Jersey, while other states are actively in pursuit of enforceable legislation, such as New York. There are some states with considerable PFAS contamination but no statewide action, including Alabama, New Mexico, and Kentucky. Figure adapted from Hu et al. (2018).

Table 1.

Common legacy per- and polyfluoroalkyl substances.

Chemical name	CAS	Abbr	Family	# Carbons w/fluorine	Carbon chain length	Type
Perfluorooctanoic acid	335-67-1	PFOA	PFCA	7	8	Legacy
Perfluorohexanoic acid	307-24-4	PFHxA	PFCA	5	6	Legacy
Perfluoropentanoic acid	2706-90-3	PFPeA	PFCA	4	5	Legacy
Perfluoroheptanoic acid	375-85-9	PFHpA	PFCA	6	7	Legacy
Perfluorononanoic acid	375-95-1	PFNA	PFCA	8	9	Legacy
Perfluorodecanoic acid	335-76-2	PFDA	PFCA	9	10	Legacy
Perfluorobutanoic acid	375-22-4	PFBA	PFCA	3	4	Legacy & replacement
Perfluorobutane sulfonic acid	375-73-5	PFBS	PFSA	4	4	Legacy & replacement
Perfluorohexane sulfonic acid	355-46-4	PFHxS	PFSA	6	6	Legacy
Perfluorooctane sulfonic acid	1763-23-1	PFOS	PFSA	8	8	Legacy
Perfluorooctane sulfonamide	754-9-6	PFOSA	PFSA	8	8	Legacy

Abbr: Perfluorocarboxylic acid = PFCA, perfluorosulfonic acid or amide = PFSA

Attachment 10

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Nutrition and Hydration Requirements In Children and Adults

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Definition/Introduction

A nutrient is a substance providing nourishment to the body and is necessary for both growth and maintenance. Nutrients can fall into seven groups that include carbohydrate, protein, fat, fiber, mineral, vitamin, and water. All groups are essential for the adequate functioning of the body. Macronutrients serve as a source of energy, while micronutrients play a crucial role in biochemical reactions. Among the most important nutrients is water; it serves as a solvent, a mode of transport, and a substrate for major metabolic reactions.

Issues of Concern

Children

In children, the daily caloric requirement is calculated based on the age, sex, and activity status of the child. For a child between 2 and 3 years of age, the recommended daily caloric intake is 1000 to 1400 kcal/day; this requirement increases with the age of the child. Children during a growth spurt, require higher amounts of calories to maintain the body as well as to grow. The daily recommended caloric intake for children 11 to 12 years range between 1800 and 2200 kcal/day. Another way to generalize caloric need is that an infant needs 100cal/kg/day, ages 1 to 3 years need 80 kcal/kg/day, 4 to 5 years needs 70kcal/kg/day, 6 to 8 years needs 60 to 65 kcal/kg/day and 9+ needs 35 to 45 kcal/kg/day. Growth charts are vital in directing nutritional counseling in children.

The daily recommended intake (DRI) of water depends on age, sex, weight, activity status, air temperature, and humidity. Plain water serves as the best way to fulfill this requirement. In a recent study, adequate plain water intake in children was more in high-income households, while 75% of children fail to meet the DRI.[1] For infants weighing between 3.5 kg to 10 kg, the daily fluid requirement is 100 ml/kg. For children 11 kg to 20 kg, the daily water requirement is 100 ml/kg for the first 10 kg and 50 ml/kg for every kg above 10 kg. For children above 20 kg, the fluid requirement is calculated as 1500ml for 20 kg and 20 ml/kg for every kg above 20 kg, but more than 2400ml of fluid should not be administered at once.

Another way to calculate daily fluid requirements is the 4-2-1 rule with 4ml/kg/hr for the first 10kg of weight and then 40ml/hr +2ml/kg/hr for kg 10 to 20 and then 60ml/hr +1ml/kg for every kg >20. With this formula, a 5kg child would need 20ml/hr or 480ml/day, and a 25kg child would need 65ml/hr or 1,5860 ml/day. Under-nutrition accounts for more than 3 million deaths in children < 5 years per year globally. Factors resulting in a diet that is low in quality include lack of knowledge, poverty, palatability, time scarcity, and lack of availability.[2][3]

Adults

The daily-recommended caloric intake for adult males and females is 2600-2800 kcal/day and 2000-2200 kcal/day, respectively. This requirement is not static and depends significantly on the activity status and the physical condition of the body. Imbalance in the diet leads to under-nutrition and over-nutrition, both of which are harmful to the body. The daily water requirement of the body depends on age, weight, sex, and air temperature. The DRI of water for men and women aged 19 to 30 years is 3.7 L/day and 2.7 L/day, respectively. In an analysis done in the USA, the estimated median total water intake of males and females aged between 19 to 50 years was 3.5 L/day and 3.0 L/day, respectively.[4] In a recent study, 83% of females and 95% of males ≥71 years of age failed to meet the DRI of water.[5]

Pregnant Women

Nutrition plays a vital role in pregnancy. The recommended weight gain during pregnancy depends on the prepregnancy body mass index (BMI). Underweight women (BMI<18.5) before pregnancy are advised to gain 28 to 40 lbs throughout their pregnancy, normal (BMI 18.5 to 24.9) 25 to 35 lbs, overweight (BMI 25 to 29.9) 15 to 25 lbs, and obese (BMI>30) 11 to 20 lbs. Pregnant women do not need to increase their daily calories during the first trimester. During the second trimester, added 340 calories per day are recommended, and then 450 extra calories per day in the third trimester.

Excess weight gain during pregnancy can lead to maternal and fetal complications. Maternal complications include cesarean delivery, retention of weight after delivery, and postpartum depression. An increased incidence of obesity, allergy, asthma, and cancer is seen in children of mothers who had excess weight gain during pregnancy. The National Research Council guidelines also recommend a range of weight gain for women carrying twin fetuses. Women with normal pre-pregnancy weight should gain 17kg-25 kg, while overweight and obese women should gain, 14kg-23kg and 11kg-19kg, respectively. It is important to ensure that women conceive while they are in the normal weight category; preconception counseling and adequate contraception should be discussed. The healthcare provider should track the weight gain during pregnancy and should guide the pregnant females regarding adequate dietary changes.

A prenatal vitamin should be taken before conception and then throughout pregnancy and breastfeeding. Adequate intake of folate (400 mcg/day) in the first trimester decreases neural tube defects. The recommended intake of iron doubles to 30 mg/day to assist with increased blood production. Vitamin D requirements increase to 600 IU per day, and calcium intake remains 1000 mg/day. Protein requirement increases from 0.8g/kg/day to 1.1g/kg/day. Fluid requirements also increase to 3 liters per day. Women should not avoid highly allergenic foods as a prophylactic measure during pregnancy. Women who follow certain diets may continue to do so with the assistance of their physician to ensure the meeting of all dietary needs.

Athletes

The nutritional requirements for athletes vary based on intensity and type of training. Physicians need to consider body composition and not just body weight when determining the needs of athletes. Special circumstances to consider would be a desire to gain weight, lose weight, build muscle, training in excess heat, training at high altitudes, and how much time in a day is spent in training. Hydration is important for maximal performance, so athletes should be sure to hydrate the 24 hours before an event, in the hour before their event, during their event, and then recovery after their event.[6]

Clinical Significance

The deficiency of any one of these nutrients can cause serious health concerns. Hence, it is essential to consume a diet that is rich in both macronutrients and micronutrients.

Carbohydrates

About 50 to 55% of the daily calories should come from carbohydrates, which are composed of monosaccharides that include fructose, glucose, and galactose. Each gram of carbohydrate contains energy equivalent to 4 kcal. Complex carbohydrates with a low glycemic index steadily raise the blood sugar level and are preferred over simple carbohydrates such as dextrose.[7] The limitation of simple sugars should be 5 to 10% of the daily caloric requirement. Legumes, whole grains, beans, fruits, and vegetables should be consumed to fulfill the daily requirement of carbohydrates.[8]

Proteins

Proteins are comprised of subunits called amino acids. These subunits provide energy and are essential for the construction of structural units of the body e.g., muscle, bone, and ligaments. Around 30% of the dry body weight is attributed to proteins. Approximately 20% of daily calories should come from sources rich in protein such as red and white meat, egg, and legumes. The daily recommendation for protein intake is 1.6 g/kg body weight for an adult. Some amino acids e.g., leucine and valine, are called essential; these are not synthesized by the body and must be obtained in the diet. Plant-sourced proteins, when consumed in replacement to animal proteins, have been shown to decrease cancer and cardiovascular disease-related mortality in a large prospective study.[9]

Marasmus is a type of protein-energy malnutrition resulting from the deficiency of energy-producing nutrients such as carbohydrates, proteins, and fats. On physical examination, the patient has generalized wasting, loss of subcutaneous fat, and muscle bulk. Another type of protein-energy malnutrition is kwashiorkor, which occurs in children consuming a diet that may be rich in energy but is deficient in proteins. The presence of skin findings e.g., pedal edema, dermatitis, skin depigmentation, hair loss, and loosening of teeth, differentiate kwashiorkor from marasmus. However, a child with marasmus can develop pitting edema due to protein deficiency; this is marasmic-kwashiorkor.[10]

Fats

Fats are composed of glycerol and fatty acids; these are high energy molecules that help the body grow, keep it warm, and serve as an inventory in case of emergency. Certain fatty acids (essential), e.g., omega-3 and omega-6, are required for the synthesis of eicosanoids such as prostaglandins and leukotrienes and should be consumed in the diet. About 25 to 30% of the daily calories should come from fats, out of which saturated fats should not be more than 10%.[11]

Cholesterol can be synthesized by the human body and hence is not essentially necessary in the diet. However, when consumed, it should not be more than 300 mg/day. A high-fat diet can lead to the development of obesity and is associated with an increased risk of cardiovascular disease.[12][11] Intake of fats can be reduced by replacing red meats, fried food, and fat-containing dairy products with white meat and fat sources that are rich in monosaturated fats e.g., olive oil, avocado, nuts, and flaxseed. A recent study reported that people consuming a diet rich in monosaturated fats were at a decreased risk of developing cardiovascular disease, type II diabetes mellitus, and cognitive decline.[8]

Dietary Fiber

Fiber improves digestive health by creating bulk in the stool and stimulating peristalsis. It prevents constipation and diarrhea and is a protector against colon cancer. Fruits and vegetables are the chief sources of fiber, and the recommendation is that one should consume at least five servings/day. The daily recommended amount of dietary fiber intake is 38 gram/day and 25 gram/day for men and women age 19 to 50 years, respectively. In children, the

goal fiber intake is age+5 grams. Consuming a diet rich in fiber can help improve the lipid profile, increase tolerability to statins, and reduce the risk of developing atherosclerosis hence preventing cardiovascular disease. [13]

Minerals and Trace Elements

Calcium and phosphorus are required for healthy bone development, while potassium, sodium, and chloride are the major electrolytes in the intracellular and extracellular compartments. An imbalance of these electrolytes can lead to drastic fluid shifts. Trace elements such as chromium, copper, and selenium also play an essential role in metabolic reactions, and their deficiency can lead to various diseases. The recommended daily allowance (RDA) of calcium is 1000 mg for both male and female adults. Females require an increased quantity of iron as compared to men due to the cyclic loss of blood during menstruation; hence the RDA for iron is 18 mg in females as compared to 8 mg in males. RDA for copper, zinc, and selenium is 30 µg, 900 µg, and 55 µg, respectively. Salt intake should be limited to fewer than 6 grams per day, as an increased quantity could lead to the development of hypertension.

The DASH diet, which is low in sodium and fat, helps improve hypertension and total cholesterol. In a recent study, the consumption of the DASH diet led to a 13% reduction in 10 years of Framingham Risk Score for cardiovascular disease in the subjects.[14] Iron deficiency can cause microcytic hypochromic anemia, as iron is an essential component of hemoglobin. In a study by Sehar et al. done in Pakistan, an estimated 500 mg of the iron reserve is necessary to meet the increased demands of pregnancy, while only 20% of the females have this reserve.[15] The thyroid gland uses iodine for the formation of thyroxine and triiodothyronine. The deficiency of iodine causes a decreased production of thyroid hormone, which leads to increased production of thyroid-stimulating hormone (TSH). Increased TSH upregulates thyroid hormone production and also causes the growth of the thyroid gland resulting in goiter. Calcium and phosphorus are vital for healthy bones, and their deficiency can lead to diseases such as osteoporosis and hypophosphatemic rickets.

Vitamins

Water-soluble (B, C) and fat-soluble (A, D, E, and K) vitamins have several vital roles. Vitamin A, also called retinol (RDA= 700 µg-900 µg retinol activity equivalents (RAE)/day), plays an essential role in the regeneration of epithelial cells and the development of rhodopsin, a photoreceptor pigment in the retina. Deficiency of vitamin A can cause xerophthalmia, keratomalacia, and night-blindness. A cross-sectional study done on pregnant and lactating women in Ethiopia revealed that 13.7% of the women had night blindness, and 0.4% had Bitot's spot. [16]

Thiamine (vitamin B1, RDA= 1.1mg/day) in the form of thiamine pyrophosphate (TPP) serves as a coenzyme in catabolic reactions of sugars and amino acids. Deficiency of vitamin B1 can cause wet beriberi, dry beriberi, and Wernicke-Korsakoff syndrome. Wernicke syndrome has distinct features of ophthalmoplegia, gait disturbances, and confusion, while Korsakoff syndrome includes confabulation and amnesia. It is a medical emergency and should be treated with intravenous thiamine and dextrose.

Scurvy presents with symptoms of skin bruises, petechiae, loosening of teeth, bleeding gums, slow wound healing, and mood changes. It occurs due to deficiency of vitamin C (RDA= 90 mg/day), which acts as a cofactor for both prolyl hydroxylase and lysyl hydroxylase, which help stabilize collagen. Collagen is a structural protein and is essential for healthy blood vessels, bones, cartilage, and connective tissue.

Vitamin D (RDA= 600IU/day) helps the absorption of calcium from both the gut and kidneys. A deficiency of vitamin D in childhood and adulthood can cause rickets and osteomalacia, respectively. On physical examination, children with rickets present with frontal bossing, pigeon chest deformity, bowing of legs, and rachitic rosary.

Vitamin E (RDA= 33IU/day [synthetic]) is an antioxidant, and its deficiency can lead to neurotoxicity and anemia.

Vitamin K (RDA= 120µg/day) plays an important role in the coagulation cascade. The gut flora helps convert vitamin K1 into vitamin K2, which is one of the main sources of the vitamin.

Water

Dehydration can occur due to inadequate consumption of water and classifies into three categories based on the percentage of body fluid loss. Loss of <5%, 5% to 10%, and >10% of body weight loss categorizes as mild, moderate, and severe dehydration, respectively. WHO has classified dehydration into no, some, and severe dehydration based on the physical examination. Patients with severe dehydration are lethargic, have sunken eyes, skin pinch goes back slowly, and the patient cannot drink on his own.

Patients with some dehydration are irritable, drink eagerly, have sunken eyes, and the skin pinch goes back slowly. Those with normal physical features are labeled as having no dehydration. Mild to moderate dehydration is treatable with oral fluids, while patients with severe dehydration or shock should be treated with intravenous fluid replacement. A recent study reported that people consuming less than the recommended amount of water per day have a constantly elevated level of serum arginine vasopressin (AVP). This hormone promotes reabsorption of water from kidneys and constricts arterioles to raise blood pressure.[17]

In a recent systematic review, decreased intake of water was related to a higher incidence of urolithiasis. While adequate water intake does not diminish the incidence of obesity or type II diabetes mellitus, it most certainly reduces the daily caloric intake.[18] Plain water is the ideal beverage to consume to fulfill the daily water requirement.[19]

Nursing, Allied Health, and Interprofessional Team Interventions

Every patient should be interviewed, examined, and investigated for potential malnutrition or overnutrition. Patients with dehydration may present with low blood pressure and increased heart rate. Nursing staff should be cautious and should work in collaboration with the physician to administer the right type and quantity of fluid. In severely dehydrated patients, it is necessary to have two wide bore cannulas in place. 0.9% normal saline is the fluid of choice.

In children, a bolus of 20 ml/kg of 0.9% normal saline should be administered in 10 to 20 minutes. If the vitals do not improve, the bolus dose can be given again. In adults, a 500 ml bolus of crystalloid fluid e.g., 0.9% normal saline, should be administered in 10 to 20 minutes. If no improvement occurs even after the administration of 2000 ml of fluid, then expert help should be taken.

Primary care providers should keep an eye on the nutritional status and development of new signs and symptoms in their patients. Clinicians practicing emergency medicine often get to see patients with a history of alcohol abuse. They can diagnose nutritional deficiency and the diseases related to it. Gynecologists and primary care physicians should pay special attention to females planning to conceive; multivitamin supplements, which include folic acid, iron, and calcium, should be prescribed. In children or elderly with severe malnutrition, cautious refeeding should be started, electrolyte abnormalities should be corrected, and the clinical team should initate activity to prevent hypoglycemia.

Review Questions

- Access free multiple choice questions on this topic.

- Comment on this article.

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Figures

Daily Recommended Caloric Intake in Children (kcal)				
Age (years)	Male		Female	
	Sedentary	Active	Sedentary	Active
2	1000	1000	1000	1000
3	1000	1400	1000	1200
4-5	1200	1400	1200	1400
6	1400	1600	1200	1400
7	1400	1600	1200	1600
8	1400	1600	1400	1600
9	1600	1800	1400	1600
10	1600	1800	1400	1800
11	1800	2000	1600	1800
12	1800	2200	1600	2000
13	2000	2200	1600	2000
14	2000	2400	1800	2000
15	2200	2600	1800	2000

Daily Recommended Caloric Intake in Children. Made by Unaiza Faizan

Daily Recommended Caloric Intake in Adults (kcal)				
Age (years)	Male		Female	
	Sedentary	Active	Sedentary	Active
16-18	2400	2800	1800	2000
19-20	2600	2800	2000	2200
21-25	2400	2800	2000	2200
26-40	2400	2600	1800	2000
41-15	2200	2600	1800	2000
46-50	2200	2400	1800	2000
51-60	2200	2400	1600	1800
61-65	2000	2400	1600	1800
66 and above	2000	2200	1600	1800

Daily Recommended Caloric Intake in Adults. Made by Unaiza Faizan

Bookshelf ID: NBK562207 PMID: 32965878

Attachment 11

METHOD 533: DETERMINATION OF PER- AND POLYFLUOROALKYL SUBSTANCES IN DRINKING WATER BY ISOTOPE DILUTION ANION EXCHANGE SOLID PHASE EXTRACTION AND LIQUID CHROMATOGRAPHY/TANDEM MASS SPECTROMETRY

Technical questions concerning this analytical method should be addressed to:

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Weck Laboratories, Inc. (City of Industry, CA)
Vogon Laboratory Services Ltd. (Cochrane, Alberta, Canada)

Disclaimer

This analytical method may support a variety of monitoring applications, which include the analysis of multiple short-chain per- and polyfluoroalkyl substances (PFAS) that cannot be measured by Method 537.1. This publication meets an agency commitment identified within the 2019 EPA PFAS Action Plan. Publication of the method, in and of itself, does not establish a requirement, although the use of this method may be specified by the EPA or a state through independent actions. Terms such as "must" or "required," as used in this document, refer to procedures that are to be followed to conform with the method. References to specific brands and catalog numbers are included only as examples and do not imply endorsement of the products. Such reference does not preclude the use of equivalent products from other vendors or suppliers.

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Tables

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1 Scope and Application

This is a solid phase extraction (SPE) liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for the determination of select per- and polyfluoroalkyl substances (PFAS) in drinking water. Method 533 requires the use of MS/MS in Multiple Reaction Monitoring (MRM) mode to enhance selectivity. Accuracy and precision data have been generated in reagent water and drinking water for the compounds included in the Analyte List.

This method is intended for use by analysts skilled in the performance of solid phase extractions, the operation of LC-MS/MS instrumentation, and the interpretation of the associated data.

Analyte List

Analyte[a]	Abbreviation	CASRN
11-Chloroeicosafluoro-3-oxaundecane-1-sulfonic acid	11Cl-PF3OUdS	763051-92-9
9-Chlorohexadecafluoro-3-oxanonane-1-sulfonic acd	9Cl-PF3ONS	756426-58-1
4,8-Dioxa-3*H*-perfluorononanoic acid	ADONA	919005-14-4
Hexafluoropropylene oxide dimer acid	HFPO-DA	13252-13-6
Nonafluoro-3,6-dioxaheptanoic acid	NFDHA	151772-58-6
Perfluorobutanoic acid	PFBA	375-22-4
Perfluorobutanesulfonic acid	PFBS	375-73-5
1*H*,1*H*, 2*H*, 2*H*-Perfluorodecane sulfonic acid	8:2FTS	39108-34-4
Perfluorodecanoic acid	PFDA	335-76-2
Perfluorododecanoic acid	PFDoA	307-55-1
Perfluoro(2-ethoxyethane)sulfonic acid	PFEESA	113507-82-7
Perfluoroheptanesulfonic acid	PFHpS	375-92-8
Perfluoroheptanoic acid	PFHpA	375-85-9
1*H*,1*H*, 2*H*, 2*H*-Perfluorohexane sulfonic acid	4:2FTS	757124-72-4
Perfluorohexanesulfonic acid	PFHxS	355-46-4
Perfluorohexanoic acid	PFHxA	307-24-4
Perfluoro-3-methoxypropanoic acid	PFMPA	377-73-1
Perfluoro-4-methoxybutanoic acid	PFMBA	863090-89-5
Perfluorononanoic acid	PFNA	375-95-1
1*H*,1*H*, 2*H*, 2*H*-Perfluorooctane sulfonic acid	6:2FTS	27619-97-2
Perfluorooctanesulfonic acid	PFOS	1763-23-1
Perfluorooctanoic acid	PFOA	335-67-1
Perfluoropentanoic acid	PFPeA	2706-90-3
Perfluoropentanesulfonic acid	PFPeS	2706-91-4
Perfluoroundecanoic acid	PFUnA	2058-94-8

a. Some PFAS are commercially available as ammonium, sodium, and potassium salts. This method measures all forms of the analytes as anions while the identity of the counterion is inconsequential. Analytes may be purchased as acids or as any of the corresponding salts.

1.1 Detection of PFAS Isomers

Both branched and linear PFAS isomers may be found in the environment. This method includes procedures for summing the contribution of multiple isomers to the final reported concentration. In those cases where standard materials containing multiple isomers are commercially available, laboratories should obtain such standards for the method analytes.

1.2 Lowest Concentration Minimum Reporting Limits

The lowest concentration minimum reporting level (LCMRL) is the lowest concentration for which the future recovery is predicted to fall between 50 and 150% with high confidence (99%). Single-laboratory LCMRLs determined for the method analytes during method development are reported in **Table 7**. It should be noted that most of the LCMRL values determined during the second laboratory evaluation were lower than the values listed in **Table 7**. The values that a laboratory can obtain are dependent on the design and capability of the instrumentation used. The procedure used to determine the LCMRL is described elsewhere.[1,2] Laboratories using this method are not required to determine LCMRLs, but they must demonstrate that they are able to meet the minimum reporting level (MRL) (Sect. 3.15) for each analyte per the procedure described in Section 9.1.4.

1.3 Method Flexibility

The laboratory may select LC columns, LC conditions, and MS conditions different from those used to develop the method. At a minimum, the isotope dilution standards and the isotope performance standards specified in the method must be used, if available. The laboratory may select the aqueous sample volume within the range of 100–250 mL that meets their objectives. During method development, 250 mL aqueous samples were extracted using a 500 mg solid phase extraction (SPE) sorbent bed volume. The ratio of sorbent mass to aqueous sample volume may not be decreased. If a laboratory uses 100 mL aqueous samples, the sorbent mass must be at least 200 mg. Changes may not be made to sample preservation, the quality control (QC) requirements, or the extraction procedure. The chromatographic separation should minimize the number of compounds eluting within a retention window to obtain a sufficient number of scans across each peak. Instrumental sensitivity (or signal-to-noise) will decrease if too many compounds are permitted to elute within a retention time window. Method modifications should be considered only to improve method performance. In all cases where method modifications are proposed, the analyst must perform the procedures outlined in the Initial Demonstration of Capability (IDC, Sect. 9.1), verify that all QC acceptance criteria in this method (Sect. 9.2) are met, and verify method performance in a representative sample matrix (Sect. 9.3.2).

2 Method Summary

A 100–250 mL sample is fortified with isotopically labeled analogues of the method analytes that function as isotope dilution standards. The sample is passed through an SPE cartridge containing polystyrene divinylbenzene with a positively charged diamino ligand to extract the method analytes and isotope dilution analogues. The cartridge is rinsed with sequential washes of aqueous ammonium acetate followed by methanol, then the compounds are eluted from the solid phase sorbent with methanol containing ammonium hydroxide. The extract is concentrated to dryness with nitrogen in a heated water bath. The extract volume is adjusted to 1.0 mL with 20% water in methanol (v/v), and three isotopically labeled isotope performance standards are added. Extracts are analyzed by LC-MS/MS

in the MRM detection mode. The concentration of each analyte is calculated using the isotope dilution technique. For QC purposes, the percent recoveries of the isotope dilution analogues are calculated using the integrated peak areas of isotope performance standards, which are added to the final extract and function as traditional internal standards, exclusively applied to the isotope dilution analogues.

3 Definitions

3.1 Analysis Batch

A set of samples that are analyzed on the same instrument during a 24-hour period that begins and ends with the analysis of the appropriate Continuing Calibration Check (CCC) standards. Additional CCCs may be required depending on the length of the Analysis Batch and the number of field samples.

3.2 Calibration Standard

A solution of the method analytes, isotope dilution analogues, and isotope performance standards prepared from the Primary Dilution Standards and stock standards. The calibration standards are used to calibrate the instrument response with respect to analyte concentration.

3.3 Continuing Calibration Check (CCC)

A calibration standard that is analyzed periodically to verify the accuracy of the existing calibration.

3.4 Extraction Batch

A set of up to 20 field samples (not including QC samples) extracted together using the same lot of solid phase extraction devices, solvents, and fortifying solutions.

3.5 Field Duplicates (FD)

Separate samples collected at the same time and sampling location, shipped and stored under identical conditions. Method precision, including the contribution from sample collection procedures, is estimated from the analysis of Field Duplicates. Field Duplicates are used to prepare Laboratory Fortified Sample Matrix and Laboratory Fortified Sample Matrix Duplicate QC samples. For the purposes of this method, Field Duplicates are collected to support potential repeat analyses (if the original field sample is lost or if there are QC failures associated with the analysis of the original field sample).

3.6 Field Reagent Blank (FRB)

An aliquot of reagent water that is placed in a sample container in the laboratory and treated as a sample in all respects, including shipment to the sampling site, exposure to sampling site conditions, storage, and all analytical procedures. The purpose of the FRB is to determine if method analytes or other interferences are introduced into the sample from shipping, storage, and the field environment.

3.7 Isotope Dilution Analogues

Isotopically labeled analogues of the method analytes that are added to the sample prior to extraction in a known amount. Note: Not all target PFAS currently have an isotopically labelled analogue. In these cases, an alternate isotopically labelled analogue is used as recommended in **Table 5**.

3.8 Isotope Dilution Technique

An analytical technique for measuring analyte concentration using the ratio of the peak area of the native analyte to that of an isotopically labeled analogue, added to the original sample in a known amount and carried through the entire analytical procedure.

3.9 Isotope Performance Standards

Quality control compounds that are added to all standard solutions and extracts in a known amount and used to measure the relative response of the isotopically labelled analogues that are components of the same solution. For this method, the isotope performance standards are three isotopically labeled analogues of the method analytes. The isotope performance standards are indicators of instrument performance and are used to calculate the recovery of the isotope dilution analogues through the extraction procedure. In this method, the isotope performance standards are not used in the calculation of the recovery of the native analytes.

3.10 Laboratory Fortified Blank (LFB)

An aliquot of reagent water to which known quantities of the method analytes and isotope dilution analogues are added. The results of the LFB verify method performance in the absence of sample matrix.

3.11 Laboratory Fortified Sample Matrix (LFSM)

An aliquot of a field sample to which known quantities of the method analytes and isotope dilution analogues are added. The purpose of the LSFM is to determine whether the sample matrix contributes bias to the analytical results. Separate field samples are required for preparing fortified matrix so that sampling error is included in the accuracy estimate.

3.12 Laboratory Fortified Sample Matrix Duplicate (LFSMD)

A Field Duplicate of the sample used to prepare the LFSM that is fortified and analyzed identically to the LFSM. The LFSMD is used instead of the Field Duplicate to assess method precision when the method analytes are rarely found at concentrations greater than the MRL.

3.13 Laboratory Reagent Blank (LRB)

An aliquot of reagent water fortified with the isotope dilution analogues and processed identically to a field sample. An LRB is included in each Extraction Batch to determine if the method analytes or other interferences are introduced from the laboratory environment, the reagents, glassware, or extraction apparatus.

3.14 Lowest Concentration Minimum Reporting Level (LCMRL)

The single-laboratory LCMRL is the lowest spiking concentration such that the probability of spike recovery in the 50% to 150% range is at least 99%.[1,2]

3.15 Minimum Reporting Level (MRL)

The minimum concentration that may be reported by a laboratory as a quantified value for a method analyte. For each method analyte, the concentration of the lowest calibration standard must be at or

below the MRL and the laboratory must demonstrate its ability to meet the MRL per the criteria defined in Section 9.1.4.

3.16 Precursor Ion

The gas-phase species corresponding to the method analyte that is produced in the electrospray ionization interface. During tandem mass spectrometry, or MS/MS, the precursor ion is mass selected and fragmented by collision-activated dissociation to produce distinctive product ions of smaller mass to charge (*m/z*) ratio. For this method, the precursor ion is usually the deprotonated molecule ($[M - H]^-$) of the method analyte, except for HFPO-DA. For this analyte, the precursor ion is formed by decarboxylation of HFPO-DA.

3.17 Primary Dilution Standard (PDS)

A solution that contains method analytes (or QC analytes) prepared from stock standards. PDS solutions are used to fortify QC samples and diluted to prepare calibration standards.

3.18 Product Ion

One of the fragment ions that is produced in MS/MS by collision-activated dissociation of the precursor ion.

3.19 Quality Control Standard (QCS)

A calibration standard prepared independently from the primary calibration solutions. For this method, the QCS is a repeat of the entire dilution scheme starting with the same stock materials (neat compounds or purchased stock solutions) used to prepare the primary calibration solutions. Independent sources and separate lots of the starting materials are not required, provided the laboratory has obtained the purest form of the starting materials commercially available. The purpose of the QCS is to verify the integrity of the primary calibration standards.

3.20 Quantitative Standard

A quantitative standard of assayed concentration and purity traceable to a Certificate of Analysis.

3.21 Stock Standard Solution

A concentrated standard that is prepared in the laboratory using assayed reference materials or that is purchased from a commercial source with a Certificate of Analysis.

3.22 Technical-Grade Standard

As defined for this method, a technical-grade standard includes a mixture of the branched and linear isomers of a method analyte. For the purposes of this method, technical-grade standards are used to identify retention times of branched and linear isomers of method analytes.

4 Interferences

4.1 Labware, Reagents and Equipment

Method interferences may be caused by contaminants in solvents, reagents (including reagent water), sample bottles and caps, and other sample processing hardware that lead to discrete artifacts or

elevated baselines in the chromatograms. The analytes in this method can also be found in many common laboratory supplies and equipment, such as PTFE (polytetrafluoroethylene) products, LC solvent lines, methanol, aluminum foil, deactivated syringes, SPE sample transfer lines, etc.[3] Laboratories must demonstrate that these items are not contributing to interference by analyzing LRBs as described in Section 9.2.1.

4.2 Sample Contact with Glass

Aqueous samples should not come in contact with any glass containers or pipettes as PFAS analytes can potentially adsorb to glass surfaces. Standards dissolved in organic solvent may be purchased in glass ampoules. These standards in organic solvent are acceptable and subsequent transfers may be performed using glass syringes and pipets. Following extraction, the eluate must be collected in a polypropylene tube prior to concentration to dryness. Concentration to dryness in glass tubes may cause poor recovery.

4.3 Matrix Interferences

Matrix interferences may be caused by contaminants that are co-extracted from the sample. The extent of matrix interferences will vary considerably from source to source, depending upon the nature of the water. Humic and fulvic material may be co-extracted during SPE and high levels may cause enhancement or suppression in the electrospray ionization source.[4] Inorganic salts may cause low recoveries during the anion-exchange SPE procedure.

4.3.1 Co-extracted Organic Material

Under the LC conditions used during method development, matrix effects due to co-extracted organic material enhanced the ionization of 4:2 FTS appreciably. Total organic carbon (TOC) is a good indicator of humic content of the sample.

4.3.2 Inorganic Salts

The authors confirmed acceptable method performance for matrix ion concentrations up to 250 mg/L chloride, 250 mg/L sulfate, and 340 mg/L hardness measured as $CaCO_3$. Acceptable performance was defined as recovery of the isotope dilution analogues between 50–200%.

4.3.3 Ammonium Acetate

Relatively large quantities of ammonium acetate are used as a preservative. The potential exists for trace-level organic contaminants in this reagent. Interferences from this source should be monitored by analysis of LRBs, particularly when new lots of this reagent are acquired.

4.3.4 SPE Cartridges

Solid phase extraction cartridges may be a source of interferences. The analysis of LRBs provides important information regarding the presence or absence of such interferences. Each brand and lot of SPE devices must be monitored to ensure that contamination does not preclude analyte identification and quantitation. SPE cartridges should be sealed while in storage to prevent ambient contamination of the SPE sorbent.

4.4 Bias Caused by Isotopically Labeled Standards

During method development, no isotopically labeled standard solution yielded any signal that gave the same mass and retention time as any native analyte. However, due to isotopic impurity, the $^{13}C_3$-PFBA isotope performance standard contained a small amount of $^{13}C_4$-PFBA, slightly contributing to the signal of the isotope dilution analogue. Further, due to natural abundance of ^{34}S, the native telomer sulfonates produced a small contribution to the $^{13}C_2$ labeled telomer sulfonate isotope dilution analogues. The effects on quantitation are insignificant. However, these cases are described below in Sections 4.4.2 and 4.4.3 to alert the user that these situations could occur.

4.4.1 Method Analytes

At the concentrations used to collect method performance data, the authors could not detect any contribution from the isotope dilution analogues or isotope performance standards to the corresponding native analyte response. However, the user should evaluate each source of isotopically labeled analogues and isotope performance standards to verify that they do not contain any native analyte at concentrations greater than 1/3 of the MRL.

4.4.2 Isotopic purity of $^{13}C_3$-PFBA

In this method, $^{13}C_3$-PFBA is used as an isotope performance standard and $^{13}C_4$-PFBA is used as an isotope dilution analogue. Both share the same product ion, *m/z* 172. Ten nanograms per liter of $^{13}C_4$-PFBA is added to the sample prior to extraction (10 ng/mL extract concentration assuming 100% recovery), and 10 ng/mL of $^{13}C_3$-PFBA is added to the final extract. Because the natural abundance of ^{13}C is 1.1%, there is a 1.1% contribution to the $^{13}C_4$-PFBA area from the lone, unlabeled ^{12}C atom in $^{13}C_3$-PFBA. The authors confirmed this contribution empirically. Users of this method may consider this bias to the area of the PFBA isotope dilution analogue insignificant.

4.4.3 Isotopic purity of $^{13}C_4$-PFBA

A trace amount of $^{13}C_3$-PFBA was detected in the $^{13}C_4$-PFBA. The contribution was no greater than 1%. The contribution of the isotope performance standard to the isotope dilution analogue is insignificant.

4.4.4 Telomer Sulfonates

Each of the three telomer sulfonates in the analyte list (4:2FTS, 6:2FTS, and 8:2FTS) are referenced to their $^{13}C_2$ isotope dilution analogue. The mass difference between the telomer sulfonates and the isotope dilution analogues is 2 mass units. The single sulfur atom in each of the unlabeled molecules has a naturally occurring M+2 isotope (^{34}S) at 4.25%. Thus, the precursor ions of the $^{13}C_2$ isotopically labeled analogues and the naturally occuring ^{34}S analogues present in the native analytes have the same nominal masses. The product ions of the telomer sulfonate isotope dilution analogues listed in **Table 6** would contain a small contribution from the ^{34}S analogue of the native telomer sulfonates. At the concentrations used in this study, the contribution of the ^{34}S analogue to the isotope dilution analogue was not greater than 2.7%. Alternate product ions may be used if there is sufficient abundance.

5 Safety

Each chemical should be treated as a potential health hazard and exposure to these chemicals should be minimized. Each laboratory is responsible for maintaining an awareness of OSHA regulations regarding

safe handling of chemicals used in this method. A reference file of safety data sheets should be made available to all personnel involved in the chemical analysis.

6 Equipment and Supplies

References to specific brands and catalog numbers are included as examples only and do not imply endorsement of the products. Such reference does not preclude the use of equivalent products from other vendors or suppliers. Due to potential adsorption of analytes onto glass, polypropylene containers were used for sample preparation and extraction steps. Other plastic materials (e.g., polyethylene) that meet the QC requirements of Section 9 may be substituted.

6.1 Sample Containers

Polypropylene bottles with polypropylene screw caps (for example, 250 mL bottles, Fisher Scientific, Cat. No. 02-896-D or equivalent).

6.2 Polypropylene Vials

These vials are used to store stock standards and PDS solutions (4 mL, VWR Cat. No. 16066-960 or equivalent).

6.3 Centrifuge Tubes

Conical polypropylene centrifuge tubes (15 mL) with polypropylene screw caps for storing standard solutions and for collection of the eluate during the extraction procedure (Thomas Scientific Cat. No. 2602A10 or equivalent).

6.4 Autosampler Vials

Polypropylene autosampler vials (ThermoFisher, Cat. No. C4000-14) with polypropylene caps (ThermoFisher, Cat. No. C5000-50 or equivalent). Note: Polypropylene vials and caps are necessary to prevent contamination of the sample from PTFE coated septa. However, polypropylene caps do not reseal, creating the potential for evaporation to occur after injection. Multiple injections from the same vial are not permissible unless the cap is replaced immediately after injection.

6.5 Micro Syringes

Suggested sizes include 10, 25, 50, 100, 250, 500 and 1000 µL.

6.6 Pipets

Polypropylene or glass pipets may be used for methanolic solutions.

6.7 Analytical Balance

Capable of weighing to the nearest 0.0001 g.

6.8 Solid Phase Extraction (SPE) Apparatus

6.8.1 SPE Cartridges

SPE cartridges containing weak anion exchange, mixed-mode polymeric sorbent (polymeric backbone and a diamino ligand), particle size approximately 33 µm. The SPE sorbent must have a pKa above 8 so that it remains positively charged during extraction. SPE cartridges containing 500 mg sorbent

(Phenomenex Cat. No. 8B-S038-HCH) were used during method development. Use of 200 mg cartridges is acceptable for the extraction of 100 mL samples.

6.8.2 Vacuum Extraction Manifold

Equipped with flow and vacuum control [Supelco Cat. No. 57030-U, UCT Cat. No. VMF016GL (the latter requires UCT Cat. No. VMF02116 control valves), or equivalent systems]. Automated devices designed for use with SPE cartridges may be used; however, all extraction and elution steps must be the same as in the manual procedure. Care must be taken with automated SPE systems to ensure that Teflon tubing and other PTFE components commonly used in these systems, do not contribute to unacceptable analyte concentrations in LRBs.

6.8.3 Sample Delivery System

Use of large volume sampling lines, constructed with polyethylene tubing, are recommended, but not mandatory. Large volume sample transfer lines, constructed with PTFE tubing, are commercially available for standard extraction manifolds (Supelco Cat. No. 57275 or equivalent). The PTFE tubing can be replaced with 1/8" o.d. x 1/16" i.d. polyethylene tubing [Freelin-Wade (McMinnville, Oregon) LLDPE or equivalent] cut to an appropriate length. This prevents potential contamination from PTFE transfer lines. Other types of non-PTFE tubing may be used provided it meets the LRB and LFB QC requirements. PTFE tubing may be used, but an LRB must be run on each individual transfer line and the QC requirements in Section 9.2.1 must be met. In the case of automated SPE, the removal of PTFE lines may not be feasible; therefore, acceptable performance for the LRB must be met for each port during the IDC (Sect 9.1.1). LRBs must be rotated among the ports during routine analyses thereafter. Plastic reservoirs are difficult to rinse during elution and their use may lead to lower recovery.

6.9 Extract Concentration System

Extracts are concentrated by evaporation with high-purity nitrogen using a water bath set no higher than 60 °C [N-Evap, Model 11155, Organomation Associates (Berlin, MA), Inc., or equivalent].

6.10 Laboratory Vacuum System

Sufficient capacity to maintain a vacuum of approximately 15 to 20 inches of mercury for extraction cartridges.

6.11 pH Meter

Used to verify the pH of the phosphate buffer and to measure the pH of the aqueous sample prior to anion exchange SPE.

6.12 LC-MS/MS System

6.12.1 LC System

The LC system must provide consistent sample injection volumes and be capable of performing binary linear gradients at a constant flow rate. On some LC systems, PFAS may build up in PTFE transfer lines when the system is idle for more than one day. To prevent long delays in purging high levels of PFAS from the LC solvent lines, it may be useful to replace PTFE tubing with PEEK™ tubing and the PTFE solvent frits with stainless steel frits. These modifications were not used on the LC system used for method development. However, a delay column, HLB Direct Connect 2.1 x 30 mm (Waters 186005231),

was placed in the mobile phase flow path immediately before the injection valve. This direct connect column may have reduced the co-elution of PFAS originating from sources prior to the sample loop from the PFAS injected in the sample. It may not be possible to remove all PFAS background contamination.

6.12.2 Analytical Column

C18 liquid chromatography column (2 x 50 mm) packed with 3 µm C18 solid phase particles (Phenomenex Part Number 00B-4439-B0 or equivalent).

6.12.3 Electrospray Ionization Tandem Mass Spectrometer (ESI-MS/MS)

The mass spectrometer must be capable of electrospray ionization in the negative ion mode. The system must be capable of performing MS/MS to produce unique product ions for the method analytes within specified retention time segments. A minimum of 10 scans across the chromatographic peak is needed to ensure adequate precision. Some ESI-MS/MS instruments may not be suitable for PFAS analysis. See the procedures in Section 10.1.2.1 to ensure that the selected MS/MS platform is capable of monitoring all the required MS/MS transitions for the method analytes.

6.12.4 MS/MS Data System

An interfaced data system is required to acquire, store, and output MS data. The computer software must have the capability of processing stored data by recognizing a chromatographic peak within a given retention time window. The software must allow integration of the abundance of any specific ion between specified time or scan number limits. The software must be able to construct a linear regression or quadratic regression calibration curve and calculate analyte concentrations using the internal standard technique.

7 Reagents and Standards

Reagent grade or better chemicals must be used. Unless otherwise indicated, all reagents must conform to the specifications of the Committee on Analytical Reagents of the American Chemical Society (ACS), where such specifications are available. Other grades may be used if the reagent is demonstrated to be free of analytes and interferences and all requirements of the IDC are met when using these reagents.

7.1 Reagent Water

Purified water which does not contain any measurable quantities of any method analytes or interfering compounds greater than one-third of the MRL for each method analyte. It may be necessary to flush the water purification unit to rinse out any build-up of PFAS in the system prior to collection of reagent water.

7.2 Methanol

CH_3OH, CASRN 67-56-1, LC grade (Fisher Scientific, Cat. No. A456 or equivalent).

7.3 Ammonium Acetate

$NH_4C_2H_3O_2$, CASRN 631-61-8, HPLC grade, molecular weight equals 77.08 g/mole.

7.3.1 20 mM Ammonium Acetate

Chromatographic mobile phase. To prepare 1 L, add 1.54 g ammonium acetate to 1 L of reagent water. This solution is volatile and must be replaced at least once per week. More frequent replacement may be necessary if unexplained losses in sensitivity or retention time shifts are encountered.

7.3.2 1 g/L Ammonium Acetate

Used to rinse SPE cartridges after loading the aqueous sample and prior to the methanol rinse. Prepare in reagent water.

7.4 Concentrated Ammonium Hydroxide Reagent

NH_4OH, CASRN 1336-21-6, approximately 56.6% in water as ammonium hydroxide (w/w), approximately 28% in water as ammonia, approximately 14.5 N (Fisher Scientific, Cat. No. A669, Certified ACS Plus grade, or equivalent).

7.5 Solution of Ammonium Hydroxide in Methanol

Used for elution of SPE cartridges. Dilute 2 mL of concentrated ammonium hydroxide (56.6% w/w) in 100 mL methanol. This solution should be made fresh on the day of extraction.

7.6 Sodium Phosphate Dibasic (Na_2HPO_4)

Used for creating the aqueous buffer for conditioning the SPE cartridges. Dibasic sodium phosphate may be purchased in either the anhydrous or any hydrated form. The formula weight will vary based on degree of hydration.

7.7 Sodium Phosphate Monobasic (NaH_2PO_4)

Used for creating the aqueous buffer for conditioning the SPE cartridges. Monobasic sodium phosphate may be purchased in either the anhydrous or any hydrated form. The formula weight will vary based on degree of hydration.

7.8 0.1 M Phosphate Buffer pH 7.0

Mix 500 mL of 0.1 M dibasic sodium phosphate with approximately 275 mL of 0.1 M monobasic sodium phosphate. Verify that the solution pH is approximately 7.0.

7.9 Nitrogen

7.9.1 Nitrogen Nebulizer Gas

Nitrogen used as a nebulizer gas in the ESI interface and as collision gas in some MS/MS platforms should meet or exceed the instrument manufacturer's specifications.

7.9.2 Nitrogen used for Concentrating Extracts

Ultra-high-purity-grade nitrogen should be used to concentrate sample extracts.

7.10 Argon

Used as collision gas in MS/MS instruments. Argon should meet or exceed instrument manufacturer's specifications. Nitrogen may be used as the collision gas if recommended by the instrument manufacturer.

7.11 Sodium Hydroxide

May be purchased as pellets or as aqueous solution of known concentration. Added to methanolic solutions of PFAS to prevent esterification.

7.12 Acetic Acid (glacial)

May be necessary to adjust pH of aqueous samples. The pH of the aqueous sample containing 1 g/L ammonium acetate must be between 6 and 8.

7.13 Standard Solutions

7.13.1 Stability of Methanolic Solutions

Fluorinated carboxylic acids will esterify in anhydrous acidic methanol. To prevent esterification, standards must be stored under basic conditions. If base is not already present, this may be accomplished by the addition of sodium hydroxide (approximately 4 mole equivalents) when standards are diluted in methanol. When calculating molarity for solutions containing multiple PFAS, the molecular weight can be estimated as 250 atomic mass units (amu). It is necessary to include sodium hydroxide in solutions of both isotopically labeled and native analytes. The amount of sodium hydroxide needed may be calculated using the following equation:

$$\frac{Total\ PFAS\ mass\ (g) \times 160(\frac{g}{mol})}{250\ (\frac{g}{mol})} = Mass\ of\ NaOH\ Required\ (g)$$

7.13.2 Preparation of Standards

When a compound purity is assayed to be 96% or greater, the weight can be used without correction to calculate the concentration of the stock standard. Sorption of PFAS analytes in methanol solution to glass surfaces after prolonged storage has not been evaluated. PFAS analyte and isotopically labeled analogues commercially purchased in glass ampoules are acceptable; however, all subsequent transfers or dilutions performed by the analyst must be stored in polypropylene containers.
Solution concentrations listed in this section were used to develop this method and are included as examples. Alternate concentrations may be used as necessary depending on instrument sensitivity and the calibration range used. Standards for sample fortification generally should be prepared in the smallest volume that can be accurately measured to minimize the addition of excess organic solvent to aqueous samples. Laboratories should use standard QC practices to determine when standards need to be replaced. The analyte supplier's guidelines may be helpful when making this determination.

7.14 Storage Temperatures for Standards Solutions

Store stock standards at less than 4 °C unless the vendor recommends otherwise. The Primary Dilution Standards may be stored at any temperature, but cold storage is recommended to prevent solvent evaporation. During method development, the PDS was stored at –20 °C and no change in analyte concentrations was observed over a period of 6 months.

7.15 Isotope Performance Standards

This method requires three isotope performance standards listed in the table below. These isotopically labeled compounds were chosen during method development to include the analogues of three method analytes: two carboxylates with different chain lengths and a sulfonate.

Obtain the isotope performance standards as certified standard solutions, if available, or as the neat compounds. During method development, the isotope performance standards were obtained from Wellington Laboratories (Guelph, ON, Canada) as certified stocks in basic methanol. Note that Chemical Abstracts Registry Numbers are not currently available for these compounds. The concentrations of the stocks supplied by Wellington are listed in the table below.

Isotope Performance Standards	Abbreviation	Wellington Stock, µg/mL	PDS, ng/µL
Perfluoro-*n*-[2,3,4-$^{13}C_3$]butanoic acid	$^{13}C_3$-PFBA	50	1.0
Perfluoro-[1,2-$^{13}C_2$]octanoic acid	$^{13}C_2$-PFOA	50	1.0
Sodium perfluoro-1-[1,2,3,4-$^{13}C_4$]octanesulfonate	$^{13}C_4$-PFOS	50[a]	3.0

a. 47.8 µg/mL as the anion.

All the isotope performance standards listed in this section must be used, if available. Additional isotope performance standards may be used provided they are isotopically labeled analytes or labeled analytes with similar functional groups as the method analytes. Linear isomers are recommended to simplify peak integration. Method modification QC requirements must be met (Sect. 9.3) whenever additional isotope performance standards are used.

7.15.1 Isotope Performance Standard PDS

Prepare the isotope performance standard PDS in methanol and add sodium hydroxide if not already present to prevent esterification as described in Section 7.13.1. The PDS concentrations used to develop the method are listed in the table above (Sect. 7.15). During collection of method performance data, the final extracts were fortified with 10 µL of the PDS to yield a concentration of 10 ng/mL for $^{13}C_3$-PFBA and $^{13}C_2$-PFOA, and 30 ng/mL for $^{13}C_4$-PFOS (28.7 ng/mL as the anion).

7.16 Isotope Dilution Analogues

Obtain the isotopically labeled analogues listed in the table in this section as individual certified standard solutions or as certified standard mixes. All listed isotope dilution analogues must be used, if available. Linear isomers are recommended to simplify peak integration. During method development, the isotope dilution analogues were obtained from Wellington Laboratories (Guelph, ON, Canada) as certified stocks in basic methanol. These analogues were chosen during method development because they encompass most of the functional groups, as well as the molecular weight range of the method analytes. Note that Chemical Abstracts Registry Numbers are not currently available for these isotopically labeled analogues.

Isotope Dilution Standards	Abbreviation	PDS, ng/µL[a]
Perfluoro-*n*-[1,2,3,4-$^{13}C_4$]butanoic acid	$^{13}C_4$-PFBA	0.50
Perfluoro-*n*-[1,2,3,4,5-$^{13}C_5$]pentanoic acid	$^{13}C_5$-PFPeA	0.50
Sodium perfluoro-1-[2,3,4-$^{13}C_3$]butanesulfonate	$^{13}C_3$-PFBS	0.50
Sodium 1*H*,1*H*,2*H*,2*H*-perfluoro-1-[1,2-$^{13}C_2$]hexane sulfonate	$^{13}C_2$-4:2FTS	2.0
Perfluoro-*n*-[1,2,3,4,6-$^{13}C_5$]hexanoic acid	$^{13}C_5$-PFHxA	0.50
2,3,3,3-Tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy-$^{13}C_3$-propanoic acid	$^{13}C_3$-HFPO-DA	0.50
Perfluoro-*n*-[1,2,3,4-$^{13}C_4$]heptanoic acid	$^{13}C_4$-PFHpA	0.50
Sodium perfluoro-1-[1,2,3-$^{13}C_3$]hexanesulfonate	$^{13}C_3$-PFHxS	0.50
Sodium 1*H*,1*H*,2*H*,2*H*-perfluoro-1-[1,2-13C_2]-octane sulfonate	$^{13}C_2$-6:2FTS	2.0
Perfluoro-*n*-[$^{13}C_8$]octanoic acid	$^{13}C_8$-PFOA	0.50
Perfluoro-*n*-[$^{13}C_9$]nonanoic acid	$^{13}C_9$-PFNA	0.50
Sodium perfluoro-[$^{13}C_8$]octanesulfonate	$^{13}C_8$-PFOS	0.50
Sodium 1*H*,1*H*,2*H*,2*H*-perfluoro-1-[1,2-$^{13}C_2$]-decane sulfonate	$^{13}C_2$-8:2FTS	2.0
Perfluoro-*n*-[1,2,3,4,5,6-$^{13}C_6$]decanoic acid	$^{13}C_6$-PFDA	0.50
Perfluoro-*n*-[1,2,3,4,5,6,7-$^{13}C_7$]undecanoic acid	$^{13}C_7$-PFUnA	0.50
Perfluoro-*n*-[1,2-$^{13}C_2$]dodecanoic acid	$^{13}C_2$-PFDoA	0.50

a. Concentrations used during method development.

As additional isotopically labelled PFAS analogues become commercially available they may be integrated into the method provided they have similar functional groups as the method analytes or are isotopically labeled analogues of the method analytes. Method modification QC requirements must be met (Sect. 9.3) whenever new analogues are proposed.

7.16.1 Isotope Dilution Analogue PDS

Prepare the isotope dilution analogue PDS in methanol and add sodium hydroxide if not already present to prevent esterification as described in Section 7.13.1. The PDS concentrations used during method development are listed in the table above. Method performance data were collected using 20 µL of this PDS to yield concentrations of 40–160 ng/L in the 250 mL aqueous samples. Note that the concentrations of sulfonates in the isotope dilution analogue PDS is based on the weight of the salt. It is not necessary to account for difference in the formula weight of the salt compared to the free acid for sample quantitation.

7.17 Analyte Standard Materials

Analyte standards may be purchased as certified standard solutions or prepared from neat materials of assayed purity. If available, the method analytes should be purchased as technical-grade (as defined in Sect. 3.22) to ensure that linear and branched isomers are represented. Standards or neat materials that contain only the linear isomer can be substituted if technical-grade analytes are not available as quantitative standards.

During method development, analyte standards were obtained from AccuStandard, Inc. (New Haven, CT), Absolute Standards (Hamden, CT), Wellington Laboratories (Guelph, Ontario, Canada), Santa Cruz Biotechnology (Dallas, TX), and Synquest Laboratories, Inc. (Alachua, FL). Stock standards are made by dilution in methanol containing 4 mole equivalents of sodium hydroxide as described in Section 7.13.1

7.17.1 PFOA

A quantitative standard for PFOA is currently available only for the linear isomer; however, a technical-grade standard (Sect. 3.22) is available for PFOA that contains the linear and branched isomers (Wellington Labs, Cat. No. T-PFOA, or equivalent). This product or a similar technical-grade PFOA standard must be used to identify the retention times of the branched and linear PFOA isomers. However, the linear-only PFOA standard must be used for quantitation until a quantitative PFOA standard containing the branched and linear isomers becomes commercially available.

7.17.2 PFHxS and PFOS

Technical grade, quantitative PFHxS and PFOS standards containing branched and linear isomers must be used when available.

7.17.3 Correction for Analytes Obtained in the Salt Form

This method measures all forms of the analytes as anions while the identity of the counterion is inconsequential. Analytes may be commercially available as neat materials or as certified stock standards as their corresponding ammonium, sodium, or potassium salts. These salts are acceptable standards provided the measured mass, or concentration, is corrected for the salt content. The equation for this correction is provided below.

$$mass(acid\ form) = mass(salt\ form) \times \frac{MWacid}{MWsalt}$$

7.17.4 Analyte PDS

The analyte PDS is used to prepare the calibration standards and to fortify the LFBs, LFSMs and LFSMDs with the method analytes. Prepare the analyte PDS by combining and diluting the analyte stock standards in 100% methanol and add sodium hydroxide if not already present to prevent esterification as described in Section 7.13.1. Select nominal analyte concentrations for the PDS such that between 5 and 100 µL of the PDS is used to fortify samples and prepare standard solutions. More than one PDS concentration may be necessary to meet this requirement. During method development, the analyte PDS was prepared at an identical concentration for all analytes, 0.5 ng/µL. The user may modify the concentrations of the individual analytes based on the confirmed MRLs and the desired monitoring range. If the PDS is stored cold, warm the vials to room temperature and vortex prior to use.

7.17.5 Calibration Standards

Prepare a series of calibration standards of at least five levels by diluting the analyte PDS into methanol containing 20% reagent water. The lowest calibration standard must be at or below the MRL for each analyte. The calibration standards may also be used as Continuing Calibration Checks (CCCs). Using the PDS solutions, add a constant amount of the isotope performance standards and the isotope dilution analogues to each calibration standard. The concentration of the isotope dilution analogues should match the concentration of the analogues in sample extracts, assuming 100% recovery through the extraction process. During method development, the concentrations of the isotope dilution analogues were 40 ng/mL extract concentration (160 ng/L in the aqueous sample) for 4:2FTS, 6:2FTS and 8:2FTS, and 10 ng/mL (40 ng/L) for all others. The analyte calibration ranged from approximately 0.50 ng/mL to 25 ng/mL extract concentration.

8 Sample Collection, Preservation, and Storage

8.1 Sample Bottles

Samples must be collected in plastic bottles: polypropylene bottles fitted with polypropylene screw-caps, or polyethylene bottles with polypropylene screw caps. Discard sample bottles after a single use. The bottle volume should approximate the volume of the sample. Subsampling from a single bottle is not permitted except as described in Section 12.5.

8.2 Sample Preservation

Based on sample volume, add ammonium acetate to each sample bottle as a solid (prior to shipment to the field or immediately prior to sample collection) to achieve a 1g/L concentration of ammonium acetate. Ammonium acetate will sequester free chlorine to form chloramine.

8.3 Sample Collection

8.3.1 Precautions against Contamination

Workers must wash their hands before sampling and wear nitrile gloves while filling and sealing the sample bottles. Users should seek to minimize accidental contamination of the samples.

8.3.2 Collection Procedure

Open the tap and allow the system to flush until the water temperature has stabilized. Collect samples from the flowing system. Samples do not need to be collected headspace free. After collecting the sample, cap the bottle and agitate by hand until the preservative is dissolved. Keep the sample sealed from time of collection until extraction.

8.4 Field Reagent Blanks (FRB)

Each sample set must include an FRB. A sample set is defined as samples collected from the same site and at the same time. The same lot of preservative must be used for the FRBs as for the field samples.

8.4.1 Analysis of Reagent Water used for FRBs

Reagent water used for the FRBs must be analyzed prior to shipment to ensure the water has minimal residual PFAS. Extract an LRB prepared with reagent water using the same lot of sample bottles destined for shipment to the sampling site and ensure that analyte concentrations are less than one-third the MRL, as described in Section 9.2.1. This will ensure that any significant contamination detected in the FRBs originated from exposure in the field.

8.4.2 Field Reagent Blank Procedure

In the laboratory, fill the FRB sample bottle with the analyzed reagent water (Sect. 8.4.1), then seal and ship to the sampling site with the sample bottles. For each FRB shipped, a second FRB sample bottle containing only preservative must also be shipped. At the sampling site, open the FRB bottle and pour the reagent water into the second sample bottle containing preservative; seal and label this bottle as the FRB with the date, time and location of the site.

8.5 Sample Shipment and Storage

Samples must be shipped on ice. Samples are valid if any ice remains in the cooler when it is received at the laboratory or bottles are received within 2 days of collection and below 10 ^{0}C. Once at the laboratory, samples must be stored at or below 6 °C until extraction. Samples must not be frozen.

8.6 Sample and Extract Holding Times

Analyze samples as soon as possible. Samples must be extracted within 28 days of collection. Extracts are generally stored at room temperature and must be analyzed within 28 days after extraction.

9 Quality Control

QC procedures include the IDC and ongoing QC requirements. This section describes each QC parameter, its required frequency, and the performance criteria that must be met in order to satisfy method objectives. The QC criteria discussed in the following sections are summarized in **Table 16** and **Table 17**. These QC requirements are considered the minimum for an acceptable QC program. Laboratories are encouraged to institute additional QC practices to meet their specific needs.

9.1 Initial Demonstration of Capability

The IDC must be successfully performed prior to analyzing field samples. The IDC must be repeated if changes are made to analytical parameters not previously validated during the IDC. This may include, for example, changing the sample volume, selecting alternate quantitation ions, extending the calibration range, adding additional isotope performance standards, or adding additional isotope dilution analogues. Prior to conducting the IDC, the analyst must meet the calibration requirements outlined in Section 10. The same calibration range used during the IDC must be used for the analysis of field samples.

9.1.1 Demonstration of Low System Background

Analyze an LRB immediately after injecting the highest calibration standard in the selected calibration range. Confirm that the blank is free from contamination as defined in Section 9.2.1. If an automated extraction system is used, an LRB must be extracted on each port to fulfil this requirement.

9.1.2 Demonstration of Precision

Prepare, extract, and analyze seven replicate LFBs in a valid Extraction Batch (seven LFBs and an LRB). Fortify the LFBs near the midpoint of the initial calibration curve. The percent relative standard deviation (%RSD) of the concentrations of the replicate analyses must be less than 20% for all method analytes.

9.1.3 Demonstration of Accuracy

Using the same set of replicate data generated for Section 9.1.2, calculate the average percent recovery. The average recovery for each analyte must be within a range of 70–130%.

9.1.4 Minimum Reporting Level (MRL) Confirmation

Establish a target concentration for the MRL (Sect. 3.15) based on the intended use of the method. If there is a programmatic MRL requirement, the laboratory MRL must be set at or below this level. In doing so, one should consider that establishing the MRL concentration too low may cause repeated failure of ongoing QC requirements.

Perform initial calibration following the procedures in Section 10.3. The lowest calibration standard used to establish the initial calibration (as well as the low-level CCC) must be at, or below, the MRL. Confirm the laboratory's ability to meet the MRL following the procedure outlined below.

9.1.4.1 Prepare and Analyze MRL Samples

Fortify, extract, and analyze seven replicate LFBs at, or below, the proposed MRL concentration.

9.1.4.2 Calculate MRL Statistics

Calculate the mean and standard deviation for each analyte in these replicates. Determine the Half Range for the Prediction Interval of Results (HR_{PIR}) using the following equation:

$$HR_{PIR} = 3.963S$$

Where,

S = the standard deviation and 3.963 is a constant value for seven replicates.[1]

Calculate the Upper and Lower Limits for the Prediction Interval of Results (*PIR* = *Mean* ± HR_{PIR}) as shown below. These equations are only defined for seven replicate samples.

$$Upper\ PIR\ Limit = \frac{Mean + HR_{PIR}}{Fortified\ Concentration} \times 100$$

$$Lower\ PIR\ Limit = \frac{Mean - HR_{PIR}}{Fortified\ Concentration} \times 100$$

9.1.4.3 MRL Acceptance Criteria

The laboratory's ability to meet the MRL is confirmed if the *Upper PIR Limit* is less than, or equal to, 150%; and the *Lower PIR Limit* is greater than, or equal to, 50%. If these criteria are not met, the MRL has been set too low and must be confirmed again at a higher concentration.

9.1.5 Calibration Verification

Analyze a QCS (Sect. 9.2.9) to confirm the accuracy of the primary calibration standards.

9.2 Ongoing QC Requirements

This section describes the ongoing QC elements that must be included when processing and analyzing field samples.

9.2.1 Laboratory Reagent Blank (LRB)

Analyze an LRB with each Extraction Batch. Background concentrations of method analytes must be less than one-third the MRL. If method analytes are detected in the LRB at concentrations greater than or equal to this level, then all positive field sample results (i.e., results at or above the MRL) for those analytes are invalid for all samples in the Extraction Batch. Subtracting blank values from sample results is not permitted.

9.2.1.1 Estimating Background Concentrations

Although quantitative data below the MRL may not be accurate enough for data reporting, such data are useful in determining the magnitude of background interference. Therefore, the analyte concentrations in the LRB may be estimated by extrapolation when results are below the MRL.

9.2.1.2 Influence of Background on Selection of MRLs

Because background contamination can be a significant problem, some MRLs may be background limited.

9.2.1.3 Evaluation of Background when Analytes Exceed the Calibration Range

After analysis of a sample in which method analytes exceed the calibration range, one or more LRBs must be analyzed (to detect potential carryover) until the system meets the LRB acceptance criteria. If this occurs during an automated sequence, examine the results of samples analyzed following the sample that exceeded the calibration range. If the analytes that exceeded the calibration range in the previous sample are detected at, or above, the MRL, these samples are invalid. If the affected analytes do not exceed the MRL, these subsequent samples may be reported.

9.2.2 Continuing Calibration Check (CCC)

Analyze CCC standards at the beginning of each Analysis Batch, after every tenth field sample, and at the end of the Analysis Batch. See Section 10.4 for concentration requirements and acceptance criteria for CCCs.

9.2.3 Laboratory Fortified Blank

An LFB is required with each Extraction Batch. The concentration of the LFB must be rotated between low, medium, and high concentrations from batch to batch.

9.2.3.1 LFB Concentration Requirements

Fortify the low concentration LFB near the MRL. The high concentration LFB must be near the high end of the calibration range.

9.2.3.2 Evaluate Analyte Recovery

Results for analytes fortified at concentrations near or at the MRL (within a factor of two times the MRL concentration) must be within 50–150% of the true value. Results for analytes fortified at all other concentrations must be within 70–130% of the true value. If the LFB results do not meet these criteria, then all data for the problem analytes must be considered invalid for all samples in the Extraction Batch.

9.2.4 Isotope Performance Standard Areas

The analyst must monitor the peak areas of the isotope performance standards in all injections of the Analysis Batch. The isotope performance standard responses (as indicated by peak area) in any chromatographic run must be within 50–150% of the average area measured during the initial calibration. Random evaporation losses have been observed with the polypropylene caps causing high-biased isotope performance standard areas. If an isotope performance standard area for a sample does not meet these criteria, reanalyze the extract in a subsequent Analysis Batch. If the isotope performance standard area fails to meet the acceptance criteria in the repeat analysis, extraction of the sample must be repeated, provided the sample is still within holding time.

9.2.5 Isotope Dilution Analogue Recovery

Calculate the concentration of each isotope dilution analogue in field and QC samples using the average area in the initial calibration and the internal standard technique. Calculate the percent recovery (%R) for each analogue as follows:

$$\%R = \frac{A}{B} \times 100$$

Where,
A = measured concentration of the isotope dilution analogue, and
B = fortification concentration of the isotope dilution analogue.

The percent recovery for each analogue must be within a range of 50–200%.

9.2.5.1 Corrective Action for Failed Analogue Recovery

If an isotope dilution analogue fails to meet the recovery criterion, evaluate the area of the isotope performance standard to which the analogue is referenced and the recovery of the analogues in the CCCs. If necessary, recalibrate and service the LC-MS/MS system. Take corrective action, then analyze the failed extract in a subsequent Analysis Batch. If the repeat analysis meets the 50–200% recovery criterion, report only data for the reanalyzed extract. If the repeat analysis fails the recovery criterion after corrective action, extraction of the sample must be repeated provided a sample is available and still within the holding time.

9.2.6 Laboratory Fortified Sample Matrix (LFSM)

Within each Extraction Batch, analyze a minimum of one LFSM. The native concentrations of the analytes in the sample matrix must be determined in a separate field sample and subtracted from the measured values in the LFSM. If various sample matrices are analyzed regularly, for example, drinking water processed from ground water and surface water sources, collect performance data for each source.

9.2.6.1 Prepare the LFSM

Prepare the LFSM by fortifying a Field Duplicate with an appropriate amount of the analyte PDS (Sect. 7.17.4) and isotope dilution analogue PDS (Sect. 7.16.1). Generally, select a spiking concentration that is greater than or equal to the native concentration for the analytes. Selecting a duplicate aliquot of a sample that has already been analyzed aids in the selection of an appropriate spiking level. If this is not possible, use historical data when selecting a fortifying concentration.

9.2.6.2 Calculate the Percent Recovery

Calculate the percent recovery (%R) using the equation:

$$\%R = \frac{(A - B)}{C} \times 100$$

Where,
A = measured concentration in the fortified sample,
B = measured concentration in the unfortified sample, and
C = fortification concentration.

In order to obtain meaningful percent recovery results, correct the measured values in the LFSM and LFSMD for the native levels in the unfortified samples, even if the native values are less than the MRL.

9.2.6.3 Evaluate Analyte Recovery in the LFSM

Results for analytes fortified at concentrations near or at the MRL (within a factor of two times the MRL concentration) must be within 50–150% of the true value. Results for analytes fortified at all other concentrations must be within 70–130% of the true value. If the accuracy for any analyte falls outside the designated range, and the laboratory performance for that analyte is shown to be in control in the CCCs and in the LFB, the recovery is judged matrix biased. Report the result for the corresponding analyte in the unfortified sample as "suspect–matrix".

9.2.7 Laboratory Fortified Sample Matrix Duplicate (LFSMD) or Field Duplicate (FD)

Within each Extraction Batch, analyze a minimum of one Field Duplicate or one Laboratory Fortified Sample Matrix Duplicate. If the method analytes are not routinely observed in field samples, analyze an LFSMD rather than an FD.

9.2.7.1 Calculate the RPD for the LFSM and LFSMD

If an LFSMD is analyzed instead of a Field Duplicate, calculate the RPD using the equation:

$$RPD = \frac{|LFSMD - LFSM|}{(LFSMD + LFSM)/2} \times 100$$

9.2.7.2 Acceptance Criterion for the RPD of the LFSM and LFSMD

RPDs for duplicate LFSMs must be less than, or equal to, 30% for each analyte. Greater variability may be observed when the matrix is fortified at analyte concentrations near or at the MRL (within a factor of two times the MRL concentration). LFSMs at these concentrations must have RPDs that are less than or equal to 50%. If the RPD of an analyte falls outside the designated range, and the laboratory performance for the analyte is shown to be in control in the CCCs and in the LFB, the precision is judged matrix influenced. Report the result for the corresponding analyte in the unfortified sample as "suspect–matrix".

9.2.7.3 Calculate the RPD for Field Duplicates

Calculate the relative percent difference (RPD) for duplicate measurements. (FD1 and FD2) using the equation:

$$RPD = \frac{|\mathrm{FD}_1 - \mathrm{FD}_2|}{(\mathrm{FD}_1 + \mathrm{FD}_2)/2} \times 100$$

9.2.7.4 Acceptance Criterion for Field Duplicates

RPDs for Field Duplicates must be less than, or equal to, 30% for each analyte. Greater variability may be observed when Field Duplicates have analyte concentrations that are near or at the MRL (within a factor of two times the MRL concentration). At these concentrations, Field Duplicates must have RPDs that are less than or equal to 50%. If the RPD of an analyte falls outside the designated range, and the laboratory performance for the analyte is shown to be in control in the CCC and in the LFB, the precision is judged matrix influenced. Report the result for the corresponding analyte in the unfortified sample as "suspect–matrix"

9.2.8 Field Reagent Blank (FRB)

The purpose of the FRB is to ensure that PFAS measured in the field samples were not inadvertently introduced into the sample during sample collection and handling. The FRB is processed, extracted, and analyzed in exactly the same manner as a field sample. Analysis of the FRB is required only if a field

sample contains a method analyte or analytes at, or above, the MRL. If a method analyte found in the field sample is present in the FRB at a concentration greater than one-third of the MRL, then the results for that analyte are invalid for all samples associated with the failed FRB.

9.2.9 Calibration Verification using QCS

A QCS must be analyzed during the IDC, and then quarterly thereafter. For this method, the laboratory is not required to obtain standards from a source independent of the primary calibration standards. Instead, the laboratory should acquire the best available quantitative standards (Sect. 3.20) and use these to prepare both the primary calibration standards and the QCS. The QCS must be an independent dilution beginning with the common starting materials. Preparation by a second analyst is recommended. The acceptance criterion for the QCS is 70–130% of the true value. If the accuracy for any analyte fails the recovery criterion, prepare fresh standard dilutions and repeat the Calibration Verification.

9.3 Method Modification QC Requirements

The analyst is permitted to modify the chromatographic and MS/MS conditions. Examples of permissible method modifications include alternate LC columns, MRM transitions, and additional QC analytes proposed for use with the method. Any method modifications must be within the scope of the established method flexibility and must retain the basic chromatographic elements of this method (Sect. 2). The following are required after a method modification.

9.3.1 Repeat the IDC

Establish an acceptable initial calibration (Sect. 10.3) using the modified conditions. Repeat the procedures of the IDC (Sect. 9.1).

9.3.2 Document Performance in Representative Sample Matrices

The analyst is also required to evaluate and document method performance for the modifications in real matrices that span the range of waters that the laboratory analyzes. This additional step is required because modifications that perform acceptably in the IDC, which is conducted in reagent water, could fail ongoing method QC requirements in real matrices. This is particularly important for methods subject to matrix effects, such as LC-MS/MS-based methods. For example, a laboratory may routinely analyze finished drinking water from municipal treatment plants that process ground water, surface water, or a blend of surface and ground water. In this case, the method modification requirement could be accomplished by assessing precision (Sect. 9.1.2) and accuracy (Sect. 9.1.3) in finished drinking waters derived from a surface water with moderate to high total organic carbon (e.g., 2 mg/L or greater) and from a hard ground water (e.g., 250 mg/L as calcium carbonate ($CaCO_3$) equivalent, or greater).

10 Calibration and Standardization

Demonstration and documentation of acceptable MS calibration and initial analyte calibration are required before performing the IDC and prior to analyzing field samples. The initial calibration should be repeated each time a major instrument modification or maintenance is performed.

10.1 MS/MS Optimization

10.1.1 Mass Calibration

Calibrate the mass spectrometer with the calibration compounds and procedures specified by the manufacturer.

10.1.2 MS Parameters

During the development of this method, instrumental parameters were optimized for the precursor and product ions listed in **Table 6**. Product ions other than those listed may be selected; however, the analyst should avoid using ions with lower mass or common ions that may not provide sufficient discrimination between the analytes of interest and co-eluting interferences.

10.1.2.1 Requirement for Branched Isomers

There have been reports that not all product ions in the linear PFOS are produced in all branched PFOS isomers.[5] (This phenomenon may exist for many of the PFAS.) For this method, the *m/z* 80 product ion must be used for PFOS and PFHxS to minimize this problem and promote comparability between laboratories. Some MS/MS instruments, may not be able to scan a product ion with such a wide mass difference from the precursor ion. These instruments may not be used for this method if PFOS or PFHxS analysis is to be conducted.

10.1.2.2 Precursor Ion

Optimize the response of the precursor ion ($[M - H]^-$ or $[M - CO_2 - H]^-$) for each analyte following manufacturer's guidance. Analyte concentrations of 1.0 µg/mL were used for this step during method development. Vary the MS parameters (source voltages, source and desolvation temperatures, gas flows, etc.) until optimal analyte responses are determined. The electrospray parameters used during method development are listed in **Table 2**. The analytes may have different optimal parameters, requiring some compromise on the final operating conditions. See **Table 6** for ESI-MS conditions used to collect method performance data.

10.1.2.3 Product Ion

Optimize the product ion for each analyte following the manufacturer's guidance. Typically, the carboxylic acids have similar MS/MS conditions and the sulfonic acids have similar MS/MS conditions. See **Table 6** for MS/MS conditions used to collect method performance data.

10.2 Chromatographic Conditions

Establish LC operating parameters that optimize resolution and peak shape. Suggested LC conditions can be found in **Table 1**. Modifying the solvent composition of the standard or extract by increasing the aqueous content to better focus early eluting compounds on the column is not permitted. A decrease in methanol concentration could lead to lower or imprecise recovery of the more hydrophobic method analytes, while higher methanol concentration could lead to the precipitation of salts in some extracts. The peak shape of the early eluting compounds may be improved by increasing the volume of the injection loop or increasing the aqueous content of the initial mobile phase composition.

10.2.1 Minimizing PFAS Background

LC system components, as well as the mobile phase constituents, may contain many of the analytes in this method. Thus, these PFAS will build up on the head of the LC column during mobile phase equilibration. To minimize the background PFAS peaks and to keep baseline levels constant, the time the LC column sits at initial conditions must be kept constant and as short as possible (while ensuring reproducible retention times). In addition, priming the mobile phase and flushing the column with at least 90% methanol before initiating a sequence may reduce background contamination.

10.2.2 Establishing Branched vs. Linear Isomer Profiles

Prepare and analyze the technical-grade standard of PFOA, discussed in Section 7.17.1, at a mid- to high-level concentration. Identify the retention times of the branched isomers of PFOA present in the technical-grade PFOA standard. When PFOA is chromatographed on a reversed-phase column, the branched isomers elute prior to the linear isomer. Repeat the procedure in this section for PFHxS and PFOS discussed in Section 7.17.2, and any other analytes for which technical-grade standards have been acquired. The branched isomer identification checks must be repeated any time chromatographic changes occur that alter analyte retention times.

10.2.3 Establish LC-MS/MS Retention Times and MRM Segments

Inject a mid- to high-level calibration standard under optimized LC-MS/MS conditions to obtain the retention times of each method analyte. Divide the chromatogram into segments that contain one or more chromatographic peaks. For maximum sensitivity, minimize the number of MRM transitions that are simultaneously monitored within each segment. Ensure that the retention time window used to collect data for each analyte is of sufficient width to detect earlier eluting branched isomers.
The retention times observed during collection of the method performance data are listed in **Table 3**, **Table 4**, and **Table 5**.

10.3 Initial Calibration

This method has three isotope performance standards that are used as reference compounds for the internal standard quantitation of the isotope dilution analogues. The suggested isotope performance standard reference for each isotope dilution analogue is listed in **Table 4**. The sixteen isotope dilution analogues are used as reference compounds to quantitate the native analyte concentrations. The suggested isotope dilution analogue references for the native analytes are listed in **Table 5**.

10.3.1 Calibration Standards

Prepare a set of at least five calibration standards as described in Section 7.17.5. The analyte concentrations in the lowest calibration standard must be at or below the MRL.

10.3.2 Calibration Curves of Native Analytes

Quantitate the native analytes using the internal standard calibration technique. The internal standard technique calculates concentration based on the ratio of the peak area of the native analyte to that of the isotope dilution analogue. Calibrate the LC-MS/MS and fit the calibration points with either a linear or quadratic regression. Weighting may be used. Forcing the calibration curve through the origin is mandatory for this method. Forcing zero allows for a better estimate of the background levels of

method analytes. The MS/MS instrument used during method development was calibrated using weighted (1/x) quadratic regression with forced zero.

10.3.3 Calibration of Isotope Dilution Analogues

The isotope dilution analogues are quantified using the internal standard calibration technique. Because isotope dilution analogues are added at a single concentration level to the calibration standards, calibrate for each of these using an average response factor.

10.3.4 Calibration of Isotope Performance Standards

Because Isotope performance standards are added at a single concentration level to the calibration standards, calibrate for each of these using an average response factor.

10.3.5 Calibration Acceptance Criteria

Evaluate the initial calibration by calculating the concentration of each analyte as an unknown against its regression equation. For calibration levels that are less than or equal to the MRL, the result for each analyte should be within 50–150% of the true value. All other calibration points should be within 70–130% of their true value. If these criteria cannot be met, the analyst could have difficulty meeting ongoing QC criteria. In this case, corrective action is recommended such as reanalyzing the calibration standards, restricting the range of calibration, or performing instrument maintenance. If the cause for failure to meet the criteria is due to contamination or standard degradation, prepare fresh calibration standards and repeat the initial calibration.

10.4 Continuing Calibration

Analyze a CCC to verify the initial calibration at the beginning of each Analysis Batch, after every tenth field sample, and at the end of each Analysis Batch. The beginning CCC for each Analysis Batch must be at, or below, the MRL for each analyte. This CCC verifies instrument sensitivity prior to the analysis of samples. If standards have been prepared such that all low calibration levels are not in the same solution, it may be necessary to analyze two standards to meet this requirement. Alternatively, the nominal analyte concentrations in the analyte PDS may be customized to meet these criteria. Alternate subsequent CCCs between the mid and high calibration levels. Verify that the CCC meets the criteria in the following sections.

10.4.1 CCC Isotope Performance Standard Responses

The absolute area of the quantitation ion for each of the three isotope performance standards must be within 50–150% of the average area measured during the initial calibration. If these limits are exceeded, corrective action is necessary (Sect. 10.5).

10.4.2 CCC Isotope Dilution Analogue Recovery

Using the average response factor determined during the initial calibration and the internal standard calibration technique, calculate the percent recovery of each isotope dilution analogue in the CCC. The recovery for each analogue must be within a range of 70–130%. If these limits are exceeded, corrective action is necessary (Sect. 10.5).

10.4.3 CCC Analyte Responses

Calculate the concentration of each method analyte in the CCC. Each analyte fortified at a level less than or equal to the MRL must be within 50–150% of the true value. The concentration of the analytes in CCCs fortified at all other levels must be within 70–130%. If these limits are exceeded, then all data for the failed analytes must be considered invalid. Any field samples analyzed since the last acceptable CCC that are still within holding time must be reanalyzed after an acceptable calibration has been restored.

10.4.3.1 Exception for High Recovery

If the CCC fails because the calculated concentration is greater than 130% (150% for the low-level CCC) for a method analyte, and field sample extracts show no concentrations above the MRL for that analyte, non-detects may be reported without re-analysis.

10.5 Corrective Action

Failure to meet the CCC QC performance criteria requires corrective action. Following a minor remedial action, such as servicing the autosampler or flushing the column, check the calibration with a mid-level CCC and a CCC at the MRL, or recalibrate according to Section 10.3. If isotope performance standard and calibration failures persist, maintenance may be required, such as servicing the LC-MS/MS system or replacing the LC column. These latter measures constitute major maintenance and the analyst must return to the initial calibration step (Sect. 10.3).

11 Procedure

This procedure may be performed manually or in an automated mode using a robotic or automatic sample preparation device. The data published in this method (Sect. 17) demonstrate acceptable performance using manual extraction. The authors did not evaluate automated extraction systems. If an automated system is used to prepare samples, follow the manufacturer's operating instructions, but all extraction and elution steps must be the same as in the manual procedure. Extraction and elution steps may not be changed or omitted to accommodate the use of an automated system. If an automated system is used, the LRBs should be rotated among the ports to ensure that all the valves and tubing meet the LRB requirements (Sect. 9.2.1).

11.1 Sample Bottle Rinse

Some of the PFAS adsorb to surfaces, including polypropylene. During the elution step of the procedure, sample bottles must be rinsed with the elution solvent whether extractions are performed manually or by automation.

11.2 Reuse of Extraction Cartridges

The SPE cartridges described in this section are designed for a single use. They may not be reconditioned for subsequent analyses.

11.3 Sample Preparation

11.3.1 Sample Volume

Determine sample volume. An indirect measurement may be done in one of two ways: by marking the level of the sample on the bottle or by weighing the sample and bottle to the nearest 1 gram. After

extraction, proceed to Section 11.5 to complete the volume measurement. Some of the PFAS adsorb to surfaces, thus the sample may not be transferred to a graduated cylinder for volume measurement. The LRB, LFB and FRB must have the same volume as that of the field samples and may be prepared by measuring reagent water with a graduated cylinder.

11.3.2 Verifying Sample pH

Verify that the sample containing 1 g/L ammonium acetate has a pH between 6.0 and 8.0. Acetic acid may be added as needed to reduce the pH

11.3.3 Fortify QC Samples

Fortify LFBs, LFSMs, and LFSMDs, with an appropriate volume of Analyte PDS (Sect. 7.17.4). Cap and invert each sample several times to mix.

11.3.4 Addition of Isotope Dilution Analogues

Add an aliquot of the isotope dilution analogue PDS (Sect. 7.16.1) to each sample, then cap and invert to mix. During method development, a 20 µL aliquot of the PDS (0.50–2.0 ng/µL) was added to achieve a final concentration of 40 ng/L of the isotopically labeled carboxylates and perfluorinated sulfonates, and 160 ng/L of the telomer sulfonates.

11.4 Extraction Procedure

11.4.1 Cartridge Cleaning and Conditioning

Do not allow cartridge packing material to go dry during any of the conditioning steps. If the cartridge goes dry during the conditioning phase, the conditioning must be repeated. Rinse each cartridge with 10 mL of methanol. Next, rinse each cartridge with 10 mL of aqueous 0.1 M phosphate buffer (Sect. 7.8) without allowing the water to drop below the top edge of the packing. Close the valve and add 2–3 mL of phosphate buffer to the cartridge reservoir and fill the remaining volume with reagent water.

11.4.2 Cartridge Loading

Attach the sample transfer tubes (Sect. 6.8.3) and adjust the vacuum to approximately 5 inches Hg. Begin adding sample to the cartridge. Adjust the vacuum and control valves so that the approximate flow rate is 5 mL/min. Do not allow the cartridge to go dry before all the sample has passed through. Flow rates above 5 mL/min during loading may cause low analyte recovery.

11.4.3 Sample Bottle Rinse and Cartridge Drying

After the entire sample has passed through the cartridge, rinse the sample bottle with a 10 mL aliquot of 1 g/L ammonium acetate in reagent water. Draw the rinsate through the sample transfer tubes and the cartridges. Add 1 mL of methanol to the sample bottle and draw through the transfer tube and SPE cartridge. This step is designed to remove most of the water from the transfer line and cartridge resulting in the reduction of the salt and water present in the eluate. The methanol rinse may also reduce interferences by removing weakly retained organic material prior to elution. If plastic reservoirs are used instead of transfer lines, the reservoirs must be rinsed with the ammonium acetate solution and the 1 mL aliquot of methanol.

11.4.4 Cartridge Drying

Draw air or nitrogen through the cartridge for 5 min at high vacuum (15–20 in. Hg).

11.4.5 Sample Bottle and Cartridge Elution

After the drying step, release the vacuum on the extraction manifold and place a collection tube under each sample position. Rinse the sample bottles with 5 mL of the elution solvent, methanol with 2% ammonium hydroxide (v/v), then elute the analytes from the cartridges by pulling the elution solvent through the sample transfer tubes and the cartridges. Use a low vacuum such that the solvent exits the cartridge in a dropwise fashion. Repeat sample bottle rinse and cartridge elution with a second 5 mL aliquot of elution solvent. If plastic reservoirs are used instead of transfer lines, attempt to rinse the entire inner surface of the reservoir with the elution solvent.

11.4.6 Extract Concentration

Concentrate the extract to dryness under a gentle stream of nitrogen in a heated water bath (55–60 °C). Reconstitute the extract with 1.0 mL of 20% reagent water in methanol (v/v). Add the isotope performance standards to the extract and vortex.

11.4.7 Extract Transfer and Storage

Transfer the final extract to a polypropylene autosampler vial. Store extracts at room temperature. Recap vials as soon as possible after injection to prevent evaporation losses; the polypropylene caps do not reseal after puncture. Alternatively, extracts can be stored in the 15 mL collection tubes after extraction. A small aliquot can be removed for analysis if the autosampler vial and injection system accommodate small volumes.

11.5 Sample Volume Determination

Use a graduated cylinder to measure the volume of water required to fill the original sample bottle to the mark made prior to extraction. If using weight to determine the volume, weigh the empty bottle to the nearest 1 gram and subtract this value from the weight recorded prior to extraction. Assume a sample density of 1.0 g/mL. Record the sample volumes for use in the final calculations of analyte concentrations.

11.6 Sample Analysis

11.6.1 Establish LC-MS/MS Operating Conditions

Establish MS/MS operating conditions per the procedures in Section 10.1 and chromatographic conditions per Section 10.2. Establish a valid initial calibration following the procedures in Section 10.3 or confirm that the existing calibration is still valid by analyzing a low-level CCC. If establishing an initial calibration for the first time, complete the IDC prior to analyzing field samples. Analyze field and QC samples in a properly sequenced Analysis Batch as described in Section 11.7.

11.6.2 Verify Retention Time Windows

The analyst must ensure that each method analyte elutes entirely within the assigned window during each Analysis Batch. Make this observation by viewing the quantitation ion for each analyte in the CCCs analyzed during an Analysis Batch. If an analyte peak drifts out of the assigned window, then data for

that analyte is invalid in all injections acquired since the last valid CCC. In addition, all peaks representing multiple isomers of an analyte must elute entirely within the same MRM window.

11.7 Analysis Batch Sequence

An Analysis Batch is a sequence of samples, analyzed within a 24-hour period, of no more than 20 field samples and includes all required QC samples (LRB, CCCs, the LFSM and LFSMD (or FD)). The required QC samples are not included in counting the maximum field sample total of 20. LC-MS/MS conditions for the Analysis Batch must be the same as those used during calibration.

11.7.1 Analyze Initial CCC

After a valid calibration is established, begin every Analysis Batch by analyzing an initial low-level CCC at or below the MRL. This initial CCC must be within 50–150% of the true value for each method analyte and must pass both the isotope performance standard area response criterion (Sect. 10.4.1) and the isotope dilution analogue recovery criterion (Sect. 10.4.2). The initial CCC confirms that the calibration is still valid. Failure to meet the QC criteria may indicate that recalibration is required prior to analyzing samples.

11.7.2 Analyze Field and QC Samples

After the initial CCC, continue the Analysis Batch by analyzing an LRB, followed by the field samples and QC samples. Analyze a mid- or high-level CCC after every ten field samples and at the end each Analysis Batch. Do not count QC samples (LRBs, FDs, LFSMs, LFSMDs) when calculating the required frequency of CCCs.

11.7.3 Analyze Final CCC

The last injection of the Analysis Batch must be a mid- or high-level CCC. The acquisition start time of the final CCC must be within 24 hours of the acquisition start time of the low-level CCC at the beginning of the Analysis Batch. More than one Analysis Batch within a 24-hour period is permitted. An Analysis Batch may contain field and QC samples from multiple extraction batches.

11.7.4 Initial Calibration Frequency

A full calibration curve is not required before starting a new Analysis Batch. A previous calibration can be confirmed by running an initial, low-level CCC followed by an LRB. If a new calibration curve is analyzed, an Analysis Batch run immediately thereafter must begin with a low-level CCC and an LRB.

12 Data Analysis and Calculations

Because environmental samples may contain both branched and linear isomers of the method analytes, but quantitative standards that contain branched isomers do not exist for all method analytes, integration and quantitation of the PFAS is dependent on the type of standard materials available.

12.1 Identify Peaks by Retention Times

At the conclusion of data acquisition, use the same software settings established during the calibration procedure to identify analyte peaks in the predetermined retention time windows. Confirm the identity of each analyte by comparison of its retention time with that of the corresponding analyte peak in an

initial calibration standard or CCC. Proceed with quantitation based on the type of standard available for each method analyte.

12.1.1 Method Analytes without Technical-Grade Standards

If standards containing the branched and linear isomers cannot be purchased (i.e., only the linear isomer is available), only the linear isomer can be identified and quantitated in field samples and QC samples because the retention time of the branched isomers cannot be confirmed.

12.1.2 PFHxS, PFOS, and other Analytes with Technical-Grade Standards

During method development, multiple chromatographic peaks, representing branched and linear isomers, were observed for standards of PFHxS and PFOS using the LC conditions in **Table 1**. For PFHxS and PFOS, all the chromatographic peaks observed in the standard must be integrated and the areas summed. Chromatographic peaks in all field samples and QC samples must be integrated in the same way as the calibration standard for analytes with quantitative standards containing the branched and linear isomers.

12.1.3 PFOA

For PFOA, identify the branched and linear isomers by analyzing a technical-grade standard that includes both linear and branched isomers as directed in Section 10.2.2 and ensure that all isomers elute within the same acquisition segment. Quantitate field samples and fortified matrix samples by integrating the total response, accounting for peaks that are identified as linear and branched isomers. Quantitate based on the initial calibration with the quantitative PFOA standard containing just the linear isomer.

12.2 Calculate Analyte Concentrations

Calculate analyte concentrations using the multipoint calibration and the measured sample volume. Report only those values that fall between the MRL and the highest calibration standard.

12.3 Calculate Isotope Dilution Analogue Recovery

Calculate the concentration of each isotope dilution analogue using the multipoint calibration and the measured sample volume. Verify that the percent recovery is within 50–200% of the true value.

12.4 Significant Figures

Calculations must use all available digits of precision, but final reported concentrations should be rounded to an appropriate number of significant figures (one digit of uncertainty), typically two, and not more than three significant figures.

12.5 Exceeding the Calibration Range

The analyst must not extrapolate beyond the established calibration range. If an analyte result exceeds the range of the initial calibration curve, a field duplicate of the sample must be extracted, if available. Dilute an aliquot of the field duplicate with reagent water to a final volume equal to that used for the IDC. Add ammonium acetate to a final concentration of 1 g/L and process the diluted sample. Report all concentrations measured in the original sample that do not exceed the calibration range. Report concentrations of analytes that exceeded the calibration range in the in the original sample based on measurement in a diluted sample. Incorporate the dilution factor into final concentration calculations

and the resulting data must be annotated as a dilution. This is the only circumstance when subsampling is permitted.

13 Method Performance

13.1 Precision, Accuracy, and LCMRL Results

Tables for these data are presented in Section 17. LCMRLs are presented in **Table 7**. Single-laboratory precision and accuracy data are presented for three water matrices: reagent water (**Table 8**), finished ground water (**Table 10**), and a drinking water matrix from a surface water source (**Table 12)**. The mean isotope dilution analogue recoveries measured in the replicate samples used in these studies are presented in **Table 9** for reagent water, **Table 11** for finished groundwater, and **Table 13** for the surface water matrix.

13.2 Analyte Stability Study

Chlorinated (finished) surface water samples were inoculated with microbial-rich water from an impacted surface source and fortified with 40 ng/L of the PFAS method analytes. These samples were stored as required in this method. The percent change from the initial analyzed concentration observed after 7, 14, 21, and 28 days is presented in Section 17, **Table 14**.

13.3 Extract Storage Stability

Extract storage stability studies were conducted on extracts obtained from the analyte stability study (Sect. 13.2). The percent change from the initial analyzed concentration observed after 14, 21, and 27 days storage is presented in Section 17, **Table 15**.

14 Pollution Prevention

For information about pollution prevention applicable to laboratory operations described in this method, consult: Less is Better, Guide to Minimizing Waste in Laboratories, a publication available from the American Chemical Society (accessed April 2019) at www.acs.org.

15 Waste Management

Laboratory waste management practices should be consistent with all applicable rules and regulations, and that laboratories protect the air, water, and land by minimizing and controlling all releases from fume hoods and bench operations. In addition, compliance is required with any sewage discharge permits and regulations, particularly the hazardous waste identification rules and land disposal restrictions.

16 References

1. US EPA. *Statistical Protocol for the Determination of the Single-Laboratory Lowest Concentration Minimum Reporting Level (LCMRL) and Validation of Laboratory Performance at or Below the Minimum Reporting Level (MRL)*; EPA 815-R-05-006; Office of Water: Cincinnati, OH, November 2004.
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4. Cahill, J.D., et al. Determination of Pharmaceutical Compounds in Surface- and Ground-Water Samples by Solid-Phase Extraction and High-Performance Liquid Chromatography Electrospray Ionization Mass Spectrometry. *J. Chromatography A*, 2004, 1041, 171–180.
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17 Tables, Figures and Method Performance Data

Table 1. HPLC Method Conditions[a]

Time (min)	% 20 mM ammonium acetate	% Methanol
Initial	95.0	5.0
0.5	95.0	5.0
3.0	60.0	40.0
16.0	20.0	80.0
18.0	20.0	80.0
20.0	5.0	95.0
22.0	5.0	95.0
25.0	95.0	5.0
35.0	95.0	5.0

[a] Phenomenex Gemini® C18, 2 x 50 mm, 3.0 µm silica with TMS end-capping. Flow rate of 0.25 mL/min; run time 35 minutes; 10 µL injection into a 50 µL loop. The chromatogram in **Figure 1** was obtained under these conditions.

Table 2. ESI-MS Method Conditions

ESI Conditions for Waters (Milford, MA) Xevo TQD	
Polarity	Negative ion
Capillary needle voltage	-2.7 kV
Cone gas flow	40 L/hour
Nitrogen desolvation gas	800 L/hour
Desolvation gas temperature	300 °C

Table 3. Isotopically Labeled Isotope Performance Standards and Retention Times

Isotope Performance Standard	Peak # (Figure 1)	RT (min)
$^{13}C_3$-PFBA	1	4.14
$^{13}C_2$-PFOA	26	12.19
$^{13}C_4$-PFOS	32	13.73

Table 4. Isotope Dilution Analogues: RTs and Suggested Isotope Performance Standard References

Isotopically Labeled Analyte	Peak # (Fig. 1)	RT (min)	Suggested Isotope Performance Standard
$^{13}C_4$-PFBA	2	4.14	$^{13}C_3$-PFBA
$^{13}C_5$-PFPeA	5	6.13	$^{13}C_3$-PFBA
$^{13}C_3$-PFBS	7	6.62	$^{13}C_4$-PFOS
$^{13}C_2$-4:2FTS	12	8.12	$^{13}C_4$-PFOS
$^{13}C_5$-PFHxA	14	8.35	$^{13}C_2$-PFOA
$^{13}C_3$-HFPO-DA	17	9.06	$^{13}C_2$-PFOA
$^{13}C_4$-PFHpA	19	10.34	$^{13}C_2$-PFOA
$^{13}C_3$-PFHxS	21	10.61	$^{13}C_4$-PFOS
$^{13}C_2$-6:2FTS	24	12.05	$^{13}C_4$-PFOS
$^{13}C_8$-PFOA	27	12.19	$^{13}C_2$-PFOA
$^{13}C_9$-PFNA	30	13.70	$^{13}C_2$-PFOA
$^{13}C_8$-PFOS	33	13.73	$^{13}C_4$-PFOS
$^{13}C_2$-8:2FTS	36	14.94	$^{13}C_4$-PFOS
$^{13}C_6$-PFDA	38	15.00	$^{13}C_2$-PFOA
$^{13}C_7$-PFUnA	40	16.14	$^{13}C_2$-PFOA
$^{13}C_2$-PFDoA	43	17.13	$^{13}C_2$-PFOA

Table 5. Method Analytes, Retention Times and Suggested Isotope Dilution Analogue References

Analyte	Peak # (Figure 1)	RT (min)	Isotope Dilution Analogue
PFBA	3	4.15	$^{13}C_4$-PFBA
PFMPA	4	4.84	$^{13}C_4$-PFBA
PFPeA	6	6.13	$^{13}C_5$-PFPeA
PFBS	8	6.62	$^{13}C_3$-PFBS
PFMBA	9	6.81	$^{13}C_5$-PFPeA
PFEESA	10	7.53	$^{13}C_3$-PFBS
NFDHA	11	8.01	$^{13}C_5$-PFHxA
4:2FTS	13	8.12	$^{13}C_2$-4:2FTS
PFHxA	15	8.36	$^{13}C_5$-PFHxA
PFPeS	16	8.69	$^{13}C_3$-PFHxS
HFPO-DA	18	9.06	$^{13}C_3$-HFPO-DA
PFHpA	20	10.42	$^{13}C_4$-PFHpA
PFHxS	22	10.62	$^{13}C_3$-PFHxS
ADONA	23	10.73	$^{13}C_4$-PFHpA
6:2FTS	25	12.04	$^{13}C_2$-6:2FTS
PFOA	28	12.19	$^{13}C_8$-PFOA
PFHpS	29	12.28	$^{13}C_8$-PFOS
PFNA	31	13.70	$^{13}C_9$-PFNA
PFOS	34	13.74	$^{13}C_8$-PFOS
9Cl-PF3ONS	35	14.53	$^{13}C_8$-PFOS
8:2 FTS	37	14.94	$^{13}C_2$-8:2FTS
PFDA	39	15.00	$^{13}C_6$-PFDA
PFUnA	41	16.14	$^{13}C_7$-PFUnA
11Cl-PF3OUdS	42	16.70	$^{13}C_8$-PFOS
PFDoA	44	17.13	$^{13}C_2$-PFDoA

Table 6. MS/MS Method Conditions[a]

Segment[b]	Analyte	Precursor Ion[c] (*m/z*)	Product Ion[c,d] (*m/z*)	Cone Voltage (v)	Collision Energy[e] (v)
1	PFBA	213	169	22	10
1	$^{13}C_3$-PFBA	216	172	22	10
1	$^{13}C_4$-PFBA	217	172	22	10
1	PFMPA	229	85	23	10
2	PFPeA	263	219	20	8
2	$^{13}C_5$-PFPeA	268	223	20	8
2	$^{13}C_3$-PFBS	302	80	45	30
2	PFBS	299	80	45	30
2	PFMBA	279	85	22	10
3	PFEESA	315	135	44	20
3	NFDHA	295	201	14	8
3	$^{13}C_2$-4:2FTS	329	309	40	18
3	4:2FTS	327	307	40	18
3	$^{13}C_5$-PFHxA	318	273	20	8
3	PFHxA	313	269	20	8
3	PFPeS	349	80	45	35
3	$^{13}C_3$-HFPO-DA	287[f]	169	15	5
3	HFPO-DA	285[f]	169	15	5
4	$^{13}C_4$-PFHpA	367	322	15	8
4	PFHpA	363	319	15	8
4	$^{13}C_3$-PFHxS[g]	402	80	45	40
4	PFHxS[h]	399	80	45	40
4	ADONA	377	251	15	10
5	$^{13}C_2$-6:2FTS	429	409	47	22
5	6:2FTS	427	407	47	22
5	$^{13}C_2$-PFOA	415	370	18	10
5	$^{13}C_8$-PFOA	421	376	18	10
5	PFOA	413	369	18	10
5	PFHpS	449	80	45	40
6	$^{13}C_9$-PFNA	472	427	17	10
6	PFNA	463	419	17	10
6	$^{13}C_4$-PFOS[g]	503	80	45	45
6	$^{13}C_8$-PFOS[g]	507	80	45	45
6	PFOS[h]	499	80	45	45
7	9Cl-PF3ONS	531	351	55	25
7	$^{13}C_2$-8:2FTS	529	509	53	28
7	8:2FTS	527	507	53	28
7	$^{13}C_6$-PFDA	519	474	22	10
7	PFDA	513	469	22	10

Segment[b]	Analyte	Precursor Ion[c] *(m/z)*	Product Ion[c,d] *(m/z)*	Cone Voltage (v)	Collision Energy[e] (v)
8	$^{13}C_7$-PFUnA	570	525	24	10
8	PFUnA	563	519	24	10
8	11Cl-PF3OUdS	631	451	60	30
8	$^{13}C_2$-PFDoA	615	570	22	10
8	PFDoA	613	569	22	10

a. An LC-MS/MS chromatogram of the analytes obtained using these parameters is shown in **Figure 1**.

b. Segments are time durations in which single or multiple scan events occur.

c. Precursor and product ions listed in this table are nominal masses. During MS and MS/MS optimization, the analyst should determine precursor and product ion masses to one decimal place by locating the apex of the mass spectral peak (e.g., *m/z* 498.9→79.9 for PFOS). These precursor and product ion masses (with at least one decimal place) should be used in the MS/MS method for all analyses.

d. Ions used for quantitation purposes.

e. Argon used as collision gas.

f. HFPO-DA is not stable in the ESI source and the $[M - H]^-$ yields a weak signal under typical ESI conditions. The precursor ion used during method development was $[M - CO_2 - H]^-$.

g. The isotope dilution analogue used during method development was composed of the linear isomer exclusively.

h. Analyte has multiple resolved chromatographic peaks due to linear and branched isomers. All peaks summed for quantitation purposes. To reduce bias regarding detection of branched and linear isomers, the *m/z* 80 product ion must be used for this analyte.

Table 7. LCMRL Results

Analyte	LCMRL Fortification Levels (ng/L)	Calculated LCMRL (ng/L)
PFBA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	13
PFMPA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.8
PFPeA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.9
PFBS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.5
PFMBA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.7
PFEESA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	2.6
NFDHA	4.0, 6.0, 10, 14, 20, 41, 82	16
4:2FTS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	4.7
PFHxA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	5.3
PFPeS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	6.3
HFPO-DA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.7
PFHpA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	2.6
PFHxS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.7
ADONA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.4
6:2FTS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	14
PFOA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	3.4
PFHpS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	5.1
PFNA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	4.8
PFOS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	4.4
9Cl-PF3ONS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	1.4
8:2FTS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	9.1
PFDA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	2.3
PFUnA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	2.7
11Cl-PF3OUdS	1.0, 2.0, 4.0, 6.0, 10, 14, 20	1.6
PFDoA	1.0, 2.0, 4.0, 6.0, 10, 14, 20	2.2

Table 8. Precision and Accuracy Data for Reagent Water

Analyte	Low Fortification (ng/L)	Mean %R[a] (*n*=7)	%RSD[a]	High Fortification (ng/L)	Mean %R (*n*=5)	%RSD
PFBA	10	128	8.6	80	98.4	2.4
PFMPA	10	108	4.5	80	98.1	2.2
PFPeA	10	107	4.9	80	99.6	3.6
PFBS	10	102	9.1	80	96.2	2.9
PFMBA	10	111	6.8	80	101	3.4
PFEESA	10	107	10	80	98.8	4.0
NFDHA	10	110	15	80	98.5	5.4
4:2FTS	10	94.4	14	80	100	5.7
PFHxA	10	102	8.0	80	97	7.7
PFPeS	10	99.5	19	80	101	7.8
HFPO-DA	10	102	9.7	80	102	4.7
PFHpA	10	108	7.0	80	104	4.1
PFHxS	10	103	9.0	80	97.7	5.5
ADONA	10	96.3	3.1	80	96.8	5.6
6:2FTS	10	109	15	80	111	11
PFOA	10	108	7.4	80	98.5	6.9
PFHpS	10	98.8	8.9	80	102	7.0
PFNA	10	109	6.2	80	99.6	5.6
PFOS	10	104	8.7	80	98.0	4.3
9Cl-PF3ONS	10	99.7	4.6	80	103	6.8
8:2FTS	10	100	17	80	100	13
PFDA	10	100	4.2	80	100	1.8
PFUnA	10	102	10	80	97.3	8.1
11Cl-PF3OUdS	10	106	5.3	80	102	6.1
PFDoA	10	101	6.2	80	96.3	5.1

[a] %R = percent recovery; %RSD = percent relative standard deviation

Table 9. P&A in Reagent Water: Isotope Dilution Analogue Recovery Data[a]

Analyte	Analogue Fortification (ng/L)	Mean %R[b,c] (*n*=7) P&A Low	%RSD[b,c]	Mean %R (*n*=5) P&A High	%RSD
$^{13}C_4$-PFBA	40	95.6	11	92.5	3.4
$^{13}C_5$-PFPeA	40	93.4	9.3	91.7	4.6
$^{13}C_3$-PFBS	40	98.6	9.6	107	6.6
$^{13}C_2$-4:2FTS	160	102	6.7	108	3.5
$^{13}C_5$-PFHxA	40	92.5	6.4	92.8	11
$^{13}C_3$-HFPO-DA	40	88.6	6.5	88.8	7.4
$^{13}C_4$-PFHpA	40	98.0	4.0	94.0	8.3
$^{13}C_3$-PFHxS	40	101	11	106	8.2
$^{13}C_2$-6:2FTS	160	109	9.5	99.8	4.7
$^{13}C_8$-PFOA	40	98.0	4.1	91.5	8.7
$^{13}C_9$-PFNA	40	97.1	4.9	92.1	8.4
$^{13}C_8$-PFOS	40	98.8	6.5	96.5	5.0
$^{13}C_2$-8:2FTS	160	106	13.9	108	8.7
$^{13}C_6$-PFDA	40	104	7.7	104	6.1
$^{13}C_7$-PFUnA	40	107	6.0	98.8	7.5
$^{13}C_2$-PFDoA	40	100	5.7	94.0	6.7

a. P&A = “precision and accuracy”.

b. %R = percent recovery; %RSD = percent relative standard deviation.

c. Mean and %RSD of the isotope dilution analogue results for the fortified samples in the P&A study; number of replicates given in the header row of the table.

Table 10. Precision and Accuracy Data for Finished Ground Water[a]

Analyte	Low Fortification (ng/L)	Mean %R[b] (*n*=5)	%RSD[b]	High Fortification (ng/L)	Mean %R (*n*=5)	%RSD
PFBA	10	127	15	80	98.0	4.0
PFMPA	10	100	8.3	80	103	9.8
PFPeA	10	105	11	80	105	5.1
PFBS	10	111	12	80	101	10
PFMBA	10	99.0	4.6	80	100	2.3
PFEESA	10	101	3.5	80	107	8.8
NFDHA	10	95.1	17	80	98.5	18
4:2FTS	10	70.5	20	80	116	9.2
PFHxA	10	104	18	80	111	17
PFPeS	10	87.5	5.0	80	106	6.2
HFPO-DA	10	105	7.4	80	103	7.5
PFHpA	10	102	6.8	80	101	6.4
PFHxS	10	86.6	18	80	108	6.8
ADONA	10	97.6	8.1	80	94.2	6.9
6:2FTS	10	99.9	15	80	100	12
PFOA	10	95.8	8.1	80	104	9.8
PFHpS	10	94.0	6.3	80	113	6.0
PFNA	10	95.1	7.2	80	108	3.3
PFOS	10	[c]	[c]	80	109	5.8
9Cl-PF3ONS	10	92.7	7.2	80	111	7.9
8:2FTS	10	108	19	80	102	3.2
PFDA	10	90.8	9.8	80	104	7.1
PFUnA	10	98.3	8.8	80	105	3.0
11Cl-PF3OUdS	10	94.6	8.3	80	110	9.3
PFDoA	10	92.7	7.8	80	102	6.3

a. Finished water from a ground water source. Hardness = 320 mg/L as $CaCO_3$. pH = 7.88 at 17 °C. Free Cl_2 = 0.64 mg/L. Total Cl_2 = 0.74 mg/L.

b. %R = percent recovery, corrected for native concentration; %RSD = percent relative standard deviation.

c. The spike level was below the ambient PFOS concentration of 25 ng/L.

Table 11. P&A in Finished Ground Water: Isotope Dilution Analogue Recovery Data[a]

Analyte	Analogue Fortification (ng/L)	Mean %R[b,c] (*n*=6) P&A Low	%RSD[b,c]	Mean %R (*n*=6) P&A High	%RSD
$^{13}C_4$-PFBA	40	89.5	4.4	81.3	7.8
$^{13}C_5$-PFPeA	40	94.0	4.2	84.6	7.7
$^{13}C_3$-PFBS	40	103	1.7	93.6	8.5
$^{13}C_2$-4:2FTS	160	107	6.1	105	2.6
$^{13}C_5$-PFHxA	40	93.8	9.8	75.8	16
$^{13}C_3$-HFPO-DA	40	77.8	8.5	72.0	9.8
$^{13}C_4$-PFHpA	40	90.5	8.4	83.3	10
$^{13}C_3$-PFHxS	40	101	7.8	94.7	6.4
$^{13}C_2$-6:2FTS	160	101	5.2	101	4.5
$^{13}C_8$-PFOA	40	89.5	5.7	82.8	10
$^{13}C_9$-PFNA	40	103	6.6	78.0	11
$^{13}C_8$-PFOS	40	101	7.6	89.7	4.5
$^{13}C_2$-8:2FTS	160	97.2	7.4	94.0	8.0
$^{13}C_6$-PFDA	40	98.7	6.3	82.3	15
$^{13}C_7$-PFUnA	40	102	4.3	82.6	8.0
$^{13}C_2$-PFDoA	40	98.8	4.6	81.2	10

a. P&A = “precision and accuracy”.

b. %R = percent recovery; %RSD = percent relative standard deviation.

c. Mean and %RSD of the isotope dilution analogue results for the unfortified matrix sample and the fortified samples in the P&A study; number of replicates given in the header row of the table.

Table 12. Precision and Accuracy Data for a Surface Water Matrix[a]

Analyte	Low Fortification (ng/L)	Mean %R[b,c] (*n*=5)	%RSD[b]	High Fortification (ng/L)	Mean %R (*n*=5)	%RSD
PFBA	10	95.4	19	80	106	4.8
PFMPA	10	108	16	80	102	5.9
PFPeA	10	93	13	80	101	6.0
PFBS	10	111	17	80	98.3	2.7
PFMBA	10	93.0	12	80	103	3.0
PFEESA	10	95.6	15	80	99.1	2.4
NFDHA	10	102	14	80	101	2.5
4:2FTS	10	70.9	17	80	91.1	7.8
PFHxA	10	96.9	19	80	103	4.2
PFPeS	10	87.5	14	80	104	4.9
HFPO-DA	10	109	8.7	80	105	7.0
PFHpA	10	95.9	11	80	105	4.8
PFHxS	10	78.5	8.2	80	97.1	5.3
ADONA	10	94.3	7.9	80	95.8	6.0
6:2FTS	10	86.5	6.3	80	101	9.7
PFOA	10	91.9	9.8	80	98.7	4.9
PFHpS	10	88.4	14	80	106	3.4
PFNA	10	89.7	9.5	80	95.9	2.8
PFOS	10	95.1	11	80	105	8.0
9Cl-PF3ONS	10	82.4	5.0	80	94.1	3.9
8:2FTS	10	102	7.6	80	101	4.0
PFDA	10	87.3	12	80	98.5	8.0
PFUnA	10	96.9	5.4	80	95.2	2.7
11Cl-PF3OUdS	10	82.4	8.9	80	93.0	4.4
PFDoA	10	94.6	2.3	80	98.4	4.1

a. Surface water matrix was sampled after the clarifier and prior to granular activated carbon within the drinking water treatment plant and chlorinated in our laboratory. pH = 8.1 at 20 °C. Free Cl_2 = 0.98 mg/L. Total Cl_2 = 1.31 mg/L. Total Organic Carbon (TOC) = 3.8 mg/L C.

b. %R = percent recovery; %RSD = percent relative standard deviation.

c. Corrected for native concentration.

Table 13. P&A in Surface Water Matrix: Isotope Dilution Analogue Recovery Data[a]

Analyte	Analogue Fortification (ng/L)	Mean %R[b,c] (*n*=6) P&A Low	%RSD[b,c]	Mean %R (*n*=6) P&A High	%RSD
$^{13}C_4$-PFBA	40	86.9	18	86.3	6.5
$^{13}C_5$-PFPeA	40	105	15	102	5.7
$^{13}C_3$-PFBS	40	98.6	11	99.8	4.5
$^{13}C_2$-4:2FTS	160	136	13	138	6.3
$^{13}C_5$-PFHxA	40	88.8	16	84.8	4.5
$^{13}C_3$-HFPO-DA	40	78.4	14	75.4	13
$^{13}C_4$-PFHpA	40	91.6	12	89.3	6.0
$^{13}C_3$-PFHxS	40	98.2	6.5	96.0	9.6
$^{13}C_2$-6:2FTS	160	110	9.7	109	8.4
$^{13}C_8$-PFOA	40	90.1	14	86.6	4.5
$^{13}C_9$-PFNA	40	91.0	14	87.2	6.0
$^{13}C_8$-PFOS	40	98.8	15	95.6	5.0
$^{13}C_2$-8:2FTS	160	101	9.8	97.3	11
$^{13}C_6$-PFDA	40	92.0	16	86.6	10
$^{13}C_7$-PFUnA	40	92.2	16	90.0	5.6
$^{13}C_2$-PFDoA	40	91.2	14	90.8	10

a. P&A = “precision and accuracy”.

b. %R = percent recovery; %RSD = percent relative standard deviation.

c. Mean and %RSD of the isotope dilution analogue results for the unfortified matrix sample and the fortified samples in the P&A study; number of replicates given in the header row of the table.

Table 14. Aqueous Sample Holding Time Data[a]

Analyte	Fortified Conc. (ng/L)	Day Zero Mean (ng/L)	Day Zero %RSD	Day 7 %Change[b]	Day 7 %RSD	Day 14 %Change	Day 14 %RSD	Day 21 %Change	Day 21 %RSD	Day 28 %Change	Day 28 %RSD
PFBA	40	42	4.6	9.1	2.3	3.1	7.2	5.1	5.4	4.2	5.0
PFMPA	40	41	5.2	5.5	2.2	-7.8	5.1	1.0	6.3	-10	3.1
PFPeA	40	43	4.1	1.2	1.9	-2.2	6.5	-0.29	2.5	-6.5	5.8
PFBS	40	43	9.7	-1.9	3.6	-6.1	1.8	-4.0	2.5	-7.6	8.9
PFMBA	40	40	3.0	-2.5	3.7	-5.7	4.3	0.20	5.0	-6.6	6.3
PFEESA	40	39	3.2	2.6	5.7	-1.8	6.7	-2.4	4.5	-1.7	2.6
NFDHA	40	39	6.5	-4.0	7.2	-11	6.9	-3.8	5.2	-2.9	8.0
4:2FTS	40	43	9.7	-1.7	3.8	-2.6	9.6	-2.0	6.1	-0.34	5.3
PFHxA	40	42	5.2	-0.37	4.6	-2.61	5.6	-1.7	5.8	-2.3	7.6
PFPeS	40	41	3.2	5.6	7.5	-3.1	2.6	6.0	9.2	-11	9.4
HFPO-DA	40	42	5.1	6.2	4.8	3.2	9.2	2.1	2.1	-3.5	4.2
PFHpA	40	41	4.6	-0.042	2.4	-4.7	1.7	-2.9	3.6	-3.0	5.4
PFHxS	40	41	4.3	1.8	3.0	-1.8	1.8	-1.8	9.0	-0.99	6.8
ADONA	40	39	4.2	-4.3	3.1	-12	5.7	-6.2	5.9	-2.3	3.1
6:2FTS	40	41	7.5	-4.3	4.4	-0.74	9.4	2.5	6.0	-1.5	6.0
PFOA	40	41	5.4	-1.5	6.7	1.6	5.1	-2.0	4.9	-6.5	7.2
PFHpS	40	41	4.7	-2.4	5.4	1.2	3.1	0.30	3.2	2.9	7.2
PFNA	40	42	4.1	2.05	0.57	-6.0	4.9	-6.1	3.4	-9.5	3.4
PFOS	40	41	7.0	-2.1	4.7	-1.8	5.2	1.0	5.8	-1.6	5.3
9Cl-PF3ONS	40	40	3.5	1.6	4.8	-0.34	1.8	4.0	4.8	-2.6	10
8:2FTS	40	44	7.9	-0.36	2.5	-1.4	6.7	0.026	3.8	-3.6	6.9
PFDA	40	41	5.0	0.12	3.1	-2.7	3.8	-1.4	3.8	-2.4	7.0
PFUnA	40	39	3.9	-1.3	4.7	-12	1.2	3.7	3.1	-6.7	3.5
11Cl-PF3OUdS	40	40	4.9	-1.1	4.5	-9.4	5.1	-11.0	4.7	-12	7.3
PFDoA	40	39	4.4	9.5	6.5	-4.8	6.0	-3.4	5.8	-16	6.1

a. Finished water from a surface water source. pH = 8.84 at 18 °C; total organic carbon (TOC) = 0.75 mg/L C (mean of 2019 first quarter plant records); free chlorine = 0.87 mg/L, total chlorine = 1.04 mg/L. Day Zero: *n*=7. All other events: *n*=5.

b. %Change = percent change from Day Zero calculated as follows: (Day X mean concentration – Day Zero mean concentration) / Day Zero mean concentration * 100%, where X is the analysis day.

Table 15. Extract Holding Time Data[a]

Analyte	Fortified Conc. (ng/L)	Day Zero Mean (ng/L)	Day Zero %RSD	Day 14 %Change[b]	Day 14 %RSD	Day 21 %Change	Day 21 %RSD	Day 27 %Change	Day 27 %RSD
PFBA	40	42	4.6	-8.0	4.2	-4.4	0.89	-12	6.4
PFMPA	40	41	5.2	-3.9	4.5	-0.10	5.1	-3.9	12
PFPeA	40	43	4.1	-6.0	6.0	-0.55	4.8	-5.4	1.1
PFBS	40	43	9.7	2.6	2.0	6.6	2.3	2.9	3.6
PFMBA	40	40	3.0	-10	7.1	-4.8	5.3	-8.8	2.7
PFEESA	40	39	3.2	1.3	8.9	-3.6	2.1	-4.9	3.6
NFDHA	40	39	6.5	-10	3.9	-13	6.8	-11	3.1
4:2FTS	40	43	9.7	-4.7	8.5	-6.2	8.8	-7.3	8.5
PFHxA	40	42	5.2	-4.6	6.3	-20	3.0	-14	4.7
PFPeS	40	41	3.2	-6.7	8.6	-11	5.2	-10	4.5
HFPO-DA	40	42	5.1	-4.9	4.9	-4.7	5.1	-4.4	7.7
PFHpA	40	41	4.6	-1.9	1.9	-6.1	4.8	-8.7	7.8
PFHxS	40	41	4.3	-19	9.9	-21	8.4	-22	11
ADONA	40	39	4.2	-1.2	1.9	-7.8	6.4	-7.5	5.0
6:2FTS	40	41	7.5	-5.3	13	-7.6	5.8	-8.4	14
PFOA	40	41	5.4	-5.7	6.3	-2.2	4.2	-2.4	3.3
PFHpS	40	41	4.7	-8.7	7.3	-6.0	5.2	-3.2	4.2
PFNA	40	42	4.1	-5.8	5.6	0.17	3.2	-2.0	6.0
PFOS	40	41	7.0	-3.8	10	-4.2	2.5	-3.7	4.4
9Cl-PF3ONS	40	40	3.5	-5.8	7.7	-9.3	4.0	-8.6	4.7
8:2FTS	40	44	7.9	-4.7	6.3	-1.3	5.8	-6.4	2.9
PFDA	40	41	5.0	-3.7	5.3	-1.8	5.6	-4.8	3.1
PFUnA	40	39	3.9	6.2	4.0	0.63	7.5	-2.8	5.2
11Cl-PF3OUdS	40	40	4.9	-12	5.9	-18	4.6	-10	6.3
PFDoA	40	39	4.4	1.9	5.5	1.0	6.4	-2.6	3.3

a. Finished water from a surface water source. pH = 8.84 at 18 °C; total organic carbon (TOC) = approximately 0.75 mg/L C (2019 first quarter plant records); free chlorine = 0.87 mg/L, total chlorine = 1.04 mg/L. Day Zero: *n*=7. All other events: *n*=7.

b. %Change = percent change from Day Zero calculated as follows: (Day X mean concentration – Day Zero mean concentration) / Day Zero mean concentration * 100%, where X is the analysis day.

Table 16. Initial Demonstration of Capability (IDC) Quality Control Requirements

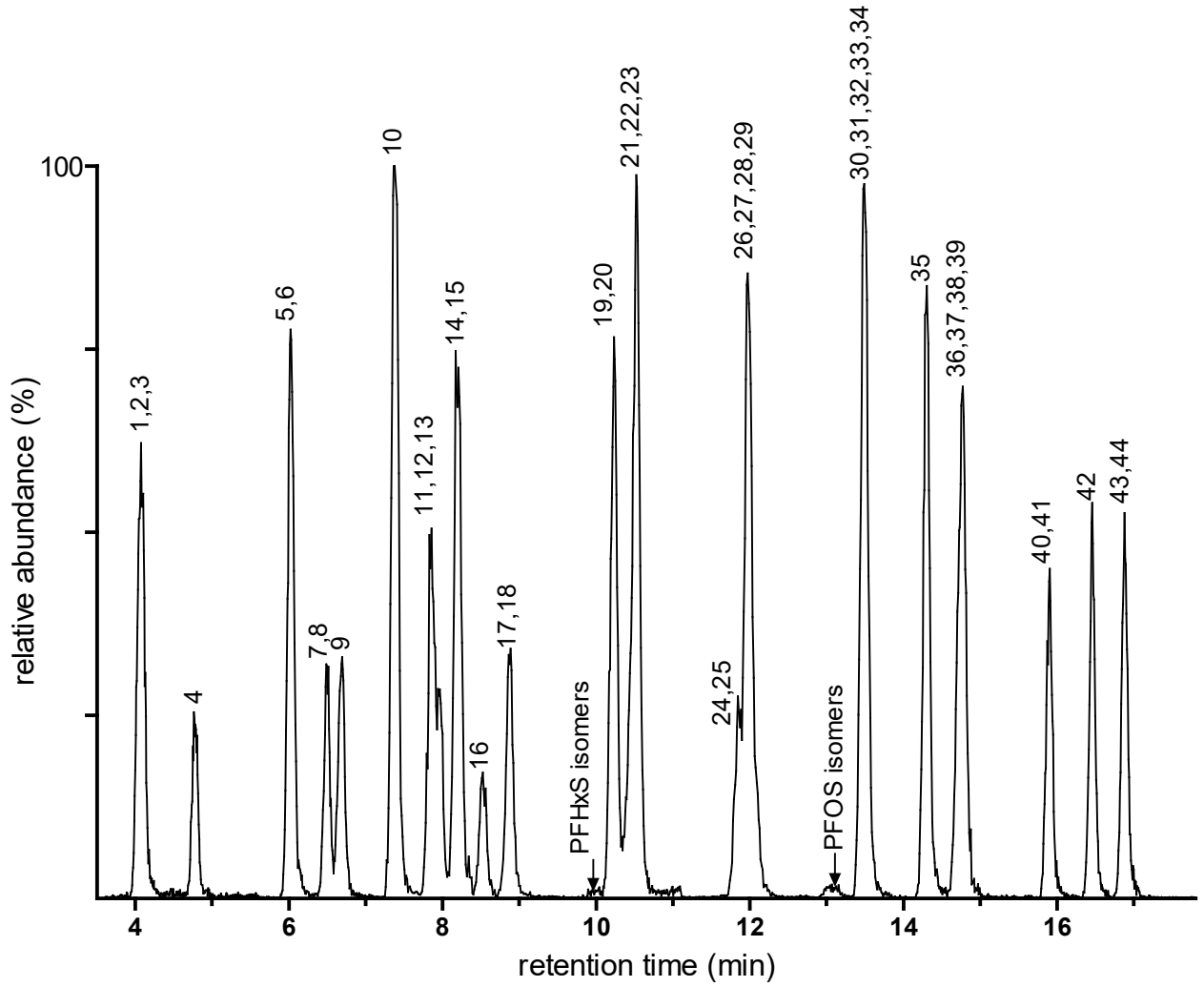
Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Section 10.2.2	Establish retention times for branched isomers	Each time chromatographic conditions change	All isomers of each analyte must elute within the same MRM window.
Section 9.1.1	Demonstration of low system background	Analyze a Laboratory Reagent Blank (LRB) after the highest standard in the calibration range.	Demonstrate that the method analytes are less than one-third of the Minimum Reporting Level (MRL).
Section 9.1.2	Demonstration of precision	Extract and analyze 7 replicate Laboratory Fortified Blanks (LFBs) near the mid-range concentration.	Percent relative standard deviation must be ≤20%.
Section 9.1.3	Demonstration of accuracy	Calculate mean recovery for replicates used in Section 9.1.2.	Mean recovery within 70–130% of the true value.
Section 9.1.4	MRL confirmation	Fortify and analyze 7 replicate LFBs at the proposed MRL concentration. Confirm that the Upper Prediction Interval of Results (PIR) and Lower PIR meet the recovery criteria.	Upper PIR ≤150% Lower PIR ≥50%
Section 9.1.5	Calibration Verification	Analyze mid-level QCS.	Results must be within 70–130% of the true value.

Table 17. Ongoing Quality Control Requirements

Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Section 10.3	Initial calibration	Use the isotope dilution calibration technique to generate a linear or quadratic calibration curve. Use at least 5 standard concentrations. Evaluate the calibration curve as described in Section 10.3.5.	When each calibration standard is calculated as an unknown using the calibration curve, analytes fortified at or below the MRL should be within 50–150% of the true value. Analytes fortified at all other levels should be within 70–130% of the true value.
Section 9.2.1	Laboratory Reagent Blank (LRB)	Include one LRB with each Extraction Batch. Analyze one LRB with each Analysis Batch.	Demonstrate that all method analytes are below one-third the Minimum Reporting Level (MRL), and that possible interference from reagents and glassware do not prevent identification and quantitation of method analytes.

Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Section 9.2.3	Laboratory Fortified Blank	Include one LFB with each Extraction Batch.	For analytes fortified at concentrations ≤2 x the MRL, the result must be within 50–150% of the true value; 70–130% of the true value if fortified at concentrations greater than 2 x the MRL.
Section 10.4	Continuing Calibration Check (CCC)	Verify initial calibration by analyzing a low-level CCC (concentrations at or below the MRL for each analyte) at the beginning of each Analysis Batch. Subsequent CCCs are required after every tenth field sample and to complete the batch.	The lowest level CCC must be within 50–150% of the true value. All other levels must be within 70–130% of the true value.
Section 9.2.4	Isotope performance standards	Isotope performance standards are added to all standards and sample extracts.	Peak area counts for each isotope performance standard must be within 50–150% of the average peak area in the initial calibration.
Section 9.2.5	Isotope dilution analogues	Isotope dilution analogues are added to all samples prior to extraction.	50%–200% recovery for each analogue
Section 9.2.6	Laboratory Fortified Sample Matrix (LFSM)	Include one LFSM per Extraction Batch. Fortify the LFSM with method analytes at a concentration close to but greater than the native concentrations (if known).	For analytes fortified at concentrations ≤2 x the MRL, the result must be within 50–150% of the true value; 70–130% of the true value if fortified at concentrations greater than 2 x the MRL.
Section 9.2.7	Laboratory Fortified Sample Matrix Duplicate (LFSMD) or Field Duplicate (FD)	Include at least one LFSMD or FD with each Extraction Batch.	For LFSMDs or FDs, relative percent differences must be ≤30% (≤50% if analyte concentration ≤2 x the MRL).
Section 9.2.8	Field Reagent Blank (FRB)	Analyze the FRB if any analyte is detected in the associated field samples.	If an analyte detected in the field sample is present in the associated FRB at greater than one-third the MRL, the results for that analyte are invalid.
Section 9.2.9	Calibration Verification using QCS	Perform a Calibration Verification at least quarterly.	Results must be within 70–130% of the true value.

Figure 1. Example Chromatogram for Reagent Water Fortified with Method Analytes at 80 ng/L[a]



a. Numbered peaks are identified in **Table 3**, **Table 4**, and **Table 5**.

Attachment 12

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METHOD 537.1 DETERMINATION OF SELECTED PER- AND POLYFLUORINATED ALKYL SUBSTANCES IN DRINKING WATER BY SOLID PHASE EXTRACTION AND LIQUID CHROMATOGRAPHY/TANDEM MASS SPECTROMETRY (LC/MS/MS)

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J.A. Shoemaker (Office of Research and Development), P.E. Grimmett (Office of Research and Development), B.K. Boutin (National Council on Aging), Method 537, Rev 1.1 (2009)

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METHOD 537.1

DETERMINATION OF SELECTED PER- AND POLYFLUORINATED ALKYL SUBSTANCES IN DRINKING WATER BY SOLID PHASE EXTRACTION AND LIQUID CHROMATOGRAPHY/TANDEM MASS SPECTROMETRY (LC/MS/MS)

1. SCOPE AND APPLICATION

1.1. This is a solid phase extraction (SPE) liquid chromatography/tandem mass spectrometry (LC/MS/MS) method for the determination of selected per- and polyfluorinated alkyl substances (PFAS) in drinking water. Accuracy and precision data have been generated in reagent water and drinking water for the compounds listed in the table below.

Analyte[a]	Acronym	Chemical Abstract Services Registry Number (CASRN)
Hexafluoropropylene oxide dimer acid	HFPO-DA	13252-13-6[b]
N-ethyl perfluorooctanesulfonamidoacetic acid	NEtFOSAA	2991-50-6
N-methyl perfluorooctanesulfonamidoacetic acid	NMeFOSAA	2355-31-9
Perfluorobutanesulfonic acid	PFBS	375-73-5
Perfluorodecanoic acid	PFDA	335-76-2
Perfluorododecanoic acid	PFDoA	307-55-1
Perfluoroheptanoic acid	PFHpA	375-85-9
Perfluorohexanesulfonic acid	PFHxS	355-46-4
Perfluorohexanoic acid	PFHxA	307-24-4
Perfluorononanoic acid	PFNA	375-95-1
Perfluorooctanesulfonic acid	PFOS	1763-23-1
Perfluorooctanoic acid	PFOA	335-67-1
Perfluorotetradecanoic acid	PFTA	376-06-7
Perfluorotridecanoic acid	PFTrDA	72629-94-8
Perfluoroundecanoic acid	PFUnA	2058-94-8
11-chloroeicosafluoro-3-oxaundecane-1-sulfonic acid	11Cl-PF3OUdS	763051-92-9[c]
9-chlorohexadecafluoro-3-oxanonane-1-sulfonic acid	9Cl-PF3ONS	756426-58-1[d]
4,8-dioxa-3H-perfluorononanoic acid	ADONA	919005-14-4[e]

[a] Some PFAS are commercially available as ammonium, sodium and potassium salts. This method measures all forms of the analytes as anions while the counterion is inconsequential. Analytes may be purchased as acids or as any of the corresponding salts (see Section 7.2.3 regarding correcting the analyte concentration for the salt content).

[b] HFPO-DA and the ammonium salt of HFPO-DA are components of the GenX processing aid technology and both are measured as the anion of HFPO-DA by this method.

[c] 11Cl-PF3OUdS is available in salt form (e.g. CASRN of potassium salt is 83329-89-9).

[d] 9Cl-PF3ONS analyte is available in salt form (e.g. CASRN of potassium salt is 73606-19-6)

[e] ADONA is available as the sodium salt (no CASRN) and the ammonium salt (CASRN is 958445-44-8).

1.2. Minimum Reporting Level (MRL) is the lowest analyte concentration that meets Data Quality Objectives (DQOs) that are developed based on the intended use of this method. The single laboratory lowest concentration MRL (LCMRL) is the lowest true concentration for which the future recovery is predicted to fall, with high confidence (99%), between 50 and 150% recovery. Single laboratory LCMRLs for analytes in this method range from 0.53-6.3 ng/L and are listed in Table 5. The procedure used to determine the LCMRL is described elsewhere.[1]

1.3. Laboratories using this method will not be required to determine the LCMRL for this method, but will need to demonstrate that their laboratory MRL for this method meets requirements described in Section 9.2.6.

1.4. Determining the Detection Limit (DL) for analytes in this method is optional (Sect. 9.2.8). Detection limit is defined as the statistically calculated minimum concentration that can be measured with 99% confidence that the reported value is greater than zero.[2] The DL is compound dependent and is dependent on extraction efficiency, sample matrix, fortification concentration, and instrument performance.

1.5. This method is intended for use by analysts skilled in solid phase extractions, the operation of LC/MS/MS instruments, and the interpretation of the associated data.

1.6. METHOD FLEXIBILITY – In recognition of technological advances in analytical systems and techniques, the laboratory is permitted to modify the evaporation technique, separation technique, LC column, mobile phase composition, LC conditions and MS and MS/MS conditions (Sect. 6.12, 9.1.1, 10.2, and 12.1). **Changes may not be made to sample collection and preservation (Sect. 8), the sample extraction steps (Sect. 11.4), or to the quality control requirements (Sect. 9).** Method modifications should be considered only to improve method performance. Modifications that are introduced in the interest of reducing cost or sample processing time, but result in poorer method performance, should not be used. Analytes must be adequately resolved chromatographically to permit the mass spectrometer to dwell on a minimum number of compounds eluting within a retention time window. Instrumental sensitivity (or signal-to-noise) will decrease if too many compounds are permitted to elute within a retention time window. In all cases where method modifications are proposed, the analyst must perform the procedures outlined in the initial demonstration of capability (IDC, Sect. 9.2), verify that all Quality Control (QC) acceptance criteria in this method (Sect. 9) are met, and that acceptable method performance can be verified in a real sample matrix (Sect. 9.3.6).

NOTE: The above method flexibility Section is intended as an abbreviated summation of method flexibility. Sections 4-12 provide detailed information of specific portions of the method that may be modified. If there is any perceived conflict between the general method flexibility statement in Section 1.6 and specific information in Sections 4-12, Sections 4-12 supersede Section 1.6.

2. SUMMARY OF METHOD

A 250-mL water sample is fortified with surrogates and passed through an SPE cartridge containing polystyrenedivinylbenzene (SDVB) to extract the method analytes and surrogates. The compounds are eluted from the solid phase sorbent with a small amount of methanol. The extract is concentrated to dryness with nitrogen in a heated water bath, and then adjusted to a 1-mL volume with 96:4% (vol/vol) methanol:water and addition of the internal standards. A 10-µL injection is made into an LC equipped with a C18 column that is interfaced to an MS/MS. The analytes are separated and identified by comparing the acquired mass spectra and retention times to reference spectra and retention times for calibration standards acquired under identical LC/MS/MS conditions. The concentration of each analyte is determined by using the internal standard technique. Surrogate analytes are added to all Field and QC Samples to monitor the extraction efficiency of the method analytes.

3. DEFINITIONS

3.1. ANALYSIS BATCH – A set of samples that is analyzed on the same instrument during a 24-hour period, including no more than 20 Field Samples, that begins and ends with the analysis of the appropriate Continuing Calibration Check (CCC) standards. Additional CCCs may be required depending on the length of the analysis batch and/or the number of Field Samples.

3.2. CALIBRATION STANDARD (CAL) – A solution prepared from the primary dilution standard solution and/or stock standard solution, internal standard(s), and the surrogate(s). The CAL solutions are used to calibrate the instrument response with respect to analyte concentration.

3.3. COLLISIONALLY ACTIVATED DISSOCIATION (CAD) – The process of converting the precursor ion's translational energy into internal energy by collisions with neutral gas molecules to bring about dissociation into product ions.

3.4. CONTINUING CALIBRATION CHECK (CCC) – A calibration standard containing the method analytes, internal standard(s) and surrogate(s). The CCC is analyzed periodically to verify the accuracy of the existing calibration for those analytes.

3.5. DETECTION LIMIT (DL) – The minimum concentration of an analyte that can be identified, measured, and reported with 99% confidence that the analyte concentration is greater than zero. This is a statistical determination of precision (Sect. 9.2.8), and accurate quantitation is not expected at this level.2

3.6. EXTRACTION BATCH – A set of up to 20 Field Samples (not including QC samples) extracted together by the same person(s) during a work day using the same lot of SPE devices, solvents, surrogate, internal standard and fortifying solutions. Required QC samples include Laboratory Reagent Blank, Laboratory Fortified Blank, Laboratory Fortified Sample Matrix, and either a Field Duplicate or Laboratory Fortified Sample Matrix Duplicate.

3.7. FIELD DUPLICATES (FD1 and FD2) – Two separate samples collected at the same time and place under identical circumstances and treated exactly the same throughout field and laboratory procedures. Analyses of FD1 and FD2 give a measure of the precision associated with sample collection, preservation, and storage, as well as laboratory procedures.

3.8. FIELD REAGENT BLANK (FRB) – An aliquot of reagent water that is placed in a sample container in the laboratory and treated as a sample in all respects, including shipment to the sampling site, exposure to sampling site conditions, storage, preservation, and all analytical procedures. The purpose of the FRB is to determine if method analytes or other interferences are present in the field environment.

3.9. INTERNAL STANDARD (IS) – A pure chemical added to an extract or standard solution in a known amount(s) and used to measure the relative response of other method analytes and surrogates that are components of the same solution. The internal standard must be a chemical that is structurally similar to the method analytes, has no potential to be present in water samples, and is not a method analyte.

3.10. LABORATORY FORTIFIED BLANK (LFB) – A volume of reagent water or other blank matrix to which known quantities of the method analytes and all the preservation compounds are added in the laboratory. The LFB is analyzed exactly like a sample, and its purpose is to determine whether the methodology is in control, and whether the laboratory is capable of making accurate and precise measurements.

3.11. LABORATORY FORTIFIED SAMPLE MATRIX (LFSM) – A preserved field sample to which known quantities of the method analytes are added in the laboratory. The LFSM is processed and analyzed exactly like a sample, and its purpose is to determine whether the sample matrix contributes bias to the analytical results. The background concentrations of the analytes in the sample matrix must be determined in a separate sample extraction and the measured values in the LFSM corrected for background concentrations.

3.12. LABORATORY FORTIFIED SAMPLE MATRIX DUPLICATE (LFSMD) – A duplicate of the Field Sample used to prepare the LFSM. The LFSMD is fortified, extracted, and analyzed identically to the LFSM. The LFSMD is used instead of the Field Duplicate to assess method precision when the occurrence of method analytes is low.

3.13. LABORATORY REAGENT BLANK (LRB) – An aliquot of reagent water or other blank matrix that is treated exactly as a sample including exposure to all glassware, equipment, solvents and reagents, sample preservatives, internal standard, and surrogates that are used in the analysis batch. The LRB is used to determine if method analytes or other interferences are present in the laboratory environment, the reagents, or the apparatus.

3.14. LOWEST CONCENTRATION MINIMUM REPORTING LEVEL (LCMRL) – The single laboratory LCMRL is the lowest true concentration for which a future recovery is expected, with 99% confidence, to be between 50 and 150% recovery.1

3.15. MINIMUM REPORTING LEVEL (MRL) – The minimum concentration that can be reported as a quantitated value for a method analyte in a sample following analysis. This defined concentration can be no lower than the concentration of the lowest calibration standard for that analyte and can only be used if acceptable QC criteria for this standard are met. A procedure for verifying a laboratory's MRL is provided in Section 9.2.6.

3.16. PRECURSOR ION – For the purpose of this method, the precursor ion is the deprotonated molecule ([M-H]-) of the method analyte. In MS/MS, the precursor ion is mass selected and fragmented by collisionally activated dissociation to produce distinctive product ions of smaller m/z.

3.17. PRIMARY DILUTION STANDARD (PDS) SOLUTION – A solution containing the analytes prepared in the laboratory from stock standard solutions and diluted as needed to prepare calibration solutions and other needed analyte solutions.

3.18. PRODUCT ION – For the purpose of this method, a product ion is one of the fragment ions produced in MS/MS by collisionally activated dissociation of the precursor ion.

3.19. QUALITATIVE STANDARD – A qualitative standard is a standard for which either the concentration is estimated or method analyte impurities exist at a concentration >1/3 of the MRL in the highest concentration calibration standard. For the purposes of this method, qualitative standards are used to identify retention times of branched isomers of method analytes and are not used for quantitation purposes.

3.20. QUALITY CONTROL SAMPLE (QCS) – A solution of method analytes of known concentrations that is obtained from a source external to the laboratory and different from the source of calibration standards. The second source SSS is used to fortify the QCS at a known concentration. The QCS is used to check calibration standard integrity.

3.21. QUANTITATIVE STANDARD – A quantitative standard is a standard of known concentration and purity. The quantitative standard must not contain any of the method analytes as impurities at concentrations >1/3 of the MRL in the highest concentration calibration standard.

3.22. SAFETY DATA SHEET (SDS) – Written information provided by vendors concerning a chemical's toxicity, health hazards, physical properties, fire, and reactivity data including storage, spill, and handling precautions.

3.23. STOCK STANDARD SOLUTION (SSS) – A concentrated solution containing one or more method analytes prepared in the laboratory using assayed reference materials or purchased from a reputable commercial source.

3.24. SURROGATE ANALYTE (SUR) – A pure chemical which chemically resembles method analytes and is extremely unlikely to be found in any sample. This chemical is added to a sample aliquot in known amount(s) before processing and is measured with the same procedures used to measure other method analytes. The purpose of the SUR is to monitor method performance with each sample.

4. INTERFERENCES

4.1. All glassware must be meticulously cleaned. Wash glassware with detergent and tap water, rinse with tap water, followed by a reagent water rinse. Non-volumetric glassware can be heated in a muffle furnace at 400 °C for 2 h or solvent rinsed. Volumetric glassware should be solvent rinsed and not be heated in an oven above 120 °C. Store clean glassware inverted or capped. **Do not cover with aluminum foil because PFAS can be potentially transferred from the aluminum foil to the glassware.**

NOTE: Samples and extracts should not come in contact with any glass containers or pipettes as these analytes can potentially adsorb to glass surfaces. PFAS analyte, IS and SUR standards commercially purchased in glass ampoules are acceptable; however, all subsequent transfers or dilutions performed by the analyst must be prepared and stored in polypropylene containers.

4.2. Method interferences may be caused by contaminants in solvents, reagents (including reagent water), sample bottles and caps, and other sample processing hardware that lead to discrete artifacts and/or elevated baselines in the chromatograms. The analytes in this method can also be found in many common laboratory supplies and equipment, such as PTFE (polytetrafluoroethylene) products, LC solvent lines, methanol, aluminum foil, SPE sample transfer lines, etc.[3] All items such as these must be routinely demonstrated to be free from interferences (less than 1/3 the MRL for each method analyte) under the conditions of the analysis by analyzing laboratory reagent blanks as described in Section 9.3.1. **Subtracting blank values from sample results is not permitted.**

4.3. Matrix interferences may be caused by contaminants that are co-extracted from the sample. The extent of matrix interferences will vary considerably from source to source, depending upon the nature of the water. Humic and/or fulvic material can be co-extracted during SPE and high levels can cause enhancement and/or suppression in the electrospray ionization source or low recoveries on the SPE sorbent.[4-5] Total organic carbon (TOC) is a good indicator of humic content of the sample. Under the LC conditions used during method development, matrix effects due to total organic carbon (TOC) were not observed.

4.4. Relatively large quantities of the preservative (Sect. 8.1.2) are added to sample bottles. The potential exists for trace-level organic contaminants in these reagents. Interferences from these sources should be monitored by analysis of laboratory reagent blanks (Sect. 9.3.1), particularly when new lots of reagents are acquired.

4.5. SPE cartridges can be a source of interferences. The analysis of field and laboratory reagent blanks can provide important information regarding the presence or absence of such interferences. Brands and lots of SPE devices should be tested to ensure that contamination does not preclude analyte identification and quantitation.

5. SAFETY

5.1. The toxicity or carcinogenicity of each reagent used in this method has not been precisely defined. Each chemical should be treated as a potential health hazard, and exposure to these chemicals should be minimized. Each laboratory is responsible for maintaining an awareness of OSHA regulations regarding safe handling of chemicals used in this method. A reference file of SDSs should be made available to all personnel involved in the chemical analysis. Additional references to laboratory safety are available.[6-8]

5.2. PFOA has been described as likely to be carcinogenic to humans.[9] Pure standard materials and stock standard solutions of these method analytes should be handled with suitable protection to skin and eyes, and care should be taken not to breathe the vapors or ingest the materials.

6. EQUIPMENT AND SUPPLIES

(Brand names and/or catalog numbers are included for illustration only, and do not imply endorsement of the product.) Due to potential adsorption of analytes onto glass, polypropylene containers were used for all standard, sample and extraction preparations. Other plastic materials (e.g., polyethylene) which meet the QC requirements of Section 9 may be substituted.

6.1. SAMPLE CONTAINERS – 250-mL polypropylene bottles fitted with polypropylene screw caps.

6.2. POLYPROPYLENE BOTTLES – 4-mL narrow-mouth polypropylene bottles (VWR Cat. No.: 16066-960 or equivalent).

6.3. CENTRIFUGE TUBES – 15-mL conical polypropylene tubes with polypropylene screw caps for storing standard solutions and for collection of the extracts (Thomas Scientific Cat. No.: 2602A10 or equivalent).

6.4. AUTOSAMPLER VIALS – Polypropylene 0.4-mL autosampler vials (ThermoFisher Cat. No.: C4000-11) with polypropylene caps (ThermoFisher Cat. No.: C5000-50 or equivalent).

NOTE: Polypropylene vials and caps are necessary to prevent contamination of the sample from PTFE coated septa. However, polypropylene caps do not reseal, so evaporation occurs after injection. Thus, multiple injections from the same vial are not possible.

6.5. POLYPROPYLENE GRADUATED CYLINDERS – Suggested sizes include 25, 50, 100 and 1000-mL cylinders.

6.6. MICRO SYRINGES – Suggested sizes include 5, 10, 25, 50, 100, 250, 500 and 1000-µL syringes.

6.7. PLASTIC PIPETS – Polypropylene or polyethylene disposable pipets (Fisher Cat. No.: 13-711-7 or equivalent).

6.8. ANALYTICAL BALANCE – Capable of weighing to the nearest 0.0001 g.

6.9. SOLID PHASE EXTRACTION (SPE) APPARATUS FOR USING CARTRIDGES

6.9.1. SPE CARTRIDGES – 0.5 g, 6-mL SPE cartridges containing styrenedivinyl-benzene (SDVB) polymeric sorbent phase (Agilent Cat. No.: 1225-5021 or equivalent). The sorbent may not be modified with monomers other than SDVB.

6.9.2. VACUUM EXTRACTION MANIFOLD – A manual vacuum manifold with Visiprep™ large volume sampler (Supelco Cat. No. 57030 and 57275 or equivalent) for cartridge extractions, or an automatic/robotic sample preparation system designed for use with SPE cartridges, may be used if all QC requirements discussed in Section 9 are met. Extraction and/or elution steps may not be changed or omitted to accommodate the use of an automated system. Care must be taken with automated SPE systems to ensure the PTFE commonly used in these systems does not contribute to unacceptable analyte concentrations in the LRB (Sect. 9.3.1).

6.9.3. SAMPLE DELIVERY SYSTEM – Use of a polypropylene transfer tube system, which transfers the sample directly from the sample container to the SPE cartridge, is recommended, but not mandatory. Standard extraction manifolds come equipped with PTFE transfer tube systems. These can be replaced with 1/8" O.D. x 1/16" I.D. polypropylene or polyethylene tubing (Hudson Extrusions LLDPE or equivalent) cut to an appropriate length to ensure no sample contamination from the sample transfer lines. Other types of non-PTFE tubing may be used provided it meets the LRB (Sect. 9.3.1) and LFB (Sect. 9.3.3) QC requirements. The PTFE transfer tubes may be used, but an LRB must be run on each PTFE transfer tube and the QC requirements in Section 9.3.1 must be met. In the case of automated SPE, the removal of PTFE lines may not be feasible; therefore, LRBs will need to be rotated among the ports and must meet the QC requirements of Sections 9.2.2 and 9.3.1.

6.10. EXTRACT CONCENTRATION SYSTEM – Extracts are concentrated by evaporation with nitrogen using a water bath set no higher than 65 °C (Meyer N-Evap, Model 111, Organomation Associates, Inc. or equivalent).

6.11. LABORATORY OR ASPIRATOR VACUUM SYSTEM – Sufficient capacity to maintain a vacuum of approximately 10 to 15 inches of mercury for extraction cartridges.

6.12. LIQUID CHROMATOGRAPHY (LC)/TANDEM MASS SPECTROMETER (MS/MS) WITH DATA SYSTEM

6.12.1. LC SYSTEM – Instrument capable of reproducibly injecting up to 10-µL aliquots and performing binary linear gradients at a constant flow rate near the flow rate used for development of this method (0.3 mL/min). The usage of a column heater is optional.

NOTE: During the course of method development, it was discovered that while idle for more than one day, PFAS built up in the PTFE solvent transfer lines. To prevent long delays in purging high levels of PFAS from the LC solvent lines, they were replaced with PEEK™ tubing and the PTFE solvent frits were replaced with stainless steel frits. It is not possible to remove all PFAS background contamination, but these measures help to minimize their background levels.

6.12.2. LC/TANDEM MASS SPECTROMETER – The LC/MS/MS must be capable of negative ion electrospray ionization (ESI) near the suggested LC flow rate of 0.3 mL/min. The system must be capable of performing MS/MS to produce unique product ions (Sect. 3.18) for the method analytes within specified retention time segments. A minimum of 10 scans across the chromatographic peak is required to ensure adequate precision. Data are demonstrated in Tables 5-9 using a triple quadrupole mass spectrometer (Waters XEVO TQMS). See the Note in Sect. 10.2.3 pertaining to potential limitations of some MS/MS instrumentation in achieving the required MS/MS transitions.

6.12.3. DATA SYSTEM – An interfaced data system is required to acquire, store, reduce, and output mass spectral data. The computer software should have the capability of processing stored LC/MS/MS data by recognizing an LC peak within any given retention time window. The software must allow integration of the ion abundance of any specific ion within specified time or scan number limits. The software must be able to calculate relative response factors, construct linear regressions or quadratic calibration curves, and calculate analyte concentrations.

6.12.4. ANALYTICAL COLUMN – An LC C18 column (2.1 x 150 mm) packed with 5 µm dp C18 solid phase particles (Waters #: 186001301 or equivalent) was used. Any column that provides adequate resolution, peak shape, capacity, accuracy, and precision (Sect. 9) may be used.

7. REAGENTS AND STANDARDS

7.1. GASES, REAGENTS, AND SOLVENTS – Reagent grade or better chemicals should be used. Unless otherwise indicated, it is intended that all reagents shall conform to the specifications of the Committee on Analytical Reagents of the American Chemical Society, where such specifications are available. Other grades may be used, provided it is first determined that the reagent is of sufficiently high purity to permit its use without lessening the quality of the determination.

7.1.1. REAGENT WATER – Purified water which does not contain any measurable quantities of any method analytes or interfering compounds greater than 1/3 the MRL for each method analyte of interest. Prior to daily use, at least 3 L of reagent water should be flushed from the purification system to rinse out any build-up of analytes in the system's tubing.

7.1.2. METHANOL (CH3OH, CAS#: 67-56-1) – High purity, demonstrated to be free of analytes and interferences (Fisher LC/MS grade or equivalent).

7.1.3. AMMONIUM ACETATE (NH4C2H3O2, CAS#: 631-61-8) – High purity, demonstrated to be free of analytes and interferences (Sigma-Aldrich ACS grade or equivalent).

7.1.4. 20 mM AMMONIUM ACETATE/REAGENT WATER – To prepare 1 L, add 1.54 g ammonium acetate to 1 L of reagent water. This solution is volatile and must be replaced at least once a week. More frequent replacement may be necessary if unexplained loss in sensitivity or retention time shifts are encountered and attributed to loss of the ammonium acetate.

7.1.5. TRIZMA® PRESET CRYSTALS, pH 7.0 (Sigma cat# T-7193 or equivalent) – Reagent grade. A premixed blend of Tris [Tris(hydroxymethyl)aminomethane] and Tris HCL [Tris(hydroxymethyl)aminomethane hydrochloride]. Alternatively, a mix of the two components with a weight ratio of 15.5/1 Tris HCL/Tris may be used. This blend is targeted to produce a pH near 7.0 at 25 °C in reagent water. Trizma® functions as a buffer and removes free chlorine in chlorinated finished waters (Sect. 8.1.2).

7.1.6. NITROGEN – Used for the following purposes:

7.1.6.1. Nitrogen aids in aerosol generation of the ESI liquid spray and is used as collision gas in some MS/MS instruments. The nitrogen used should meet or exceed instrument manufacturer's specifications.

7.1.6.2. Nitrogen is used to concentrate sample extracts (Ultra High Purity or equivalent).

7.1.7. ARGON – Used as collision gas in MS/MS instruments. Argon should meet or exceed instrument manufacturer's specifications. Nitrogen gas may be used as the collision gas provided sufficient sensitivity (product ion formation) is achieved.

7.2. STANDARD SOLUTIONS – When a compound purity is assayed to be 96% or greater, the weight can be used without correction to calculate the concentration of the stock standard. PFAS analyte, IS and SUR standards commercially purchased in glass ampoules are acceptable; however, all subsequent transfers or dilutions performed by the analyst must be prepared and stored in polypropylene containers. Solution concentrations listed in this Section were used to develop this method and are included as an example. Alternate concentrations may be used as necessary depending on instrument sensitivity and the calibration range used. Standards for sample fortification generally should be prepared in the smallest volume that can be accurately measured to minimize the addition of excess organic solvent to aqueous samples. PDS and calibration standards were found to be stable for, at least, one month during method development. Laboratories should use standard QC practices to determine when standards need to be replaced. The target analyte manufacturer's guidelines may be helpful when making the determination.

NOTE: Stock standards (Sect. 7.2.1.1, 7.2.2.1 and 7.2.3.1) were stored at ≤4 °C. Primary dilution standards (Sect.7.2.1.2, 7.2.2.2 and 7.2.3.2) were stored at room temperature to prevent adsorption of the method analytes onto the container surfaces that may occur when refrigerated. Storing the standards at room temperature will also minimize daily imprecision due to the potential of inadequate room temperature stabilization. However, standards may be stored cold provided the standards are allowed to come to room temperature and vortexed well prior to use.

7.2.1. INTERNAL (IS) STOCK STANDARD SOLUTIONS – This method uses three IS compounds listed in the table below. These isotopically labeled IS(s) were carefully chosen during method development because they encompass all the functional groups of the method analytes. Although alternate IS standards may be used provided they are isotopically labeled compounds with similar functional groups as the method analytes, the analyst must have documented reasons for using alternate IS(s). Alternate IS(s) must meet the QC requirements in Section 9.3.4. Note that different isotopic labels of the same IS(s) are acceptable (e.g., $^{13}C_2$-PFOA and $^{13}C_4$-PFOA) but will require modification of the MS/MS precursor and product ions.

Internal Standards	**Acronym**
Perfluoro-[1,2-$^{13}C_2$]octanoic acid	$^{13}C_2$-PFOA
Sodium perfluoro-1-[1,2,3,4-$^{13}C_4$]octanesulfonate	$^{13}C_4$-PFOS
N-deuteriomethylperfluoro-1-octanesulfonamidoacetic acid	d_3-NMeFOSAA

7.2.1.1. IS STOCK STANDARD SOLUTIONS (IS SSS) – These IS stocks can be obtained as individual certified stock standard solutions. The ISs can also be purchased as PDSs, making the preparation of individual SSSs unnecessary. Analysis of the IS(s) is less complicated if the IS(s) purchased contains only the linear isomer.

7.2.1.2. INTERNAL STANDARD PRIMARY DILUTION (IS PDS) STANDARD (1-4 ng/µL) – Prepare, or purchase commercially, the IS PDS at a suggested concentration of 1-4 ng/µL. The IS PDS (in methanol with 4 molar equivalents of sodium hydroxide) was purchased from Wellington Labs. Alternatively, the IS PDS can be prepared in methanol containing 4% reagent water. Use 10 µL of this 1-4 ng/µL solution to fortify the final 1-mL extracts (Sect. 11.5). This will yield a concentration of 10-40 ng/mL of each IS in the 1-mL extracts.

IS	Final Conc. of IS PDS (ng/µL)
$^{13}C_2$-PFOA	1.0
$^{13}C_4$-PFOS	3.0
d_3-NMeFOSAA	4.0

7.2.2. SURROGATE (SUR) STANDARD SOLUTIONS – The four SUR(s) listed in the table below were purchased from Wellington Labs as linear only isomers. These isotopically labeled SUR standards were carefully chosen during method development because they encompass most of the functional groups, as well as the water solubility range of the method analytes. Although alternate SUR standards may be used provided they are isotopically labeled compounds with similar functional groups as the method analytes, the analyst must have documented reasons for using alternate SUR standards. The alternate SUR standards chosen must still span the water solubility range of the method analytes. In addition, alternate SUR standards must meet the QC requirements in Section 9.3.5.

Surrogates	Acronym
Perfluoro-n-[1,2-$^{13}C_2$]hexanoic acid	$^{13}C_2$-PFHxA
Perfluoro-n-[1,2-$^{13}C_2$]decanoic acid	$^{13}C_2$-PFDA
N-deuterioethylperfluoro-1-octanesulfonamidoacetic acid	d_5-NEtFOSAA
Tetrafluoro-2-heptafluoropropoxy-$^{13}C_3$-propanoic acid	$^{13}C_3$-HFPO-DA

7.2.2.1. SUR STOCK STANDARD SOLUTIONS (SUR SSS) – These SUR stocks can be obtained as individual certified stock standard solutions. The SURs can also be purchased as PDSs, making the preparation of individual SSSs

unnecessary. Analysis of the SUR(s) is less complicated if the SUR(s) purchased contains only the linear isomer.

7.2.2.2. SURROGATE PRIMARY DILUTION STANDARD (SUR PDS) (1-4 ng/µL) – Prepare, or purchase commercially, the SUR PDS at a suggested concentration of 1-4 ng/µL. The SUR PDS (in methanol with 4 molar equivalents of sodium hydroxide) was purchased from Wellington Labs. Alternatively, the SUR PDS can be prepared in methanol containing 4% reagent water. Use 10 µL of this 1-4 ng/µL solution to fortify all QC and Field Samples. (Sect. 11.5). This will yield SUR concentrations of 40-160 ng/L in the 250 mL aqueous samples.

SUR	Final Conc. of SUR PDS (ng/µL)
$^{13}C_2$-PFHxA	1.0
$^{13}C_2$-PFDA	1.0
d_5-NEtFOSAA	4.0
$^{13}C_3$-HFPO-DA	1.0

7.2.3. ANALYTE STANDARD SOLUTIONS – Analyte standards may be purchased commercially as ampoulized solutions or prepared from neat materials. If commercially available, the method analytes must be purchased as technical grade (linear and branched isomers) standards or neat materials. Standards or neat materials that contain only the linear isomer can be substituted only if technical grade (linear and branched isomers) standards or neat material cannot be purchased as quantitative standards (see note below regarding PFOA). At the time of this method development, PFHxS, PFOS, NEtFOSAA and NMeFOSAA are available as technical grade (containing branched and linear isomers) and therefore must be purchased as technical grade.

A qualitative standard (Sect. 3.19) is available for PFOA that contains the linear and branched isomers (Wellington Labs, Cat. No. T-PFOA, or equivalent). This qualitative PFOA standard must be purchased and used to identify the retention times of the branched PFOA isomers, but the linear only PFOA standard must be used for quantitation (Sect. 12.2) until a quantitative PFOA standard containing the branched and linear isomers becomes commercially available.

PFHxS, PFOS, ADONA, 9Cl-PF3ONS and 11Cl-PF3OUdS may not be available as the acids listed in Section 1.1, but rather as their corresponding salts, such as NH_4^+, Na^+ and K^+. These salts are acceptable starting materials for the stock standards provided the measured mass is corrected for the salt content according to the equation below. Prepare the Analyte Stock and Primary Dilutions Standards as described below.

$$Mass_{acid} = MeasuredMass_{salt} \times \frac{MW_{acid}}{MW_{salt}}$$

where:

MW_{acid} = the molecular weight of PFAS
MW_{salt} = the molecular weight of purchased salt

7.2.3.1. ANALYTE STOCK STANDARD SOLUTION (SSS) – Analyte standards may be purchased commercially as ampoulized solutions prepared from neat materials. Commercially prepared SSSs are available for all method analytes. During method development, mixes or individual stocks were obtained from Accustandard, Absolute, Wellington Labs and Synquest. When using these stock standards to prepare a PDS, care must be taken to ensure that these standards are at room temperature and adequately vortexed.

7.2.3.2. ANALYTE PRIMARY DILUTION STANDARD (PDS) SOLUTION (0.5-2.5 ng/µL) – The analyte PDS contains all the method analytes of interest at various concentrations in methanol containing 4% water (or in methanol containing 4 molar equivalents of sodium hydroxide). The ESI and MS/MS response varies by compound; therefore, a mix of concentrations may be needed in the analyte PDS. See Tables 5-9 in Section 17 for suggested concentrations for each analyte. During method development, the analyte PDS was prepared such that approximately the same instrument response was obtained for all the analytes. The analyte PDS is prepared by dilution of the combined Analyte Stock Standard Solutions and is used to prepare the CAL standards, and fortify the LFBs, LFSMs, and LFSMDs with the method analytes. If the PDS is stored cold, care must be taken to ensure that these standards are at room temperature and adequately vortexed before usage.

7.2.4. CALIBRATION STANDARDS (CAL) – At least five calibration concentrations are required to prepare the initial calibration curve spanning a 20-fold concentration range (Sect. 10.2). Larger concentration ranges will require more calibration points. Prepare the CAL standards over the concentration range of interest from dilutions of the analyte PDS in methanol containing 4% reagent water. The suggested analyte concentrations found in Tables 5-9 can be used as a starting point for determining the calibration range. The IS and SUR are added to the CAL standards at a constant concentration. During method development, the concentrations of the SUR(s) were 10-40 pg/µL in the standard (40-160 ng/L in the sample) and the IS(s) were 10-40 ng/mL. The lowest concentration CAL standard must be at or below the MRL, which may depend on system sensitivity. The CAL standards may also be used as CCCs (Sect. 9.3.2).

8. SAMPLE COLLECTION, PRESERVATION, AND STORAGE

8.1. SAMPLE BOTTLE PREPARATION

8.1.1. Samples must be collected in a 250-mL polypropylene bottle fitted with a polypropylene screw-cap.

8.1.2. The preservation reagent, listed in the table below, is added to each sample bottle as a solid prior to shipment to the field (or prior to sample collection).

Compound	Amount	Purpose
Trizma® (Sect. 7.1.5)	5.0 g/L	buffering reagent and removes free chlorine

8.2. SAMPLE COLLECTION

8.2.1. The sample handler must wash their hands before sampling and wear nitrile gloves while filling and sealing the sample bottles. PFAS contamination during sampling can occur from a number of common sources, such as food packaging and certain foods and beverages. Proper hand washing and wearing nitrile gloves will aid in minimizing this type of accidental contamination of the samples.

8.2.1. Open the tap and allow the system to flush until the water temperature has stabilized (approximately 3 to 5 min). Collect samples from the flowing system.

8.2.2. Fill sample bottles, taking care not to flush out the sample preservation reagent. Samples do not need to be collected headspace free.

8.2.3. After collecting the sample, cap the bottle and agitate by hand until preservative is dissolved. Keep the sample sealed from time of collection until extraction.

8.3. FIELD REAGENT BLANKS (FRB)

8.3.1. An FRB must be handled along with each sample set. The sample set is composed of samples collected from the same sample site and at the same time. At the laboratory, fill the field blank sample bottle with reagent water, then seal, and ship to the sampling site along with the sample bottles. For each FRB shipped, a second FRB bottle containing only the preservative must also be shipped. At the sampling site, the sampler must open the shipped FRB and pour the preserved reagent water into the empty shipped sample bottle, seal and label this bottle as the FRB. The FRB is shipped back to the laboratory along with the samples and analyzed to ensure that PFAS were not introduced into the sample during sample collection/handling.

8.3.2. The same batch of preservative must be used for the FRBs as for the field samples.

8.3.3. The reagent water used for the FRBs must be initially analyzed for method analytes as a LRB (using the same lot of sample bottles as the field samples) and must meet the LRB criteria in Section 9.3.1 prior to use. This requirement will ensure samples are not being discarded due to contaminated reagent water or sample bottles rather than contamination during sampling.

8.4. SAMPLE SHIPMENT AND STORAGE – Samples must be chilled during shipment and must not exceed 10 °C during the first 48 hours after collection. Sample temperature must be confirmed to be at or below 10 °C when the samples are received at the laboratory. Samples stored in the lab must be held at or below 6 °C until extraction but must not be frozen.

NOTE: Samples that are significantly above 10° C, at the time of collection, may need to be iced or refrigerated for a period of time, in order to chill them prior to shipping. This will allow them to be shipped with sufficient ice to meet the above requirements.

8.5. SAMPLE AND EXTRACT HOLDING TIMES – Results of the sample storage stability study (Table 10) indicated that all compounds listed in this method have adequate stability for 14 days when collected, preserved, shipped and stored as described in Sections 8.1, 8.2, and 8.4. Therefore, water samples should be extracted as soon as possible but must be extracted within 14 days. Extracts must be stored at room temperature and analyzed within 28 days after extraction. The extract storage stability study data are presented in Table 11.

9. QUALITY CONTROL

9.1. QC requirements include the Initial Demonstration of Capability (IDC) and ongoing QC requirements that must be met when preparing and analyzing Field Samples. This Section describes the QC parameters, their required frequencies, and the performance criteria that must be met in order to meet EPA quality objectives. The QC criteria discussed in the following sections are summarized in Table 12 and Table 13. These QC requirements are considered the minimum acceptable QC criteria. Laboratories are encouraged to institute additional QC practices to meet their specific needs.

9.1.1. METHOD MODIFICATIONS – The analyst is permitted to modify LC columns, LC conditions, evaporation techniques, internal standards or surrogate standards, and MS and MS/MS conditions. Each time such method modifications are made, the analyst must repeat the procedures of the IDC. **Modifications to LC conditions should still produce conditions such that co-elution of the method analytes is minimized to reduce the probability of suppression/enhancement effects.**

9.2. INITIAL DEMONSTRATION OF CAPABILITY – The IDC must be successfully performed prior to analyzing any Field Samples. Prior to conducting the IDC, the

analyst must first generate an acceptable Initial Calibration following the procedure outlined in Section 10.2.

9.2.1. INITIAL DEMONSTRATION OF BRANCHED vs LINEAR ISOMER PROFILE for PFOA IN A QUALITATIVE STANDARD – Prepare and analyze a qualitative standard used for identifying retention times of branch isomers of PFOA. Identify the retention times of branched isomers of PFOA in the purchased technical grade PFOA standard. This qualitative PFOA standard is not used for quantitation (see Section 12.2). This branched isomer identification check must be repeated any time changes occur that affect the analyte retention times.

9.2.2. INITIAL DEMONSTRATION OF LOW SYSTEM BACKGROUND – Any time a new lot of SPE cartridges, solvents, centrifuge tubes, disposable pipets, and autosampler vials are used, it must be demonstrated that an LRB is reasonably free of contamination and that the criteria in Section 9.3.1 are met. If an automated extraction system is used, an LRB should be extracted on each port to ensure that all the valves and tubing are free from potential PFAS contamination.

9.2.3. INITIAL DEMONSTRATION OF PRECISION (IDP) – Prepare, extract, and analyze four to seven replicate LFBs fortified near the midrange of the initial calibration curve according to the procedure described in Section 11.4. Sample preservatives as described in Section 8.1.2 must be added to these samples. The relative standard deviation (RSD) of the results of the replicate analyses must be less than 20%.

9.2.4. INITIAL DEMONSTRATION OF ACCURACY (IDA) – Using the same set of replicate data generated for Section 9.2.3, calculate average recovery. The average recovery of the replicate values must be within ± 30% of the true value.

9.2.5. INITIAL DEMONSTRATION OF PEAK ASYMMETRY FACTOR – Peak asymmetry factors must be calculated using the equation in Section 9.3.9 for the first two eluting peaks (if only two analytes are being analyzed, both must be evaluated) in a mid-level CAL standard. The peak asymmetry factors must fall in the range of 0.8 to 1.5. See guidance in Section 10.2.4.1 if the calculated peak asymmetry factors do not meet the criteria.

9.2.6. MINIMUM REPORTING LEVEL (MRL) CONFIRMATION – Establish a target concentration for the MRL based on the intended use of the method. The MRL may be established by a laboratory for their specific purpose or may be set by a regulatory agency. Establish an Initial Calibration following the procedure outlined in Section 10.2. The lowest CAL standard used to establish the Initial Calibration (as well as the low-level CCC, Section 10.3) must be at or below the concentration of the MRL. Establishing the MRL concentration too low may cause repeated failure of ongoing QC requirements. Confirm the MRL following the procedure outlined below.

9.2.6.1. Fortify, extract, and analyze seven replicate LFBs at the proposed MRL concentration. These LFBs must contain all method preservatives described in Section 8.1.2. Calculate the mean measured concentration (*Mean*) and standard deviation for these replicates. Determine the Half Range for the prediction interval of results (HR_{PIR}) using the equation below

$$HR_{PIR} = 3.963s$$

where

s = the standard deviation
3.963 = a constant value for seven replicates.[1]

9.2.6.2. Confirm that the upper and lower limits for the Prediction Interval of Result ($PIR = Mean \pm HR_{PIR}$) meet the upper and lower recovery limits as shown below

The Upper PIR Limit must be ≤150% recovery.

$$\frac{Mean + HR_{PIR}}{Fortified\,Concentration} \times 100\% \leq 150\%$$

The Lower PIR Limit must be ≥ 50% recovery.

$$\frac{Mean - HR_{PIR}}{Fortified\,Concentration} \times 100\% \geq 50\%$$

9.2.6.3. The MRL is validated if both the Upper and Lower PIR Limits meet the criteria described above (Sect. 9.2.6.2). If these criteria are not met, the MRL has been set too low and must be determined again at a higher concentration.

9.2.7. CALIBRATION CONFIRMATION – Analyze a QCS as described in Section 9.3.10 to confirm the accuracy of the standards/calibration curve.

9.2.8. DETECTION LIMIT DETERMINATION *(optional) – While DL determination is not a specific requirement of this method, it may be required by various regulatory bodies associated with compliance monitoring. It is the responsibility of the laboratory to determine if DL determination is required based upon the intended use of the data.*

9.2.8.1. Replicate analyses for this procedure should be done over at least three days (i.e., both the sample extraction and the LC/MS/MS analyses should be done over at least three days). Prepare at least seven replicate LFBs at a concentration estimated to be near the DL. This concentration may be estimated by selecting a concentration at 2-5 times the noise level. The DLs in Table 5 were calculated from LFBs fortified at various concentrations as

indicated in the table. The appropriate fortification concentrations will be dependent upon the sensitivity of the LC/MS/MS system used. All preservation reagents listed in Section 8.1.2 must also be added to these samples. Analyze the seven replicates through all steps of Section 11.

NOTE: If an MRL confirmation data set meets these requirements, a DL may be calculated from the MRL confirmation data, and no additional analyses are necessary.

Calculate the *DL* using the following equation

$$DL = s \times t_{(n-1,\,1-\alpha=0.99)}$$

where

s = standard deviation of replicate analyses
$t_{(n\text{-}1,\ 1\text{-}\alpha=0.99)}$ = Student's t value for the 99% confidence level with n-1 degrees of freedom
n = number of replicates.

NOTE: Do not subtract blank values when performing DL calculations. The DL is a statistical determination of precision only.[2] If the DL replicates are fortified at a low enough concentration, it is likely that they will not meet the precision and accuracy criteria for CCCs. Therefore, no precision and accuracy criteria are specified.

9.2.8.2. If a laboratory is establishing their own MRL, the calculated DLs should not be used as the MRL for analytes that commonly occur as background contaminants. Method analytes that are seen in the background should be reported as present in Field Samples, only after careful evaluation of the background levels. It is recommended that a MRL be established at the mean LRB concentrations + 3σ or 3 times the mean LRB concentration, whichever is greater. This value should be calculated over a period of time, to reflect variability in the blank measurements. It is recommended that this value be used as an MRL in order to avoid reporting false positive results.

9.3. ONGOING QC REQUIREMENTS – This Section summarizes the ongoing QC criteria that must be followed when processing and analyzing Field Samples.

9.3.1. LABORATORY REAGENT BLANK (LRB) – An LRB is required with each extraction batch (Sect. 3.6) to confirm that potential background contaminants are not interfering with the identification or quantitation of method analytes. If more than 20 Field Samples are included in a batch, analyze an LRB for every 20 samples. If the LRB produces a peak within the retention time window of any analyte that would prevent the determination of that analyte, determine the source of contamination and eliminate the interference before processing samples. Background contamination must be reduced to an acceptable level before

proceeding. Background from method analytes or other contaminants that interfere with the measurement of method analytes must be below 1/3 of the MRL. Blank contamination is estimated by extrapolation, if the concentration is below the lowest CAL standard. This extrapolation procedure is not allowed for sample results as it may not meet data quality objectives. If the method analytes are detected in the LRB at concentrations equal to or greater than this level, then all data for the problem analyte(s) must be considered invalid for all samples in the extraction batch. Because background contamination is a significant problem for several method analytes, maintaining a historical record of LRB data is highly recommended.

9.3.2. CONTINUING CALIBRATION CHECK (CCC) – CCC Standards are analyzed at the beginning of each analysis batch, after every 10 Field Samples, and at the end of the analysis batch. See Section 10.3 for concentration requirements and acceptance criteria.

9.3.3. LABORATORY FORTIFIED BLANK (LFB) – An LFB is required with each extraction batch (Sect. 3.6). The fortified concentration of the LFB must be rotated between low, medium, and high concentrations from batch to batch. The low concentration LFB must be as near as practical to, but no more than two times, the MRL. Similarly, the high concentration LFB should be near the high end of the calibration range established during the initial calibration (Sect. 10.2). Results of the low-level LFB analyses must be 50-150% of the true value. Results of the medium and high-level LFB analyses must be 70-130% of the true value. If the LFB results do not meet these criteria for method analytes, then all data for the problem analyte(s) must be considered invalid for all samples in the extraction batch.

9.3.4. INTERNAL STANDARDS (IS) – The analyst must monitor the peak areas of the IS(s) in all injections during each analysis day. The IS responses (peak areas) in any chromatographic run must be within 70-140% of the response in the most recent CCC and must not deviate by more than 50% from the average area measured during initial analyte calibration. If the IS areas in a chromatographic run do not meet these criteria, inject a second aliquot of that extract aliquotted into a new capped autosampler vial. Random evaporation losses have been observed with the polypropylene caps causing high IS(s) areas.

9.3.4.1. If the reinjected aliquot produces an acceptable IS response, report results for that aliquot.

9.3.4.2. If the reinjected extract fails again, the analyst should check the calibration by reanalyzing the most recently acceptable CAL standard. If the CAL standard fails the criteria of Section 10.3, recalibration is in order per Section 10.2. If the CAL standard is acceptable, extraction of the sample may need to be repeated provided the sample is still within the holding time.

Otherwise, report results obtained from the reinjected extract, but annotate as suspect. Alternatively, collect a new sample and re-analyze.

9.3.5. SURROGATE RECOVERY – The SUR standard is fortified into all samples, CCCs, LRBs, LFBs, LFSMs, LFSMDs, FD, and FRB prior to extraction. It is also added to the CAL standards. The SUR is a means of assessing method performance from extraction to final chromatographic measurement. Calculate the recovery (%R) for the SUR using the following equation

$$\%R = \left(\frac{A}{B}\right) \times 100$$

where

A = calculated SUR concentration for the QC or Field Sample
B = fortified concentration of the SUR.

9.3.5.1. SUR recovery must be in the range of 70-130%. When SUR recovery from a sample, blank, or CCC is less than 70% or greater than 130%, check 1) calculations to locate possible errors, 2) standard solutions for degradation, 3) contamination, and 4) instrument performance. Correct the problem and reanalyze the extract.

9.3.5.2. If the extract reanalysis meets the SUR recovery criterion, report only data for the reanalyzed extract.

9.3.5.3. If the extract reanalysis fails the 70-130% recovery criterion, the analyst should check the calibration by injecting the last CAL standard that passed. If the CAL standard fails the criteria of Section 10.3, recalibration is in order per Section 10.2. If the CAL standard is acceptable, extraction of the sample should be repeated provided the sample is still within the holding time. If the re-extracted sample also fails the recovery criterion, report all data for that sample as suspect/SUR recovery to inform the data user that the results are suspect due to SUR recovery. Alternatively, collect a new sample and re-analyze.

9.3.6. LABORATORY FORTIFIED SAMPLE MATRIX (LFSM) – Analysis of an LFSM is required in each extraction batch and is used to determine that the sample matrix does not adversely affect method accuracy. Assessment of method precision is accomplished by analysis of a Field Duplicate (FD) (Sect. 9.3.7); however, infrequent occurrence of method analytes would hinder this assessment. If the occurrence of method analytes in the samples is infrequent, or if historical trends are unavailable, a second LFSM, or LFSMD, must be prepared, extracted, and analyzed from a duplicate of the Field Sample. Extraction batches that contain LFSMDs will not require the extraction of a FD. If a variety of different sample matrices are analyzed regularly, for example, drinking water from groundwater and surface water sources, method performance should be

established for each. Over time, LFSM data should be documented by the laboratory for all routine sample sources.

9.3.6.1. Within each extraction batch (Sect. 3.6), a minimum of one Field Sample is fortified as an LFSM for every 20 Field Samples analyzed. The LFSM is prepared by spiking a sample with an appropriate amount of the Analyte PDS (Sect. 7.2.3.2). Select a spiking concentration that is greater than or equal to the matrix background concentration, if known. Use historical data and rotate through the low, mid and high concentrations when selecting a fortifying concentration.

9.3.6.2. Calculate the percent recovery (%*R*) for each analyte using the equation

$$\%R = \frac{(A - B)}{C} \times 100$$

where

A = measured concentration in the fortified sample
B = measured concentration in the unfortified sample
C = fortification concentration.

9.3.6.3. Analyte recoveries may exhibit matrix bias. For samples fortified at or above their native concentration, recoveries should range between 70-130%, except for low-level fortification near or at the MRL (within a factor of 2-times the MRL concentration) where 50-150% recoveries are acceptable. If the accuracy of any analyte falls outside the designated range, and the laboratory performance for that analyte is shown to be in control in the CCCs, the recovery is judged to be matrix biased. The result for that analyte in the unfortified sample is labeled suspect/matrix to inform the data user that the results are suspect due to matrix effects.

9.3.7. FIELD DUPLICATE OR LABORATORY FORTIFIED SAMPLE MATRIX DUPLICATE (FD or LFSMD) – Within each extraction batch (not to exceed 20 Field Samples, Sect. 3.6), a minimum of one FD or LFSMD must be analyzed. Duplicates check the precision associated with sample collection, preservation, storage, and laboratory procedures. If method analytes are not routinely observed in Field Samples, an LFSMD should be analyzed rather than an FD.

9.3.7.1. Calculate the relative percent difference (*RPD*) for duplicate measurements (*FD1* and *FD2*) using the equation

$$RPD = \frac{|FD1 - FD2|}{(FD1 + FD2)/2} \times 100$$

9.3.7.2. RPDs for FDs should be ≤30%. Greater variability may be observed when FDs have analyte concentrations that are within a factor of 2 of the MRL. At these concentrations, FDs should have RPDs that are ≤50%. If the RPD of

any analyte falls outside the designated range, and the laboratory performance for that analyte is shown to be in control in the CCC, the recovery is judged to be matrix biased. The result for that analyte in the unfortified sample is labeled suspect/matrix to inform the data user that the results are suspect due to matrix effects.

9.3.7.3. If an LFSMD is analyzed instead of a FD, calculate the relative percent difference (RPD) for duplicate LFSMs (LFSM and LFSMD) using the equation

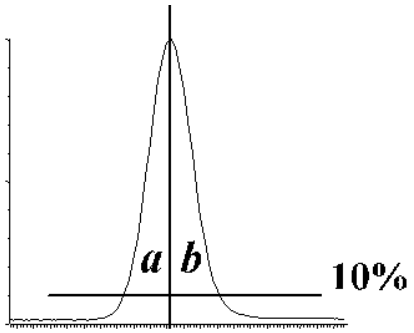
$$RPD = \frac{|LFSM - LFSMD|}{(LFSM + LFSMD)/2} \times 100$$

9.3.7.4. RPDs for duplicate LFSMs must be ≤30% for samples fortified at or above their native concentration. Greater variability may be observed when LFSMs are fortified at analyte concentrations that are within a factor of 2 of the MRL. LFSMs fortified at these concentrations must have RPDs that are ≤50% for samples fortified at or above their native concentration. If the RPD of any analyte falls outside the designated range, and the laboratory performance for that analyte is shown to be in control in the CCC, the recovery is judged to be matrix biased. The result for that analyte in the unfortified sample is labeled suspect/matrix to inform the data user that the results are suspect due to matrix effects.

9.3.8. FIELD REAGENT BLANK (FRB) – The purpose of the FRB is to ensure that PFAS measured in the Field Samples were not inadvertently introduced into the sample during sample collection/handling. Analysis of the FRB is required only if a Field Sample contains a method analyte or analytes at or above the MRL. The FRB is processed, extracted and analyzed in exactly the same manner as a Field Sample. If the method analyte(s) found in the Field Sample is present in the FRB at a concentration greater than 1/3 the MRL, then all samples collected with that FRB are invalid and must be recollected and reanalyzed.

9.3.9. PEAK ASYMMETRY FACTOR – A peak asymmetry factor must be calculated using the equation below during the IDC and every time chromatographic changes are made that may affect peak shape. The peak asymmetry factor for the first two eluting peaks in a mid-level CAL standard (if only two analytes are being analyzed, both must be evaluated) must fall in the range of 0.8 to 1.5. Modifying the standard or extract composition to more aqueous content to prevent poor shape is not permitted. See guidance in Section 10.2.4.1 if the calculated peak asymmetry factors do not meet the criteria.

$$A_s = \frac{b}{a}$$



where:

A_s = peak asymmetry factor

B = width of the back half of the peak measured (at 10% peak height) from the trailing edge of the peak to a line dropped perpendicularly from the peak apex

a = the width of the front half of the peak measured (at 10% peak height) from the leading edge of the peak to a line dropped perpendicularly from the apex.

9.3.10. QUALITY CONTROL SAMPLES (QCS) – As part of the IDC (Sect. 9.2), each time a new Analyte PDS (Sect. 7.2.3.2) is prepared, and at least quarterly, analyze a QCS sample from a source different from the source of the CAL standards. If a second vendor is not available, then a different lot of the standard should be used. The QCS should be prepared at a mid-level concentration and analyzed just like a CCC. Acceptance criteria for the QCS are identical to the CCCs; the calculated amount for each analyte must be ± 30% of the expected value. If measured analyte concentrations are not of acceptable accuracy, check the entire analytical procedure to locate and correct the problem.

10. CALIBRATION AND STANDARDIZATION

10.1. Demonstration and documentation of acceptable initial calibration is required before any samples are analyzed. After the initial calibration is successful, a CCC is required at the beginning and end of each period in which analyses are performed, and after every tenth Field Sample.

10.2. INITIAL CALIBRATION

10.2.1. ESI-MS/MS TUNE

10.2.1.1. Calibrate the mass scale of the MS with the calibration compounds and procedures prescribed by the manufacturer.

10.2.1.2. Optimize the $[M-H]^-$ or $[M-CO_2]^-$ for each method analyte by infusing approximately 0.5-1.0 µg/mL of each analyte (prepared in the initial mobile phase conditions) directly into the MS at the chosen LC mobile phase flow

rate (approximately 0.3 mL/min). This tune can be done on a mix of the method analytes. The MS parameters (voltages, temperatures, gas flows, etc.) are varied until optimal analyte responses are determined. The method analytes may have different optima requiring some compromise between the optima. See Table 2 for ESI-MS conditions used in method development.

10.2.1.3. Optimize the product ion (Sect. 3.18) for each analyte by infusing approximately 0.5-1.0 µg/mL of each analyte (prepared in the initial mobile phase conditions) directly into the MS at the chosen LC mobile phase flow rate (approximately 0.3 mL/min). This tune can be done on a mix of the method analytes. The MS/MS parameters (collision gas pressure, collision energy, etc.) are varied until optimal analyte responses are determined. Typically, the carboxylic acids have very similar MS/MS conditions and the sulfonic acids have similar MS/MS conditions. See Table 4 for MS/MS conditions used in method development.

10.2.2. Establish LC operating parameters that optimize resolution and peak shape. Suggested LC conditions can be found in Table 1. The LC conditions listed in Table 1 may not be optimum for all LC systems and may need to be optimized by the analyst (See Sect. 10.2.4.1). Modifying the standard or extract composition to more aqueous content to prevent poor shape is not permitted.

Cautions: LC system components, as well as the mobile phase constituents, contain many of the analytes in this method. Thus, these PFAS will build up on the head of the LC column during mobile phase equilibration. To minimize the background PFAS peaks and to keep background levels constant, the time the LC column sits at initial conditions must be kept constant and as short as possible (while ensuring reproducible retention times). In addition, prior to daily use, flush the column with 100% methanol for at least 20 min before initiating a sequence. It may be necessary on some systems to flush other LC components such as wash syringes, sample needles or any other system components before daily use.

Mobile phase modifiers other than 20 mM ammonium acetate may be used at the discretion of the analyst, provided that the retention time stability criteria in Sect. 11.7.2 can be met over a period of two weeks. During method development, retention times shifted to shorter and shorter times as days progressed when mobile phases with less than 20 mM ammonium acetate were used.

10.2.3. Inject a mid-level CAL standard under LC/MS conditions to obtain the retention times of each method analyte. Divide the chromatogram into retention time windows each of which contains one or more chromatographic peaks. During MS/MS analysis, fragment a small number of selected precursor ions ($[M-H]^-$; Sect. 3.16) for the analytes in each window and choose the most abundant product

ion. The product ions (also the quantitation ions) chosen during method development are in Table 4, although these will be instrument dependent. For maximum sensitivity, small mass windows of ±0.5 daltons around the product ion mass were used for quantitation.

NOTE: There have been reports[10] that not all product ions in the linear PFOS are produced in all branched PFOS isomers. (This phenomenon may exist for many of the PFAS.) Thus, to reduce PFOS, PFBS and PFHxS bias, it is required that the precursor *m/z* → *m/z* 80 transition be used as the quantitation transition. Some MS/MS instruments, may not be able to scan a product ion with such a wide mass difference from the precursor ion; therefore, if the MS/MS cannot measure the precursor *m/z* → *m/z* 80 transition they may not be used for this method if PFOS, PFBS, or PFHxS analysis is to be conducted.

10.2.4. Inject a mid-level CAL standard under optimized LC/MS/MS conditions to ensure that each method analyte is observed in its MS/MS window and that there are at least 10 scans across the peak for optimum precision.

NOTE: Ensure that the retention time window used to collect data for each analyte is sufficient to detect earlier eluting branched isomers.

10.2.4.1. If broad, split or fronting peaks are observed for the first two eluting chromatographic peaks (if only two analytes are being analyzed, both must be evaluated), change the initial mobile phase conditions to higher aqueous content until the peak asymmetry ratio for each peak is 0.8 – 1.5. The peak asymmetry factor is calculated as described in Section 9.3.9 on a mid-level CAL standard. The peak asymmetry factor must meet the above criteria for the first two eluting peaks during the IDC and every time a new calibration curve is generated. Modifying the standard or extract composition to more aqueous content to prevent poor shape is not permitted.

10.2.4.2. Most PFAS are produced by two different processes. One process gives rise to linear PFAS only while the other process produces both linear and branched isomers. Thus, both branched and linear PFAS can potentially be found in the environment. Refer to Section 12.2 for guidance on integration and quantitation of PFAS.

10.2.5. Prepare a set of at least five CAL standards as described in Section 7.2.4. The lowest concentration CAL standard must be at or below the MRL, which may depend on system sensitivity. It is recommended that at least four of the CAL standards are at a concentration greater than or equal to the MRL.

10.2.6. The LC/MS/MS system is calibrated using the IS technique. Use the LC/MS/MS data system software to generate a linear regression or quadratic calibration curve

for each of the analytes. This curve **must always** be forced through zero and may be concentration weighted, if necessary. Forcing zero allows for a better estimate of the background levels of method analytes.

10.2.7. CALIBRATION ACCEPTANCE CRITERIA – Validate the initial calibration by calculating the concentration of each analyte as an unknown against its regression equation. For calibration levels that are ≤ MRL, the result for each analyte must be within ± 50% of the true value. All other calibration points must calculate to be within ± 30% of their true value. If these criteria cannot be met, the analyst will have difficulty meeting ongoing QC criteria. It is recommended that corrective action is taken to reanalyze the CAL standards, restrict the range of calibration, or select an alternate method of calibration (forcing the curve through zero is still required).

CAUTION: When acquiring MS/MS data, LC operating conditions must be carefully reproduced for each analysis to provide reproducible retention times. If this is not done, the correct ions will not be monitored at the appropriate times. As a precautionary measure, the chromatographic peaks in each window must not elute too close to the edge of the segment time window.

10.3. CONTINUING CALIBRATION CHECK (CCC) – Minimum daily calibration verification is as follows. Verify the initial calibration at the beginning and end of each group of analyses, and after every tenth sample during analyses. In this context, a "sample" is considered to be a Field Sample. LRBs, CCCs, LFBs, LFSMs, FDs FRBs and LFSMDs are not counted as samples. The beginning CCC of each analysis batch must be at or below the MRL to verify instrument sensitivity prior to any analyses. If standards have been prepared such that all low CAL points are not in the same CAL solution, it may be necessary to analyze two CAL standards to meet this requirement. Alternatively, the analyte concentrations in the analyte PDS may be customized to meet these criteria. Subsequent CCCs should alternate between a medium and high concentration CAL standard.

10.3.1. Inject an aliquot of the appropriate concentration CAL standard and analyze with the same conditions used during the initial calibration.

10.3.2. Determine that the absolute areas of the quantitation ions of the IS(s) are within 70-140% of the areas measured in the most recent continuing calibration check, and within 50-150% from the average areas measured during initial calibration. If any of the IS areas has changed by more than these amounts, adjustments must be made to restore system sensitivity. These adjustments may include cleaning of the MS ion source, or other maintenance as indicated in Section 10.3.4. Major instrument maintenance requires recalibration (Sect. 10.2) and verification of sensitivity by analyzing a CCC at or below the MRL (Sect. 10.3). Control charts are useful aids in documenting system sensitivity changes.

10.3.3. Calculate the concentration of each analyte and SUR in the CCC. The calculated amount for each analyte and SUR for medium and high level CCCs must be within ± 30% of the true value. The calculated amount for the lowest calibration point for each analyte must be within ± 50% and the SUR must be within ± 30% of the true value. If these conditions do not exist, then all data for the problem analyte must be considered invalid, and remedial action should be taken (Sect. 10.3.4) which may require recalibration. Any Field or QC Samples that have been analyzed since the last acceptable calibration verification that are still within holding time must be reanalyzed after adequate calibration has been restored, with the following exception. **If the CCC fails because the calculated concentration is greater than 130% (150% for the low-level CCC) for a particular method analyte, and Field Sample extracts show no detection for that method analyte, non-detects may be reported without re-analysis.**

10.3.4. REMEDIAL ACTION – Failure to meet CCC QC performance criteria may require remedial action. Major maintenance, such as cleaning the electrospray probe, atmospheric pressure ionization source, cleaning the mass analyzer, replacing the LC column, etc., requires recalibration (Sect. 10.2) and verification of sensitivity by analyzing a CCC at or below the MRL (Sect. 10.3)

11. PROCEDURE

11.1. This procedure may be performed manually or in an automated mode using a robotic or automatic sample preparation device. The data presented in Tables 5-11 demonstrate data collected by manual extraction. If an automated system is used to prepare samples, follow the manufacturer's operating instructions, but all extraction and elution steps must be the same as in the manual procedure. Extraction and/or elution steps may not be changed or omitted to accommodate the use of an automated system. If an automated system is used, the LRBs should be rotated among the ports to ensure that all the valves and tubing meet the LRB requirements (Sect. 9.3.1).

11.2. Some of the PFAS adsorb to surfaces, including polypropylene. Therefore, the aqueous sample bottles must be rinsed with the elution solvent (Sect. 11.4.4) whether extractions are performed manually or by automation. The bottle rinse is passed through the cartridge to elute the method analytes and is then collected (Sect. 11.4.4).

NOTE: The SPE cartridges and sample bottles described in this Section are designed as single use items and must be discarded after use. They may not be refurbished for reuse in subsequent analyses.

11.3. SAMPLE PREPARATION

11.3.1. Samples are preserved, collected and stored as presented in Section 8. All Field and QC Samples, including the LRB, LFB and FRB, must contain the dechlorinating agent listed in Section 8.1.2. Before extraction, verify that the sample pH is 7 ± 0.5. Determine sample volume. An indirect measurement may

be done in one of two ways: by marking the level of the sample on the bottle or by weighing the sample and bottle to the nearest 1 g. After extraction, proceed to Section 11.6 for final volume determination. Some of the PFAS adsorb to surfaces, thus the sample volume may **NOT** be transferred to a graduated cylinder for volume measurement. The LRB, LFB and FRB may be prepared by measuring 250 mL of reagent water with a polypropylene graduated cylinder or filling a 250-mL sample bottle to near the top.

11.3.2. Add an aliquot of the SUR PDS (Sect. 7.2.2.2) to each sample, cap and invert to mix. During method development, a 10-µL aliquot of the 1-4 ng/µL SUR PDS (Sect. 7.2.2.2) was added to 250 mL of sample for a final concentration of 40 ng/L for $^{13}C_2$-PFHxA, $^{13}C_3$-HFPO-DA, and $^{13}C_2$-PFDA and 160 ng/L for d_5-NEtFOSAA.

11.3.3. In addition to the SUR(s) and dechlorination agent, if the sample is an LFB, LFSM, or LFSMD, add the necessary amount of analyte PDS (Sect. 7.2.3.2). Cap and invert each sample to mix.

11.4. CARTRIDGE SPE PROCEDURE

11.4.1. CARTRIDGE CLEAN-UP AND CONDITIONING – DO NOT allow cartridge packing material to go dry during any of the conditioning steps. Rinse each cartridge with 15 mL of methanol. Next, rinse each cartridge with 18 mL of reagent water, without allowing the water to drop below the top edge of the packing. If the cartridge goes dry during the conditioning phase, the conditioning must be started over. Add 2-3 mL of reagent water to each cartridge, attach the sample transfer tubes (Sect. 6.9.3), turn on the vacuum, and begin adding sample to the cartridge.

NOTE: If low recoveries are observed for PFBS and PFHxA during the IDC, recoveries may be improved by allowing a one- or two-minute soak time after each addition of the methanol and water used in the clean-up and conditioning step.

11.4.2. SAMPLE EXTRACTON – Adjust the vacuum so that the approximate flow rate is 10-15 mL/min. Do not allow the cartridge to go dry before all the sample has passed through.

11.4.3. SAMPLE BOTTLE AND CARTRIDGE RINSE – After the entire sample has passed through the cartridge, rinse the sample bottles with two 7.5-mL aliquots of reagent water and draw each aliquot through the sample transfer tubes and the cartridges. Draw air or nitrogen through the cartridge for 5 min at high vacuum (10-15 in. Hg).

NOTE: If empty plastic reservoirs are used in place of the sample transfer tubes to pass the samples through the cartridges, these reservoirs

must be treated like the transfer tubes. After the entire sample has passed through the cartridge, the reservoirs must be rinsed to waste with reagent water.

11.4.4. SAMPLE BOTTLE AND CARTRIDGE ELUTION – Turn off and release the vacuum. Lift the extraction manifold top and insert a rack with collection tubes into the extraction tank to collect the extracts as they are eluted from the cartridges. Rinse the sample bottles with 4 mL of methanol and elute the analytes from the cartridges by pulling the 4 mL of methanol through the sample transfer tubes and the cartridges. Use a low vacuum such that the solvent exits the cartridge in a dropwise fashion. Repeat sample bottle rinse and cartridge elution with a second 4-mL aliquot of methanol.

NOTE: If low recoveries are observed for PFBS and PFHxA during the IDC, recoveries may be improved by allowing a one or two-minute soak time after each four mL addition of the methanol and water used in the clean-up and conditioning step.

NOTE: If empty plastic reservoirs are used in place of the sample transfer tubes to pass the samples through the cartridges, these reservoirs must be treated like the transfer tubes. After the reservoirs have been rinsed in Section 11.4.3, the elution solvent used to rinse the sample bottles must be swirled down the sides of the reservoirs while eluting the cartridge to ensure that any method analytes on the surface of the reservoirs are transferred to the extract.

11.5. EXTRACT CONCENTRATION – Concentrate the extract to dryness under a gentle stream of nitrogen in a heated water bath (60-65 °C) to remove all the water/methanol mix. Add the appropriate amount of 96:4% (vol/vol) methanol:water solution and the IS PDS (Sect. 7.2.1.2) to the collection vial to bring the volume to 1 mL and vortex. (10 µL of the 1-4 ng/µL IS PDS for extract concentrations of 10-40 ng/mL were used for method development). Transfer a small aliquot with a plastic pipet (Sect. 6.7) to a polypropylene autosampler vial.

NOTE: It is recommended that the entire 1-mL aliquot not be transferred to the autosampler vial because the polypropylene autosampler caps do not reseal after injection. Therefore, do not store the extracts in the autosampler vials as evaporation losses occur in these autosampler vials. Extracts can be stored in 15-mL centrifuge tubes (Sect. 6.3).

11.6. SAMPLE VOLUME DETERMINATION – If the level of the sample was marked on the sample bottle, use a graduated cylinder to measure the volume of water required to fill the original sample bottle to the mark made prior to extraction. Determine to the nearest 2 mL. If using weight to determine volume, weigh the empty bottle to the nearest 1 g and determine the sample weight by subtraction of the empty bottle weight from the original sample weight (Sect. 11.3.1). Assume a sample density of 1.0 g/mL.

In either case, the sample volume will be used in the final calculations of the analyte concentration (Sect. 12.3).

11.7. EXTRACT ANALYSIS

11.7.1. Establish operating conditions equivalent to those summarized in Tables 1-4 of Section 17. Instrument conditions and columns should be optimized prior to the initiation of the IDC.

11.7.2. Establish an appropriate retention time window for each analyte. This should be based on measurements of actual retention time variation for each method analyte in CAL standard solutions analyzed on the LC over the course of time. A value of plus or minus three times the standard deviation of the retention time obtained for each method analyte while establishing the initial calibration and completing the IDC can be used to calculate a suggested window size. However, the experience of the analyst should weigh heavily on the determination of the appropriate retention window size.

11.7.3. Calibrate the system by either the analysis of a calibration curve (Sect. 10.2) or by confirming the initial calibration is still valid by analyzing a CCC as described in Section 10.3. If establishing an initial calibration for the first time, complete the IDC as described in Section 9.2.

11.7.4. Begin analyzing Field Samples, including QC samples, at their appropriate frequency by injecting the same size aliquots (10 µL was used in method development), under the same conditions used to analyze the CAL standards.

11.7.5. At the conclusion of data acquisition, use the same software that was used in the calibration procedure to identify peaks of interest in predetermined retention time windows. Use the data system software to examine the ion abundances of the peaks in the chromatogram. Identify an analyte by comparison of its retention time with that of the corresponding method analyte peak in a reference standard. Comparison of the MS/MS mass spectra is not particularly useful given the limited ±0.5 dalton mass range around a single product ion for each method analyte.

11.7.6. The analyst must not extrapolate beyond the established calibration range. If an analyte peak area exceeds the range of the initial calibration curve, the extract may be diluted with 96%:4% (vol/vol) methanol:water solution and the appropriate amount of IS added to match the original concentration. Re-inject the diluted extract. Incorporate the dilution factor into the final concentration calculations. Acceptable SUR performance (Sect. 9.3.5.1) should be determined from the undiluted sample extract. The resulting data must be documented as a dilution and MRLs adjusted accordingly.

12. DATA ANALYSIS AND CALCULATION

12.1. Complete chromatographic resolution is not necessary for accurate and precise measurements of analyte concentrations using MS/MS. In validating this method, concentrations were calculated by measuring the product ions listed in Table 4. Other ions may be selected at the discretion of the analyst.

12.2. Because environmental samples may contain both branched and linear isomers for method analytes, but quantitative standards that contain the linear and branched isomers do not exist for all method analytes, integration and quantitation of the PFAS is dependent on type of standard available for each PFAS. It is recognized that some of the procedures described below for integration of standards, QC samples and Field Samples may cause a small amount of unavoidable bias in the quantitation of the method analytes due to the current state of the commercially available standards.

12.2.1. During method development, multiple chromatographic peaks were observed for standards of PFHxS, PFOS, NMeFOSAA, and NEtFOSAA using the LC conditions in Table 1 due to chromatographic resolution of the linear and branched isomers of these compounds. For PFHxS, PFOS, NMeFOSAA and NEtFOSAA, all the chromatographic peaks observed in the standard must be integrated and the areas summed. Chromatographic peaks in all Field Samples and QC samples must be integrated in the same way as the CAL standard for analytes with quantitative standards containing the branched and linear isomers.

12.2.2. For PFOA, identify the branched isomers by analyzing a qualitative standard that includes both linear and branched isomers and compare retention times and tandem mass spectrometry transitions. Quantitate Field Samples and QC samples by integrating the total response (i.e., accounting for peaks that are identified as linear and branched isomers) and relying on the initial calibration with a linear-isomer quantitative PFOA standard.

12.2.3. If standards containing the branched and linear isomers cannot be purchased (i.e., only linear isomer is available), only the linear isomer can be identified and quantitated in Field Samples and QC samples using the linear standard because the retention time of the branched isomers cannot be confirmed.

12.3. Calculate analyte and SUR concentrations using the multipoint calibration as described in Section 10.2. Do not use daily calibration verification data to quantitate analytes in samples. Adjust final analyte concentrations to reflect the actual sample volume determined in Section 11.6.

12.4. Prior to reporting the data, the chromatogram should be reviewed for any incorrect peak identification or poor integration.

12.5. Calculations must utilize all available digits of precision, but final reported concentrations should be rounded to an appropriate number of significant figures (one digit of uncertainty), typically two, and not more than three significant figures.

NOTE: Some data in Section 17 of this method are reported with more than two significant figures. This is done to better illustrate the method performance.

13. METHOD PERFORMANCE

13.1. PRECISION, ACCURACY, AND MINIMUM REPORTING LEVELS – Tables for these data are presented in Section 17. LCMRLs and DLs for each method analyte are presented in Table 5. Precision and accuracy are presented for four water matrices: reagent water (Table 6); chlorinated (finished) ground water (Table 7); chlorinated (finished) surface water (Table 8); and private well water (Table 9).

13.2. SAMPLE STORAGE STABILITY STUDIES – An analyte storage stability study was conducted by fortifying the analytes into chlorinated surface water samples that were collected, preserved, and stored as described in Section 8. The precision and mean recovery (n=4) of analyses, conducted on Days 0, 8, and 14 are presented in Table 10.

13.3. EXTRACT STORAGE STABILITY STUDIES – Extract storage stability studies were conducted on extracts obtained from a chlorinated surface water fortified with the method analytes. The precision and mean recovery (n=4) of injections conducted on Days 0, 8, 14, 22, and 28 are reported in Table 11.

13.4. MULTI-LABORATORY DEMONSTRATION – The performance of this method was demonstrated by multiple laboratories, with results similar to those reported in Section 17. The authors wish to acknowledge the work of 1) EPA Region 2 in Edison, NJ., 2) Eurofins Eaton Analytical, LLC in Monrovia, CA, and 3) New Jersey Department of Health in Ewing, NJ.

14. POLLUTION PREVENTION

14.1. This method utilizes SPE to extract analytes from water. It requires the use of very small volumes of organic solvent and very small quantities of pure analytes, thereby minimizing the potential hazards to both the analyst and the environment as compared to the use of large volumes of organic solvents in conventional liquid-liquid extractions.

14.2. For information about pollution prevention that may be applicable to laboratory operations, consult "Less is Better: Laboratory Chemical Management for Waste Reduction" available from the American Chemical Society's Department of Government Relations and Science Policy, 1155 16th Street N.W., Washington, D.C., 20036 or on-line at http://membership.acs.org/c/ccs/pub_9.htm (accessed August 2008).

15. WASTE MANAGEMENT

The analytical procedures described in this method generate relatively small amounts of waste since only small amounts of reagents and solvents are used. The matrices of concern are finished drinking water or source water. However, laboratory waste management practices must be conducted consistent with all applicable rules and regulations, and that laboratories protect the air, water, and land by minimizing and controlling all releases from fume hoods and bench operations. Also, compliance is required with any sewage discharge permits and regulations, particularly the hazardous waste identification rules and land disposal restrictions.

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17. TABLES, DIAGRAMS, FLOWCHARTS AND VALIDATION DATA

Table 1. LC Method Conditions

Time (min)	% 20 mM ammonium acetate	% Methanol
Initial	60.0	40.0
1.0	60.0	40.0
25.0	10.0	90.0
32.0	10.0	90.0
32.1	60.0	40.0
37.0	60.0	40.0
Waters Atlantis® dC_{18} 2.1 x 150 mm packed with 5.0 µm C_{18} stationary phase Flow rate of 0.3 mL/min 10 µL injection into a 50 µL loop		

Table 2. ESI-MS Method Conditions

ESI Conditions	
Polarity	Negative ion
Capillary needle voltage	-3 kV
Cone gas flow	50 L/hr
Nitrogen desolvation gas	800 L/hr
Desolvation gas temp.	350°C

Table 3. Method Analytes, Retention Times (RT) and Suggested IS References

Analyte	Peak # (Fig. 1)	RT (min)	IS# Ref
PFBS	1	7.62	2
PFHxA	2	10.42	1
HFPO-DA	4	11.38	1
PFHpA	6	13.40	1
PFHxS	7	13.58	2
ADONA	8	13.73	1
PFOA	9	15.85	1
PFOS	11	17.91	2
PFNA	13	17.92	1
9Cl-PF3ONS	14	18.91	2
PFDA	15	19.69	1
NMeFOSAA	17	20.50	3
PFUnA	19	21.21	1
NEtFOSAA	20	21.26	3
11Cl-PF3OUdS	22	21.84	2
PFDoA	23	22.52	1
PFTrDA	24	23.66	1
PFTA	25	24.64	1
$^{13}C_2$-PFHxA	3	10.42	1
$^{13}C_3$-HFPO-DA	5	11.40	1
$^{13}C_2$-PFDA	16	19.69	1
d_5-NEtFOSAA	21	21.24	3
$^{13}C_2$-PFOA– IS#1	10	15.85	-
$^{13}C_4$-PFOS– IS#2	12	17.91	-
d_3-NMeFOSAA–IS#3	18	20.49	-

Table 4. MS/MS Method Conditions[a]

Segment[b]	Analyte	Precursor Ion[c] *(m/z)*	Product Ion[c,d] *(m/z)*	Cone Voltage (v)	Collision Energy[e] (v)
1	PFBS[g]	299	80	42	30
1	PFHxA	313	269	14	10
1	HFPO-DA	285[f]	169	12	8
2	PFHpA	363	319	12	10
2	PFHxS[g,h]	399	80	46	32
2	ADONA	377	251	14	12
3	PFOA	413	369	14	10
3	PFOS[g,h]	499	80	52	42
3	PFNA	463	419	16	12
4	9Cl-PF3ONS	531	351	34	24
4	PFDA	513	469	14	10
4	NMeFOSAA[g]	570	419	30	20
4	PFUnA	563	519	12	10
4	NEtFOSAA[g]	584	419	30	20
4	11Cl-PF3OUdS	631	451	40	24
4	PFDoA	613	569	18	10
5	PFTrDA	663	619	14	14
5	PFTA	713	669	14	12
1	$^{13}C_2$-PFHxA	315	270	16	10
1	$^{13}C_3$-HFPO-DA	287	169	10	6
4	$^{13}C_2$-PFDA	515	470	18	10
4	d_5-NEtFOSAA	589	419	28	22
3	$^{13}C_2$-PFOA	415	370	16	10
3	$^{13}C_4$-PFOS	503	80	58	42
4	d_3-NMeFOSAA	573	419	28	14

[a] An LC/MS/MS chromatogram of the analytes is shown in Figure 1.

[b] Segments are time durations in which single or multiple scan events occur.

[c] Precursor and product ions listed in this table are nominal masses. During MS and MS/MS optimization, the analyst should determine precursor and product ion masses to one decimal place by locating the apex of the mass spectral peak place (e.g., *m/z* 498.9→79.9 for PFOS). These precursor and product ion masses (with at least one decimal place) should be used in the MS/MS method for all analyses.

[d] Ions used for quantitation purposes.

[e] Argon used as collision gas at a flow rate of 0.15 mL/min.

[f] HFPO-DA is not stable in the ESI source and the $[M-H]^-$ is not observed under typical ESI conditions. The precursor ion used during method development was $[M-CO_2]^-$.

[g] Analyte has multiple resolved chromatographic peaks due to linear and branched isomers. All peaks summed for quantitation purposes.

[h] To reduce bias regarding detection of branch and linear isomers, the *m/z* 80 product ion must be used for this analyte.

Table 5. DLs and LCMRLs in Reagent Water

Analyte	Fortified Conc. (ng/L)[a]	DL[b] (ng/L)	LCMRL[c] (ng/L)
PFBS	4.0	1.8	6.3
PFHxA	4.0	1.0	1.7
HFPO-DA	4.0	1.9	4.3
PFHpA	4.0	0.71	0.63
PFHxS	4.0	1.4	2.4
ADONA	4.0	0.88	0.55
PFOA	4.0	0.53	0.82
PFOS	4.0	1.1	2.7
PFNA	4.0	0.70	0.83
9Cl-PF3ONS	4.0	1.4	1.8
PFDA	4.0	1.6	3.3
NMeFOSAA	4.0	2.4	4.3
PFUnA	4.0	1.6	5.2
NEtFOSAA	4.0	2.8	4.8
11Cl-PF3OUdS	4.0	1.5	1.5
PFDoA	4.0	1.2	1.3
PFTrDA	4.0	0.72	0.53
PFTA	4.0	1.1	1.2

[a] Spiking concentration used to determine DL.

[b] Detection limits were determined by analyzing seven replicates over three days according to Section 9.2.8.

[c] LCMRLs were calculated according to the procedure in reference 1.

Table 6. Precision and Accuracy (n=8) of PFAS in Fortified Reagent Water

18. Analyte	Fortified Conc. (ng/L)	Mean % Recovery	% RSD	Fortified Conc. (ng/L)	Mean % Recovery	% RSD
PFBS	16.0	90.8	6.8	80.0	85.1	6.7
PFHxA	16.0	101	8.0	80.0	96.5	4.6
HFPO-DA	16.0	97.8	1.8	80.0	96.8	5.1
PFHpA	16.0	105	3.3	80.0	104	2.7
PFHxS	16.0	109	6.7	80.0	107	4.4
ADONA	16.0	108	1.3	80.0	106	3.6
PFOA	16.0	106	1.8	80.0	104	3.1
PFOS	16.0	111	4.7	80.0	107	4.8
PFNA	16.0	110	2.6	80.0	104	3.6
9Cl-PF3ONS	16.0	108	8.8	80.0	101	3.8
PFDA	16.0	111	2.4	80.0	107	3.6
NMeFOSAA	16.0	104	5.2	80.0	102	5.4
PFUnA	16.0	107	2.8	80.0	101	1.3
NEtFOSAA	16.0	97.7	6.8	80.0	101	2.5
11Cl-PF3OUdS	16.0	109	3.4	80.0	103	6.1
PFDoA	16.0	101	7.2	80.0	107	3.7
PFTrDA	16.0	108	2.6	80.0	99.1	3.6
PFTA	16.0	110	0.9	80.0	97.2	3.6
$^{13}C_2$-PFHxA	40.0	88.5	6.4	40.0	97.0	4.9
$^{13}C_3$-HFPO-DA	40.0	94.5	3.2	40.0	101	9.9
$^{13}C_2$-PFDA	40.0	99.1	3.4	40.0	106	2.7
d_5-NEtFOSAA	160	90.0	2.6	160	99.5	4.8

Table 7. Precision and Accuracy (n=4) of PFAS in Tap Water[a] from a Ground Water Source

19. Analyte	Fortified Conc. (ng/L)	Mean % Recovery	% RSD	Fortified Conc. (ng/L)	Mean % Recovery	% RSD
PFBS	16.0	104	3.1	80.0	90.2	2.1
PFHxA	16.0	105	3.5	80.0	91.6	3.9
HFPO-DA	16.0	99.6	4.0	80.0	90.6	2.9
PFHpA	16.0	101	3.4	80.0	91.2	4.2
PFHxS	16.0	110.0	3.3	80.0	93.5	4.8
ADONA	16.0	104	3.9	80.0	92.2	4.7
PFOA	16.0	105	2.7	80.0	91.1	4.8
PFOS	16.0	108	3.3	80.0	93.9	3.8
PFNA	16.0	105	2.4	80.0	92.4	6.9
9Cl-PF3ONS	16.0	101	8.1	80.0	92.4	4.9
PFDA	16.0	102	4.5	80.0	92.5	7.7
NMeFOSAA	16.0	92.6	7.4	80.0	87.1	9.4
PFUnA	16.0	104	4.8	80.0	92.8	5.6
NEtFOSAA	16.0	108	18.4	80.0	94.1	6.7
11Cl-PF3OUdS	16.0	103	3.4	80.0	95.4	5.4
PFDoA	16.0	99.4	4.6	80.0	92.0	5.0
PFTrDA	16.0	98.8	4.1	80.0	93.1	5.9
PFTA	16.0	102	3.7	80.0	93.9	5.0
$^{13}C_2$-PFHxA	40.0	97.7	3.4	40.0	87.0	6.2
$^{13}C_3$-HFPO-DA	40.0	97.2	3.9	40.0	88.8	6.2
$^{13}C_2$-PFDA	40.0	97.5	5.3	40.0	86.0	10
d_5-NEtFOSAA	160	94.7	8.8	160	80.8	10

[a] TOC = 0.53 mg/L and hardness = 377 mg/L measured as calcium carbonate.

Table 8. Precision and Accuracy (n=4) Of PFAS in Tap Water[a] from a Surface Water Source

20. Analyte	Fortified Conc. (ng/L)	Mean % Recovery	% RSD	Fortified Conc. (ng/L)	Mean % Recovery	% RSD
PFBS	16.0	91.6	3.8	80.0	91.9	7.1
PFHxA	16.0	92.0	5.5	80.0	99.3	4.0
HFPO-DA	16.0	88.6	1.3	80.0	102	2.2
PFHpA	16.0	95.5	3.6	80.0	101	3.3
PFHxS	16.0	99.1	2.5	80.0	102	0.9
ADONA	16.0	95.5	2.9	80.0	102	3.5
PFOA	16.0	97.9	5.2	80.0	98.8	3.9
PFOS	16.0	93.5	5.9	80.0	101	2.4
PFNA	16.0	96.4	3.4	80.0	101	2.8
9Cl-PF3ONS	16.0	93.1	4.6	80.0	102	3.3
PFDA	16.0	95.3	1.7	80.0	99.2	3.3
NMeFOSAA	16.0	99.3	7.2	80.0	94.9	4.5
PFUnA	16.0	99.8	1.7	80.0	100	4.1
NEtFOSAA	16.0	93.3	8.0	80.0	90.5	3.9
11Cl-PF3OUdS	16.0	97.6	6.7	80.0	97.5	3.1
PFDoA	16.0	88.0	1.8	80.0	97.0	2.7
PFTrDA	16.0	94.7	2.5	80.0	95.5	1.8
PFTA	16.0	94.1	5.9	80.0	97.8	3.3
$^{13}C_2$-PFHxA	40.0	86.3	2.8	40.0	90.6	4.1
$^{13}C_3$-HFPO-DA	40.0	92.9	2.4	40.0	101	1.8
$^{13}C_2$-PFDA	40.0	89.3	4.3	40.0	95.8	2.2
d_5-NEtFOSAA	160	86.5	5.4	160	83.1	4.4

[a] TOC = 2.4 mg/L and hardness = 103 mg/L measured as calcium carbonate.

Table 9. Precision and Accuracy (n=4) Of PFAS in Tap Water[a] from a Private Well

21. Analyte	Fortified Conc. (ng/L)	Mean % Recovery	% RSD
PFBS	80.0	99.7	3.1
PFHxA	80.0	96.3	2.7
HFPO-DA	80.0	94.2	4.3
PFHpA	80.0	97.4	1.9
PFHxS	80.0	99.4	4.0
ADONA	80.0	98.7	2.8
PFOA	80.0	97.2	1.5
PFOS	80.0	100	1.9
PFNA	80.0	99.4	1.3
9Cl-PF3ONS	80.0	101	2.2
PFDA	80.0	98.7	2.3
NMeFOSAA	80.0	93.2	4.6
PFUnA	80.0	98.8	1.7
NEtFOSAA	80.0	94.4	0.6
11Cl-PF3OUdS	80.0	99.8	2.5
PFDoA	80.0	99.3	1.9
PFTrDA	80.0	96.2	1.3
PFTA	80.0	97.9	1.2
$^{13}C_2$-PFHxA	40.0	89.9	2.7
$^{13}C_3$-HFPO-DA	40.0	95.7	5.3
$^{13}C_2$-PFDA	40.0	92.3	1.8
d_5-NEtFOSAA	160	86.3	4.5

[a] TOC = 0.56 mg/L and hardness = 394 mg/L measured as calcium carbonate.

Table 10. Aqueous Sample Holding Time Data for Tap Water Samples from a Surface Water Source[a], Fortified with Method Analytes and Preserved and Stored According to Section 8 (n=4)

Analyte	Fortified Conc. (ng/L)	Day 0 Mean % Recovery	Day 0 % RSD	Day 8 Mean % Recovery	Day 8 % RSD	Day 14 Mean % Recovery	Day 14 % RSD
PFBS	80.0	91.9	7.1	99.4	4.2	93.4	11
PFHxA	80.0	99.3	4.0	101	5.4	93.4	7.9
HFPO-DA	80.0	102	2.2	101	5.3	100	11
PFHpA	80.0	101	3.3	99.2	2.2	101	3.6
PFHxS	80.0	102	0.9	103	4.0	107	4.5
ADONA	80.0	102	3.5	102	4.7	101	4.4
PFOA	80.0	98.8	3.9	99.8	0.63	100	3.5
PFOS	80.0	101	2.4	101	3.6	106	6.8
PFNA	80.0	101	2.8	101	0.87	105	4.8
9Cl-PF3ONS	80.0	102	3.3	100	2.2	102	4.4
PFDA	80.0	99.2	3.3	99.6	1.6	102	5.5
NMeFOSAA	80.0	94.9	4.5	98.0	3.5	95.4	7.3
PFUnA	80.0	100	4.1	101	4.4	100	6.2
NEtFOSAA	80.0	90.5	3.9	102	5.3	96.5	7.7
11Cl-PF3OUdS	80.0	97.5	3.1	101	4.5	102	5.5
PFDoA	80.0	97.0	2.7	98.4	3.5	103	3.8
PFTrDA	80.0	95.5	1.8	99.5	3.2	99.4	3.8
PFTA	80.0	97.8	3.3	102	3.2	96.2	2.1
$^{13}C_2$-PFHxA	40.0	90.6	4.1	93.6	5.5	93.0	8.8
$^{13}C_3$-HFPO-DA	40.0	101	1.8	101	3.1	91.5	12
$^{13}C_2$-PFDA	40.0	95.8	2.2	92.6	6.8	104	2.8
d_5-NEtFOSAA	160	83.1	4.4	87.6	2.6	95.2	4.3

[a] TOC = 2.4 mg/L and hardness = 103 mg/L measured as calcium carbonate.

Table 11. Extract Holding Time Data for Tap Water Samples from a Surface Water Source, Fortified with Method Analytes and Preserved and Stored According to Section 8 (n=4)

Analyte	Fortified Conc. (ng/L)	Day 0 Mean % Recovery	Day 0 % RSD	Day 8 Mean % Recovery	Day 8 % RSD	Day 14 Mean % Recovery	Day 14 % RSD	Day 28 Mean % Recovery	Day 28 % RSD
PFBS	80.0	91.9	7.1	96.9	5.1	90.6	10	99.4	5.3
PFHxA	80.0	99.3	4.0	10	1.3	94.1	2.9	105	2.6
HFPO-DA	80.0	102	2.2	103	1.4	98.7	2.6	103	1.1
PFHpA	80.0	101	3.3	102	2.9	98.3	1.0	104	3.5
PFHxS	80.0	102	0.9	105	2.9	99.7	1.8	107	2.5
ADONA	80.0	102	3.5	104	3.7	98.6	2.5	106	2.5
PFOA	80.0	98.8	3.9	106	3.7	101	1.8	106	2.8
PFOS	80.0	101	2.4	102	1.1	103	1.8	109	2.2
PFNA	80.0	101	2.8	105	1.8	103	2.3	107	2.4
9Cl-PF3ONS	80.0	102	3.3	99.4	3.1	97.6	2.9	107	2.2
PFDA	80.0	99.2	3.3	104	1.9	101.2	0.9	107	3.4
NMeFOSAA	80.0	94.9	4.5	101	3.9	90.5	5.2	105	6.8
PFUnA	80.0	100	4.1	104	5.5	102	4.2	106	3.0
NEtFOSAA	80.0	90.5	3.9	104	3.1	93.6	7.7	102	2.9
11Cl-PF3OUdS	80.0	97.5	3.1	103	1.9	97.3	1.6	108	2.7
PFDoA	80.0	97.0	2.7	102	3.7	99.8	3.3	106	2.6
PFTrDA	80.0	95.5	1.8	102	3.0	97.2	1.6	104	3.1
PFTA	80.0	97.8	3.3	105	4.2	98.8	2.1	108	2.5
$^{13}C_2$-PFHxA	40.0	90.6	4.1	101	1.2	101	2.6	114	2.1
$^{13}C_3$-HFPO-DA	40.0	101	1.8	95.5	3.2	96.5	2.7	111	2.5
$^{13}C_2$-PFDA	40.0	95.8	2.2	100	2.7	109	1.9	124	4.4
d_5-NEtFOSAA	160	83.1	4.4	94.7	1.6	91.4	4.8	113	9.1

Table 12. Initial Demonstration of Capability Quality Control Requirements

Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Sect. 9.2.2	Initial Demonstration of Low System Background	Analyze LRB prior to any other IDC steps.	Demonstrate that all method analytes are below 1/3 the MRL and that possible interferences from extraction media do not prevent the identification and quantification of method analytes.
Sect. 9.2.3	Initial Demonstration of Precision (IDP)	Analyze four to seven replicate LFBs fortified near the midrange calibration concentration.	%RSD must be <20%
Sect. 9.2.4	Initial Demonstration of Accuracy (IDA)	Calculate average recovery for replicates used in IDP.	Mean recovery ± 30% of true value
Sect. 9.2.5	Initial Demonstration of Peak Asymmetry Factor	Calculate the peak asymmetry factor using the equation in Section 9.3.9 for the first two eluting chromatographic peaks in a mid-level CAL standard.	Peak asymmetry factor of 0.8 - 1.5
Sect. 9.2.6	Minimum Reporting Limit (MRL) Confirmation	Fortify, extract and analyze seven replicate LFBs at the proposed MRL concentration. Calculate the Mean and the Half Range (HR). Confirm that the upper and lower limits for the Prediction Interval of Result (Upper PIR, and Lower PIR, Sect. 9.2.6.2) meet the recovery criteria.	Upper PIR ≤ 150% Lower PIR ≥ 50%
Sect. 9.2.7 and 9.3.10	Quality Control Sample (QCS)	Analyze a standard from a second source, as part of IDC.	Results must be within 70-130% of true value.
Sect. 9.2.8	Detection Limit (DL) Determination (optional)	Over a period of three days, prepare a minimum of seven replicate LFBs fortified at a concentration estimated to be near the DL. Analyze the replicates through all steps of the analysis. Calculate the DL using the equation in Sect. 9.2.8.1.	Data from DL replicates are not required to meet method precision and accuracy criteria. If the DL replicates are fortified at a low enough concentration, it is likely that they will not meet precision and accuracy criteria.

NOTE: Table 12 is intended as an abbreviated summary of QC requirements provided as a convenience to the method user. Because the information has been abbreviated to fit the table format, there may be issues that need additional clarification, or areas where important additional information from the method text is needed. In all cases, the full text of the QC in Section 9 supersedes any missing or conflicting information in this table.

Table 13. Ongoing Quality Control Requirements (Summary)

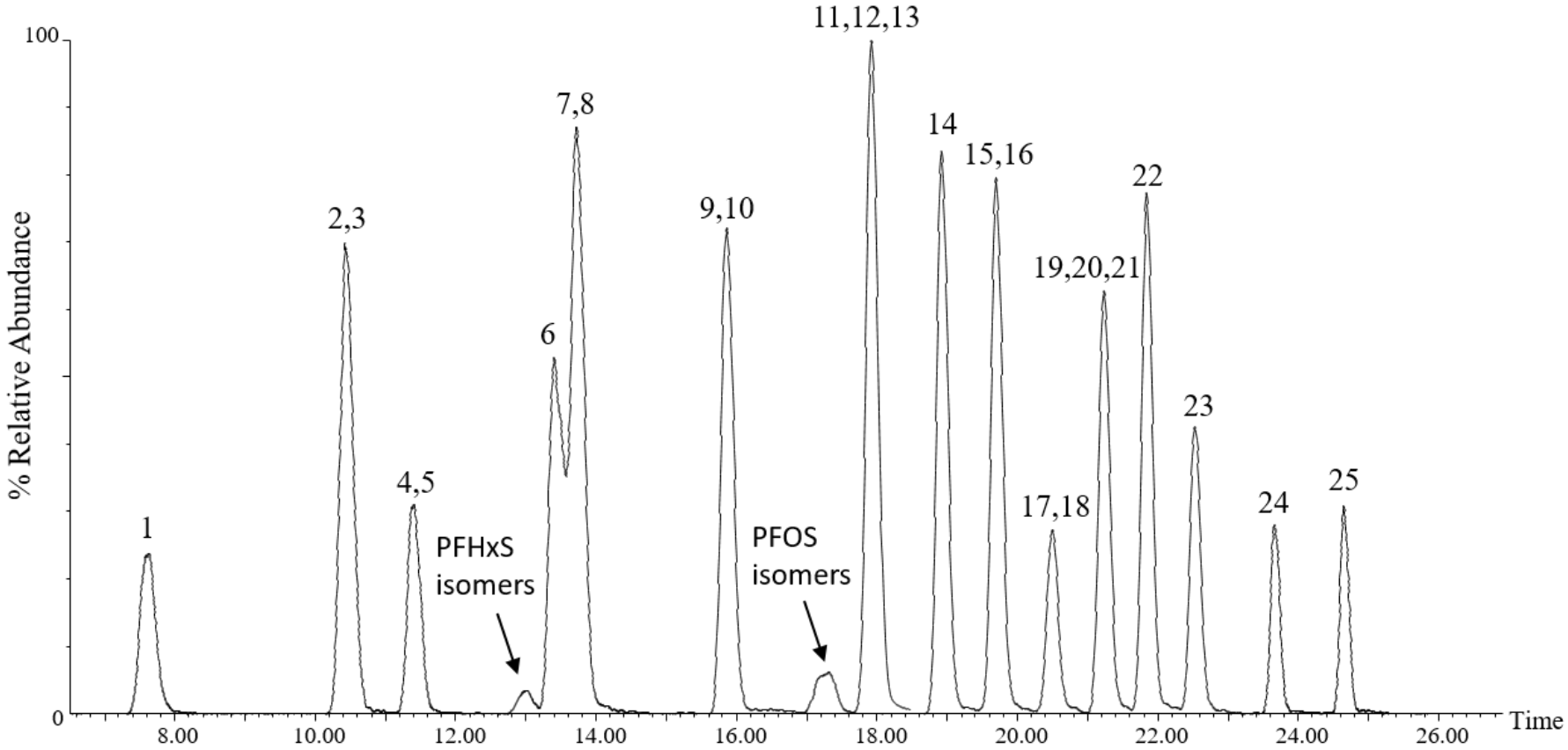
Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Sect. 8.1 - Sect. 8.5	Sample Holding Time	14 days with appropriate preservation and storage as described in Sections 8.1-8.5.	Sample results are valid only if samples are extracted within the sample holding time.
Sect. 8.5	Extract Holding Time	28 days when stored at room temperature in polypropylene centrifuge tubes.	Extract results are valid only if extracts are analyzed within the extract holding time.
Sect. 9.3.1	Laboratory Reagent Blank (LRB)	One LRB with each extraction batch of up to 20 samples.	Demonstrate that all method analytes are below 1/3 the MRL and confirm that possible interferences do not prevent quantification of method analytes. If targets exceed 1/3 the MRL or if interferences are present, results for these subject analytes in the extraction batch are invalid.
Sect. 9.3.3	Laboratory Fortified Blank (LFB)	One LFB is required for each extraction batch of up to 20 Field Samples. Rotate the fortified concentrations between low, medium and high amounts.	Results of LFB analyses must be 70-130% of the true value for each method analyte for all fortified concentrations except the lowest CAL point. Results of the LFBs corresponding to the lowest CAL point for each method analyte must be 50-150% of the true value.
Sect. 9.3.4	Internal Standard (IS)	Internal standards, $^{13}C_2$-PFOA (IS#1), $^{13}C_4$-PFOS (IS#2), and d_3-NMeFOSAA (IS#3), are added to all standards and sample extracts, including QC samples. Compare IS areas to the average IS area in the initial calibration and to the most recent CCC.	Peak area counts for all ISs in all injections must be within ± 50% of the average peak area calculated during the initial calibration and 70-140% from the most recent CCC. If ISs do not meet this criterion, corresponding target results are invalid.
Sect. 9.3.5	Surrogate Standards (SUR)	Surrogate standards, $^{13}C_2$-PFHxA, $^{13}C_3$-HFPO-DA, $^{13}C_2$-PFDA, and d_5-NEtFOSAA, are added to all CAL standards and samples, including QC samples. Calculate SUR recoveries.	SUR recoveries must be 70-130% of the true value. If a SUR fails this criterion, report all results for sample as suspect/SUR recovery.

Table 13. (Continued)

Method Reference	Requirement	Specification and Frequency	Acceptance Criteria
Sect. 9.3.6	Laboratory Fortified Sample Matrix (LFSM)	Analyze one LFSM per extraction batch (20 samples or less) fortified with method analytes at a concentration close to but greater than the native concentration, if known. Calculate LFSM recoveries.	Recoveries at mid and high levels must be within 70-130% and within 50-150% at the low-level fortified amount (near the MRL). If these criteria are not met, results are labeled suspect due to matrix effects.
Sect. 9.3.7	Laboratory Fortified Sample Matrix Duplicate (LFSMD) or Field Duplicates (FD)	Extract and analyze at least one FD or LFSMD with each extraction batch (20 samples or less). A LFSMD may be substituted for a FD when the frequency of detects are low. Calculate RPDs.	Method analyte RPDs for the LFMD or FD must be ≤30% at mid and high levels of fortification and ≤50% near the MRL. If these criteria are not met, results are labeled suspect due to matrix effects.
Sect. 9.3.8	Field Reagent Blank (FRB)	Analysis of the FRB is required only if a Field Sample contains a method analyte or analytes at or above the MRL. The FRB is processed, extracted and analyzed in exactly the same manner as a Field Sample.	If the method analyte(s) found in the Field Sample is present in the FRB at a concentration greater than 1/3 the MRL, then all samples collected with that FRB are invalid and must be recollected and reanalyzed.
Sect. 9.3.9	Peak Asymmetry Factor	Calculate the peak asymmetry factor for the first two eluting chromatographic peaks in a mid-level CAL standard during IDC and when chromatographic changes are made that affect peak shape.	Peak asymmetry factor of 0.8 - 1.5
Sect. 9.3.10	Quality Control Sample (QCS)	Analyze at least quarterly or when preparing new standards, as well as during the IDC.	Results must be within 70-130% of true value.
Sect. 10.2 and Sect. 9.3.2	Initial Calibration	Use IS calibration technique to generate a first or second order calibration curve forced through zero. Use at least five standard concentrations. Check the calibration curve as described in Sect. 10.2.4.4.	When each CAL standard is calculated as an unknown using the calibration curve, the analyte and SUR results must be 70-130% of the true value for all except the lowest standard, which must be 50-150% of the true value. Recalibration is recommended if these criteria are not met.
Sect. 9.3.2 and Sect. 10.3	Continuing Calibration Check (CCC)	Verify initial calibration by analyzing a low level (at the MRL or below) CCC prior to analyzing samples. CCCs are then injected after every 10 samples and after the last sample, rotating concentrations to cover the calibrated range of the instrument.	Recovery for each analyte and SUR must be within 70-130% of the true value for all but the lowest level of calibration. Recovery for each analyte in the lowest CAL level CCC must be within 50-150% of the true value and the SUR must be within 70-130% of the true value.

NOTE: Table 13 is intended as an abbreviated summary of QC requirements provided as a convenience to the method user. Because the information has been abbreviated to fit the table format, there may be issues that need additional clarification, or areas where important additional information from the method text is needed. In all cases, the full text of the QC in Sections 8-10 supersedes any missing or conflicting information in this table.

Figure 1. Example Chromatogram for Reagent Water Fortified with Method 537.1 Analytes at 80 ng/L. Numbered Peaks are Identified in Table 3



Attachment 13

Perfluorooctanoic Acid

Informational Links

Chemicals Dashboard	CCL3	Health advisory	Information
UCMR3	FAQs	Analytical Method	

Contaminant Navigation

Overview | Treatment Processes | Properties | Fate and Transport | References

Treatment Processes

The following processes were found to be effective for the removal of perfluorooctanoic acid: GAC (up to > 99 percent removal), membrane separation &ndash high pressure membranes such as nanofiltration and reverse osmosis (up to > 99 percent removal), anion exchange (up to 99 percent removal), and powdered activated carbon (up to 95 percent removal). Various types of novel adsorptive media have also been found to effectively remove PFOA (up to > 99 percent removal), but results for these media published to date have been limited to batch tests at bench scale. The exact percentage removal a water system may achieve with a given technology will be dependent upon a variety of factors, including source water quality and water system characteristics. Adsorptive media, GAC, and anion exchange are non-steady state technologies where the media will need to be periodically replaced or reactivated/regenerated to prevent contaminant breakthrough.

Based on the available literature, the following are not considered effective for the removal of perfluorooctanoic acid: conventional treatment (comprised of the unit processes coagulation, flocculation, clarification, and filtration, and is typically followed by disinfection at full-scale) (no removal) and UV at wavelengths greater than 185 nm and irradiation times less than 24 hours (4 percent to 34 percent removal). Conventional ozonation was ineffective but a demonstration study of a patented ozofractionation process, which used ozone gas to separate PFOA into a foam residual, found greater than 97 percent removal.

Other treatment processes with varying results include UV irradiation using 185 nm UV wavelength and irradiation times of 2 to 4 hours (57 to 99 percent removal). UV bench scale studies at 220-460 nm wavelength with irradiation times of 72 hours showed 89.5 percent removal. UV/hydrogen peroxide treatment (35 percent removal) was less effective in comparison to UV alone (45 percent removal) after 24 hours of irradiation. Certain other chemicals/catalysts were found to increase UV degradation of PFOA (60 to > 99 percent removal) with contact times of one hour or more.

Low-pressure membrane filtration - such as microfiltration or ultrafiltration varied in effectiveness (2 to 56 percent removal). Some of the percent removal values reported (e.g., UV, low-pressure membrane filtration) are higher than reasonably anticipated due to a variety of factors such as study conditions differing from the conditions of typical drinking water facilities, outlier data points, or multiple treatment processes being run simultaneously.

Studies were identified evaluating the following treatment technologies for the removal of perfluorooctanoic acid:

Adsorptive Media

Bench-scale studies tested adsorption of PFOA using novel media including: magnetic nanoparticles with different polymer coatings [2535], functionalized and hybrid hydrogel sorbents [2617, 2606], adsorptive photocatalysts [2623], swellable modif...

See more

Aeration and Air Stripping

At a full-scale site, packed tower aeration was not effective for removing PFOA [2441].

See more

Biological Filtration

A full-scale study [2175] of a plant treating reclaimed domestic wastewater found biological filtration to be ineffective for removing PFOA.

See more

Biological Treatment

Removal of PFOA from water using biological treatment was found to be ineffective. One bench-scale study [2161] reported removal of 0 to 8 percent using supernatant from a domestic wastewater activated sludge process as a microbial sourc...

See more

Chemical Treatment

One lab study observed >90% removal of PFOA via oxidation by persulfate in hot (85 degrees C) water after 30 hours reaction time. Removal in cooler water (25 degrees C) was negligible. The presence of iron reduced PFOA oxidation somewhat. Degra...

See more

Chlorine

Chlorination was ineffective for removing PFOA at seven full-scale sites [2441, 2509, 2619].

See more

Chlorine Dioxide

Chlorine dioxide was ineffective for removing PFOA at a full-scale site [2441].

See more

Conventional Treatment

Bench scale studies [2536, 2548, 2553] were able to achieve moderate removals (up to 58 percent) of perfluorooctanoic acid (PFOA) by coagulation, but only by using high coagulant dosage and/or low pH. Removals at lower doses and neutral pH we...

See more

GAC Isotherm

Isotherm data are available for adsorption onto various types of granular activated carbon and onto other media, including powdered activated carbon, anion exchange resin, and novel adsorbents.

See more

Granular Activated Carbon

Removal of perfluorooctanoic acid (PFOA) by granular activated carbon (GAC) can be effective. Bench and pilot tests, including rapid small scale column tests, showed removals from less than zero to greater than 99 percent, depending on carbon type...

See more

Ion Exchange

Removal of perfluorooctanoic acid (PFOA) using anion exchange resins was found to be effective up to greater than 99 percent removal in bench- and pilot-scale studies [2427, 2503, 2504, 2515, 2523, 2534, 2535, 2538, 2559, 2562, 2563, 2564, 2576, 2...

See more

Membrane Filtration

Removal of PFOA from water by membrane filtration varied in effectiveness in full scale studies with 2 to 56 percent removal achieved. The first study [1756] found that membrane filtration (type not specified) together with chlorinati...

See more

Membrane Separation

Removal of perfluorooctanoic acid (PFOA) from water using membrane separation was found to be quite effective. Bench [2423, 2441, 2514, 2530, 2610], pilot [2569, 2573, 2624], and full-scale [2175, 2424, 2428, 2441, 2509] studies evaluating several...

See more

Other Treatment

Other processes that have been evaluated for the treatment of perfluorooctanoic acid (PFOA) in groundwater or at environmentally relevant concentrations (e.g., 1 milligram per liter or less) include electrochemical treatment [2629, 2630] and plasm...

See more

Ozone

Several full-scale studies [2174, 2175, 2441, 2508, 2509, 2518, 2619] found conventional ozonation ineffective for removal of PFOA. A demonstration study of a patented ozofractionation process, which used ozone gas to separate PFAS into a foam res...

See more

Ozone and Hydrogen Peroxide

A bench-scale study [2635] achieved up to greater than 63 percent removal of perfluorooctanoic acid (PFOA) using ozone, followed by increasing pH to 11, followed by hydrogen peroxide addition. The study did not test the treatment process at natura...

See more

Powdered Activated Carbon

Bench [1700, 2536, 2542, 2544, 2546, 2548, 2621] and pilot scale [2518] tests have shown that PAC can achieve up to 95 percent removal of perfluorooctanoic acid. Removal depends on factors including PAC dosage, PAC particle size, contact time, and...

See more

Precipitative Softening

See more

Ultraviolet Irradiation

In a full-scale facility treating groundwater using UV, effluent PFOA exceeded influent [2441]. Bench-scale studies have found that PFOA degradation by UV irradiation depends on UV wavelength and UV contact time. Tests that included 185 nm UV ligh...

See more

Ultraviolet Irradiation and Hydrogen Peroxide

In a bench scale study, PFOA removal with UV (220-460nm) in combination with H_2O_2 was not significant. The study reported 35 percent removal after 24 hours of irradiation; removal was less effective in comparison t...

See more

Ultraviolet Irradiation and Ozone

See more

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Attachment 14

Perfluorooctane Sulfonate

Informational Links

Chemicals Dashboard Analytical Method

Contaminant Navigation

Overview Treatment Processes Properties Fate and Transport References

Treatment Processes

The following processes were found to be effective for the removal of PFOS: GAC (up to > 99 percent removal), membrane separation - high pressure membranes such as nanofiltration and reverse osmosis (up to > 99 percent removal), anion exchange (up to > 99 percent removal), and powdered activated carbon (up to 99 percent removal). Various types of novel adsorptive media have also been found to effectively remove PFOS (up to > 99 percent removal), but results for these media published to date have been limited to batch tests, primarily at bench scale. The exact percentage removal a water system may achieve with a given technology will be dependent upon a variety of factors, including source water quality and water system characteristics. Adsorptive media, GAC, and anion exchange are non-steady state technologies where the media will need to be periodically replaced or reactivated/regenerated to prevent contaminant breakthrough.

Processes ineffective for the removal of PFOS were biological treatment (0 to 10 percent removal), chloramines (-96 percent removal), conventional treatment (comprised of the unit processes coagulation, flocculation, clarification, and filtration, and is typically followed by disinfection at full-scale) (-222 to 59 percent removal), hydrogen peroxide (0 to 2 percent removal), ozone (-11 to 7 percent removal), ozone plus hydrogen peroxide (2 percent removal), slow sand filtration (-21 to 15 percent removal), UV photocatalysis using titanium dioxide (15 percent removal), and UV irradiation plus ozone (-2 percent removal).

Other treatment processes with varying results include low-pressure membrane filtration - such as microfiltration or ultrafiltration (-15 to 43 percent) and permanganate (1 to 53 percent). Negative values indicate that a study found a higher concentration in effluent water than in influent water possibly due to the analytical uncertainties or the oxidation of PFOS precursors into PFOS within the process. Some of the percent removal values reported (e.g., conventional treatment, permanganate) are higher than reasonably anticipated due to a variety of factors such as study conditions differing from the conditions of typical drinking water facilities, outlier data points, or multiple treatment processes being run simultaneously.

Research was identified evaluating the following treatment technologies for the removal of PFOS:

Adsorptive Media

A pilot study achieved greater than 89 percent removal of PFOS from groundwater using a batch reactor with an aluminum- based sorbent that was not replaced between batches over a period of 14 days [2570].

One bench-scale study found re...

See more

Aeration and Air Stripping

At a full-scale site, packed tower aeration was not effective for removing PFOS [2441].

See more

Biological Filtration

Removal of PFOS with a biologically active GAC filter was found to be successful in removing low levels of the contaminant (> 48 percent) within a treatment plant treating reclaimed water [2175]. In one sampling event, PFOS was removed to below...

See more

Biological Treatment

Removal of PFOS from water using biological treatment was found to be ineffective. One bench-scale study [2161] reported removal of 0 to 10 percent using supernatant from a domestic wastewater activated sludge process as a microbial source in both...

See more

Chloramine

A full-scale study [2175] found that chloramines are ineffective in removing PFOS (-96 percent removal) in combination with a primary settling process at a treatment plant treating reclaimed water. The author stated that the difficulty in assessin...

See more

Chlorine

Chlorination was ineffective for removing PFOS at seven full-scale sites [2441, 2509, 2619].

See more

Chlorine Dioxide

Chlorine dioxide was ineffective for removing PFOS at a full-scale site [2441].

See more

Conventional Treatment

Bench scale studies [2536, 2548, 2553, 2642] were able to achieve moderate to high removals (50 to 95 percent) of perfluorooctane sulfonate (PFOS) by coagulation, but only by using high coagulant dosage and/or low pH. Removals at lower doses and n...

See more

GAC Isotherm

Isotherm data are available for adsorption onto various types of granular activated carbon and onto other media, including powdered activated carbon, anion exchange resin, and novel adsorbents.

See more

Granular Activated Carbon

Removal of perfluorooctane sulfonate (PFOS) by granular activated carbon (GAC) was found to be effective in bench and pilot scale studies and in full-scale treatment when GAC replacement was frequent. In bench and pilot tests, including rapid smal...

See more

Hydrogen Peroxide

Removal of PFOS from water using hydrogen peroxide was found to be ineffective in two studies [2160]. One bench-scale study achieved 2 percent PFOS removal with an H_2O_2 dose of 3.0 mg/L. Also, a bench-scale Fenton's reag...

See more

Ion Exchange

Removal of perfluorooctane sulfonate (PFOS) using anion exchange resins was found to be effective (greater than 90 to 99 percent removal) in bench- and pilot-scale studies [2426, 2427, 2503, 2504, 2515, 2523, 2535, 2538, 2559, 2562, 2563, 2564, 25...

See more

Membrane Filtration

Removal of perfluorooctane sulfonate (PFOS) from water by membrane filtration varied in effectiveness in full-scale studies with -30 to 43 percent removal achieved. One study found PFOS concentration of the ultrafiltration filt...

See more

Membrane Separation

Removal of perfluorooctane sulfonate (PFOS) from water using membrane separation was found to be quite effective. Bench [2163, 2173, 2423, 2441, 2514, 2530, 2642], pilot [2568, 2571, 2642], and full-scale [2175, 2424, 2428, 2441, 2509] studies eva...

See more

Other Treatment

Other processes that have been evaluated for the treatment of perfluorooctane sulfonate (PFOS) in groundwater or at environmentally relevant concentrations (e.g., 1 milligram per liter or less) include electrocoagulation [2608], electrochemical tr...

See more

Ozone

Removal of PFOS with ozone in drinking water applications was found to be ineffective. A bench-scale study [2160] demonstrated a removal of only 7 percent with an applied dose of 2.6 gO_3/hr and a contact time of 120 minutes. Several ful...

See more

Ozone and Hydrogen Peroxide

One bench-scale study [2160] found removal of PFOS from water using ozone and hydrogen peroxide to be ineffective. It achieved 2 percent removal with an applied ozone dose of 2.6 grams per hour and hydrogen peroxide dose of 3.0 mg/L. The lack of ...

See more

Permanganate

Removal of PFOS from water using permanganate was found to be somewhat effective in a bench-scale study [2162]. The study found contaminant removal of between 1 and 53 percent. Generally, removal was enhanced when dose, temperature,...

See more

Powdered Activated Carbon

Bench [2158, 2521, 2536, 2542, 2544, 2548] and pilot scale [2518] tests have shown that PAC can achieve up to 99 percent removal of perfluorooctane sulfonate. Removal depends on factors including PAC dosage, PAC particle size, contact time, and in...

See more

Slow Sand Filtration

Removal of perfluorooctane sulfonate (PFOS) from water by slow sand filtration was not effective in two full-scale studies. Both studies found PFOS concentration of the treated water to exceed that of the raw water. One study found that slow sand ...

See more

Ultraviolet Irradiation

One full scale study found partial removal (an average of 38 percent) of PFOS using UV [2441]. One study using a photocatalytic reactor membrane pilot system, employing UV/TiO_2 photocatalysis, found 15 percent photodegradation for surfa...

See more

Ultraviolet Irradiation and Hydrogen Peroxide

A single full-scale study found limited removal (9 percent) of PFOS by UV and hydrogen peroxide [2441].

See more

Ultraviolet Irradiation and Ozone

Removal of PFOS from water using a combination of ozone and UV irradiation was found to be ineffective based on data from one bench-scale study [2160]. In this study, a removal of -2 percent was achieved. The lack of removal was thought to be due ...

See more

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Attachment 15

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Removal of per- and polyfluoroalkyl substances (PFASs) in a full-scale drinking water treatment plant: Long-term performance of granular activated carbon (GAC) and influence of flow-rate

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ABSTRACT

Per- and polyfluoroalkyl substances (PFASs) have been ubiquitously detected in drinking water which poses a risk for human exposure. In this study, the treatment efficiency for the removal of 15 PFASs was examined in a full-scale drinking water treatment plant (DWTP) in the City of Uppsala, Sweden, over a period of two years (2015–2017). Removal of the five frequently detected PFASs was influenced by the total operation time of granular activated carbon (GAC) filters, GAC type and surface loading rate. The average removal efficiency of PFASs ranged from 92 to 100% for "young" GAC filters and decreased to 7.0–100% for "old" GAC filters (up to 357 operation days, 29 300 bed volumes (BV) treated). Flow-rates were adjusted in two full-scale GAC filters of different operational age to examine the removal of PFAS and organic matter depending on GAC operational age and operating flow. The decrease in flow-rate by 10 L s^{-1} from 39 to 29 L s^{-1} led to an average increase of 14% and 6.5% in total PFAS removal efficiency for an "old" (264 operation days, 21 971 BV treated) and a "young" GAC filter (63 operation days, 5 725 BV treated), respectively. A cost-analysis for various operation scenarios illustrated the dominating effect of treatment goals and costs for GAC regeneration on overall GAC operation costs. The unit costs for GAC filters ranged from 0.08 to 0.10 € m^{-3} water treated and 0.020-0.025 € m^{-3} water treated for a treatment goal of 10 ng L^{-1} and 85 ng L^{-1}, respectively, for $\sum_{11}$PFAS. Furthermore, it was concluded that prolonging the GAC service life by lowering the flow-rates after reaching the treatment goal could lead to a 26% cost-deduction. The results and methods presented in this study give drinking water providers valuable tools for the operation of a full-scale treatment train for the removal of PFAS in contaminated raw water.

1. Introduction

Per- and polyfluoroalkyl substances (PFASs) are found ubiquitously in the abiotic and biotic environment (Ahrens, 2011). Due to their unique physico-chemical properties, PFASs have a wide range of applications and are for instance used in food packaging materials, textiles and in aqueous film forming foams (AFFFs) for firefighting (Buck et al., 2011; Appleman et al., 2014; Biegel-Engler et al., 2017). PFASs are highly persistent and many have half-lives of several years to decades in the human body (Lindstrom et al., 2011). Exposure to PFASs has been linked to adverse health effects, e.g. increased risk of high cholesterol and blood lipid levels, decreased fertility and certain types of cancer (Lindstrom et al., 2011; Post et al., 2012; Biegel-Engler et al., 2017). PFASs have been detected in drinking water in several European countries and the USA (Ericson et al., 2009; Post et al., 2009; Ullah et al., 2011). In 2016, the US EPA therefore recommended a health advisory limit of 70 ng L^{-1} for sum of PFOS and PFOA in drinking water (USEPA, 2016). The National Food Agency in Sweden recommends an action level of 90 ng L^{-1} for the sum of 11 PFASs (i.e. C3–C9 perfluoroalkyl carboxylic acids (PFCAs): PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA; C4, C6, C8 perfluoroalkyl sulfonic acid (PFSAs): PFBS, PFHxS, PFOS; 6:2 fluorotelomer sulfonic acid: 6:2 FTSA) in drinking water and advises the level should be reduced as low as possible (Ankarberg and Lindberg, 2016). In the future, the drinking water guidelines are becoming more strict (e.g. including a larger number of compounds and lower guideline

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levels) due to revised recommendations on the acceptable daily intake (ADI) value (Knutsen et al., 2018). PFAS emissions can occur through point sources such as wastewater treatment plants, landfill leachate, industries, and fire training facilities which have used PFAS containing AFFFs (Post et al., 2012). Nonpoint sources include surface runoff or precipitation (Ahrens, 2011). Once PFASs are released into the aquatic environment, they pose a risk for our drinking water, as conventional treatment processes such as sand-filtration, coagulation, flocculation, sedimentation, oxidation and disinfection are ineffective for the removal of PFASs during the treatment of contaminated ground or surface water (Rahman et al., 2014). The occurrence of PFASs in potable water at levels greater than regulatory limits therefore requires development and operation of efficient removal methods for drinking water treatment plants (DWTPs). Filtration through virgin or freshly regenerated ("young") granular activated carbon (GAC) or ion exchange and membrane techniques like nanofiltration and reverse osmosis are effective methods for PFAS removal (Vecitis et al., 2009; Carter and Farrell, 2010; Eschauzier et al., 2012; Flores et al., 2013; Appleman et al., 2014; Chularueangaksorn et al., 2014; Rahman et al., 2014; Zhang et al., 2016; Zaggia et al., 2016; Franke et al., 2019). While it is recognized, that membrane filtration techniques like nanofiltration and reverse osmosis and adsorption to synthetic materials like anion exchange resins show superior PFAS removal compared to GAC, filtration through GAC remains a go-to method, as it is reliable, straight forward to operate and has been used in drinking water production for decades (Merino et al., 2016; Crittenden et al., 2012). GAC treatment also entails a commercially available method for regeneration without creating an additional waste stream. Today, filtration through GAC is commonly applied in DWTPs treating PFAS contaminated water. If deployed as a chemical barrier for the removal of PFASs, GAC filtration, however, needs to be closely monitored for PFAS breakthrough and regenerated or replaced relatively frequently. Short-chain PFASs (PFSAs with $\leq$ 6 carbons and PFCAs with $\leq$ 7) break through rapidly (Flores et al., 2013; Zaggia et al., 2016) and even long-chain PFASs break through after a limited time (Takagi et al., 2011; Eschauzier et al., 2012; Rahman et al., 2014; Zaggia et al., 2016; McCleaf et al., 2017). Drinking water treatment and respective GAC filtration should therefore be optimized to the best extent, not the least in order to save costs arising due to the frequently necessary regeneration or exchange of filter material (Takagi et al., 2011; Rahman et al., 2014). Until this point, little is known concerning optimization and long-term removal efficiency of PFASs in full-scale DWTPs.

In this study, the removal of PFASs in a full-scale DWTP in the City of Uppsala, Sweden, was examined. PFAS contamination of groundwater in Uppsala was detected in 2012 and is likely linked to historic use of PFAS-containing AFFFs in the aquifer catchment (Gyllenhammar et al., 2015). Affected wells show sum concentrations of up to 250 ng L^{-1} PFASs. After process modifications, Uppsala's Bäcklösa DWTP began treating water from two contaminated wellfields in April 2015 using ten GAC gravity filters. PFAS concentrations were monitored throughout the full treatment train where evaluated treatment methods included aeration, softening and filtration, sand filtration, the plant's GAC filtration system and a disinfection step. The specific objectives of this study included to i) investigate the removal of PFAS in a full-scale DWTP, ii) evaluate the long-term performance of GAC for the removal of PFASs, iii) assess the impact of the GAC age and flow-rate on the removal of PFASs, and iv) to estimate the operations costs for the removal of PFASs using GAC at different treatment scenarios.

2. Materials and methods

2.1. PFAS analytes

In total, 27 PFASs were analyzed including C_4, $C_{6\text{-}8}$, C_{10} PFSAs (i.e. PFBS, PFHxS, PFHpS, PFOS, PFDS), $C_{3\text{-}13}$, C_{15}, C_{17} PFCAs (i.e. PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTriDA, PFTeDA, PFHxDA, PFOcDA), perfluorooctanesulfonamide (FOSA), methyl- and ethyl FOSA (i.e. MeFOSA, EtFOSA), perfluorooctanesulfonamidoacetic acid (FOSAA), methyl- and ethyl FOSAA (i.e. MeFOSAA, EtFOSAA), methyl- and ethyl perfluorooctanesulfonamido-ethanol (MeFOSE, EtFOSE) and 6:2 FTSA (all > 98%, Wellington Laboratories, Canada). For internal calibration, 16 mass-labelled PFASs internal standards (IS) were used: $^{18}O_2$-PFHxS, $^{13}C_4$-PFOS,$^{13}C_4$-PFBA, $^{13}C_2$-PFHxA, $^{13}C_4$-PFOA, $^{13}C_5$-PFNA, $^{13}C_2$-PFDA, $^{13}C_2$-PFUnDA, $^{13}C_2$-PFDoDA, $^{13}C_8$-FOSA, d_3-N-MeFOSA, d_5-N-EtFOSA, d_3-N-MeFOSAA, d_5-N-EtFOSAA, d_7-N-MeFOSE and d_9-N-EtFOSE (all > 98%, Wellington Laboratories, Canada). In addition, a mass-labelled injection standard (InjS) (i.e. $^{13}C_8$-PFOA: 97.9%, Wellington Laboratories, Canada) was applied. For details on PFAS analysis, see Tables S1 and S2 in the Supporting Information (SI).

2.2. Sampling

The DWTP contains five treatment steps: aeration, softening (fluidized bed pellet reactor type), dual media (granular carbon/sand) filtration, GAC filtration and disinfection with free chlorine. Samples were taken to investigate i) the full-scale treatment efficiency on November 24, 2016 (Table S4 in the SI), ii) the influence of flow-rate on the removal of PFASs between 28 November and December 21, 2016, and iii) long-term performance of granular activated carbon (GAC) between April 28, 2015 and February 7, 2017 (Fig. 1, Table S3 in SI). Samples taken for i) and ii) were analyzed at SLU, while samples for investigation of iii) were sent to the accredited commercial laboratories of ALS Scandinavia (see below). In all cases, samples were collected in clean 1 L polypropylene (PP) bottles and stored in the dark at 8 °C until analysis. Evaluation of the PFAS removal performance of the full-scale DWTP is based on grab samples during one day and should not be considered representative of the PFAS concentrations over time.

PFAS concentrations were determined for samples taken after or just downstream of each respective process stage with the exception of the sample taken after the disinfection step, which was taken after free chlorine disinfection and after storage in an underground reservoir which has a residence time of approximately 6 h. The removal efficiencies of each GAC filter and of the whole DWTP are listed in Tables S5 and S6 in the SI.

The performance of one "young" GAC filter (GAC 10, 63 operation days, 5 725 bed volumes treated) and one "old" GAC filter (GAC 5, 264 operation days, 21 971 bed volumes treated) consisting of Filtrasorb® 400 were evaluated at full-scale. Flow-rates of initially 35 L s^{-1} to 45 L s^{-1} (1st sampling round, n = 6), were first adjusted to 30 L s^{-1} (2nd, n = 12) and then to 15 L s^{-1} (3rd, n = 9). The average flow-rates on the sampling days were calculated based on the following equation:

$$r = \frac{V_{treated}}{t} \quad (1)$$

where r [L s^{-1}] is the average flow-rate, $V_{treated}$ [L] is the volume treated in the period between the sampling days and t [s] is the time in operation in the period between the sampling days. After each change of the flow-rate, the GAC filter adsorption process was allowed to stabilize. PFAS removal was assumed to stabilize when

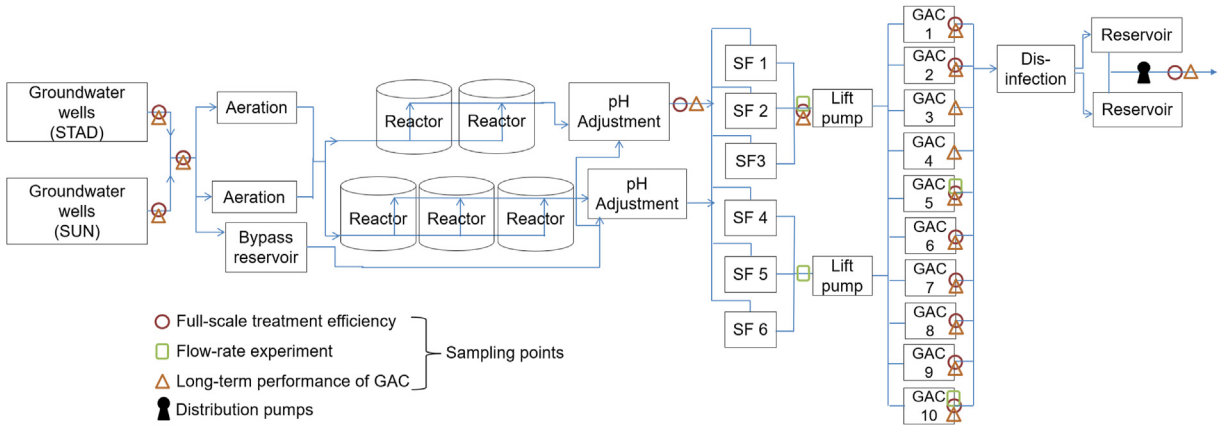

Fig. 1. Conceptual scheme of the drinking water treatment plant Bäcklösa in Uppsala, Sweden. Samples were taken to investigate the i) full-scale treatment efficiency (circles), ii) the influence of flow-rate on the removal of PFASs (squares) and iii) long-term performance of granular activated carbon (GAC) (triangles). SF = dual media filtration, GAC = granular activated carbon, STAD = Stadstädgården, SUN = Sunnersta.

Table 1
Specifications of the granular active carbon materials evaluated in this study, Filtrasorb® 400 (F400) (Calgon Carbon Corporation, 2004) and AquaSorb® 2000 (A2000) (Jakobi Carbons Group, 2012).

	F400	A2000
GAC ID number (Fig. 1)	1–6, 10	7–9
Iodine number [mg g^{-1}]	1050	1000
Surface area [m^2 g^{-1}][a]	1050	950
MB number [mL g^{-1}][b]	300	180
Effective size [mm]	0.6–0.7	0.6

[a] Surface area analysis according to Brunauer, Emmett and Teller (BET) (Brunauer et al., 1938).
[b] MB = Methylene blue.

UV adsorption stabilized. UV adsorption at 254 nm was utilized since it was a quick and accurate measurement technique. After stabilization was reached (varying between 3 and 7 days), water samples were collected and analyzed for PFASs.

2.3. Granular activated carbon (GAC) filters

The DWTP in Bäcklösa, Uppsala, Sweden has ten GAC filters with two different GAC types which are operated in parallel (Fig. 1). Six GAC filters are typically in operation at the same time. The types of GAC material applied during the course of this study were Filtrasorb® 400 and AquaSorb® 2000 (Table 1 (Calgon Carbon Corporation, 2004; Jakobi Carbons Group, 2012)).

GAC treatment efficiency was evaluated using the parameters bed volumes treated ($BV_{treated}$) and empty bed contact time (EBCT) according to Equations (2) and (3), respectively. EBCT indicates the residence or contact time of the water with the GAC granules (Applied Membranes Inc, 2020).

$$BV_{treated} = \frac{V_{treated}}{V_{GAC}} = \frac{r \cdot t}{V_{GAC}} \quad (2)$$

$$EBCT = \frac{V_{GAC}}{r} \quad (3)$$

where $V_{treated}$ [m^3] is the treated volume during operation time, V_{GAC} [35 m^3] is the volume of the GAC, r [m^3 s^{-1}] is the average flow-rate and t [s] is the operation time.

Removal efficiency (RE [%], Equation (4)) of a GAC filter was calculated by considering the concentration of a substance after the dual media filtration step, i.e. before GAC filtration (incoming water) and after GAC filtration (outgoing water):

$$RE = \frac{c_0 - c}{c_0} \cdot 100 \quad (4)$$

where c_0 [ng L^{-1}] is the concentration of the substance in the incoming water and c [ng L^{-1}] is the concentration of the substance in the outgoing water.

2.4. Sample preparation and analyses

2.4.1. PFAS analysis

Water samples sent to the commercial laboratory ALS Scandinavia were analyzed according to a method accredited for PFAS analysis. For more details, the authors refer to the laboratory (ALS Scandinavia Danderyd, 2017; ALS Scandinavia, 2017). Water samples processed at SLU were filtrated through glass microfiber filters (47 mm diameter, Whatman™, China). After filtration, samples were extracted through solid phase extraction (SPE) cartridges (Oasis® WAX, 6 cc, 500 mg, 60 μm; Waters, Ireland) using an established method described elsewhere (Ahrens et al., 2010). Briefly, the cartridges were preconditioned with 4 mL ammonium hydroxide solution (0.1% in methanol), 4 mL methanol and 4 mL Millipore water. Before loading the water samples, 100 μL of the IS mix (20 ng mL^{-1} for individual mass-labelled PFAS) were added to the samples in the PP bottles. 500 mL of the water samples were then loaded onto the cartridges with one drop per second. The cartridges were washed by adding 4 mL 25 mM ammonium acetate buffer in Millipore water. After drying the cartridges through centrifugation (3000 rpm, 2 min), the analytes were eluted from the cartridges by using 4 mL methanol and 8 mL 0.1% ammonium hydroxide in methanol. Finally, the samples were concentrated to 0.5 mL by evaporating with nitrogen (N-EVAPTM112; Organomation Associates, Inc., USA). Before injecting the samples into the LC-MS/MS, 10 μL of the InjS (200 ng mL^{-1}) were added. Blanks (n = 7) were processed in the same way as the natural samples but without loading the cartridge with any water. PFASs were analyzed using high performance liquid chromatography (HPLC) coupled to a triple quadrupole and an electrospray ionisation interface in negative-ion mode ((−)ESI-MS/MS, Agilent 6460 Triple Quadrupole System, Palo Alto, CA, USA) as described elsewhere (Ahrens et al., 2016). For HPLC (Agilent Technologies 1200 Series, Palo Alto, CA, USA), a Hypersil Gold pre-column (10 × 2.1 mm, 5 μm particle size, Thermo Scientific, Waltham, MA, USA) connected to a Betasil C18 column (50 × 2.1 mm, 5 μm particle size, Thermo Scientific,

Waltham, MA, USA) was used. For calibration, five standards with concentrations from 0.05 to 48 ng mL^{-1} (injected absolute 0.5 pg–480 pg on column) were measured. PFHpS was semi quantified using the response factors of PFHxS. The branched (B) isomers of PFHxS, PFOS and FOSA were semi-quantified using the response factor of the corresponding linear (L) isomer. Details for instrument parameters and transitions of the analytes can be found in Table S1 in the SI.

2.4.2. TOC and UV absorbance at 254 nm

For the TOC-analysis a catalytic combustion analyzer (TOC-VCPH with the autosampler ASI-V, Shimadzu, Japan) was used. Both, the total carbon (TC) and the inorganic carbon (IC) were measured after acidification (200 μL 2 M HCl in 20 mL) and purging with a carrier gas (purified air). Subsequently, the TOC concentration was calculated by subtracting the IC concentration from the TC concentration. Because of the purging step, the determined TOC is non-purgeable organic carbon (NPOC). In the following, NPOC will only be referred to as TOC as the amount of volatile OC is below the precision of the machine employed in this study ($<$ 0.3 mg L^{-1}). UV absorbance at 254 nm was determined with a combined photometer-fluorometer (Aqualog, Horiba Scientific) following the method described previously (Lavonen et al., 2015). As particulate carbon in samples that have passed a GAC filter is usually very low, NPOC is considered equivalent to DOC. According to a method described by Eaton (1996), UV absorbance at 254 nm can be used to predict DOC concentrations, as it is highly proportional to DOC concentration. In this study, the correlation between UV absorbance at 254 nm and DOC concentrations was DOC [mg L^{-1}] = 44 • UV [cm^{-1}] + 0.22 with $R^2 = 0.91$ (see Fig. S1 in the SI and for more details on TOC and UV absorption analysis, see text in the SI).

2.5. Quality control

The applied PP bottles used for PFAS analysis at SLU were machine washed and rinsed with methanol three times. All glassware and glass microfiber filters were heated at 400 °C and prior utilization, all glassware was rinsed with methanol. PFAS concentrations found in the blank samples were in the range of 0–8 ng L^{-1}. The method detection limit (MDL) was calculated based on the concentrations measured in the blanks (Equation (5)).

$$MDL = \bar{x}_{blanks} \cdot 3s \tag{5}$$

where $\bar{x}_{blanks}$ [ng L^{-1}] is the average concentration found in the blank samples and s is the standard deviation. When a compound was not detected in the blanks, the lowest detectable calibration point (signal to noise ratio $>$ 8) in the instrument was used as MDL (0.05 ng L^{-1}). The MDLs ranged between 0.05 and 15 ng L^{-1}. The recovery for the IS compounds ranged from 36% (Et-FOSA) to 135% (PFNA) (for details see Table S1 in the SI and Gobelius et al., 2018). Variations between the samples were calculated based on the collected duplicate or triplicate samples and are included in presented graphs. UV control analyses showed no variation and internal EDTA controls (nominal concentration 10 mg L^{-1}) during TOC analysis were in the range from 9.5 to 10 mg L^{-1}.

2.6. Statistical analysis

For statistical analyses, only PFASs with detection frequencies higher than 50% were evaluated. Concentrations below the MDL were set to 0.5 • MDL if not noted differently. Linear regression parameters were calculated with one-way ANOVA (analysis of variance). Pearson correlation was performed for correlation analysis between PFAS and TOC concentrations or UV absorbance (254 nm). Half-times for GAC filters (half-time [$BV_{treated}$] until 0% removal of a respective compound can be expected) were calculated according to Ahrens et al. (2009) by performing a linear regression with the logarithmic values of removal efficiencies over $BV_{treated}$ (Equation (6)):

$$t = -\frac{ln(2)}{m} \tag{6}$$

where $-1/m$ is the slope of the linear regression. Significant changes were defined with $p < 0.05$ with a confidence level of 95%. Half-times in operating days were derived by converting $BV_{treated}$ into days by multiplying with the average flow-rate (given in $BV_{treated}$ per day). Generally, operation time was defined as the time filters produced $>$ 500 m^3 water per day in order to account for operation stops of the filters. Next to the operating half-times, treatment goals were defined as receiving an outgoing $\sum_{11}$PFAS concentration of 10, 25, 50 or 85 ng L^{-1}, respectively, for each filter. For deriving the amount of $BV_{treated}$ when each of the treatment goals was reached, a linear regression was performed for the relationship of outgoing $\sum_{11}$PFAS concentration vs. $BV_{treated}$. Concentrations below MDL (removal efficiency near 100%) were disregarded in the two latter analysis as a linear regression for calculating the half-times and constant increase in outgoing concentrations should only be performed as soon as a decrease in performance is observed. Calculations and graphical visualizations were performed with the R software and the RStudio interface (R Development Core Team, 2016; R Studio Team, 2016). Smooth functions used for deriving the mean removal efficiency during GAC treatment applied the Local Regression (Loess) approach (Cleveland et al., 2017).

2.7. Economic analysis

Unit regeneration costs were calculated based on actual regeneration cost per Filtrasorb® 400 filter (i.e. 25 000 euro) divided by the volume of water treated by the filter up to each break through goal (10 ng L^{-1}, 25 ng L^{-1}, 50 ng L^{-1}, and 85 ng L^{-1}). Annual regeneration cost at Bäcklösa DWTP was calculated by multiplying unit regeneration costs by the actual annual volume of water treated at Bäcklösa DWTP (i.e. 7 million m^3). Annual operations costs were defined as annual regeneration cost plus the uniform annual cost of the actual initial purchase cost of virgin GAC for one filter (40 000 euros) over 10 years with an interest rate of 5% per year. Calculations are based on an exchange rate of 1 euro = 9.86 SEK. Finally, annual unit operations costs (in the following simplified to *unit costs*) were calculated as annual operations cost as defined above divided by the actual annual volume of water treated at Bäcklösa DWTP (i.e. 7 million m^3).

3. Results and discussion

3.1. Removal of PFASs in a full-scale DWTP

An evaluation of the full-scale treatment indicated that aeration, softening, pH adjustment and sand filtration did not decrease initial PFAS concentrations efficiently (Fig. 2). This was expected as it has been reported previously that these conventional treatment steps do not remove PFASs (Eschauzier et al., 2012; Appleman et al., 2014). However, GAC filtration (see Table 1 and Table S7 in the SI for individual filter characteristics) was effective in removing PFASs with removal efficiencies ranging from 67% to 100% (removal below MDL) depending on the filters' respective time in operation ($BV_{treated}$). This is also in agreement with previous studies (Eschauzier et al., 2012; Appleman et al., 2014; McCleaf et al., 2017).

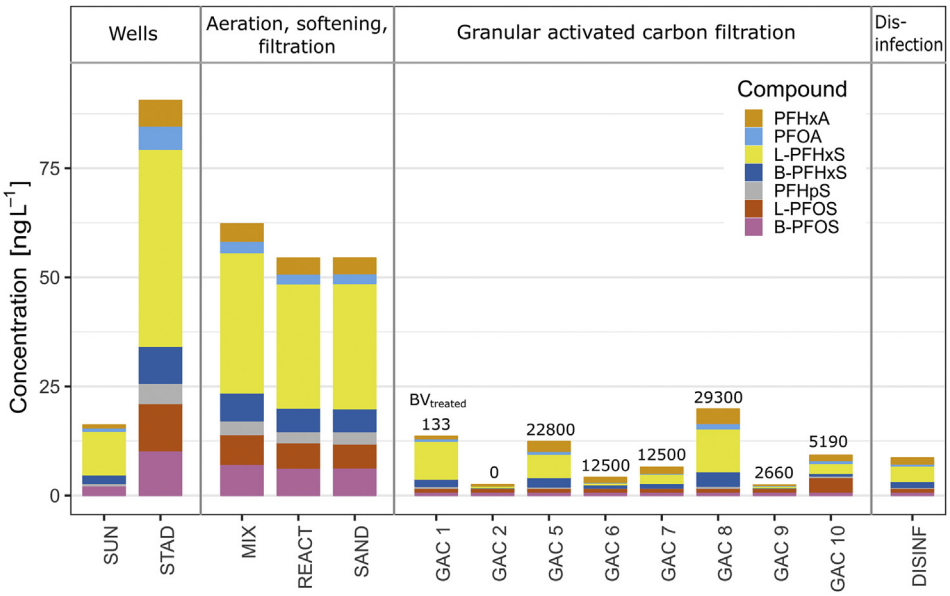

Fig. 2. PFAS concentrations detected in each step of the drinking water treatment plant (DWTP) Bäcklösa, Uppsala, Sweden. The incoming raw water from two wellfields SUN = Sunnersta, STAD = Stadsträdgården is mixed (MIX). The treatment involves aeration, softening and pH adjustment steps (REACT), followed by dual media filtration (SAND), several granular activated carbon filters (GAC) and finally a disinfection step (DISINF) (see also Fig. 1). GAC 1 and 2 were not in operation and the outgoing water of those filters was directed to the waste. Numbers on top of the bars indicate times in operation for the individual filters, expressed in bed volumes treated at the point of analysis ($BV_{treated}$).

Comparing the removal efficiency of individual PFASs, in particular the shorter chained PFCAs (i.e. PFHxA, PFHpA) showed lower removal efficiencies for GAC filters with large $BV_{treated}$ and PFSAs were generally retained better than PFCAs. For example, GAC 9 (30 d; 2 660 $BV_{treated}$) removed >99% of ∑PFAS as well as of short chained PFCAs (i.e. PFHxA, PFHpA), whereas GAC 8 (360 d; 29 300 $BV_{treated}$) removed 67% of ∑PFAS, where ∑PFCAs (i.e. PFHxA, PFHpA, PFOA) were removed to 22% (7.0% for PFHxA) and ∑PFSAs (i.e. PFHxS, PFHpS, PFOS) to 72%. When comparing removal efficiencies for linear vs. branched isomers, it was found that the removal efficiency for L-PFHxS was higher (i.e. ranging from 66% for GAC 8−100% for GAC 9) compared to B-PFHxS (i.e. from 37% for GAC 8−100% for GAC 9). This is in agreement with previous studies which found that the removal of branched PFASs through GAC is less effective than for linear PFASs due to different adsorption strengths (Eschauzier et al., 2012; McCleaf et al., 2017). McCleaf et al. (2017) found that the branched isomers of PFHxS, PFOS and FOSA showed a 8−13% lower removal efficiency than the linear isomers during GAC treatment in pilot-scale. In summary, as shown in Fig. 2, "younger" GAC filters (smaller number of $BV_{treated}$ after regeneration) had greater total removal efficiencies compared to the "older" GAC filters and were more successful in removing short-chained PFCAs (i.e. PFHxA, PFHpA). When comparing the two different GAC materials applied in the plant, it was evident that water treated by Filtrasorb® 400 (GAC6) showed slightly lower outgoing ∑PFAS concentrations (2.1 ng L^{-1}) than the AquaSorb® 2000 material (GAC7; 4.9 ng L^{-1}) despite identical operation parameters. One explanation for this observation could be that the GAC material Filtrasorb® 400 has a more defined effective particle size and wider pore size distribution as well as a higher surface area of 1050 m^2 g^{-1} for enhanced PFAS removal compared to AquaSorb® 2000 with 950 m^2 g^{-1} (Table 1). An interesting finding was that ∑PFAS concentration in the full-scale treatment was significantly correlated with TOC concentration (Pearson correlation coefficient $r_p = 0.80$, $p < 0.05$) and UV absorption (254 nm) ($r_p = 0.82$, $p < 0.05$). More specifically, concentrations of individual PFASs were significantly correlated with TOC concentration and UV absorbance ($p < 0.05$) ranging from $r_p = 0.72$ (L-PFOS) to $r_p = 0.88$ (B-PFHxS) for UV absorbance and from $r_p = 0.73$ (L-PFOS) to $r_p = 0.85$ (PFHxA, B-PFHxS) for TOC concentration. This is similar to the correlation reported by Anumol et al. (2015) between PFOS and PFOA with UV absorbance (254 nm) (r_p = 0.84 and 0.93, respectively). Thus, removal of organic carbon as determined by TOC and UV absorbance (254 nm) could potentially be used as a temporal surrogate for measuring PFAS removal efficiency, as it is both more practical and economical to measure compared to PFAS analysis. It should be kept in mind, that the relationship between the adsorption of micropollutants and organic matter might be dependent on organic matter type and composition (Matsui et al., 2002; Zietzschmann et al., 2016). The relationship between PFAS removal and removal of TOC or UV absorbance (254 nm) should therefore be determined for local conditions. Generally, measurements of TOC or UV absorbance (254 nm) should only complement and not replace the analysis of PFASs. More details of UV and TOC concentrations from each treatment stage and GAC filter for the full-scale treatment can be found in Fig. S1 and Table S8 in the SI.

3.2. Long-term performance of GAC for the removal of PFASs in a full-scale DWTP

Fastest decreasing removal efficiencies were observed for PFHxA, which was the only substance showing complete breakthrough (removal efficiency < 0%) at a GAC treatment time between 20 000 and 30 000 BV for five of the six GAC filters monitored for this specific part of the study (Fig. 3). Rapidly decreasing removal efficiencies were also observed for PFBS with removal efficiencies of 20% at approximately 30 000 BV. The removal efficiency for PFASs with longer chains, i.e. PFOA, PFHxS and PFOS, did not decline as rapidly as the above-mentioned PFASs. This is in line with earlier studies and could be due to better adsorption capacity of the GAC material for long chained PFASs, replacement of shorter chained by long chained PFASs or general blockage of pores by organic matter or other micropollutants (Eschauzier et al., 2012; McCleaf et al., 2017). PFOS was observed to

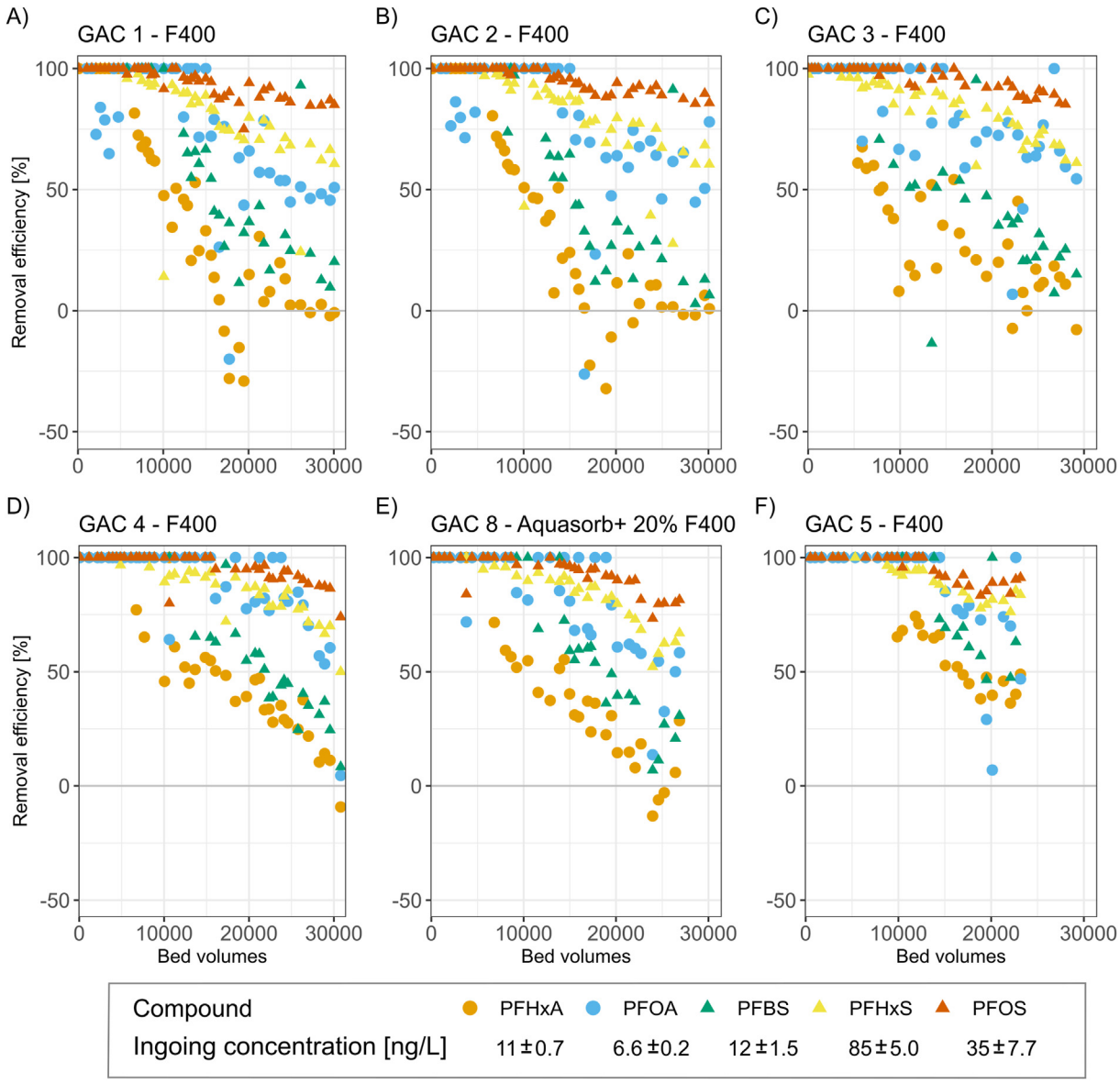

Fig. 3. PFAS removal efficiencies of A) GAC 1 (Filtrasorb® 400; "F400"), B) GAC 2 (F400), C) GAC 3 (F400), D) GAC 4 (F400), E) GAC 8 (80–90% AquaSorb® 2000 ("Aquasorb") + 10–20% F400) and F) GAC 5 (F400) for individual PFASs (detection frequency > 50%) (circle: PFCAs, triangle: PFSAs) for the DWTP Bäcklösa, Uppsala, Sweden. Average concentrations going into the GAC filters are given in the legend (arithmetic mean ± standard deviation in ng L^{-1}).

be retained best of all frequently detected PFASs by all GAC filters and removal was at 80–100% even after 30 000 treated BV for all GAC filters. Despite lower initial concentrations, PFCAs showed faster decreasing removal efficiencies compared to PFSAs (e.g. PFHxA < PFBS and PFOA < PFHxS), which has been observed before and might be explained by Pearson's concept of soft and hard acids or bases (Du et al., 2014). It can be argued that PFSAs (hard bases) are retained better than PFCAs (soft bases) by the oxide surface (hard acid) of the GAC (Du et al., 2014). Further adsorption mechanisms include the formation of hydrogen bonds between functional groups on the GAC surface (e.g. sulfides, halogenated hydrocarbons and non-aromatic ketones) and the hydrophilic group of PFCAs and PFSAs (Zhang et al., 2016a). For comparability, removal efficiencies at the greatest common $BV_{treated}$ of the six GAC filters studied are given in Table S9 in the SI. Generally, such comparisons should be made with care, as ingoing concentrations and water quality parameters like organic matter content are known to experience seasonal changes and filters were operated during slightly different times (Table S9 in the SI). This is apparent when looking at the total PFAS loading individual filters experienced over time, where e.g. GAC 1 and GAC 2 experienced similar PFAS loadings (Fig. S2 in the SI), which reflects in the breakthrough curves, even on a concentration normalized basis as expressed by removal efficiency (Fig. 3). These findings suggests an influence of other water constituents, like organic matter loading, to be responsible for the observed performance differences (Corwin and Summers, 2010).

Individual estimated operation times at which the total removal efficiency reaches 50% (operation half-times) were calculated assuming a logarithmic decrease in removal efficiencies for individual PFASs and can be found in Table S10 in the SI. Operation half-times increased with increasing chain length for both PFCAs (i.e. PFHxA (20 300 BV) < PFOA (68 300 BV)) and PFSAs (PFBS (22 300 BV) < PFHxS (91 600 BV) < PFOS (284 000 BV)).

3.3. Influence of GAC flow-rate for removal of PFASs, TOC and UV absorbance

For the evaluation of the influence of the PFAS removal by the applied flow-rate through the full-scale GAC filters, flow-rate experiments were performed on one "old" (264 days of operation; 21 971 $BV_{treated}$) and one relatively "young" GAC filter (63 days of operation; 5 725 $BV_{treated}$), see also Table S11 in the SI. As expected, removal efficiencies increased with decreasing flow-rate and thus longer EBCT (Fig. 4). For instance, a decrease of 10 L s^{-1} from 39 to 29 L s^{-1} led to an average increase of 14% and 6.5% in total PFAS removal efficiency for the "old" and the "young" GAC filter, respectively. Greatest changes were observed for PFHxA, which showed a 15% and 25% better removal efficiency for the "old" and the "young" filter, respectively. For each 10 L s^{-1} decrease in flow-rate the removal efficiency for PFHxA increased by an average of 19% and 2.5% for the "old" and "young" GAC filter, respectively. The "young" GAC filter was generally less effected by the change in flow-rate compared to the "old" GAC filter. Both GAC filters showed high PFOS removal of > 98%, with the exception of the largest flow-rate tested in the "old" filter, where L-PFOS and B-PFOS were removed by 91 and 76%, respectively.

These results highlight a beneficial influence on adsorption kinetics on PFAS adsorption, where with higher EBCT the water spends more time in contact with GAC particles and thus PFASs and other substances have more time to diffuse into pores and adsorb onto sorption sites. This might further relate to diffusion limitations "older" GAC filters experience, due to the total organic matter loading. Longer contact times will allow for longer diffusion times thus creating a diffusion gradient beneficial for PFAS adsorption. Substantially lower flow-rates of 7.5 L s^{-1} for the "young" GAC filter showed no further increase in PFAS removal efficiencies, which indicates that PFAS adsorption is dominated by thermodynamic mechanisms, rather than kinetics at flow-rates of below 15 L s^{-1} for the "young" GAC filter. Naturally, operation flow-rates cannot be lowered indefinitely since at some point water production would be too low. Results of this study indicate however, that "older" GAC filters could be operated for a longer time than they commonly are by lowering the flow-rates, thus expand their service lifetime, and still provide sufficient PFAS removal.

The Swedish drinking water guideline is 90 ng L^{-1} for $\sum_{11}$PFAS, however drinking water providers in the City of Uppsala, Sweden, are setting even stricter treatment goals in their treatment plants. On average, the treatment goals of 25 and 50 ng L^{-1} were reached at 15 176 and 23 231 $BV_{treated}$, respectively. The average amount of $BV_{treated}$ when reaching the treatment goal of outgoing $\sum_{11}$PFAS < 50 ng L^{-1} (23 231) is close to the $BV_{treated}$ of the "old" GAC filter examined in the flow-rate experiment discussed above (21 971). By decreasing the flow-rates from 39 to 18 L s^{-1} (Fig. 4), the average service lifetime of a GAC filter could potentially be extended from 23 231 to 32 976 $BV_{treated}$ targeting a treatment goal of 50 ng L^{-1}, assuming a similar decrease in removal efficiency as prior a decrease in flow-rate (Fig. 5). Based on this estimation, service life times of "old" GAC filters could potentially be increased by an additional 9 745 $BV_{treated}$ and thus expand the filter's service lifetime by almost half for the treatment goal of outgoing $\sum_{11}$PFAS < 50 ng L^{-1}. Empirical data collected for one of the filters in the full-scale DTWP suggests this assumption to hold for certain PFAS compounds, see Fig. S3 in the SI. Similar estimations could be performed for other treatment goals, in case one would have data on the influence of flow-rate for different GAC operational ages at which those were reached. Takagi et al. (2011) proposed to renew GAC filters two or three times yearly. As shown in this work, estimation of when or how often to renew GAC filters should be based on $BV_{treated}$ in combination with the applied flow-rate and treatment goal rather than solely operational time. When looking at the influence of the operating flow-rate on other water quality

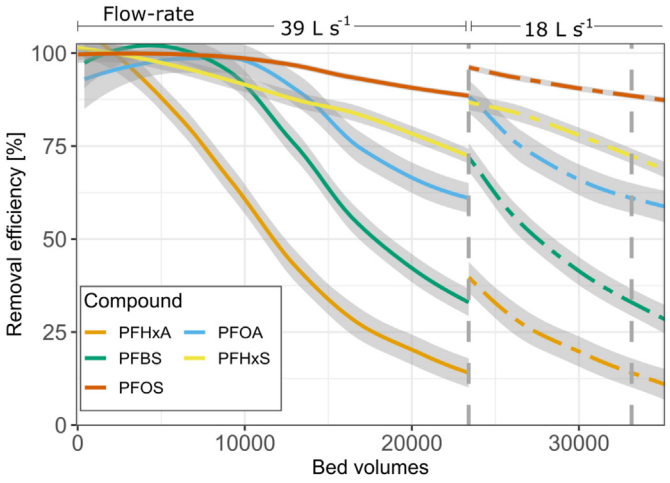

Fig. 5. Mean observed and predicted decrease in PFAS removal efficiency for all GAC filters monitored in this study. Grey shaded curves illustrate the 95% confidence intervals. Dashed lines depicted for bed volumes > 23 200 illustrate the expected behavior of removal efficiencies if flow-rates were decreased from 39 to 18 L s^{-1} at 23 200 $BV_{treated}$. Vertical dashed lines mark the average maximum amount of $BV_{treated}$ for reaching the treatment goal of outgoing $\sum_{11}$PFAS < 50 ng L^{-1} for a flow of 39 L s^{-1} and a subsequent decrease in flow-rate to 18 L s^{-1}, respectively.

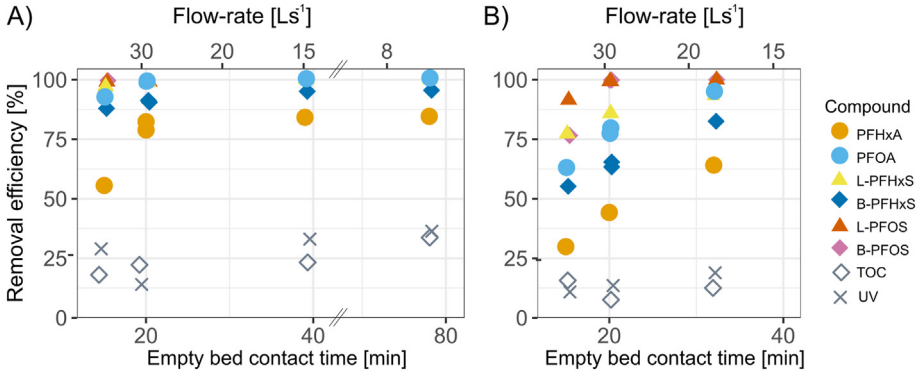

Fig. 4. Flow-rate experiment showing the removal efficiency of PFASs, total organic carbon (TOC) and UV absorption at 254 nm in % of A) a "young" GAC filter (63 operation days, 5 725 $BV_{treated}$) and B) an "old" GAC filter (264 operation days, 21 971 $BV_{treated}$) depending on the evaluated empty bed contact time (EBCT) in minutes (corresponding flow-rate in L s^{-1} shown on the upper axis). Duplicate samples were taken for each experiment with EBCT = 20 min and results from both samples are plotted.

parameters, it was found that lower flow-rates increased the removal efficiency not only for PFASs but also for organic carbon (Fig. 4). Significant changes ($p < 0.05$) in the removal of organic carbon (i.e. TOC) were observed when changing the EBCT in the "young" GAC filter from 39 to 7.5 L s^{-1} ($p = 0.017$; $r_p = 0.94$). The removal of TOC and substances responsible for UV light absorption at 254 nm was generally lower for the "older" GAC filter, for which a change in EBCT did not have a significant effect on the removal efficiency for either of the parameters. This is most likely because the "old" GAC filter already was saturated with organic matter at the time of the flow-rate experiments.

3.4. GAC operations costs for the removal of PFASs

Operational parameters and costs were derived for GAC 1 at Bäcklösa DWTP, during operation from April 28, 2015 till June 7, 2016 (406 days). Operation of this GAC filter serves as an illustrative example and is summarized in Table 2 for four different treated water goals: 10, 25, 50 and 85 ng L^{-1}, respectively. At the Bäcklösa DWTP, approximately 7 million m^3 drinking water are produced annually and distributed to about 80 000 consumers. The treatment goal for the plant is an average of 25 ng L^{-1} $\sum_{11}$PFAS while the regulatory limit is 90 ng L^{-1} for $\sum_{11}$PFAS. As shown in Table 2, the annual operation cost for the plant with a 25 ng L^{-1} treatment goal is 0.058 euro per m^{-3} treated. Treatment goals were the key factor determining service volume as shown by the 75, 244, and 318% greater service volume with a treatment goals of 25, 50, and 85 ng L^{-1}, respectively, as compared to a 10 ng L^{-1} treatment goal. Similarly, annual operations cost, which are dominated by regeneration costs, are lower if a higher treatment goal is adopted. Specifically, for treatment goals of 25, 50, and 85 ng L^{-1}, the annual operations costs are 42, 70, and 76% less, respectively, as compared to the cost with a treatment goal of 10 ng L^{-1}. This shows the impact of lowering or increasing regulatory levels for PFAS on operations costs.

Note that Table 2 costs are similar to those cited by McNamara et al., (2018) who estimated an operation cost of 0.025 euro m^{-3} (0.08 USD/1000 gal) for a simulated regenerated GAC filter, and estimated 0.038 euro m^{-3} (0.12 USD/1000 gal) for a simulated virgin GAC filter in order to achieve a water treatment goal of 70 ng L^{-1} for combined PFOA and PFOS in the treated water for a dual vessel lead-lag treatment.

3.5. Optimization of treatment costs

As discussed earlier, a number of factors affects the length of service of a GAC filter, specifically the adsorption capacity of the GAC, the treatment goals, the flow operation of the filters (EBCT), initial PFAS concentrations in the raw water and general water quality. In order to explore the GAC 1 unit costs, various cost scenarios were calculated for different treatment goals assuming hypothetically 20% lower cost for virgin GAC, 20% lower GAC regeneration cost, 10 and 20% longer service life to treatment goal, and if the service life is extended using the low flow strategy depicted in Fig. 5. Relative cost savings for each treatment goal hypothetically achieved by the different scenarios are shown in Fig. 6. Absolute unit cost are depicted as diamonds in Fig. 6 and the results again illustrate the dominating effect of treatment goals on treatment costs.

For the specific treatment goal of 50 ng L^{-1}, it can be seen that

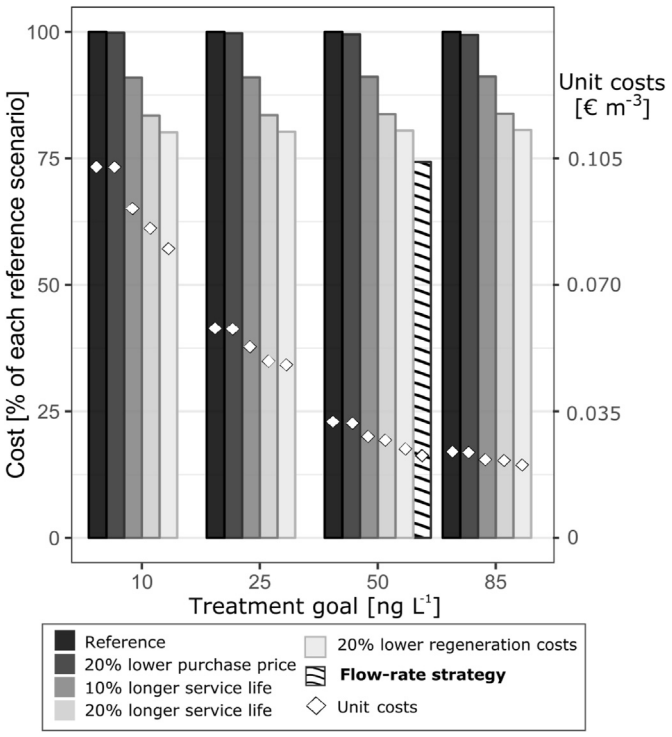

Fig. 6. Treatment costs for GAC 1 depending on treatment goal. Bars describe the relative costs for each cost scenario compared to the current (Reference) scenario. Diamonds illustrate estimations of the respective annual unit operations costs in the Bäcklösa drinking water treatment plant, i.e. unit costs.

Table 2
GAC1 treatment operational parameters and costs for PFAS removal.

Parameter	GAC filter 1 Filtrasorb® 400			
Treated water goal [ng L^{-1} $\sum_{11}$PFAS]	10	25	50	85
Average EBCT [min]	20	24	21	20
Inlet water average [ng L^{-1} $\sum_{11}$PFAS]	216	189	160	159
Service volume treated [1000 m^3]	247	433	850	1034
$BV_{treated}$	7 070	12 400	24 300	29 600
Carbon use rate [dry kg m^{-3} treated]	0.074	0.042	0.021	0.018
Total $\sum_{11}$PFAS loading [μg PFAS g^{-1} dry GAC]	2.9	4.2	6.0	6.9
Unit regeneration costs [euros m^{-3} treated][a]	0.10	0.06	0.03	0.02
Annual regeneration cost at Bäcklösa DWTP (1000 euros $year^{-1}$)[b]	707 000	404 000	206 000	169 000
Annual operations cost at Bäcklösa DWTP including regeneration and initial purchase of virgin GAC (1000 euro $year^{-1}$)[c]	712 000	409 000	211 000	174 000

[a] GAC regeneration cost 714 euro m^{-3} wet GAC.
[b] GAC regeneration cost for treatment of 7 million m^3 water per year at Bäcklösa DWTP.
[c] Virgin GAC cost 1142 euro m^{-3} wet GAC and service life 10 years with interest rate 5%.

the greatest cost savings, 26%, appears to be provided by adopting a strategy of adjusting flow-rates to extend the service life of the filter without exceeding the treatment goal (Fig. 5). A 20% reduction in regeneration costs reduces the unit costs by 20% in the case of this specific study while a reduction in the cost of virgin GAC has little effect. Utilization of a more efficient GAC which provides a 10% longer service volume decreases unit costs by 9% while a GAC providing 20% greater service volume reduces unit costs by 16%. Thus, an initial greater cost for high quality virgin GAC can be offset if greater service volume is provided. Similarly, it is economically worthwhile to reduce the cost of regeneration by competitive bidding or even by cooperation between water producers to establish joint-owned regeneration facilities.

4. Conclusions

This study confirmed that conventional treatment techniques are not efficient for PFAS removal in a full-scale DWTP. However, GAC filters present a reliable treatment method for the removal of PFASs, which is straight forward to operate and can utilize the existing competitive GAC market to minimize operations costs. The removal efficiency for GAC filters evaluated in this study was higher for long chained PFASs than for short chained PFASs and PFSAs were removed better than PFCAs. Adjusting the flow-rate through two full-scale GAC filters of different operational ages showed a positive correlation of PFAS removal with lower flow-rates (higher EBCT). The “young” GAC filter was less effected by the change in flow-rates, while the removal efficiency of the “old” GAC filter could be increased substantially by decreasing the flow. Estimations based on the six month data set for six GAC filters suggest that GAC service life could be prolonged by almost half if the flow-rate was decreased from the conventionally applied 39 to 18 L s^{-1} after having reached the treatment goal of Σ_{11}PFAS < 50 ng L^{-1} in the outgoing water.

A subsequent cost analysis indicated an overwhelming effect of the treatment goals on unit cost. A decrease of Sweden’s current regulatory guidelines of accepted 90 ng L^{-1} in finished drinking water to 50, 25 or even 10 ng L^{-1} would increase annual operations cost at the examined DWTP by 21, 135 and 314%, respectively. It was further shown, that regeneration cost is the dominant PFAS treatment cost factor at the Bäcklösa DWTP. Prolonging the overall service life time of the GAC filters by adopting a operations strategy of adjustment to low flow-rates at the end of service life could decrease operations costs. It is worth recalling that treatment performance of GAC is highly dependent on water quality and that there is a need for empirical studies for each raw water when comparing GAC filters in full-scale drinking water treatment plants. The tools and methods presented in this study can, however, easily be applied to other cases of full-scale operation and therefore provide valuable insights for drinking water providers worldwide. Future research should examine how to monitor the performance of GAC filters (i.e. good removal efficiencies for PFASs) and should attempt to quantify the influence of EBCT, ingoing PFAS concentrations and water quality parameters like organic matter concentrations for better performance and GAC service lifetime predictability.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.watres.2020.115913.

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Attachment 16

ScienceDirect

Water Research
Volume 188, 1 January 2021, 116546

Rejection of per- and polyfluoroalkyl substances (PFASs) in aqueous film-forming foam by high-pressure membranes

Charlie J. Liu ✉, Timothy J. Strathmann ✉, Christopher Bellona ✉

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Highlights

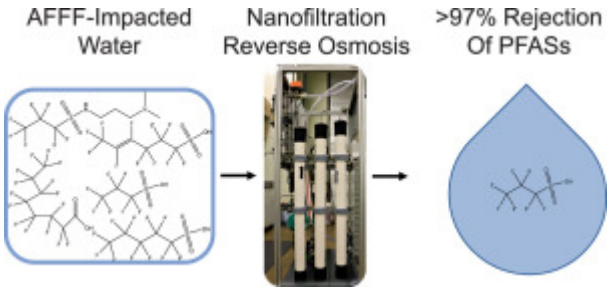
- >97% rejection of 42 different PFASs by nanofiltration and reverse osmosis.
- Membrane operating conditions marginally impacted PFAS rejection.
- Rejection reduced in groundwater matrix.
- Hydrophobic adsorption of PFASs to membranes, permeate spacer, and membrane system.
- Long-term membrane performance was not impacted by adsorption.

Abstract

The ubiquitous use and manufacturing of per- and polyfluoroalkyl substances (PFASs) have led to the contamination of water resources worldwide. High-pressure membranes, including nanofiltration (NF) and reverse osmosis (RO), are increasingly being deployed for water treatment and may be an effective barrier to PFASs. However, the impact of membrane operating

conditions, background water matrix, and solute adsorption on rejection of diverse PFASs by NF and RO remains unclear. Rejection of perfluoroalkyl acids (PFAAs) present in aqueous film-forming foam (AFFF) diluted into a laboratory electrolyte matrix by NF and RO spiral wound elements was >98% and >99%, respectively. Rejection of the same PFAAs present in an AFFF-impacted groundwater matrix by NF was lower, between 92-98%, and was attributed to background water matrix constituents. Operating conditions did not have a significant impact on rejection of PFASs with the exception of shorter chain perfluoroalkyl sulfonic acids (PFSAs) in the AFFF-impacted groundwater matrix, where rejection increased with increasing flux. Structure-activity analysis of 42 PFASs, including 10 PFAAs and 32 PFASs identified in AFFF through high-resolution mass spectrometry suspect screening methods, showed some correlation between rejection and compound molecular weight. Adsorptive losses of PFAAs, most notably longer-chain hydrophobic PFAAs, to the spiral wound membrane elements and the membrane system were observed. Adsorption of PFAAs to the permeate spacer was especially pronounced and may have implications of artificially high rejection values. Still, rejection of PFASs by NF remained consistently >98% over 13 days of continuous operation.

Graphical abstract



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Keywords

Nanofiltration; Reverse osmosis; Pilot-scale; Adsorption; Groundwater; High-resolution mass spectrometry

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Attachment 17

Basic Information about Lead in Drinking Water

Have a question that's not answered on this page? Contact the Safe Drinking Water Hotline <https://epa.gov/your-drinking-water/safe-drinking-water-hotline>.

Información relacionada disponible en español <https://espanol.epa.gov/plomo>

Infographic: Lead in Drinking Water

<https://epa.gov/node/187177>

EPA and the Centers for Disease Control and Prevention (CDC) agree that there is no known safe level of lead in a child's blood. Taking action to reduce these exposures can improve outcomes. Lead is harmful to health, especially for children.

On this page:

General Information about Lead in Drinking Water

- How lead gets into drinking water
- Health effects of being exposed to lead in drinking water
- Can I shower in lead-contaminated water?

What You Can Do

- Find out if lead is in your drinking water
- Important steps you can take to reduce lead in drinking water

- Find out if you have lead pipes in your home with the Protect Your Tap: A Quick Check for Lead guide
- Get your child tested to determine lead levels in his or her blood
- Find out if lead in drinking water is an issue in your child's school or child care facility

Drinking Water Requirements for Lead

- EPA's drinking water regulations for lead
- How EPA requires states and public water systems to protect drinking water

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General Information about Lead in Drinking Water

How Lead Gets into Drinking Water

Lead can enter drinking water when plumbing materials that contain lead corrode, especially where the water has high acidity or low mineral content that corrodes pipes and fixtures. The most common sources of lead in drinking water are lead pipes, faucets, and fixtures. In homes with lead pipes that connect the home to the water main, also known as lead services lines, these pipes are typically the most significant source of lead in the water. Lead pipes are more likely to be found in older cities and homes built before 1986. Among homes without lead service lines, the most common problem is with brass or chrome-plated brass faucets and plumbing with lead solder.

The Safe Drinking Water Act (SDWA) has reduced the maximum allowable lead content -- that is, content that is considered "lead-free" -- to be a weighted average of 0.25 percent calculated across the wetted surfaces of pipes, pipe fittings, plumbing fittings, and fixtures and 0.2 percent for solder and flux.

- Learn more about the maximum allowable content of lead in pipes, solder, fittings and fixtures <https://epa.gov/dwstandardsregulations/section-1417-safe-drinking-water-act-prohibition-use-lead-pipes-solder-and>
- Learn more about EPA's regulations to prevent lead in drinking water
- Learn how to identify lead-free certification marks on drinking water system and plumbing products (PDF)

Corrosion is a dissolving or wearing away of metal caused by a chemical reaction between water and your plumbing. A number of factors are involved in the extent to which lead enters the water, including:

- the chemistry of the water (acidity and alkalinity) and the types and amounts of minerals in the water,
- the amount of lead it comes into contact with,
- the temperature of the water,
- the amount of wear in the pipes,
- how long the water stays in pipes, and
- the presence of protective scales or coatings inside the plumbing materials.

To address corrosion of lead and copper into drinking water, EPA issued the Lead and Copper Rule (LCR) <https://epa.gov/dwreginfo/lead-and-copper-rule> under the authority of the SDWA. One requirement of the LCR is corrosion control treatment to prevent lead and copper from contaminating drinking water. Corrosion control treatment means utilities must make drinking water less corrosive to the materials it comes into contact with on its way to consumers' taps. Learn more about EPA's regulations to prevent lead in drinking water.

Health Effects of Exposures to Lead in Drinking Water*

> *The health effects information on this page is not intended to catalog all possible health effects for lead. Rather, it is intended to let you know about the most significant and probable health effects associated with lead in drinking water.

Is there a safe level of lead in drinking water?

The Safe Drinking Water Act requires EPA to determine the level of contaminants in drinking water at which no adverse health effects are likely to occur with an adequate margin of safety. These non-enforceable health goals, based solely on possible health risks, are called maximum contaminant level goals (MCLGs). EPA has set the maximum contaminant level goal for lead in drinking water at zero because lead is a toxic metal that can be harmful to human health even at low exposure levels. Lead is persistent, and it can bioaccumulate in the body over time.

Young children, infants, and fetuses are particularly vulnerable to lead because the physical and behavioral effects of lead occur at lower exposure levels in children than in adults. A dose of lead that would have little effect on an adult can have a significant effect on a child.

In children, low levels of exposure have been linked to damage to the central and peripheral nervous system, learning disabilities, shorter stature, impaired hearing, and impaired formation and function of blood cells.

The Centers for Disease Control and Prevention (CDC) recommends that public health actions be initiated when the level of lead in a child's blood is 5 micrograms per deciliter (µg/dL) or more.

It is important to recognize all the ways a child can be exposed to lead. Children are exposed to lead in paint, dust, soil, air, and food, as well as drinking water. If the level of lead in a child's blood is at or above the CDC action level of 5 micrograms per deciliter, it may be due to lead exposures from a combination of sources. EPA estimates that drinking water can make up 20 percent or more of a person's total exposure to lead. Infants who consume mostly mixed formula can receive 40 percent to 60 percent of their exposure to lead from drinking water.

Children

Even low levels of lead in the blood of children can result in:

- Behavior and learning problems
- Lower IQ and hyperactivity
- Slowed growth
- Hearing problems
- Anemia

In rare cases, ingestion of lead can cause seizures, coma and even death.

Pregnant Women

Lead can accumulate in our bodies over time, where it is stored in bones along with calcium. During pregnancy, lead is released from bones as maternal calcium and is used to help form the bones of the fetus. This is particularly true if a woman does not have enough dietary calcium. Lead can also cross the placental barrier exposing the fetus to lead. This can result in serious effects to the mother and her developing fetus, including:

- Reduced growth of the fetus
- Premature birth

Find out more about lead's effects on pregnancy:

- Effects of Workplace Hazards on Female Reproductive Health EXIT <http://www.cdc.gov/niosh/docs/99-104/> (National Institute for Occupational Safety and Health)

Lead can also be transmitted through breast milk. Read more on lead exposure in pregnancy and lactating women (PDF) EXIT <http://www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf> (302 pp, 4.3 MB, About PDF <https://epa.gov/home/pdf-files>) .

Adults

Lead is also harmful to adults. Adults exposed to lead can suffer from:

- Cardiovascular effects, increased blood pressure and incidence of hypertension
- Decreased kidney function
- Reproductive problems (in both men and women)

Related Information

- Learn more about lead and its health effects <https://epa.gov/lead/learn-about-lead>

Can I shower in lead-contaminated water?

Yes. Bathing and showering should be safe for you and your children, even if the water contains lead over EPA's action level. Human skin does not absorb lead in water.

This information applies to most situations and to a large majority of the population, but individual circumstances may vary. Some situations, such as cases involving highly corrosive water, may require additional recommendations or more stringent actions. Your local water authority is always your first source for testing and identifying lead contamination in your tap water. Many public water authorities have websites that include data on drinking water quality, including results of lead testing. Links to such data can be found on the EPA Consumer Confidence Report <https://epa.gov/ccr> website.

For more information, see CDC's "Sources of Lead: Water" Web page EXIT <http://www.cdc.gov/nceh/lead/tips/water.htm>.

What You Can Do

Find Out if Lead is in Your Drinking Water

First, learn more about the water coming into your home

EPA requires all community water systems to prepare and deliver an annual water quality report called a ***Consumer Confidence Report (CCR)*** for their customers by July 1 of each year. Contact your water utility if you'd like to receive a copy of their latest report. If your water comes from a household well or other private water supply, check with your health department, or with any nearby water utilities that use ground water, for information on contaminants of concern in your area.

- Find your local Consumer Confidence Report
- Information about CCRs for consumers <https://epa.gov/ccr/ccr-information-consumers>
- EPA's CCR home page <https://epa.gov/ccr>
- Learn more about protecting water quality from private drinking water wells <https://epa.gov/privatewells>
- Printable color fact sheet: Is There Lead in My Drinking Water?

EPA's ***Public Notification Rule*** requires public water systems to alert you if there is a problem with your drinking water.

- Learn more about the Public Notification Rule <https://epa.gov/dwreginfo/public-notification-rule>

Second, you can have your water tested for lead

Homes may have internal plumbing materials containing lead. Since you cannot see, taste, or smell lead dissolved in water, testing is the only sure way of telling whether there are harmful quantities of lead in your drinking water. A list of certified laboratories are available from your state or local drinking water authority. Testing costs between $20 and $100. Contact your water supplier as they may have useful information, including whether the service connector used in your home or area is made of lead.

You can learn on our Protect Your Family from Exposures to Lead web page <https://epa.gov/lead/protect-your-family-exposures-lead#testdw>:

- when you may want to test your drinking water; and
- what to do if your home tests positive for lead.

You can also view and print a fact sheet on testing your home's drinking water <https://epa.gov/your-drinking-water/home-drinking-water-testing-fact-sheet>.

Important Steps You Can Take to Reduce Lead in Drinking Water

- **Have your water tested**. Contact your water utility to have your water tested and to learn more about the lead levels in your drinking water.
- **Learn if you have a lead service line**. Contact your water utility or a licensed plumber to determine if the pipe that connects your home to the water main (called a service line) is made from lead.
- **Run your water.** Before drinking, flush your home's pipes by running the tap, taking a shower, doing laundry, or doing a load of dishes. The amount of time to run the water will depend on whether your home has a lead service line or not, and the length of the lead service line. Residents should contact their water utility for recommendations about flushing times in their community.
- **Learn about construction in your neighborhood.** Be aware of any construction or maintenance work that could disturb your lead service line. Construction may cause more lead to be released from a lead service line.
- **Use cold water.** Use only cold water for drinking, cooking and making baby formula. Remember, boiling water does not remove lead from water.
- **Clean your aerator.** Regularly clean your faucet's screen (also known as an aerator). Sediment, debris, and lead particles can collect in your aerator. If lead particles are caught in the aerator, lead can get into your water.
- **Use your filter properly.** If you use a filter, make sure you use a filter certified to remove lead. Read the directions to learn how to properly install and use your cartridge and when to replace it. Using the cartridge after it has expired can make it less effective at removing lead. Do not run hot water through the filter.

Learn more by reviewing EPA's Lead in Drinking Water Infographic <https://epa.gov/sites/production/files/2017-08/documents/epa_lead_in_drinking_water_final_8.21.17.pdf>.

Related Information

- Fact sheet: How to Identify Lead-Free Certification Marks for Drinking Water System & Plumbing Products (PDF)
- Factsheet: A Consumer Tool for Identifying Point of Use (POU) Drinking Water Filters Certified to Reduce Lead (PDF) <https://epa.gov/water-research/consumer-tool-identifying-pou-drinking-water-filters-certified-reduce-lead>
- How to make your home lead-safe <https://epa.gov/lead/protect-your-family#homeleadsafe>
- What you can do to protect your drinking water <https://epa.gov/sourcewaterprotection/how-can-you-help-protect-source-water>

Find out if you have lead pipes in your home with the Protect Your Tap: A Quick Check for Lead guide

Protect Your Tap: A quick check for lead <https://epa.gov/ground-water-and-drinking-water/protect-your-tap-quick-check-lead-0> **is an on-line step by step guide** to learn how to find lead pipes, called service lines, in your home. It also provides tips about reducing exposure to lead in drinking water and how to get your water tested for lead and resources to learn more.

You can learn about how this guide was developed and toolkits for sharing with others on the Protect Your Tap <https://epa.gov/ground-water-and-drinking-water/protect-your-tap-quick-check-lead> outreach page.

Tool kits for different sectors with resources to create your own campaign to get others to use Protect Your Tap:

Community Groups

Protect Your Tap: A Quick Check for Lead is for housing authorities and community organizations to help residents learn more about lead in drinking water. While providing safe affordable housing is a critical need, lead in drinking water can sometimes be overlooked.

Government

Protect Your Tap: A Quick Check for Lead is intended for use by state and municipal government officials such as water superintendents, public health officers, and building inspectors to help residents learn more about lead in drinking water.

Health

Protect Your Tap: A Quick Check for Lead is for doctors, school nurses, and community health providers to help patients learn more about lead in drinking water. Protecting children from exposure to lead is important to lifelong good health. Even low levels of lead in blood have been shown to have harmful, irreversible effects. Children six years old and younger are most susceptible to the effects of lead.

Utilities

Protect Your Tap: A Quick Check for Lead is for water utility companies to help customers learn more about lead in drinking water.

Get Your Child Tested to Determine Lead Levels in His or Her Blood

A family doctor or pediatrician can perform a blood test for lead and provide information about the health effects of lead. State, city or county departments of health can also provide information about how you can have your child's blood tested for lead. The Centers for Disease Control and Prevention recommends that public health actions be initiated when the level of lead in a child's blood is 5 micrograms per deciliter (µg/dL) or more.

Find Out if Lead in Drinking Water is an Issue in Your Child's School or Child Care Facility

Children spend a significant part of their days at school or in a child care facility. The faucets that provide water used for consumption, including drinking, cooking lunch, and preparing juice and infant formula, should be tested.

- Protect your children from lead where they learn and play: learn how to test your child, and how to check the condition of schools and child care facilities <https://epa.gov/lead/protect-your-family-exposures-lead#protect>
- How schools and child care centers can test for lead in drinking water <https://epa.gov/ground-water-and-drinking-water/3ts-reducing-lead-drinking-water-toolkit>

Drinking Water Requirements for Lead

EPA's Drinking Water Regulations for Lead

In 1974, Congress passed the Safe Drinking Water Act. This law requires EPA to determine the level of contaminants in drinking water at which no adverse health effects are likely to occur with an adequate margin of safety. These non-enforceable health goals, based solely on possible health risks are called maximum contaminant level goals (MCLGs). The MCLG for lead is zero. EPA has set this level based on the best available science which shows there is no safe level of exposure to lead. The fact that there is no safe level of exposure underscores the fact that any action to reduce exposures can have impacts on lives and livelihoods.

For most contaminants, EPA sets an enforceable regulation called a maximum contaminant level (MCL) based on the MCLG. MCLs are set as close to the MCLGs as possible, considering cost, benefits and the ability of public water systems to detect and remove contaminants using suitable treatment technologies.

However, because lead contamination of drinking water often results from corrosion of the plumbing materials belonging to water system customers, EPA established a treatment technique rather than an MCL for lead. A treatment technique is an enforceable procedure or level of technological performance which water systems must follow to ensure control of a contaminant.

The treatment technique regulation for lead (referred to as the ***Lead and Copper Rule*** <*https://epa.gov/dwreginfo/lead-and-copper-rule*>) requires water systems to control the corrosivity of the water. The regulation also requires systems to collect tap samples from sites served by the system that are more likely to have plumbing materials containing lead. If more than 10 percent of tap water samples exceed the lead action level of 15 parts per billion, then water systems are required to take additional actions including:

- Taking further steps optimize their corrosion control treatment (for water systems serving 50,000 people that have not fully optimized their corrosion control) .
- Educating the public about lead in drinking water and actions consumers can take to reduce their exposure to lead.
- Replacing the portions of lead service lines (lines that connect distribution mains to customers) under the water system's control.

EPA issued the Lead and Copper Rule in 1991 and revised the regulation in 2000, 2007 and 2021. States may set more stringent drinking water regulations than EPA.

In addition:

- EPA requires all community water systems to prepare and deliver an annual water quality report called a ***Consumer Confidence Report (CCR)*** for their customers.
    - Find your local Consumer Confidence Report
    - Information about CCRs for consumers <https://epa.gov/ccr/ccr-information-consumers>
    - EPA's CCR home page <https://epa.gov/ccr>
- EPA's ***Public Notification Rule*** requires public water systems to alert you if there is a problem with your drinking water.
    - Learn more about the Public Notification Rule. <https://epa.gov/dwreginfo/public-notification-rule>

- In 2011, changes to the Safe Drinking Water Act reduced the maximum allowable lead content -- that is, content that is considered "lead-free" -- to be a weighted average of 0.25 percent calculated across the wetted surfaces of pipes, pipe fittings, plumbing fittings, and fixture and 0.2 percent for solder and flux. Learn more about the maximum allowable content of lead in pipes, solder, fittings and fixtures.
  <https://epa.gov/dwstandardsregulations/section-1417-safe-drinking-water-act-prohibition-use-lead-pipes-solder-and>

How EPA Requires States and Public Water Systems to Protect Drinking Water

The Safe Drinking Water Act (SDWA) requires EPA to establish and enforce standards that public drinking water systems must follow. EPA delegates primary enforcement responsibility (also called ***primacy***) for public water systems to states and tribes if they meet certain requirements. Learn more about:

- The SDWA <https://epa.gov/sdwa> and SDWA standards <https://epa.gov/sdwa/background-drinking-water-standards-safe-drinking-water-act-sdwa>
- How EPA regulates drinking water contaminants <https://epa.gov/sdwa/how-epa-regulates-drinking-water-contaminants>
- Primacy enforcement responsibility for public water systems <https://epa.gov/dwreginfo/primacy-enforcement-responsibility-public-water-systems>

Related Information from Other Federal Government Agencies

Centers for Disease Control and Prevention (CDC):

- About Lead in Drinking Water EXIT <http://www.cdc.gov/nceh/lead/leadinwater/>
- Prevention Tips for Lead in Water EXIT <http://www.cdc.gov/nceh/lead/tips/water.htm>
- CDC main page on lead EXIT

Agency for Toxic Substances & Disease Registry (ATSDR):

- Public Health Statement for Lead EXIT
- ToxFAQs for Lead EXIT
- ATSDR main page on lead EXIT

- Basic Information <https://www.epa.gov/ground-water-and-drinking-water/drinking-water-your-home>
- Private Wells <https://www.epa.gov/privatewells>
- Consumer Confidence Reports <https://www.epa.gov/ccr>
- Regulatory Requirements <https://www.epa.gov/dwreginfo>
- Standards and Regulations <https://epa.gov/sdwa>
- All Drinking Water Topics <https://epa.gov/ground-water-and-drinking-water/drinking-water-topics>
- Safe Drinking Water Information System
- For Students and Teachers <https://www.epa.gov/ground-water-and-drinking-water/drinking-water-activities-kids-and-teachers>

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LAST UPDATED ON FEBRUARY 1, 2022

Attachment 18

Vocabulary Catalog

Drinking Water Technical & Legal Terms

Long Name: Drinking Water Glossary: A Dictionary of Technical and Legal Terms Related to Drinking Water

Description: A dictionary of technical and legal terms related to drinking water

Publishing Organization: Office of Water/Office of Ground Water and Drinking Water

Last Update: February 17, 2009

Program Site: https://www.epa.gov/ground-water-and-drinking-water

Terms & Acronyms

Search Terms (Contains): turbidity

Back to Search **Back to Main Results**

2 results found (Export options: Excel | XML | PDF | RTF)

Page 1 of 1 Results per page: 50

	Term
☐	**Nephelometric Turbidity Unit** **Definition:** The unit of measure for turbidity. **Acronym:** NTU
☐	**Turbidity** **Definition:** (ter-BID-it-tee) The cloudy appearance of water caused by the presence of suspended and colloidal matter. Technically, turbidity is an optical property of the water based on the amount of light reflected by suspended particles. In the waterworks field, a turbidity measurement is used to indicate the... more

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- EPA Enterprise Vocabulary
- Taxonomies

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VERSION: RELEASE/4.14.2

Attachment 19

Assessing the Benefits of Drinking Water Regulations : A Primer for Stakeholders

OGWDW (Mail Code 4607M)
EPA
www.
April 2002

ACKNOWLEDGMENTS

This report was developed as a joint product of EPA's Office of Ground Water and Drinking Water and National Center for Environmental Economics. Representatives from many different offices within EPA reviewed and provided insightful comments on earlier drafts of this report. In addition, the discussions of the Benefits Working Group of the National Drinking Water Advisory Council helped shape its content.

This document is intended to provide information on the process currently followed by EPA when assessing the benefits of drinking water regulations. It is not intended as guidance.

Table of Contents

OVERVIEW

The U.S. Environmental Protection Agency's (EPA's) Office of Ground Water and Drinking Water developed *Assessing the Benefits of Drinking Water Regulations: A Primer for Stakeholders* to provide information to stakeholders and other interested parties on analyzing the effects of regulations establishing Maximum Contaminant Levels (MCLs) for drinking water. This *Overview* summarizes the information contained in this document for those interested in a brief synopsis of key issues.

EPA created this document in response to new provisions contained in the 1996 Amendments to the Safe Drinking Water Act (SDWA), working closely with a group of stakeholders -- the Benefits Working Group of the National Drinking Water Advisory Council. The Amendments create specific requirements for assessing benefits and for using the resulting information in EPA decision-making. This document focuses on the benefits valuation issues commonly addressed by EPA's economists and policy analysts. We also briefly discuss the assessment of costs and risks, and provide references for more detailed information on these topics.

In addition to SDWA's statutory provisions, regulatory benefit-cost analyses conducted by the Federal government are subject to several other sets of requirements. Chief among these are guidelines developed by the U.S. Office of Management and Budget for all Federal agencies and guidance developed by EPA for its own programs. These documents require analysts to adhere to "best practices" as defined by the economics profession, and emphasize the need to clearly communicate (1) the rationale for decisions made in the course of the analysis; (2) the implications of the findings; and (3) the uncertainties in the resulting estimates. Regulatory analyses also comply with several statutory and administrative requirements for addressing impacts on selected groups, including small businesses and government units, low income and minority populations (i.e., environmental justice), and children. This document is based on, and consistent with, these sources of requirements for regulatory analyses.

The remainder of this *Overview* discusses five subjects: the SDWA requirements for benefits assessment; the general categories of benefits most often addressed; the measures of value preferred by economists; the general methods used to estimate these values; and the specific methods used to value benefits related to reducing the risks of mortality, morbidity and other effects. The following chapters provide more detailed information on these topics as well as references to the underlying literature.

SDWA Requirements For Benefits Analysis

EPA has used benefit-cost analysis for many years as one of several sources of information on the impacts of alternative policy choices. While there are many ways to categorize the positive and negative impacts of a regulation, traditionally EPA has

defined the "cost" side of the analysis as including estimates of the expenditures needed to comply with new regulations (e.g., of installing pollution control equipment) and of the market effects of these expenditures (e.g., on the prices charged for the products of affected industries). The "benefits" side of the analysis generally focuses on the effects of reducing contamination levels, including effects on human health, the natural environment, and man-made materials.

EPA's ability to use the results of these analyses in decision-making under SDWA was limited prior to the 1996 Amendments. The Agency's choice of regulatory levels was constrained by statutory language requiring EPA to set MCLs as close to the MCLG as is "feasible" [SDWA, Section 1412(b)(4)(B)], and defined feasible as the use of the best technology and treatment techniques examined for efficacy under field conditions, taking cost into consideration [SDWA, Section 1412(b)(4)(D)]. Under the amendments, EPA may, at its discretion, establish a less stringent MCL if the costs of achieving the lowest feasible level are not justified by its benefits.

The amendments list a number of issues that should be addressed in benefits analyses, including:

- the quantifiable and non-quantifiable health risk reduction benefits of control of the contaminant proposed for regulation at the specified MCL;
- the quantifiable and non-quantifiable health risk reduction benefits of any control of co-occurring contaminants that can be attributed solely to the proposed MCL, exclusive of compliance with other proposed or promulgated regulations;
- the quantifiable and non-quantifiable costs of compliance with the proposed MCL, including monitoring, treatment, and other costs, exclusive of costs of compliance with other proposed or promulgated regulations;
- the incremental costs and benefits associated with each alternative MCL under consideration;
- the effects of the contaminant on the general population, and on groups within the population that are likely to be at greater risk of adverse health effects from drinking water contaminants, such as infants, children, pregnant women, the elderly, and individuals with a history of serious illness;

- the increased health risks, if any, that may result from compliance with the proposed MCL, including risks associated with co-occurring contaminants; and,

- other relevant factors, including the quality of the available information supporting the analysis, the uncertainties in the analysis, and factors relating to the degree and nature of the identified risks.

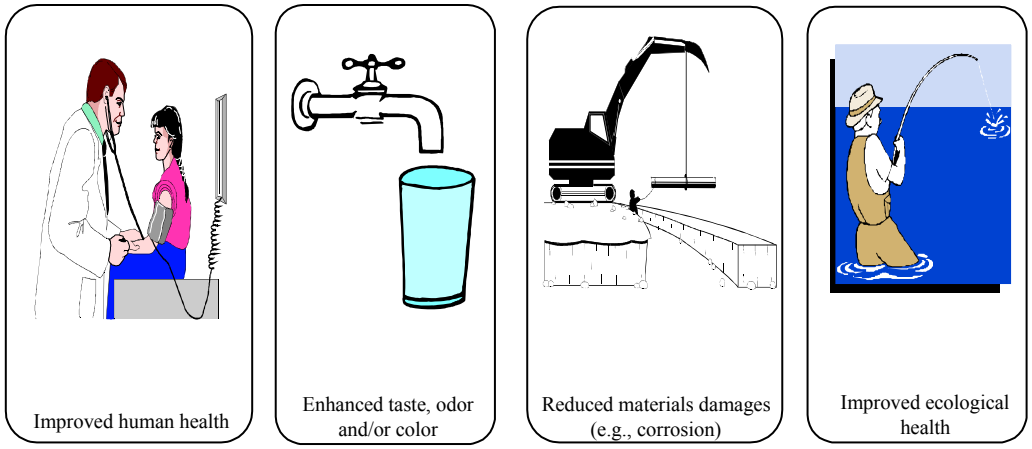
SDWA also requires that these analyses be based on the best available scientific research.

Types of Benefits

For regulations that establish MCLs, a variety of benefits may be associated with reducing the effects of contamination on users of public water supplies (including households, commercial establishments, and industry) as well as on the water system itself. Chief among these effects are reductions in human health risks. The regulations may decrease the risks of incurring particular illnesses or adverse health effects as well as the risks of dying from these illnesses.

Depending on the characteristics of the contaminants, drinking water regulations may have other types of benefits, including aesthetic effects (improved taste, odor, and/or color) and effects on man-made materials (e.g., reduced corrosion). In cases where significant increases in source water protection result from the regulation, ecological benefits may also accrue. Ecological benefits may include improved fishing and recreational opportunities, protection of biodiversity, or enhanced nonuse values (e.g., the pleasure of knowing that clean water exists). Examples of these benefits categories are illustrated in Exhibit 1.

Exhibit 1
Benefits of Drinking Water Regulations



To determine the types of benefits to be assessed for a specific regulation, analysts generally begin by developing an inclusive list of the possible effects of controlling the contaminants on all types of water users. Analysts then often conduct screening analysis of selected effects, focusing on those that are most likely to be significant. Next, analysts expand and/or refine the analysis as needed to address key sources of uncertainty. This type of sequencing is designed to focus Agency resources on addressing those issues most likely to affect the ultimate policy decision.

Definition of "Value"

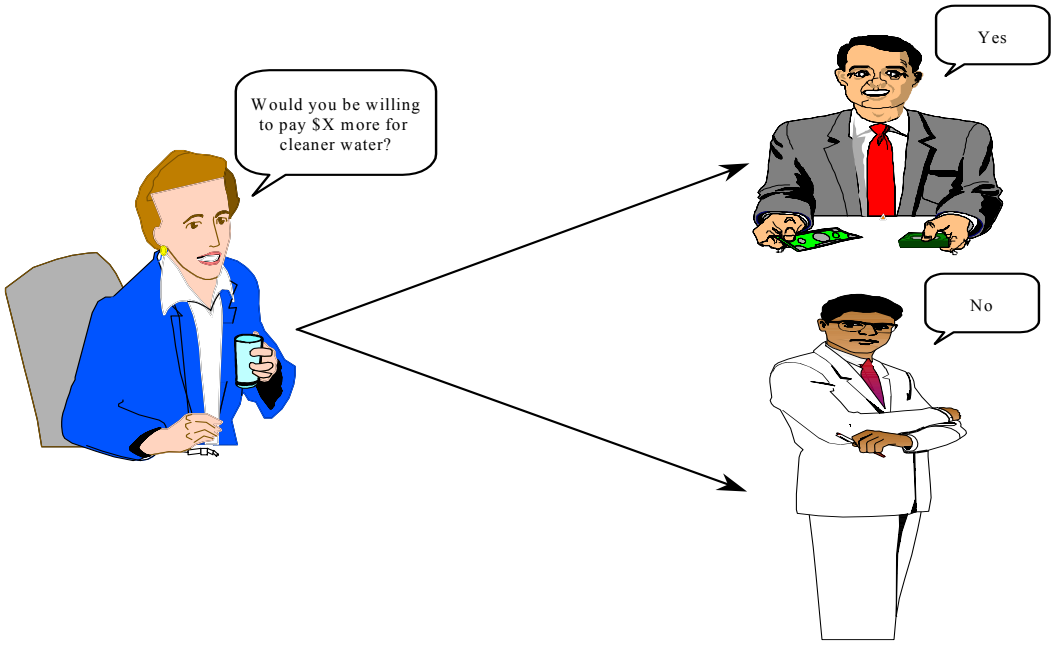
The practice of benefits assessment is based on the discipline of welfare economics. When determining the value of benefits such as those resulting from drinking water regulations, economists begin with the assumption that individuals derive utility (or a sense of satisfaction or well-being) from the goods and services they consume. Individuals can maintain the same level of utility while trading off different bundles of goods and services (e.g., one may be equally happy going to the movies or a baseball game), and their willingness to make these trade-offs can be measured in dollar terms.

In theory, the dollar value of a regulatory requirement is most appropriately measured by determining the change in income (or compensation) that has the same effect on utility (or the level of individual satisfaction) as the requirement. Because utility is difficult to measure directly, economists usually rely on estimates of *willingness to pay* to value the effects of these types of requirements. Willingness

to pay is the maximum amount of money an individual would voluntarily exchange to obtain an improvement; e.g., in drinking water quality.

Willingness to pay is a different concept than cost or price. Cost refers to the resources needed to produce a good or service; it does not measure the value of the good or service to members of society. Price is determined by the interactions of suppliers and consumers in the marketplace. Individual willingness to pay may exceed the current price, in which case the individual benefits from the fact that the market price is less than he or she is willing to pay. If price instead exceeds willingness to pay, then the individual would not purchase the good. An example of this concept is provided in Exhibit 2.

Exhibit 2
Individual's Willingness to Pay



The amount by which willingness to pay exceeds price is referred to as consumer surplus by economists, and aggregate changes in this difference (i.e., across all consumers) can be used to measure the dollar value of the social welfare effects of government policies. For example, consumers generally benefit from price decreases because willingness to pay will then exceed price by a larger amount.

Measuring the value of benefits in dollar terms has two key advantages. First, expressing both costs and benefits in monetary terms allows policymakers to more easily compare these measures of a regulation's impact. Second, valuation provides

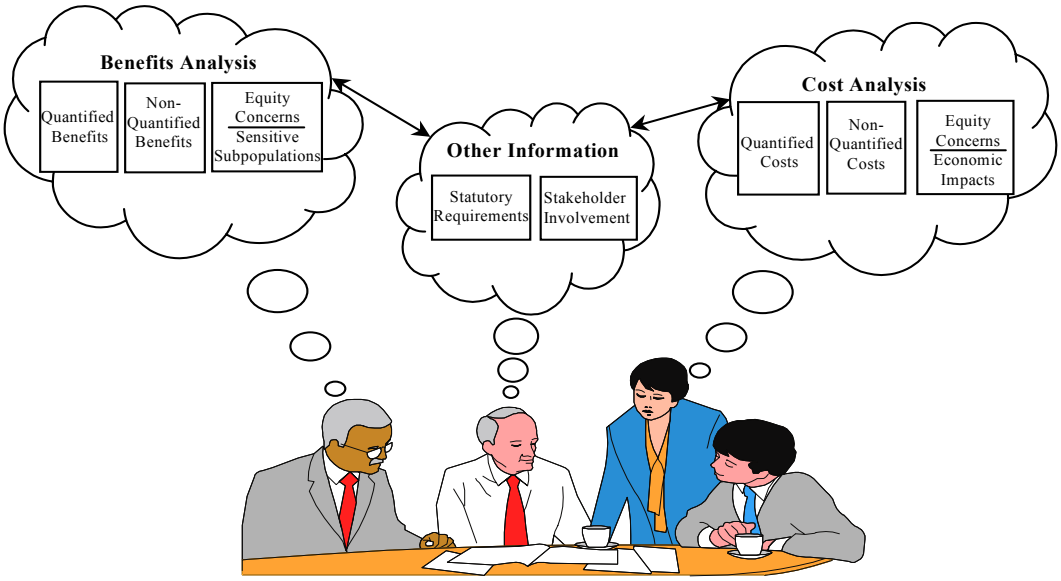
explicit information on the values held by individual members of society for the benefits of alternative policy choices.

However, critics of benefit-cost analysis are concerned that this approach does not take into account the distributional effects of a policy. For example, they argue that lower income individuals may not be treated equitably if decisions are based solely on willingness to pay (which is constrained by income). Economists traditionally focus on how individuals value changes in their own well-being -- aggregating the individual values to determine total benefits, and argue that ethical judgements about distributional effects should be addressed separately.

Because of these concerns, economic benefit-cost analyses of EPA regulations are supplemented by analyses of effects on equity. For example, analysis of environmental justice (effects on low income and minority groups) and risks to children are required for all major EPA regulations. In addition, SDWA requires that EPA consider effects on sensitive subpopulations *"such as infants, children, pregnant women, the elderly, and individuals with a history of serious illness, or other subpopulations likely to be at greater risk..."*

Also, many benefits can be difficult to quantify or may be quantifiable but difficult to value in monetary terms. EPA explicitly considers these non-quantified or non-monetized benefits in setting regulatory standards. The many factors EPA considers are illustrated in Exhibit 3 below.

Exhibit 3
Information for Decision-Making



Valuation Methods

The preferred approach for valuing the benefits of environmental regulations is generally to determine individuals' willingness to pay (WTP) by observing the market demand for related improvements. However, there is often no marketplace for directly buying and selling reductions in environmental contamination. When market data are lacking, economists may use a variety of methods to estimate WTP, which are often divided into two categories: *stated preference methods* and *revealed preference methods*.

Stated preference methods typically employ survey techniques and ask respondents to "state" what they would pay for a good or service. These methods can be used to directly value the program of concern (e.g., "how much would you be willing to pay for a program that would reduce the concentrations of arsenic in drinking water from 10 µg/L to 5 µg/L?") or to assess specific effects of the program (e.g., "how much would you be willing to pay for a program that would reduce the risks of incurring kidney disease from 10/100,000 to 5/100,000?").

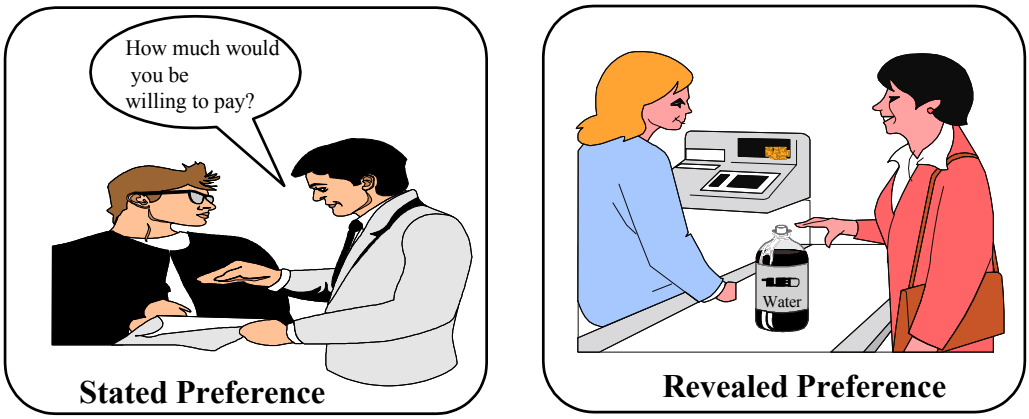
Revealed preference methods are based on observed behaviors that can "reveal" values based on prices and preferences for related market goods or services. For example, if an individual chooses to pay $50 a month to drink bottled water rather than $30 a month to drink tap water because he or she believes that the bottled water

is cleaner and safer, presumably this individual values the additional cleanliness and safety of the bottled drinking water at no less than $20 per month ($50 - $30 = $20).

Examples of revealed preference methods may include studies of wage-risk trade-offs, costs of illness, and averted costs. These methods use actual market data for related goods instead of relying on individual's predictions of their own behavior. However, there is often an imperfect match between the commodities valued in these studies and individual's' willingness to pay for the effects associated with a rulemaking. For example, bottled water purchases may not be affected by establishment of an MCL for an individual contaminant or group of contaminants, if such purchases reflect concern about a range of contaminants or about convenience, taste, odor, or color. The medical expenditures included in a cost of illness study may reflect the availability of insurance, rather than individual's true willingness to pay, and exclude the value of avoiding pain and suffering.

The types of studies often used to value the benefits of environmental regulations are illustrated in Exhibit 4 below.

Exhibit 4
Stated and Revealed Preferences



When assessing EPA regulations, analysts often transfer benefits estimates from existing studies rather than conduct new primary research. Benefit transfer involves reviewing the relevant valuation literature, selecting studies that address effects similar to those addressed by the regulations, and applying the estimates from the studies to the regulatory analysis. Key issues in conducting these transfers include ensuring that the studies used are of reasonable quality (e.g., adhere to best practices

for the particular type of research) and are applicable to the policy of concern (e.g., consider similar effects and similar populations). In some cases, it may be possible to adjust the primary research results to address differences between the study scenario and the regulatory scenario.

Valuation of Health Risks and Other Effects

Regulation of contaminants in drinking water may reduce the risks of incurring a variety of health effects, including acute or chronic illnesses that may sometimes result in death. Below, we summarize current practices for valuing mortality and morbidity risks, as well as other effects.

Mortality Risks

Mortality risk reductions are generally valued using estimates of the "value of statistical life" (VSL). VSL does not refer to the value of an identifiable life, but instead to the value of small reductions in mortality risks throughout a population. A "statistical" life can be thought of as the sum of small individual risk reductions across an entire exposed population. For example, if 100,000 people would each experience a reduction of 1/100,000 in their risk of premature death as the result of a regulation, the regulation can be said to "save" one statistical life (i.e., 100,000 * 1/100,000). If each member of the population of 100,000 were willing to pay $50 for this risk reduction, the corresponding value of a statistical life would be $5 million (i.e., $50 * 100,000). VSL estimates are appropriate only for valuing small changes in risk; they are not values for saving an individual's life.

To value mortality risks, EPA analysts often use VSL estimates applied in the recent report to Congress, *The Benefits and Costs of the Clean Air Act, 1990 to 2010,* since these estimates have been subject to substantial peer review. They are derived from 26 studies, 21 of which consider the increase in wages that workers demand for riskier jobs and five of which are based on contingent valuation surveys. The resulting values (in 2000 dollars) range from $0.8 million to $17.8 million per statistical life saved, with a mean of $6.3 million. Given the uncertainty in these estimates, a range of values are generally presented in the benefits analysis, including upper and lower bound estimates as well as the central estimate. EPA is now researching a number of topics related to improving the use of these types of estimates.

When applying this range of estimates to the effects of a particular rule, benefit analysts consider differences between the scenarios addressed in the original studies and the risk reductions addressed by the regulations. For example, the types of fatal risks assessed in the 26 studies (primarily work place accidents) differ from the types of fatal risks affected by environmental regulations (which are often cancer-related).

The subjects of the studies may differ in age, income, or baseline health status from the populations most likely to be affected by the regulations. The studies also do not address factors such as altruism; i.e., individual's willingness to pay for improvements in the health of others. The empirical literature does not provide adjustment factors for many of these (potentially counter-balancing) sources of bias, hence many of these concerns are often discussed qualitatively.

Morbidity Risks

Regulations establishing MCLs also often reduce the risks of incurring nonfatal cancers or other nonfatal health effects. Studies of total willingness to pay (WTP) to avoid an illness, which generally use contingent valuation or other stated preference methods, are available for only a limited number of health effects. Benefit transfer techniques are often used to apply these estimates of WTP to other types of effects. In some cases, analysts may instead rely on estimates using the cost of illness (COI) method. COI studies often include medical expenses (e.g., doctor visits, prescription medicine, hospital stays) and may include lost work time (e.g., foregone earnings), but generally do not address lost leisure time or pain and suffering. They focus on expenditures (which may be influenced by the availability of insurance), rather than on willingness to pay to reduce future risks. Economists believe that COI studies generally understate willingness to pay for morbidity risk reductions.

Analyses of the morbidity risk reductions attributable to drinking water regulations may include estimates of COI and/or total WTP, along with a discussion of the advantages and drawbacks of the valuation methods and an evaluation of the quality and relevance of the individual studies from which the estimates were obtained. The COI studies will provide reasonably certain estimates of averted costs that generally can be interpreted as a lower bound on WTP; the WTP estimates may be less certain (due to the methods used or specific effects studied) but more consistent with the theoretically correct definition of value.

Other Effects

In addition to effects on morbidity or mortality, some drinking water regulations may affect the aesthetic qualities of public water supplies (taste, odor, color) or the damages they cause to man-made materials (corrosion, build-up, impurities). The approach to assessing these types of effects often relies on avoided cost methods. These methods generally involve comparing the costs (e.g., for replacing corroded pipes) that are likely to be incurred in the absence of the rule to the costs likely if alternative MCLs are established. In some cases, studies of willingness to pay (e.g., using contingent valuation) may also be available. For regulations that lead to increases in source water protection, ecological benefits may also accrue -- such as improved recreational opportunities, protection of biodiversity, or nonuse values such as the pleasure of knowing clean resources exist. The methods appropriate for

valuation of these effects will depend on the types of effects considered, but may include analyses of avoided costs or use of contingent valuation surveys.

In applying these valuation methods, analysts often apply informed judgement to determine the appropriate approach for a particular rulemaking. As noted in OMB guidance on conducting economic analysis: *"You will find that you cannot write a good regulatory analysis according to a formula. The preparation of high-quality analysis requires competent professional judgement. Different regulations may call for very different emphasis in the analyses, depending on the importance and complexity of the regulatory issues and the sensitivity of the benefit and cost estimates to key assumptions."* The rationale for these judgements, the limitations and uncertainties in the analysis, and the implications for decision-making are communicated in the materials presenting the results of the analysis.

INTRODUCTION . . . . . CHAPTER 1

In 1996, Congress amended the Safe Drinking Water Act (SDWA) and substantially changed the approach for protecting the nation's drinking water supplies. These Amendments strengthened the U.S. Environmental Protection Agency's (EPA's) programs for reducing drinking water contamination by requiring the dissemination of more information to consumers, supporting better approaches for developing sound regulations, and enabling water systems to more easily implement needed improvements. This document was developed by EPA's Office of Ground Water and Drinking Water (OGWDW) for stakeholders and other interested parties to address one of the key areas affected by the 1996 Amendments: the use of benefit-cost analysis in establishing regulations for contaminants in drinking water.

EPA has used benefit-cost analysis for many years as one of several sources of information on the impacts of alternative policy choices. Traditionally, the cost side of the analysis includes estimating the expenditures needed to comply with new regulations (e.g., to install pollution control equipment) and determining the market effects of these expenditures (e.g., on the prices charged for the products of affected industries). The benefits side of the analysis generally focuses on the effects of reducing exposure to contaminants, including effects on human health and the environment.

EPA's ability to use the results of these analyses in decision-making under SDWA was limited prior to the 1996 Amendments. The Agency's choice of regulatory levels was constrained by statutory language requiring EPA to set Maximum Contaminant Levels (MCLs) as close to the MCLG as is "feasible" [SDWA, Section 1412(b)(4)(B)], and defined feasible as the use of the best technology and treatment techniques examined for efficacy under field conditions, taking cost into consideration [SDWA, Section 1412(b)(4)(D)]. Under the Amendments, EPA, at the discretion of the Administrator, may now establish less stringent MCLs if the costs of achieving the lowest feasible level are not justified by its benefits.

Because of the importance of these issues, EPA asked members of key stakeholder groups to assist in designing improved approaches to benefit-cost analysis. In 1998, EPA convened a Benefits Working Group to provide recommendations to the National Drinking Water Advisory Council on how EPA can best address the benefits of drinking water regulations. The Working Group's deliberations were carefully considered in the development of this document, and its report is included as Appendix A.

This document is divided into five chapters. The remainder of this first chapter introduces the benefits that may result from establishing MCLs for drinking water contaminants and describes the contents of the subsequent chapters in more detail. The second chapter describes the requirements for conducting benefit-cost analysis under SDWA as well as other applicable statutes and administrative orders. The third chapter describes the theory and methods for benefits analysis, focusing on the types of benefits most frequently associated with establishing drinking water MCLs. In the fourth chapter, we describe the benefit transfer technique, which is often used to estimate the value of benefits from environmental regulations. The fifth chapter provides information on how these analyses are implemented. An appendix summarizes the deliberations of the National Drinking Water Advisory Council's (NDWAC's) Benefits Working Group.

1.1 Types of Benefits

For environmental regulations, EPA generally defines benefits as the impacts of reducing the emissions of pollutants into the environment. In the case of regulations that establish MCLs (or, when necessary, treatment requirements) for public drinking water systems, these benefits result largely from reducing the adverse effects of contamination on users of this water, including households, commercial establishments, and industry.[1] The most significant effects of these regulations are improvements in human health, but other types of benefits (such as improved taste or reduced pipe corrosion) may also accrue.

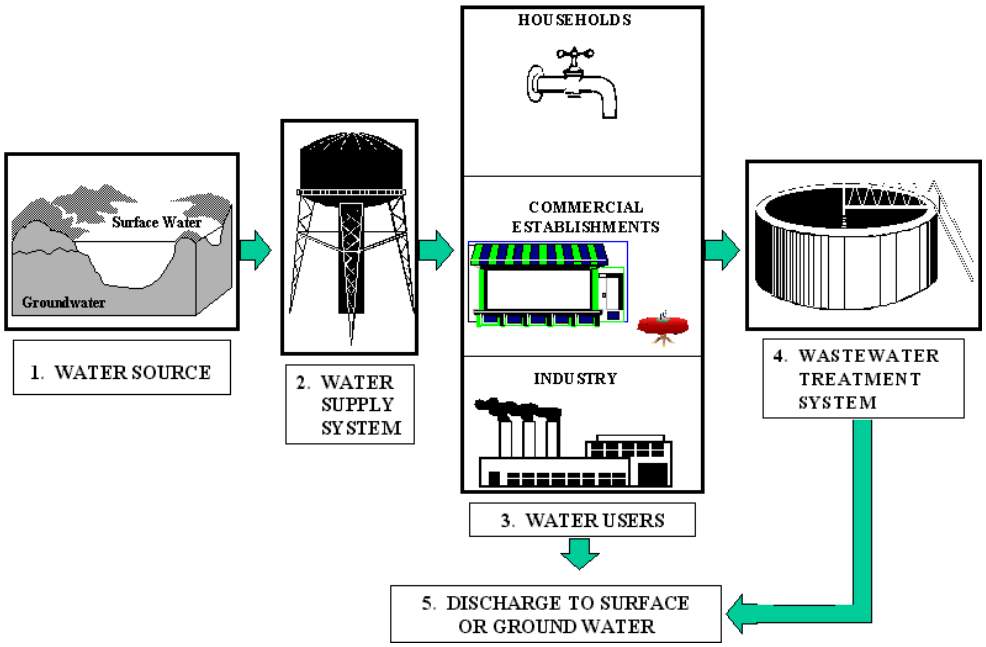
1.1.1 Water Supply Life-Cycle

In Exhibit 1-1, we provide a simple illustration of the life-cycle for publicly-supplied drinking water. This life-cycle begins with the surface or ground water sources that feed the water system. According to the U.S. Geological Survey, daily use of public water supplies totaled 40 billion gallons in the U.S. in 1995.[2] Surface waters are the source of about 62 percent of this supply; ground water sources account for the remaining 38 percent.

[1] "Public water systems" refer to systems serving the public (e.g., a community), which may be publicly or privately owned. Under the *National Primary Drinking Water Regulations* (40 CFR 141.2), these systems include those with at least 15 service connections or that regularly serve an average of at least twenty-five individuals at least 60 days per year.

[2] U.S. Geological Survey, *Estimated Use of Water in the United States in 1995,* 1997.

Exhibit 1-1
Public Water Supply Life-Cycle Overview



The water supply system collects water from these sources, treats it as necessary, and then distributes it to residential, commercial, industrial, or other users. EPA data indicate that about 47 percent of community water supplies were delivered to residential customers in 1995.[3] The remaining 53 percent includes commercial use (23 percent), industrial use (11 percent), government use (4 percent), agricultural use (1 percent), and wholesale (14 percent, primarily sales to other water systems for residential use). Once the water is used, it generally enters a sewer system and is conveyed to a wastewater treatment plant, where it is treated and discharged. Wastewater may also be directly discharged to surface water (e.g., by an industrial user) or released to ground water (e.g., when used for lawn-watering or treated by a home septic system).

Regulations establishing an MCL (or treatment requirements in lieu of an MCL) are likely to have the largest impact on the quality of water as it is delivered to the user

[3] U.S. Environmental Protection Agency, *Community Water Systems Survey, Volume 1: Overview,* January 1997.

(i.e., from Step Two to Step Three in Exhibit 1-1). The contaminants in discharges to surface and ground water (i.e., after Steps Three and Four) depend in part on the quality of the influent water supply and in part on how the water is used (e.g., for household hygiene or industrial cooling), and are generally regulated separately under the Clean Water Act and other authorities.

While MCLs focus on the quality of water delivered to end users, ground and surface water sources (Step One in Exhibit 1-1) can be affected by local decisions on how best to achieve an MCL. To comply with new regulations, systems may install treatment or blend contaminated and uncontaminated water to reduce concentration levels. Alternatively, systems may change the source of their water by connecting to a neighboring system, by developing a new well field, or by switching from ground water to surface water or vice-versa. Water systems may choose to implement source water protection measures rather than to undertake or improve water treatment.[4] They may take steps to for example, ban development in a buffer zone surrounding a water source. In the following chapters, we concentrate on the benefits associated with delivering cleaner water to users because, at a national level, these are likely to be the most significant benefits associated with new MCLs in most cases.

1.1.2 Major Benefit Categories

In this document, we organize "types of benefits" or "types of effects" into four major categories, based on the methods used to assess benefits (described in Chapter 3) within each category. This distinction is illustrated in Exhibit 1-2 and discussed below.

Exhibit 1-2
Benefits Terminology

Benefits categories represent the general types of benefits a regulation may produce. These include human health effects, ecological effects, aesthetic effects, and/or effects on materials.

Types of benefits are the specific types of effects within each category that are addressed by a regulation. For example, stomach cancer and kidney disease are two types of effects in the human health category that may be reduced by regulation of certain drinking water contaminants.

Methods for assessing benefits include both the approaches used to quantify physical effects (e.g., risk assessment) and the approaches used to determine the dollar value of the physical effects (e.g., survey research or market data).

[4] EPA also develops other types of regulations that protect water sources (e.g., by requiring industry to clean-up contaminated sites); this document focuses on regulations establishing MCLs.

Regulations establishing MCLs often have impacts that fall primarily into three categories: human health effects, aesthetic effects (e.g., taste, odor, color), and effects on materials (e.g., corrosion). The fourth category, ecological effects, may also be important in cases where the regulations increase source water protection or decrease the contamination associated with wastewater discharges or other wastes generated by water users or the system itself.

Households are often the users most significantly affected by regulations establishing MCLs both because of their level of water use and because of SDWA's focus on reducing risks to human health. Industrial or commercial establishments, who may use public supplies for drinking water or food preparation, as an input to a production process, or for cooling or cleaning, may also benefit from the establishment of MCLs. Government and agricultural use make up a relatively small proportion of the total use of publicly supplied water and often may be less substantially affected by related regulations than other types of use.

Determining the benefits categories affected by a particular regulation generally involves tracing the uses of the water supplies and the effects of changes in contamination levels on these uses. In some cases, the type of use affected may be passive; e.g., individuals may value simply knowing that clean water exists.

The relationship between use of public water supplies and potential benefits is illustrated by the examples in Exhibit 1-3 below. While the exhibit provides some examples of potential benefits for each type of user, it is not intended to be comprehensive; other types of benefits may accrue from regulation of individual contaminants. In general, analysts explore the types of benefits associated with a particular regulation on a case-by-case basis.

Exhibit 1-3

Public Water Users and Potential Benefits

User	Examples of Uses	Examples of Potential Types of Benefits From Improved Water Quality
Households	▸ Drinking water and food preparation	▸ Decreased health effects associated with ingestion; improved taste and odor
	▸ Showering and bathing	▸ Decreased health effects through dermal exposure and inhalation
Commercial establishments	▸ Drinking water and food preparation	▸ Decreased health effects associated with ingestion; improved taste and odor
	▸ Laundry and cleaning	▸ Reduced discoloration
Industry	▸ Drinking water and food preparation	▸ Decreased health effects associated with ingestion; improved taste and odor
	▸ Production input	▸ Improved product quality
	▸ Cooling and cleaning	▸ Reduced damage (e.g., corrosion, scaling) to equipment

Whether a specific use is affected by the regulations for an individual contaminant (or group of contaminants) will depend on both the characteristics of the contaminant and the changes in contamination levels attributable to the regulations. For example, in the case of a corrosive contaminant, damages to equipment or piping may be only partially reduced if the MCL is not set below the level at which noticeable damages occur. For a contaminant associated with lung disease, disease incidence may not be affected if the quantities inhaled (e.g., during showering) are not sufficient to cause the disease. The potential benefits therefore may vary substantially depending on the regulatory levels considered as well as the nature of the contaminants.

While for simplicity we have excluded the water system itself from Exhibit 1-3, benefits to the system may also accrue from regulations establishing MCLs, such as reduced damages to treatment equipment and distribution piping or changes in risks to the general public due to transportation of treatment residuals. Transportation or other risks are often best addressed as part of the risk assessment conducted for the benefits analysis (because such analysis requires the skills of health scientists), and direct savings to the system may be best addressed as part of the cost analysis (because such analysis requires the skills of water supply engineers and are an off-set to other compliance costs).

For example, if the use of new treatment techniques reduces pipe corrosion or blockage associated with the contaminant, cost analysts may choose to subtract the savings (from the reduced frequency of pipe repair or replacement) from the costs of installing and maintaining the equipment, rather than assessing the averted costs as part of the benefits analysis. To avoid double-counting, cost and benefit analysts agree in advance about whether each type of effect should be included in the cost or the benefit analysis.

As suggested by Exhibit 1-3 above, most of the benefits associated with regulations establishing MCLs fall into three categories: health effects, aesthetic effects (also referred to as amenities), and effects on materials (or materials damage). Exhibit 1-4 lists some examples of the types of effects that fall into each of these benefit categories. Methods for assessing these types of benefits are discussed in detail in Chapter 3 of this document.

Exhibit 1-4
Benefit Categories and Types of Benefits

Benefit Category	Examples of Types of Benefits
Human Health Effects	▸ Reduced mortality ▸ Decreased incidence of nonfatal cancers ▸ Decreased incidence of other nonfatal chronic and acute illnesses ▸ Reduced incidence of developmental, neurological, or reproductive effects
Aesthetic Effects	▸ Improved taste ▸ Improved odor ▸ Reduced discoloration
Effects on Materials	▸ Reduced corrosion or scaling ▸ Reduced build-up in piping ▸ Improved product quality

For regulations that lead to significant increases in source water protection, additional types of benefits may accrue. If source water protection is used in lieu of treatment to achieve an MCL, it will provide the same benefits (resulting from reducing contamination in water delivered to users of public supplies) as discussed above. In addition, source water protection may lead to ecological benefits stemming from the use of the water for recreational or commercial activities such as fishing, or from protection of biodiversity. "Nonuse" values, such as the pleasure of simply knowing that clean resources exist for current and future generations, may also be affected.

1.2 Use of this Report

The remainder of this document provides additional information on identifying and assessing these various types of benefits.

- Chapter Two, **Requirements for Benefits Analyses**, discusses the statutes, administrative orders, and other requirements that govern the conduct of benefits analysis at EPA. These requirements include those contained in SDWA as well as requirements developed by the Executive Office of the President and EPA to guide analyses of all major regulations. EPA analyses should also address several requirements for assessing impacts on business and government, as well as impacts on certain groups within the population, such as minorities, low income groups, and children.

- Chapter Three, **Methods for Benefits Analyses**, describes the theory and methods used in these analyses. It introduces several basic concepts and valuation methods, and then describes best practices for assessing effects on human health, aesthetics, and manufactured materials. Analysis of the ecological effects potentially associated with source water protection is also briefly described.

- Chapter Four, **Conducting Benefit Transfers**, provides information on how the benefit transfer technique is used to value the benefits of drinking water standards. Benefit transfer refers to the use of valuation information from one or more existing studies to assess similar, but not identical, effects.

- Chapter Five, **Implementing Benefits Analyses,** addresses the steps in the analysis and provides information on addressing data limitations and other issues. It also discusses several cross-cutting issues that arise when conducting these analyses, such as defining conditions with and without the regulations.

- Appendix A, **Report of the Benefits Working Group**, then provides the recommendations of the stakeholder group convened to advise EPA on these topics.

This appendix is followed by a list of references and an index to the major topics addressed in this document.

REQUIREMENTS FOR ECONOMIC ANALYSES CHAPTER 2

The process for developing Federal regulations has been subject to requirements for preparing supporting benefit-cost analyses for more than 20 years under an increasing variety of laws and executive orders.[5] In some cases these requirements focus on national analysis of regulatory impacts; in other cases they address effects on particular groups of concern, such as small businesses and government units, or minorities, low income groups, and children. For drinking water regulations, the Safe Drinking Water Act (SDWA) also contains several provisions that apply specifically to the analysis of benefits and costs.

This chapter summarizes the provisions of statutes, executive orders, and guidance documents that apply to the economic analysis of potential Federal regulations, with particular emphasis on the application of these requirements to the assessment of regulations establishing Maximum Contaminant Levels (MCLs) or treatment requirements for public drinking water systems. Many of these statutes, executive orders and guidance documents also contain requirements for the regulatory development process (e.g., for stakeholder involvement) and for the analysis of costs. While we allude to these other requirements, particularly where they constitute the primary purpose of an individual statute or executive order, we focus on information related to assessing benefits and comparing benefits to associated costs.

The purpose of this chapter is to introduce the requirements for the regulatory analyses described in these documents. The documents referenced in this chapter provide more detailed information on each set of requirements, as well as on the process for implementing and updating them.

2.1 The Safe Drinking Water Act

SDWA, as amended in 1996, provides the framework for developing National Primary Drinking Water Regulations, which establish MCLs or treatment techniques for controlling specific contaminants in drinking water.[6] SDWA also includes requirements for benefits assessment and for comparing benefits to costs as described below.

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[5] A concise summary of the development of the U.S. regulatory analysis program is contained in the U.S. Office of Management and Budget's *Report to Congress On the Costs and Benefits of Federal Regulations*, September 30, 1997. (The subsequent updates of this report do not provide this historical perspective.)

[6] The 1996 SDWA amendments and related information are available on EPA's Website at: http://www.epa.gov/ogwdw/sdwa/sdwa.html.

2.1.1 MCL Development Process

SDWA was originally enacted in 1974 and substantially amended in both 1986 and 1996. The 1986 Amendments specified 83 drinking water contaminants for regulation, and required EPA to regulate 25 of these contaminants every three years. EPA developed regulations for many of these contaminants before the 1996 Amendments, which changed the contaminant identification process to include risk-based prioritization of regulatory decisions with sound scientific peer review.[7]

In response to these new requirements, EPA must publish a list once every five years of unregulated contaminants it will consider for regulation [SDWA, Section 1412(b)(1)(B)]. Based on review of available information, the Agency must determine whether to regulate at least five contaminants from this list every five years. In accordance with these provisions, the Agency published its first *Contaminant Candidate List* of 60 chemical and microbial contaminants in March 1998, and will decide whether to proceed with developing regulations for at least five of these contaminants by August 2001.[8]

The 1996 Amendments maintain the Act's historic focus on the protection of public health. Specifically, SDWA Section 1412(b)(1)(A) directs the Administrator to focus on those contaminants that may have adverse human health effects, that are known or substantially likely to occur in public water systems at levels and with a frequency of concern to public health, and that present meaningful opportunities for health risk reductions if regulated. In all of these decisions, the Agency is further directed to draw data from the best available peer-reviewed science [SDWA, Section 1412(b)(3)(A)].

For each contaminant that EPA chooses to regulate, SDWA requires the Agency to publish a Maximum Contaminant Level Goal (MCLG) and issue a National Primary Drinking Water Regulation that would reduce health risks. In this regulation, EPA must either establish a Maximum Contaminant Level (MCL) and list technologies that can achieve compliance with the MCL (specifying compliance technologies for small systems), or (if it is not economically or technically feasible to monitor the contaminant in drinking water) specify a treatment technology. EPA sets the MCLG at the concentration at which there are no known or anticipated adverse health effects associated with exposure to the contaminant, taking into account an adequate margin

[7] In addition, the 1996 Amendments established specific requirements for the regulation of four contaminants: arsenic, radon, disinfection byproducts /cryptosporidium, and sulfate. The 1996 Amendments also require EPA to review and, if necessary, revise National Primary Drinking Water Regulations for currently regulated contaminants after six years.

[8] The Contaminant Candidate List and supporting information is available on EPA's Website at: http://www.epa.gov/ogwdw/ccl/cclfs.html.

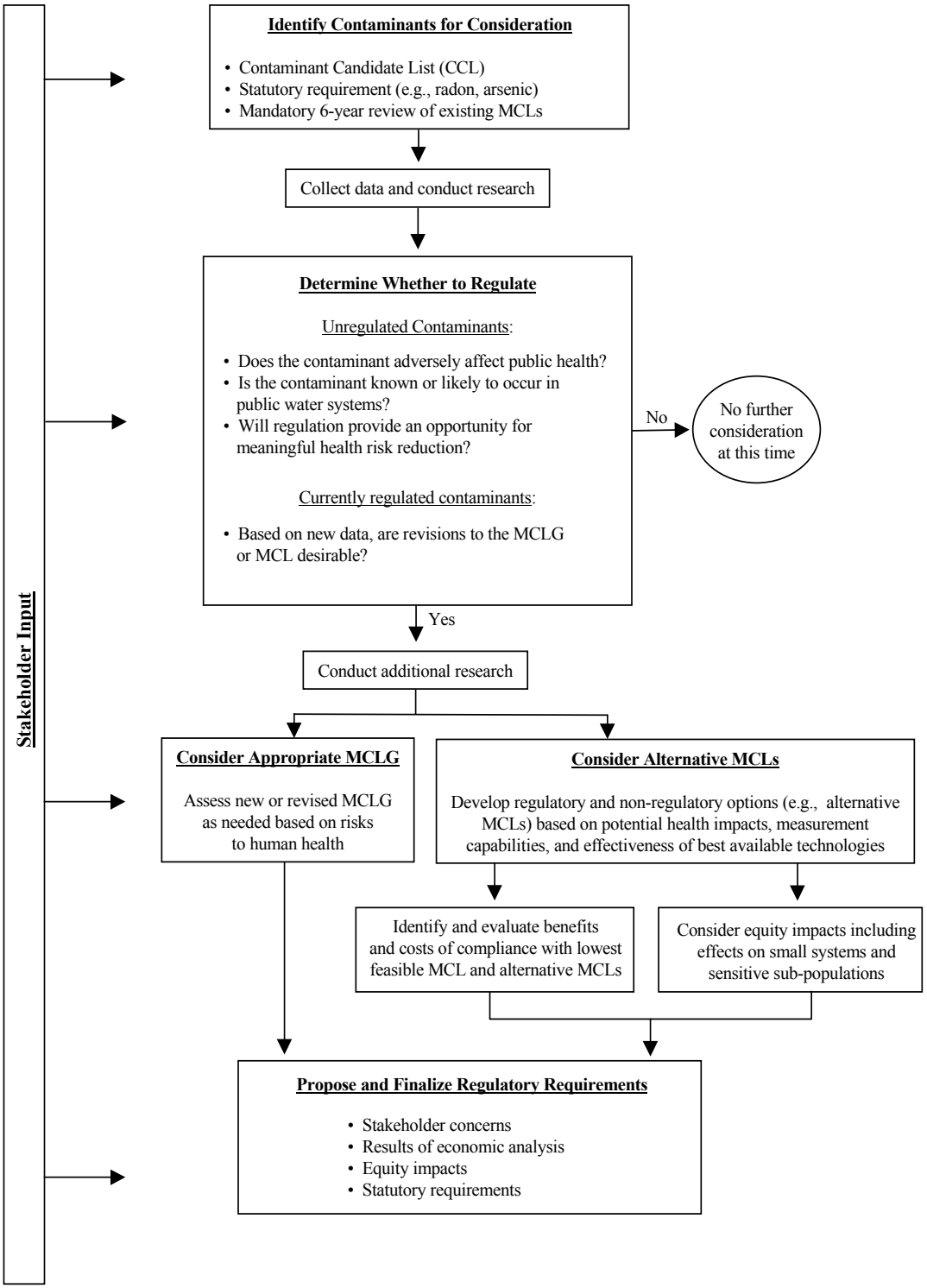
of safety and considering the effects on sensitive subpopulations. MCLGs for carcinogens are generally set at zero in the absence of data to support an alternative value. MCLGs for noncarcinogens are based on the Reference Dose (RfD, the level at which no adverse effects are likely to occur even for sensitive populations), combined with data on body weight, water consumption, and the percent of total exposure attributable to drinking water.

The 1986 SDWA amendments identified a process for setting MCLs as close to the MCLG as is "feasible" [SDWA, Section 1412(b)(4)(B)], and defined feasible as the use of the best technology and treatment techniques examined for efficacy under field conditions, taking cost into consideration [SDWA, Section 1412(b)(4)(D)]. This process was retained in the 1996 Amendments. However, under the 1996 Amendments, EPA can, at its discretion, establish a less stringent MCL that *"maximizes health risk reduction benefits at a cost that is justified by the benefits"* [SDWA, Section 1412(b)(6)(A)], with certain exceptions. In particular, SDWA Section 1412 (b)(6)(B) prohibits the Administrator from establishing a less stringent MCL if the benefits justify the costs for large water systems and those small systems not likely to gain variances, once the costs and benefits for those small systems likely to obtain variances are excluded from the analysis.

Exhibit 2-1 provides an overview of the regulatory development process under SDWA. EPA begins by selecting contaminants for regulatory consideration, then determines whether to proceed with developing new or revised regulations. These regulations may address both the MCLG and the MCL (or treatment requirements), depending on the status of the regulation and available research. The Agency considers the regulatory options and makes regulatory decisions based on stakeholder concerns, the results of the economic analysis, equity impacts, and statutory and other requirements.

Exhibit 2-1

OVERVIEW OF REGULATORY DEVELOPMENT PROCESS



2.1.2 Benefits Assessment

The 1996 SDWA Amendments impose significant new requirements on EPA for assessing benefits and for comparing benefits to costs. Specifically, when proposing any MCL, the Agency must publish an analysis of the benefits and costs of compliance with the MCL, including the following [SDWA, Section 1412(b)(3)(C)(i)]:

- the quantifiable and non-quantifiable health risk reduction benefits of control of the contaminant proposed for regulation at the specified MCL;
- the quantifiable and non-quantifiable health risk reduction benefits of any control of co-occurring contaminants that can be attributed solely to the proposed MCL, exclusive of compliance with other proposed or promulgated regulations;
- the quantifiable and non-quantifiable costs of compliance with the proposed MCL, including monitoring, treatment, and other costs, exclusive of costs of compliance with other proposed or promulgated regulations;
- the incremental costs and benefits associated with each alternative MCL under consideration;
- the effects of the contaminant on the general population, and on groups within the population that are likely to be at greater risk of adverse health effects from drinking water contaminants, such as infants, children, pregnant women, the elderly, and individuals with a history of serious illness;
- the increased health risks, if any, that may result from compliance with the proposed MCL, including risks associated with co-occurring contaminants; and,
- other relevant factors, including the quality of the available information supporting the analysis, the uncertainties in the analysis, and factors relating to the degree and nature of the identified risks.

If EPA proposes a treatment technique in lieu of establishing an MCL, the Agency must analyze the benefits and costs for the proposed treatment technique and alternatives considered, considering the same factors as listed above [SDWA, Section 1412(b)(3)(C)(ii)].

2.1.3 Comparison of Benefits to Costs

For each proposed MCL, SDWA further requires that the EPA Administrator publish a determination as to whether the benefits of the proposed regulation justify the costs [SDWA, Section 1412(b)(4)(C)], based on the analyses described above. If the benefits of setting the MCL at the feasible level would not justify the costs, *"the Administrator may, after notice and opportunity for public comment, promulgate an alternative MCL that will maximize health risk reduction benefits at a cost that would be justified by the benefits"* [SDWA, Section 1412(b)(6)(A)], with the exception (noted earlier) related to variances for small systems. These decisions are subject to judicial review [SDWA, Section 1448].

2.2 General OMB and EPA Guidance

In addition to the requirements imposed by SDWA, EPA benefit analyses must comply with more general provisions governing the assessment and promulgation of major Federal regulations. Executive Order 12866 establishes many of these requirements for major Federal regulations, defining major regulations as those that have an annual effect on the economy of $100 million or more, have other significant adverse economic impacts, are inconsistent with the actions of other agencies, alter the budgetary impact of Federal programs, or raise unusual legal or policy issues. The Office of Management and Budget (OMB) in the Executive Office of the President reviews major Federal regulations prior to promulgation under this Executive Order to ensure that they are consistent with the goals of the President and based on sound analysis and judgement.

OMB has developed guidance for preparing the benefit-cost analyses required under Executive Order 12866. This guidance focuses on ensuring that the analysis complies with "best practices" as defined by the economics profession. In addition, EPA has developed similar guidance tailored to its own regulations to ensure that the required analyses are performed consistently and accurately. This section first discusses the OMB guidance, "Guidelines to Standardize Measures of Costs and Benefits of Federal Regulations and Format of Accounting Statements" and then the EPA guidance, *Guidelines for Preparing Economic Analyses.*

2.2.1 OMB Guidance Under Executive Order 12866

Executive Order 12866, *Regulatory Planning and Review*, requires Federal agencies to conduct economic analyses of significant regulatory actions as a means to improve regulatory decision-making.[9] To assist agencies in carrying out these analyses, OMB issued guidelines to standardize benefit-cost analysis in their 2000 report to

[9] Executive Order 12866, *Regulatory Planning and Review,* September 30, 1993.

Congress.[10] As outlined in these guidelines, an economic analysis of a regulation should be designed to provide information for decision-makers on the potential benefits to society of alternative regulatory and nonregulatory approaches to risk management in comparison to potential costs, recognizing that not all benefits and costs can be described in monetary or even in quantitative terms. The guidelines focus on ensuring that decisions are based on the best available scientific, technical, and economic information.

The OMB guidelines are divided into four major sections:

- **General Considerations** discusses addressing the need for regulatory action, policy alternatives to consider, choice of a baseline, inclusion of non-monetized benefits and costs, and discounting of benefits and costs over time.

- **Benefit Estimates** describes the key concepts related to estimating benefits, valuing market and nonmarket goods, and valuing health and safety benefits.

- **Cost Estimates** provides an overview of the key concepts related to estimating costs, and the difference between real costs and transfer payments.

- **Other Key Considerations** describes methods for dealing with risk and uncertainty, use of sensitivity analysis to address alternative assumptions, distributional effects and equity considerations, and compliance assumptions.

In addition, the guidelines discuss a standard format for summarizing analytic results.

The guidelines are intended to provide a flexible framework for regulatory analyses, presenting information on practices that are consistent with the principles of economic theory. They also help standardize the measurement of benefits and costs of Federal regulatory actions. OMB emphasizes the need to clearly communicate the approach and findings of the analysis by presenting transparent analysis.

While the focus of OMB's regulatory review under Executive Order 12866 will vary depending on the characteristics of individual rules and the current priorities of the

[10] U.S. Office of Management and Budget, "Guidelines to Standardize Measures of Costs and Benefits and the Format of Accounting Statements," in *Appendix 4: Report to Congress on the Costs and Benefits of Federal Regulations,* March 22, 2000.

President, this guidance suggests that the criteria for acceptable analysis include consistency with the general principles of economics and clear justification of the analytic approach used for the particular rulemaking. The information on benefits analysis provided later in this document complies with these general principles.

2.2.2 EPA Guidelines for Economic Analyses

EPA first issued formal guidelines for the preparation of regulatory impact analyses in 1983 in response to President Reagan's Executive Order 12291(the predecessor to President Clinton's Executive Order 12866). EPA then amended these guidelines and added new appendices in 1991. Over the past four years, the Agency undertook a major effort to update and revise these guidelines, finalizing its *Guidelines for Preparing Economic Analyses* in 2000.[11]

EPA's guidelines generally follow the same framework as OMB's guidance. The EPA *Guidelines* are in part based on research commissioned by EPA's Economic Consistency Work Group and subsequent decisions made by its Regulatory Policy Council. This research focused on six areas that are central to the preparation of sound regulatory analyses: defining the baseline, selecting discount rates, valuing mortality risk reductions, addressing equity and distributional issues, evaluating uncertainty, and assessing non-quantified and non-monetized effects. The EPA *Guidelines* incorporate new advances in applied economic research, and address the analytic requirements of a number of recent statutes and executive orders.

The EPA *Guidelines* are substantially more detailed than the OMB guidelines mentioned above, but place a similar emphasis on applying best practices derived from the field of economics, using informed professional judgement to appropriately design and implement the analysis, and ensuring that the analytic methods and results are clearly communicated. The EPA *Guidelines* address the following topics:

- Statutory and executive order requirements for conducting economic analyses;
- Stating the need for the proposal, including guidance on procedures and analyses for clearly identifying the environmental problem to be addressed and for justifying Federal intervention;
- Developing regulatory and nonregulatory approaches for consideration;

[11] U.S. Environmental Protection Agency, *Guidelines for Preparing Economic Analyses*, EPA 240-R-00-003, September 2000.

- Understanding the theoretical foundations of economic analyses, as well as general guidance on specifying the baseline, predicting responses to the regulations, and assessing uncertainty;
- Approaches to social discounting;
- Assessing the benefits of environmental policies;
- Analyzing the social costs of environmental policies;
- Assessing the economic impacts and equity effects of environmental policies; and,
- Using economic analyses in evaluating policy options.

The EPA *Guidelines* include a thorough discussion of the benefits categories, general analytic approach, and methods applicable to the assessment of benefits of environmental regulations. A review of these topics, illustrated with examples of their application to drinking water regulations, is included in Chapters 3 and 4 of this document. Several other topics addressed by the EPA guidelines affect both the cost and benefit analysis (e.g., the definition of the baseline) and are briefly summarized in Chapter 5 of this document.

2.3 Requirements Related to Impacts on Government and Business Units

The increasing scope and number of environmental and other regulations have raised concerns in recent years over the economic impacts of Federal actions on state and local governments and the business community. EPA is subject to two primary sets of requirements for assessing these types of impacts.[12] The Unfunded Mandates Reform Act requires EPA to assess the impacts of Federal regulations on non-Federal government units and to minimize associated costs (when not offset by adequate Federal funding). The Small Business Regulatory Enforcement Fairness Act amends the Regulatory Flexibility Act; in combination these Acts establish analytical and procedural requirements for addressing the impacts of Federal regulations on small government and business entities. As discussed below, the guidelines for addressing these statutory requirements focus largely on the analysis

[12] In addition to these statutes, EPA is subject to Executive Order 13132, *Federalism,* which requires intergovernmental consultation. Executive Order 13084, *Consultation and Coordination with Indian Tribal Governments,* also requires consultation on potential regulatory requirements. However, these Orders do not specifically address the conduct of economic analysis.

of costs, but information on associated benefits is often useful for related decision-making.

2.3.1 The Unfunded Mandates Reform Act (UMRA)

The Unfunded Mandates Reform Act (UMRA), which Congress enacted in 1995, requires that Federal agencies assess the budgetary impacts of proposed regulations on state, local and tribal governments as well as on the private sector. The general requirements for analysis under UMRA are very similar to the requirements described in the above-mentioned OMB and EPA guidance for regulatory analysis, but focus on the effects of Federal requirements on other government entities and the private sector. Information on complying with the requirements of UMRA can be found in OMB's *Guidance for Implementing Title II of S.1*.[13] EPA is also developing draft guidance on these topics.

Title II of UMRA directs agencies to prepare an economic analysis prior to promulgating any regulation that may mandate direct expenditures of $100 million in any one year by state, local, and tribal governments combined, or by the private sector. The statute further requires that the economic analysis include:

- a qualitative and quantitative assessment of the anticipated benefits and costs of the mandate, including its effects on health, safety, and the natural environment [Section 202(a)(2)];

- an assessment of the extent to which Federal resources and financial assistance (e.g., through the Drinking Water State Revolving Fund) are available to offset the costs imposed on state, local, and tribal governments [Section 202(a)(2)(A)];

- estimates, where feasible, of disproportionate budgetary effects on any particular region, any particular state, local, or tribal government, any particular type of community (e.g., urban or rural), or particular segments of the private sector [Section 202(a)(3)(B)]; and,

- estimates, where feasible, of the proposed regulation's effects on the national economy (e.g., its effects on productivity,

[13] U.S. Office of Management and Budget, *Guidance for Implementing Title II of S.1,* Memorandum from Sally Katzen, March 31, 1995. Information on the historical relationship between UMRA and SDWA is also provided in: U.S. Congressional Budget Office, *The Safe Drinking Water Act: A Case Study of an Unfunded Federal Mandate,* September 1995.

economic growth, employment, and job creation) [Section 202(a)(4)].

To foster greater communication and coordination between all levels of government during regulatory development, UMRA also includes requirements for Federal consultation with representatives of state, local, and tribal governments so as to provide "meaningful and timely" input to the development of a regulatory proposal [UMRA, Section 204].

For each proposed rule, UMRA requires that agencies *"consider a reasonable number of regulatory alternatives and ... select the least costly, most cost-effective, or least burdensome alternative,"* unless this provision is inconsistent with applicable law. Otherwise, the Agency must publish (with the final rule) an explanation of why the least costly, most cost-effective, or least burdensome alternative was not chosen. In total, the requirements of UMRA suggest that analysts may wish to disaggregate both benefit and cost estimates so that the cost impacts of any significant unfunded mandates can be compared to their benefits for the particular types of affected entities. In addition, the requirements of UMRA must be taken into account when selecting the regulatory options to be considered in the benefit-cost analysis.

2.3.2 The Small Business Regulatory Enforcement Fairness Act (SBREFA)/Regulatory Flexibility Act (RFA)

The Small Business Regulatory Enforcement Fairness Act (SBREFA) was passed in 1996, amending the Regulatory Flexibility Act (RFA) of 1980. The purpose of these combined statutes is to ensure that agencies consider the economic impacts of their regulations on small entities, both public and private, and provide flexibility to minimize these impacts. Many of the specific requirements in these statutes apply primarily to the analysis of the direct economic impacts (i.e., costs) associated with regulatory compliance and related decision-making; however, analysts may also wish to provide information on benefits to help inform these decisions. These statutes also contain specific requirements for consulting with representatives of small entities and for publishing a small entity compliance guide. EPA guidance for implementing SBREFA and RFA is available in: *Revised Interim Guidance for EPA Rulewriters: Regulatory Flexibility Act as Amended by the Small Business Regulatory Enforcement Fairness Act* and related documents.[14]

[14] U.S. Environmental Protection Agency, *Revised Interim Guidance for EPA Rulewriters: Regulatory Flexibility Act as Amended by the Small Business Regulatory Enforcement Fairness Act,* March 1999; and U.S. Environmental Protection Agency, *1999 Update to Elements of a Reg Flex Analysis,* 1999. The U.S. Small Business Administration (SBA) has also developed guidance (*Implementation Guide for the RFA,* February 1998). However, the SBA differs from EPA in its legal and policy interpretations of some

The RFA provides definitions of small entities, including "small businesses," "small governments," and "small organizations." However, for drinking water regulations, EPA's policy has been to instead define water systems serving less than 10,000 customers as small entities.[15] Such systems account for nearly 95 percent of all community water systems nationwide, although they serve relatively small populations and hence provide a much smaller proportion of total water supplies. EPA's definition of small water systems does not correspond precisely to the definition of small entity under RFA; however, EPA has in the past consulted with and received approval from the Small Business Administration for the use of this alternative definition.[16]

Under SBREFA and RFA, EPA must evaluate the reporting, record-keeping, and other compliance requirements imposed on small entities by the proposed regulation. EPA must also consider regulatory alternatives and other measures that can minimize the economic impact of the proposed regulation on small entities while accomplishing the stated objectives of the applicable statute(s). Because the Acts' requirements are potentially resource intensive, analysts first conduct a screening analysis to determine if a full "Regulatory Flexibility Analysis" is required. A detailed analysis is not required if the agency can certify that the rule *"will not, if promulgated, have a significant economic impact on a substantial number of small entities."* It is EPA's policy, however, to consider a rule's impact on any small entities and minimize any adverse impact to the extent feasible, regardless of whether a full Regulatory Flexibility Analysis is required.

The specific requirements for these analyses focus on the adverse economic impacts of the regulations, and generally do not specifically address benefits. However, disaggregate information on the benefits to small entities may be useful in decision-making, particularly if the benefits analysis addresses cost savings (e.g., from reduced pipe corrosion) that may offset compliance costs. Decision-makers may also be interested in information on the extent to which small systems account for a disproportionately large or small share of the total benefits of the regulations. Actions taken to minimize economic impacts on small entities could include the granting of waivers or the adoption of alternative standards, which will affect overall costs and benefits under the regulations. As noted earlier (in Section 2.1 of this

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provisions of SBREFA and RFA.

[15] U.S. Environmental Protection Agency, *National Water Quality Inventory: 1994 Report to Congress,* 1994.

[16] See, for example, U.S. Environmental Protection Agency. "National Primary Drinking Water Regulations: Consumer Confidence; Proposed Rule," *Federal Register,* Vol. 63, No. 30, p. 7605, February 13, 1998.

chapter), the SDWA requirements for considering whether benefits justify costs explicitly take into consideration the availability of variances for small systems.

2.4 Requirements Related to Impacts on Subpopulations

In addition to the SDWA requirements for addressing risks to sensitive subgroups when developing MCLs (see Section 2.1 above), recent executive orders require the consideration of effects on minority and low income groups and children.[17] As mentioned in Section 2.2, both the OMB and EPA guidance also require addressing any potentially disproportionate adverse impacts on a number of groups. Below, we describe the two executive orders and related guidance that explicitly address the risks imposed on specific subpopulations: Executive Order 12898 on environmental justice, and Executive Order 13045 on children's health.

2.4.1 Environmental Justice

Under Executive Order 12898, *Federal Actions to Address Environmental Justice in Minority Populations and Low Income Populations*, each Federal agency is required to identify and address "disproportionately high and adverse human health or environmental effects of its programs, policies, and activities on minority populations and low-income populations." Specifically, the Order requires each agency to develop an environmental justice strategy. This strategy must include provisions for improving related research and data collection efforts, for ensuring greater public participation, and for identifying differential patterns of natural resource consumption among minority and low-income populations.

Accordingly, EPA's 1995 *Environmental Justice Strategy: Executive Order 12898* develops objectives for partnerships, data collection, and outreach in five mission areas central to the promotion of environmental justice:

- public participation, accountability, partnerships, outreach, and communication with stakeholders;
- research on health and environmental issues (e.g., ongoing cooperative studies of drinking water consumption patterns and resulting contaminant exposures by EPA and USDA);
- data collection, analysis, and stakeholder access to public information;
- environmental protection for American Indian, Alaska native and indigenous peoples; and

[17] In addition, as noted earlier Executive Order 13084 requires consultation with tribal groups.

- enforcement, compliance assurance, and regulatory review.[18]

EPA's *Environmental Justice Handbook*, issued in September 1993, defines environmental justice as the fair treatment of people of all races, incomes, and cultures with respect to the development, implementation, and enforcement of environmental laws, regulations and policies. To help ensure that fair treatment, the Agency has developed an *Environmental Justice Implementation Plan* designed to foster progress toward achieving the objectives specified in the *Environmental Justice Strategy*. Additional guidance for addressing environmental justice concerns in the context of the National Environmental Policy Act (NEPA) is provided by EPA and the Council on Environmental Quality.[19]

In addition, EPA's Office of Ground Water and Drinking Water and Office of Science and Technology are undertaking several efforts to address these issues. EPA published the *Safe Drinking Water Act Guide for Environmental Justice Stakeholders* and convened a meeting of these stakeholders in March 1998.[20] EPA's health scientists are also researching several issues concerning the sensitivity of various groups to drinking water contaminants. The implications of these issues for benefits analyses are two-fold. First, the analysis of health risks should consider the extent to which minority groups or low income populations may be more sensitive to the effects of contaminants than the general population, either due to baseline health conditions or patterns of exposure to drinking water contaminants. Second, any disproportionate adverse affects of contaminants on these populations should be addressed and highlighted in benefits analyses.

2.4.2 Children's Health

Recognizing the growing body of evidence that children may be more susceptible or vulnerable to adverse health effects resulting from environmental contaminants, the EPA Administrator in the fall of 1995 issued a *Policy on Evaluating Health Risks to Children*. This policy directed the Agency, when setting standards to protect public health, to explicitly and consistently consider risks to children and infants. The

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[18] U.S. Environmental Protection Agency, *Environmental Justice Strategy: Executive Order 12898*, April 1995. More information on environmental justice issues, including information on the other documents cited in this section, can be found on EPA's Environmental Justice Website: http://www.epa.gov/oeca/oej.

[19] U.S. Environmental Protection Agency, *Interim Final Guidance for Incorporating Environmental Justice Concerns in EPA's NEPA Compliance Analyses,* Office of Federal Activities, April 1998, and Council on Environmental Quality, *Guidance for Addressing Environmental Justice Under the National Environmental Policy Act*, March 1998.

[20] Information on these efforts is available on EPA's Website at http://www.epa.gov/ogwdw/ndwac/sum_ej-a.html.

Policy was subsequently reinforced by the announcement of EPA's *National Agenda to Protect Children's Health from Environmental Threats.* The Agenda stipulated that, as a matter of policy, all standards EPA sets will be protective enough to address the potentially heightened risks faced by children.

In April 1997, President Clinton issued Executive Order 13045, *Protection of Children From Environmental Health Risks and Safety Risks*, directing all Federal agencies to give high priority to the identification and assessment of disproportionate environmental health risks and safety risks to children, to coordinate research on children's health, and to ensure that their standards address disproportionate risks to children.[21] The Order further directs agencies, when proposing and promulgating regulations concerning environmental health risks or safety risks that may disproportionately affect children, to submit to OMB an evaluation of the proposed regulation's environmental health or safety effects on children, and an explanation of why the proposed regulation is preferable to other reasonably feasible alternatives considered by the agency.

In May 1997, the Administrator created the Office of Children's Health Protection (OCHP) to coordinate the implementation of Executive Order 13045 and the Agency's *National Agenda*. To assist Agency staff in the regulatory development and assessment process, OCHP and the Office of Regulatory Management and Information issued draft Interim Final Guidance on implementation of the executive order in *EPA's Rule Writer's Guide to Executive Order 13045: Guidance for Considering Risks to Children During the Establishment of Public Health-Related and Risk-Related Standards*.[22] This guidance is designed to ensure that the "analytical blueprint" for the regulatory development process includes the components required by the Executive Order; it also addresses issues related to distinguishing between risk assessment and risk characterization.

This general concern about children's health effects is also reflected in SDWA. As discussed earlier in Section 2.1, SDWA requires EPA to evaluate health risk reduction benefits for those groups within the population that are likely to be at greater risk of adverse health effects from drinking water contaminants, including infants and children. Benefits analysts therefore pay particular attention to children's health risks when assessing the effects of drinking water regulations, highlighting potentially significant impacts.

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[21] These documents and other information related to children's health effects are available on EPA's Website at: http://www.epa.gov/children.

[22] U.S. Environmental Protection Agency. *EPA's Rule Writer's Guide to Executive Order 13045: Guidance for Considering Risks to Children During the Establishment of Public Health-Related and Risk-Related Standards*, Review Draft, April 21, 1998.

2.5 An Integrated Approach

As the above discussion makes clear, the development of drinking water regulations is subject to the provisions of several statutes, executive orders, and guidance documents. One of the primary challenges for regulatory analysts and decision-makers in assessing the benefits of regulatory options is to integrate these many requirements into a coherent analytic strategy. This strategy generally includes a national benefit-cost assessment, and, as appropriate, evaluation of the effects on distinct subgroups of the affected population (e.g., small businesses, government entities, children, minorities, or low-income households).

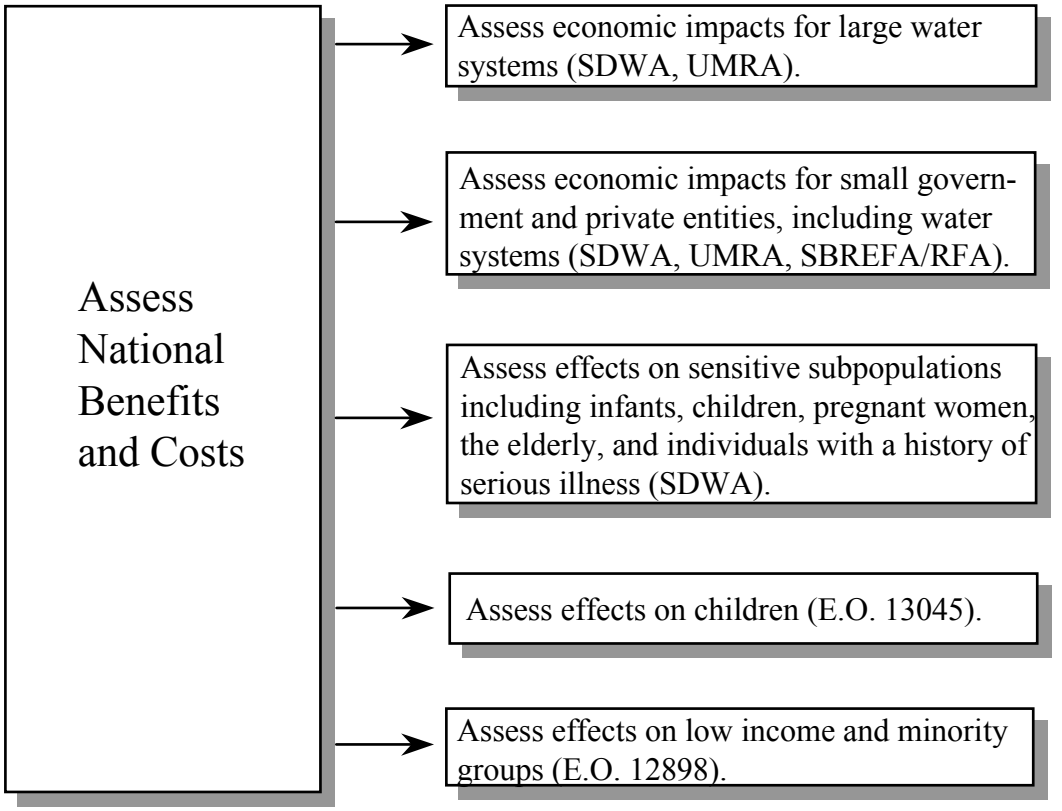
Some of the statutes and executive orders discussed earlier are applicable to all actions taken by the Agency, whereas others are applicable only to "major" regulations. Exhibit 2-2 summarizes the applicability of each set of requirements. In parentheses, we indicate the section of this chapter that provides more information on each set of requirements and that references sources of additional information on applying these criteria.

Exhibit 2-2
Applicability of Statutory and Executive Order Requirements for Benefit-Cost Analysis

Safe Drinking Water Act (see Section 2.1 above): All National Primary Drinking Water Regulations.
Executive Order 12866, "Regulatory Planning and Review" (see Section 2.2.1 above): All "significant regulatory actions" that may "(1) Have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities; (2) Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency; (3) Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or (4) Raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in this Executive Order."
Unfunded Mandates Reform Act (see Section 2.3.1 above)**:** All rules that "may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year."
EPA Guidelines for Preparing Economic Analyses (see Section 2.2.2 above): Not specified; generally applies to all economic analyses prepared by EPA.
Small Business Regulatory Enforcement Fairness Act and the Regulatory Flexibility Act (see Section 2.3.2 above): All rules that will have "a significant economic impact on a substantial number of small entities."
Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low Income Populations" (see Section 2.4.1 above): No specific criteria; generally applies to all EPA programs.
Executive Order 13045, "Protection of Children from Environmental Health Risks and Safety Risks" (see Section 2.4.2 above): All "economically significant" rules as defined under Executive Order 12866 that "concern an environmental health risk or safety risk that an agency has reason to believe may disproportionately affect children."

Exhibit 2-3 summarizes the necessary disaggregated analyses and indicates the source of the requirement (e.g., SDWA), as discussed in previous sections of this chapter.

Exhibit 2-3
Summary of Required Analyses



To meet the requirements specified in Exhibit 2-3, benefits analysts work with others, such as cost analysts, health scientists, and stakeholders, in developing the overall economic analysis. Proper assessment of disproportionate health risks to sensitive populations, for example, involves consultation with health researchers and risk assessors to integrate the latest information on health risks to children and other groups. Similarly, effective and meaningful comparison of benefits and costs for small entities involves working closely with cost analysts and representatives of small water systems to address related impacts.

METHODS FOR BENEFITS ANALYSES CHAPTER 3

Regulations establishing Maximum Contaminant Levels (MCLs) or treatment requirements under the Safe Drinking Water Act (SDWA) may have several types of benefits. On a national level, the most significant benefits generally will be improvements in human health. As described in Chapter 1, other benefits may include aesthetic effects (such as improved taste or odor) and effects on materials (such as reduced pipe corrosion). Regulations that lead to greater source water protection may also have ecological benefits, such as increased protection of biodiversity.

As discussed in Chapter 2, analysis of these types of effects is necessary to meet the SDWA requirements for assessing the extent to which the benefits of achieving the lowest feasible MCL may be commensurate with the costs. Benefit-cost analysis is also necessary for all major rulemakings under government-wide and EPA requirements. These analyses also address the impact of regulations on certain groups of concern (including state and local governmental units, private entities, minorities, low income groups, and children), as required by SDWA and several statutes and executive orders.

The practice of benefits assessment is based on the discipline of welfare economics. In this chapter, we briefly introduce the theoretical foundation and economic methods for benefits analysis, then describe "best practices" for assessing particular types of benefits.[23] Although it is generally useful to express the value of benefits in dollar terms using the methods discussed below, analysts may often find that it is not possible to quantify or value all of the benefits of drinking water regulations. In such cases, nonquantified and nonmonetized benefits are carefully described in the analysis so that they can be taken into consideration by decision-makers.

This chapter is divided into three parts. First, we introduce the economic concepts that provide the foundation for benefits analyses. Next, we describe research methods commonly used to determine the dollar value of these benefits. Finally, we describe approaches for assessing specific types of benefits in more detail. Chapter 4 discusses the transfer of benefit estimates from existing studies to the analysis of drinking water regulations, while Chapter 5 provides information and examples related to implementing these methods.

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[23] For a more detailed technical discussion of the economic theory and methods for benefits assessment described in this chapter, see: U.S. Environmental Protection Agency, *Guidelines for Preparing Economic Analyses:* EPA 240-R-00-003, September 2000; and, Freeman, A. Myrick III, *The Measurement of Environmental and Resource Values: Theory and Methods,* Resources for the Future, Washington, D.C., 1993.

3.1 The Economist's Perspective

The simplest way to value benefits from a drinking water regulation would be to use market data or survey responses to determine directly the value of decreasing contaminant concentrations. For example, if a "decrease in arsenic contaminant concentrations from 50 μg/L to 10 μg/L" was a product available for purchase, we could use market data on the demand for this product to value benefits. Alternatively, we could survey consumers and ask how much they would be willing to pay to reduce contaminant concentrations by specific amounts.

Unfortunately, we often cannot determine the value of benefits in such a straightforward manner. Because reductions in contaminant concentrations are not goods that are directly bought and sold, there is little empirical information on the prices people would be willing to pay for these reductions. In addition, people who are not familiar with the effects of individual drinking water contaminants may have difficulty responding to a survey asking them what they would be willing to pay for reduced concentrations; conducting a survey that fully informs them about each contaminant can be quite expensive and time consuming.

Faced with these difficulties, benefit analysts usually begin by listing the possible effects reduced by the regulations, then focus on valuing each specific effect (such as the changes in the risks of contracting a particular disease). Values are derived for each effect, then aggregated (taking care to avoid double-counting) to determine the total benefits of the regulations. For example, rather than directly estimating the value of a specific reduction in the concentrations of a chemical (such as arsenic or benzene), analysts generally estimate the value of the risks averted (such as the risks of incurring certain nervous system disorders or kidney cancer) and other benefits (such as improved taste or odor), then aggregate the values of these effects to determine the total benefits of the rule.

To determine the monetary value of these benefits, economists focus on what people would be willing to pay for specific health improvements and other effects of the regulations. The basis for this focus on willingness to pay, and its advantages and limitations, are described below.

3.1.1 Willingness to Pay

In considering policies that affect social welfare, economists begin with the assumption that individuals derive utility (or a sense of satisfaction or well-being) from the goods and services they consume. Conversely, people may derive disutility from negative experiences, such as illness or harm to the environment. Individuals can maintain the same level of utility while trading off different bundles of goods and services (e.g., one may be equally happy going to the movies or a baseball game), and their willingness to make these trade-offs can be measured in dollar terms.

In theory, the dollar value of the benefits associated with a regulatory requirement is most appropriately measured by determining the change in income that has the same effect on utility (or the level of individual satisfaction) as the requirement. Because utility is impossible to measure directly, economists rely instead on estimates of willingness to pay or willingness to accept compensation to value the effects of regulations and other actions that lead to improvements in environmental quality. Willingness to pay is the maximum amount of money an individual would voluntarily exchange to obtain an improvement (e.g., in drinking water quality), given his or her budget constraints. Willingness to accept is the least amount of money an individual would accept to forego the improvement.

These two measures are not necessarily equal. One reason for the difference is that the two measures have different starting points. For environmental improvements, willingness to pay uses the level of utility *without* the improvement as a reference point, while willingness to accept uses as its reference point the level of utility *with* the improvement. Under conventional assumptions, economists expect that the difference between these measures will be small in many cases; e.g., as long as the amount involved is not a significant proportion of income.[24] In practice, benefits analysts usually rely on measures of willingness to pay because of concerns about the accuracy and reliability of the methods available for estimating willingness to accept compensation.[25] Willingness to pay is generally easier to measure and quantify.

While willingness to pay is constrained by income, it is a different concept than affordability. "Affordability" is a nontechnical term that is often used to refer to peoples' judgements about what is "reasonable" to pay for a particular good or service. In contrast, willingness to pay is the maximum amount an individual would *actually* pay for a good or service, given his or her income constraints and other desired expenditures.[26]

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[24] In the case of environmental goods, additional considerations may lead to larger differences between willingness to pay and willingness to accept, as discussed in EPA's *Guidelines for Preparing Economic Analyses* and Hanemann, W.M., "Willingness to Pay and Willingness to Accept: How Much Can They Differ?," *American Economic Review*, Volume 81, Number 3, 1991, pp. 635- 647.

[25] Accuracy refers to whether the findings are correct; for example, to how well the study results mirror the value in the underlying population. Reliability refers to whether the findings can be replicated; for example, to whether applying a survey to a second sample would result in the same or similar estimates as those from the first sample.

[26] While it is reasonable to assume that individuals' donations to environmental causes or organizations reflect willingness to pay for protection and preservation of the environment, these contributions cannot be interpreted as a direct proxy for willingness to pay. Donations generally reflect only partial values; for example, some people will not make

Willingness to pay is also a different concept than cost or price. "Cost" refers to the resources needed to produce a good or service; it does not measure the value of the good or service to members of society. "Price" is determined by the interactions of suppliers and consumers in the marketplace. For some individuals, the market price may exceed willingness to pay, in which case they will not purchase the good. For other individuals, willingness to pay may exceed the current price, in which case these individuals will benefit from the fact that the market price is less than he or she is willing to pay.

Economists refer to the aggregate amount that individuals are willing to spend on a good or service over and above that required by the market price as "consumer surplus." Changes in this surplus can be used to measure the benefits of various policy options. For example, if a government program reduces the price of a good or service, consumers are likely to purchase more of the product. For some consumers, the price drop will cause the difference between price and willingness to pay to rise. These impacts will increase consumer surplus, and the dollar amount of the increase can be used to measure the social welfare benefits of the policy.[27]

Measuring the value of benefits in dollar terms, based on estimates of willingness to pay, provides useful information for decision-makers. First, it is easier to compare costs and benefits and make related decisions when both are expressed in monetary terms. Second, valuation (accompanied by discussion of uncertainties in the estimates used) provides explicit, objective information on the amount of money members of society would be willing to exchange for the benefits of alternative drinking water standards or other policy choices.

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the donation if they believe that payments by others will lead to an adequate level of environmental protection.

[27] The concept of consumer surplus, and its relationship to the analysis of benefits, is described in more detail in: EPA's *Guidelines for Preparing Economic Analyses*; Freeman (1993); and Just, R.E., D.L. Hueth, and A. Schmitz, *Applied Welfare Economics and Public Policy*, Englewood Cliffs, NJ: Prentice Hall, 1982.

3.1.2 Equity Considerations

Some critics of the use of willingness to pay to value benefits are concerned about the effect of income on these values. If policy decisions were made solely on the basis of willingness to pay, critics argue, the results would not treat lower income individuals equitably. Economists deliberately attempt to separate these types of ethical judgements from the economic analysis of efficiency. They traditionally focus on how individuals value changes in their own well-being, aggregating the individual values to determine total benefits to society. If the group of individuals who benefit from a policy could compensate the group of individuals who are adversely affected, economists argue that net social welfare is maximized and the policy is considered economically efficient.

To address the limitations of this approach, economic analyses of EPA regulations are supplemented by analyses of effects on equity. As discussed in Chapter 2, analyses of environmental justice (risks and other effects on low income and minority groups) and risks to children are required for major EPA regulations. In addition, SDWA requires that EPA consider effects on sensitive subpopulations "such as infants, children, pregnant women, the elderly, and individuals with a history of serious illness, or other subpopulations likely to be at greater risk..." [SDWA, Section 1412(b)(3)(C)(i)]. SDWA also raises concerns about "affordability," particularly for small systems [SDWA, Section 1412(b)(4)(E)].[28] Requirements under other statutes mandate consideration of the costs the regulations impose on government units and private entities, as also discussed in Chapter 2.

The language of SDWA (e.g., on sensitive subpopulations and small systems) suggests that these types of equity effects should be considered when determining whether the costs of an MCL are justified by its benefits. In other words, SDWA appears to define "benefits" broadly to include both equity and traditional economic concerns about net social welfare. Because detailed information on conducting equity assessments is provided in the references cited in Chapter 2, we focus on the economic assessment of benefits in the remainder of this document.

The economic analyses described in this document can be designed to support the equity analyses. For example, in developing new studies, analysts may wish to ensure that these groups are adequately represented in the data collection strategy. When presenting the results of the analysis, analysts may decide to provide disaggregated estimates of the benefits for each subpopulation or group of concern, as well as national totals.

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[28] Information on EPA's definition of "affordability" for SDWA requirements is available in: U.S. Environmental Protection Agency, *Announcement of Small System Compliance Technology Lists for Existing National Primary Drinking Water Regulations and Findings Concerning Variance Technologies,* 63 *FR* 42032, August 6, 1998.

3.1.3 Nonquantified and Nonmonetized Benefits

The economic framework for benefits analysis described in this document focuses on developing monetary measures for valuing benefits. Many benefits, however, can be difficult to quantify, or may be quantifiable but difficult to value in monetary terms. These types of benefits are generally described in the analysis and noted in any summary of the findings. SDWA specifically calls for consideration of such benefits, noting that "quantifiable and nonquantifiable" effects should be taken into account when establishing an MCL [SDWA, Section 1412(b)(3)(C)(i)].

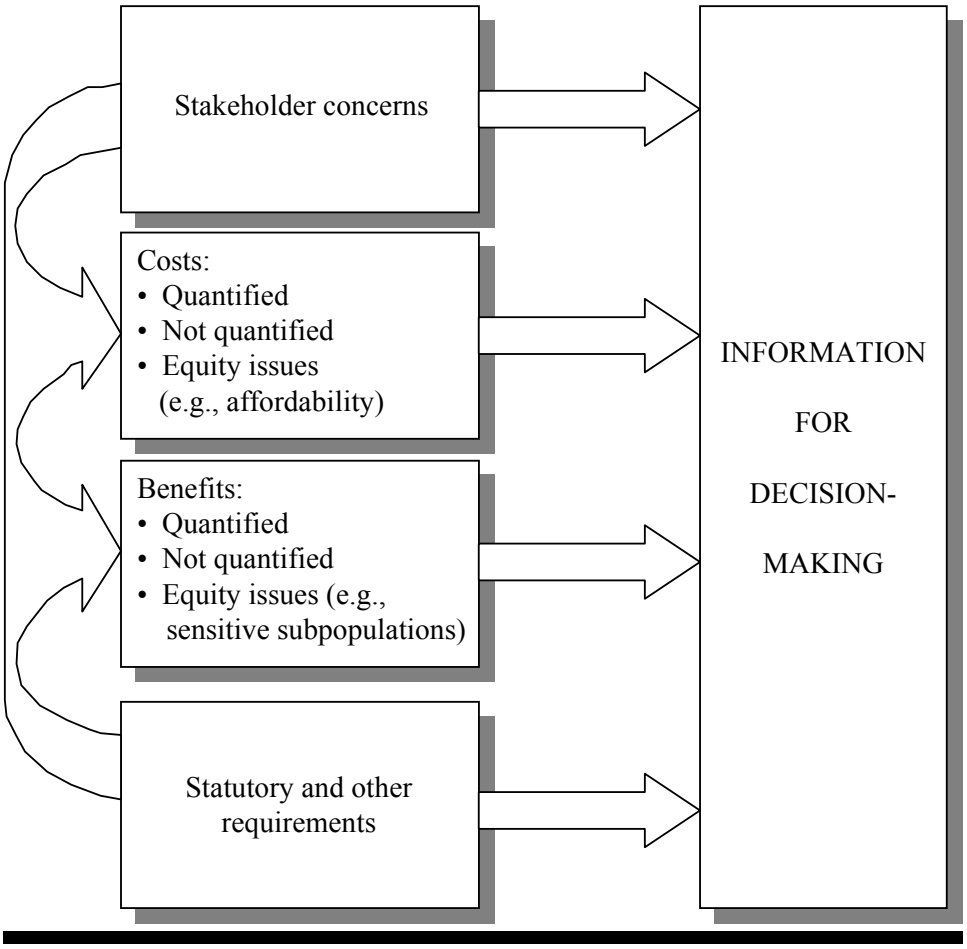
For example, EPA may know that a drinking water contaminant causes adverse health effects, but lack data on how changes in exposure levels correspond to changes in the incidence or severity of the effects. Despite this uncertainty, EPA may consider these effects when establishing regulatory levels to ensure that human health is adequately protected. These nonquantified or nonmonetized benefits are often presented in the same tables or charts as the quantified results to ensure that they are taken into account by decision-makers, along with information on the uncertainties in the estimates.

When conducting a benefit-cost analysis, analysts may find that the quantified costs exceed the monetized benefits or vice-versa. The question then becomes determining whether it is reasonable to assume that the nonquantified or nonmonetized benefits (or costs) bridge the gap between the quantified costs and benefits. In some cases, the gap may be small enough that decision-makers will conclude that benefits may be equal to, or exceed, costs if nonquantified effects are considered. Analysts may also consider whether the nonquantified impacts could disproportionately impact the results across regulatory options. For example, if consideration of a particular health effect (e.g., a type of cancer not quantified in the analysis) is likely to increase the benefits estimates by a similar percentage across all regulatory options, its consideration may not change the relative rankings of the options. However, if the impacts are uneven (e.g., some regulatory options do not reduce exposure below the threshold level at which a health effect occurs), consideration of the nonquantified benefits may affect the relationship between costs and benefits for only some of the regulatory options.

The factors to be considered by decision-makers are summarized in Exhibit 3-1. As indicated by the exhibit, the analysis of costs and benefits includes quantified and nonquantified effects and addresses concerns about the distribution (or equity) of these impacts. Statutory requirements and stakeholder concerns help shape the

contents of the analyses as well as the use of the analyses in regulatory decision-making.

Exhibit 3-1
Information for Decision-Making



3.2 Primary Valuation Methods

As discussed above, the preferred approach for valuing the benefits of environmental regulations generally is to determine individuals' willingness to pay (WTP) for the proposed improvements. When market data are not available, economists use a variety of other methods to estimate willingness to pay.[29] One of several approaches

[29] For information about market methods, see EPA's *Guidelines for Preparing Economic Analyses.*

for categorizing these methods is to divide them into two categories: *stated preference methods* and *revealed preference methods*.[30]

Stated preference methods typically employ survey techniques and ask respondents to "state" what they would pay for a good or service. These methods can be used to directly value the program of concern (e.g., "how much would you be willing to pay for a program that would reduce the concentrations of arsenic in drinking water from 10 µg/L to 5 µg/L?"), in which case they are designed to fully inform respondents about the effects of the reduction. Such studies are also used to assess specific effects (e.g., "how much would you be willing to pay for a program that would reduce the risks of incurring kidney disease from 10/100,000 to 5/100,000 annually?"). Stated preference methods are attractive in theory because they allow researchers to directly elicit values for particular effects. However, conducting a study that yields accurate and reliable results can be expensive, and relatively few have been completed that directly address the effects of concern for drinking water contaminants.

Revealed preference methods are based on observed behaviors that can "reveal" the values of nonmarket goods based on prices and preferences for related market goods or services. For example, if an individual would be charged $30 a month for tap water to drink, but instead pays $50 per month for bottled water that he or she believes to be cleaner and safer, then presumably this individual values the additional cleanliness and safety of the bottled drinking water at no less than $20 per month ($50 - $30 = $20). These methods use actual market data for related goods instead of relying on individuals' predictions of their own behavior. However, there is often an imperfect match between the commodities valued in these studies and individuals' willingness to pay for the effects associated with a particular rule.

Below, we introduce each of the primary research methods most likely to be used in valuing the effects of drinking water regulations; the footnotes provide references for more information on each method. We describe contingent valuation and conjoint analysis, wage-risk studies, cost-of-illness research, averting behavior studies, and avoided cost methods.

[30] More information on methods for valuing the benefits of drinking water regulations as well as examples of these studies is available in: Research Triangle Institute, *Valuing Water Quality: Theory, Methods, and Research Needs,* prepared for the U.S. Environmental Protection Agency, April 1998.

3.2.1 Contingent Valuation and Other Stated Preference Methods

Contingent valuation (CV) is a stated preference method that uses consumer surveys to directly elicit statements of willingness to pay for a commodity.[31] The values derived from the surveys are "contingent" on the realization of the scenarios described in the study. For example, a survey might ask individuals what they would be willing to pay for a specified reduction in the risk of developing kidney disease from long-term exposure to contaminants in drinking water. The researcher can define the scenario to address all the factors that may influence total willingness to pay, such as pain and suffering in the case of illness.

Contingent valuation surveys can be used to derive estimates for the full range of effects of environmental regulations, including changes in mortality and morbidity risks, improved aesthetic effects, reduced damages to materials, and changes in ecological risks. Contingent valuation is also the primary method used to assess the "nonuse" values of natural resources, such as the value of simply knowing that clean water exists.[32] Some examples of contingent valuation studies are provided in Exhibit 3-2.

[31] For more information on contingent valuation, see: Bjornstad, D.J. and J.R. Kahn, *The Contingent Valuation of Environmental Resources: Methodological Issues and Research Needs*, Edward Elgar: Brookfield, VT, 1996; Carson, R.T., "Contingent Valuation: A User's Guide," *Environmental Science and Technology*, Vol. 34, 2000, pp. 1413-1418; Hanemann, W. Michael, "Valuing the Environment through Contingent Valuation," *Journal of Economic Perspectives*, Fall 1994, Vol. 8, No. 4, pp. 19-43; Kopp, R., W.W. Pommerehne, and N.T. Schwarz, (eds.), *Determining the Value of Non-Marketed Goods*, Boston, MA: Kluwer Academic Publishers, 1997; and Mitchell, R. and R.T. Carson, *Using Surveys to Value Public Goods: The Contingent Valuation Method*, Resources for the Future, Washington, DC, 1989.

[32] For more information on nonuse values, see: Kopp, R.J., "Why Existence Value *Should* be Used in Cost-Benefit Analysis," *Journal of Policy Analysis and Management,* Vol. 11, No. 1, pp. 123-130, 1992; and Cummings, Ronald G. and Glenn W. Harrison, "The Measurement and Decomposition of Nonuse Values: A Critical Review," *Environmental and Resource Economics,* Vol. 4, pp. 225-247, 1995.

Exhibit 3-2

Examples of Contingent Valuation Studies[33]

Fatal Risks: Jones-Lee, et al. used contingent valuation to estimate individuals' willingness to pay to avoid the risk of death from auto accidents. The study also explored willingness to pay to reduce fatal risks for other people (e.g., passengers) and other types of fatalities (e.g., from heart disease and cancer). The researchers conducted face-to-face interviews with 1,103 persons in Great Britain and asked them to consider the value of avoiding fatalities expressed as "X" in 100,000 risks. Converted from British pounds (using the 1982 exchange rate) and inflated to 1997 dollars (using the GDP deflator), the average value of a statistical life resulting from this study is $4.6 million.

Minor Health Problems: Berger, et al. used contingent valuation to study willingness to pay to avoid an additional day of minor health problems such as headaches and itching eyes. Participants were asked to rank seven minor health problems, state values for symptom-free days, and summarize the values on a tally sheet. The researchers interviewed 119 respondents and determined, for example, that the average willingness to pay to avoid a day of headache is $109, and a day of itching eyes is $48 (1984 - 85 dollars).

Ground Water Protection: Powell studied individuals' willingness to pay for ground water protection using a contingent valuation survey conducted in 12 towns in the northeast. The survey was performed by mail and 1,041 people responded. The questionnaire presented information on contamination and asked respondents to indicate their willingness to pay for a water supply protection district funded through increased utility bills. Mean willingness to pay was $62 per household per year (1990 dollars).

Despite the widespread applicability and use of contingent valuation, the method has been heavily criticized in recent years. This criticism focuses largely on the measurement of nonuse values; the application of contingent valuation surveys to other types of effects tends to be less controversial. Contingent valuation studies need to be carefully implemented if they are to provide accurate and reliable estimates of willingness to pay, because individuals generally are not required to actually make the payments and may not fully understand the scenario presented in the survey.

Much of the debate has centered on the use of contingent valuation to assess damages to natural resources from oil spills and other contamination events as part of related litigation. The National Oceanic and Atmospheric Administration (NOAA) convened an expert panel in 1992 to develop guidelines for using

[33] Jones-Lee, Michael W., M. Hammerton and P.R. Phillips, "The Value of Safety: Results of a National Sample Survey," *Economic Journal,* Vol. 95, March 1985, pp. 49-72; Berger, M.C., et al., "Valuing Changes in Health Risks: A Comparison of Alternative Measures," *Southern Economic Journal,* Vol. 53, 1987, pp. 967-984; Powell, John R., David J. Allee, and Charles McClintock, "Groundwater Protection Benefits and Local Community Planning: Impact of Contingent Valuation Information," *American Journal of Agricultural Economics*, Vol. 76, December 1994, pp. 1068-1075.

contingent valuation to estimate nonuse values in such situations.[34] The panel made several recommendations for improving the reliability of these studies, such as encouraging in-person interviews (rather than mail or telephone surveys) and extensive pretesting of questionnaires and accompanying materials. Following the panel's recommendations can substantially increase the costs of contingent valuation research (e.g., to over $1 million per study) and very few existing studies fully comply with these guidelines. Several of the recommendations are controversial and may not be relevant to studies conducted for purposes other than assessment of nonuse values for litigation. As a result, EPA is currently developing its own guidelines to specifically address the use of contingent valuation for policy analysis.

Economists recently have been experimenting with other stated preference methods, particularly those referred to as conjoint analyses.[35] These methods are relatively complex and include presenting respondents with several scenarios involving various amenities and prices. Estimates of willingness to pay may be elicited based on the way in which respondents rank, rate, or construct equivalent sets of alternatives. For example, Adamowicz et al. asked respondents to make choices among several hypothetical fishing scenarios that differed along 13 attributes such as site terrain, average fish size, and water quality, and combined the results with data on actual site choices to value recreational opportunities.[36]

The "risk-risk trade-off" method is closely related to conjoint analysis, and has been used in research conducted by Viscusi and others to value changes in health risks. For example, Viscusi, et al. developed a computerized questionnaire that asked respondents to choose between places to live which varied with respect to the cost

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[34] National Oceanic and Atmospheric Administration (NOAA), "Appendix I - Report of the NOAA Panel on Contingent Valuation," *Federal Register*, Vol. 58, No. 10, pp. 4602-4614, January 15, 1993. The official EPA response to these guidelines can be found in: U.S. Environmental Protection Agency, "Comments on Proposed Regulations on Natural Resource Damage Assessment," 1994.

[35] For more information on conjoint methods, see: Adamowicz, Wiktor, Jordan Louviere, and Joffre Swait, *Introduction to Attribute Based Stated Choice Methods*, prepared for the National Oceanic and Atmospheric Administration, January 1998; and Smith, V.K. "Pricing What is Priceless: A Status Report on NonMarket Valuation of Environmental Resources," *The International Yearbook of Environmental and Resource Economics, 1997/1998: A Survey of Current Issues,* (H. Folmer and T. Tietenberg, eds.), 1997.

[36] Adamowicz, Wiktor, et al., "Combining Revealed Preference and Stated Preference Methods for Valuing Environmental Amenities," *Journal of Environmental Economics and Management,* Vol. 26, No. 3, pp. 271- 292, 1994.

of living, the risks of chronic bronchitis, and/or the risks of automobile fatalities.[37] The results indicated that the median value of avoiding a case of chronic bronchitis is 32 percent of the value of avoiding an automobile fatality. When asked to trade-off changes in the cost of living for changes in risk, respondents indicated that the mean value of avoiding a case of chronic bronchitis was $457,000 (1988 dollars).

3.2.2 Wage-Risk Studies

A wage-risk (or hedonic wage) study is a revealed preference method that values changes in risk by examining the additional compensation workers demand for taking jobs with higher risks. Typically, these studies focus on small changes in the risks of accidental workplace fatalities. Researchers use statistical methods to separate changes in compensation associated with changes in risks from changes in compensation associated with other job and personal characteristics.[38] An example of a wage-risk study is provided below.

Exhibit 3-3
Example of a Wage-risk Study[39]

Fatal Risks: Moore and Viscusi used data from the Bureau of Labor Statistics (BLS) and the National Institute of Occupational Safety and Health (NIOSH), combined with information on worker attributes from the Panel Study of Income Dynamics, to estimate the value of a statistical life. The mean value of the risks studied was $5x10^{-5}$ for the BLS data and $8x10^{-5}$ for the NIOSH data. The researchers found that the value of statistical life estimates resulting from the NIOSH data ($6 million to $7 million) are significantly larger than values from the BLS data ($2 million), and argue that the NIOSH values are likely to be more accurate (1986 dollars).

The wage-risk approach has several advantages. For example, the data and methods for estimating risk reduction and associated wage differentials have been well-established through a number of studies. In addition, the approach directly measures changes in the risk of premature mortality. A number of factors, however, may complicate the use of wage-risk studies to value the benefits of drinking water regulations. For example, workplace risks usually involve some degree of voluntary acceptance, while environmental risks usually affect individuals involuntarily. In addition, most wage-risk studies use data on middle-aged laborers (often male), who may not be representative of the members of the population most significantly

[37] Viscusi, W.K., Magat, W.A., and Huber, J., "Pricing Environmental Health Risks: Survey Assessments of Risk-Risk and Risk-Dollar Tradeoffs," *Journal of Environmental Economics and Management,* 1991, Vol. 201, pp. 32-57.

[38] More information on wage-risk studies is provided in: Viscusi, W.P., "The Value of Risks to Life and Health," *Journal of Economic Literature*, Vol. 31, 1993, pp. 1912-1946.

[39] Moore, Michael J. and W. Kip Viscusi, "Doubling the Estimated Value of Life: Results Using New Occupational Fatality Data," *Journal of Policy Analysis and Management,* Vol. 7, No. 3, 1988, pp. 476-490.

affected by the risks associated with drinking water contaminants. Despite these limitations, these revealed preference studies may provide the most defensible estimates of the value of mortality risk reductions and are the source of many of the estimates used by EPA when valuing these risks, as discussed in more detail later in this chapter.

3.2.3 Cost-of-Illness Studies

Cost-of-illness (COI) studies are frequently used to value morbidity (i.e., nonfatal health effects). These studies examine the actual direct (e.g., medical expenses such as doctor visits, medication, and hospital stays) and indirect (e.g., lost wages) costs incurred by affected individuals.[40] While cost-of-illness is sometimes categorized as a revealed preference method, it does not directly measure willingness to pay. In general, the logic for using these studies to value benefits is as follows: if illness imposes the costs of medical expenditures and foregone earnings, then a regulation leading to a reduction in illness yields benefits equal at minimum to the costs saved.[41]

The cost-of-illness method has several advantages, including: (1) it is well-developed, widely applied, and easily explained; (2) many of the types of costs it includes are easily measured; and (3) existing studies provide estimates for a large number of illnesses. These studies can be designed to address all expenditures associated with an illness, regardless of whether they are paid by the patient or a third party (i.e., insurance). Lost productivity can be estimated by lost wages for those in the paid labor force; however, lost productivity for unpaid labor in the home and lost leisure time can be more difficult to measure. Examples of cost-of-illness estimates are provided in Exhibit 3-4.[42]

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[40] Sources of more information on cost-of-illness methods include: U.S. Environmental Protection Agency, *Cost of Illness Handbook*, February 2001; Hartunian, N.S., C.N. Smart, and M.S. Thompson, *The Incidence of Economic Costs of Major Health Impairments*, Lexington Books: Lexington, MA, 1981; Hu, T. and F.H. Sandifer, *Synthesis of Cost-of-Illness Methodology: Part I*, report to the National Center for Health Services Research, U.S. Department of Health and Human Services, 1981.

[41] Tolley, G., D.Kenkel, and R. Fabian (Eds.), *Valuing Health for Policy: An Economic Approach*, University of Chicago Press, 1994.

[42] Although cost of illness values have been developed for both fatal and nonfatal health effects, the value of statistical life is generally the preferred valuation measure for fatalities, as discussed later in this chapter. Cost-of-illness estimates are generally applied to those nonfatal health effects for which estimates of willingness to pay are unavailable.

Exhibit 3-4
Examples of Cost of Illness Studies[43]

Stomach Cancer: Based on research conducted by Baker et al, EPA examined both the medical costs and the lost time that result from stomach cancer. For survivors diagnosed at age 70, the direct medical costs for the 10 years following diagnosis were estimated at $85,700 per case (present value, 1996 dollars, 7 percent discount rate).

Low Birth Weight: Low birth weight in infants can lead to a variety of medical disorders, including heart failure and severe developmental disabilities. Infants with low birth weight incur high medical costs in their first year, but also tend to continue to incur elevated medical costs throughout their life. Based on research conducted by Lewitt et. al, EPA examined these costs as well as non-medical costs stemming from the need for special education and grade repetition. The present value (discounted at 7 percent) of the costs over a lifetime were estimated as $80,600 per case (1996 dollars).

Contaminated Water Supply: Harrington, et al. valued the losses incurred by households as a result of a water contamination episode in Luzerne County, Pennsylvania, during 1983 to 1984. As part of this analysis, they estimated the costs due to illness resulting from water contamination, including direct medical costs (doctor visits, hospital visits, emergency room visits, laboratory tests and medication), and time costs (including time spent obtaining medical care and related travel, lost work days, lost work productivity, and lost leisure time). The study relies on survey data (mail and phone) from affected households. Depending on the wage rate assumptions, the researchers found that cost-of-illness related losses averaged between approximately $900 and $1,300 per confirmed case of giardiasis (1984 dollars).

Although these studies are widely used for valuation, they generally do not provide estimates of willingness to pay. In many cases, cost-of-illness estimates may significantly underestimate individual willingness to pay, because they do not address the value of avoiding the pain and suffering associated with the illness, costs that an individual may have incurred in order to avoid the illness, and other factors. Cost-of-illness estimates may also occasionally overstate willingness to pay because the availability of insurance may lead people to agree to treatments that they would not willingly finance themselves.

In addition, cost-of-illness estimates do not reflect value associated with an individual's risk aversion, i.e., his or her willingness to pay to avoid future risks. Treatment also often does not return people to their original health state and hence does not address all of the benefits of avoiding the illness entirely.

3.2.4 Averting Behavior Studies

Averting behavior studies are a revealed preference method that use data on consumer behavior to estimate willingness to pay for risk reductions or other

[43] EPA's *Cost of Illness Handbook*; Harrington, Winston, Alan J. Krupnick and Walter O. Spofford, Jr., "The Economic Losses of a Waterborne Disease Outbreak," *Journal of Urban Economics*, Vol. 25, 1989, pp. 116-137.

effects.[44] For example, in the absence of regulation, individuals or households may avoid the health risks and aesthetic effects associated with drinking water contaminants by using bottled water, treating water at the tap, or using water softeners. Some of these studies also consider the medical treatments sought in response to particular types of contamination. If a regulation leads people to discontinue these behaviors, then the avoided costs may be one measure of the resulting benefits.

The averting actions considered in these studies often fall into three categories: (1) the purchase of a durable good (e.g., a water filter); (2) the purchase of a nondurable good (e.g., bottled water); and (3) a change in daily activities or behavior (e.g., boiling water before use or consuming less drinking water). Some averting actions allow an individual to completely eliminate exposure to the perceived contamination, while others allow the individual to mitigate the effects of potential exposure. The costs considered in such studies are sometimes referred to as defensive expenditures.

Use of these studies for benefits valuation can pose difficult problems related to separating out different motives for the behavior. For example, bottled water purchases may reflect the desire for convenience, or for better taste, as well as the desire to avoid the perceived risks of tap water ingestion. In addition, use of bottled water may reflect concerns about a wide variety of contaminants and health effects. It may be impossible to disentangle the various complex motives for engaging in these behaviors, and several of these motives may not be addressed by the regulations under consideration.

The extent to which such studies provide an estimate of willingness to pay is a subject of debate in the literature, and depends in part on the nature of the policy problem and the types of expenditures considered by the researcher. For example, bottled water expenditures may overstate the value of risk reductions if they also reflect convenience and taste. However, studies that consider only the money and time expended on boiling or purchasing water in response to drinking water contamination are likely to understate willingness to pay to avoid the contamination,

[44] For more information on averting behavior studies see: Cropper, Maureen, and A. Myrick Freeman III, "Environmental Health Effects." *Measuring the Demand for Environmental Quality* (J.B. Branden and C.D. Kolstad, eds.), Elsevier Science Publishers: The Netherlands, 1991, pp. 165 - 213; Bartik, Timothy J., "Evaluating the Benefits of Nonmarginal Reductions in Pollution Using Information on Defensive Expenditures," *Journal of Environmental Economics and Management,* Vol. 15, 1988, pp. 111-127; Courant, Paul and Richard Porter, "Averting Expenditure and the Cost of Pollution," *Journal of Environmental Economics and Management,* Vol. 8, 1981, pp. 321-329; and Desvousges, W.H., F.R. Johnson, and H.S. Banzhaf, *Environmental Policy Analysis with Limited Information: Principles and Applications of the Transfer Method*, Northampton, MA: Edward Elgar, 1998.

since they leave out other responses to these incidents and do not address the value of averting the dread of such incidents.

In theory, researchers could combine data on averting behavior with other types of information (such as data on the associated changes in risk) to estimate willingness to pay for risk reductions. They could then apply statistical methods to separate the value of the risk reduction from the value of other effects. Because separating the value of the different effects of averting behavior is difficult (requiring a relatively large amount of data and the application of complex analytic techniques), such analysis is rarely, if ever, attempted.

In Exhibit 3-5, we provide examples of various types of averting behavior studies.

Exhibit 3-5
Examples of Averting Behavior Studies[45]

Lead Exposure: Agee and Crocker applied the averting behavior method to assess willingness to pay for reduced lead exposures. They assessed data for 256 Massachusetts children, considering the child's body burden of lead, parental decisions regarding treatment, and household characteristics such as the parent's educational level and income. They found that the mean value of a one percent reduction in child body lead burden ranged from $11 to $104 (1980 dollars).

Drinking Water Contamination -- Trichloroethylene: Abdalla, et al. researched the effect of a drinking water contamination incident in Perkasie, Pennsylvania, where trichloroethylene was detected in a well at levels far exceeding the MCL. They used a mail questionnaire to gather information about averting expenditures and behaviors in response to the contamination. They found that only 43 percent of the survey respondents knew of the contamination; of those, only 44 percent undertook averting actions such as purchasing bottled water or boiling water before use. The authors indicate that the total costs of these actions ($61,300 - $131,300 over 88 weeks; 1987-89 dollars) provide a conservative estimate of the benefits of avoiding the contamination.

Drinking Water Contamination -- Perchloroethylene: In another study, Abdalla quantified household level economic losses due to averting behavior in response to perchloroethylene groundwater contamination. Using a mail survey of residents in the affected Pennsylvania community, Abdalla determined the frequency and types of averting behaviors adopted in response to contamination, and estimated economic losses attributable to these behavior changes. He found that, on average, total household costs of averting behavior ranged from $252 to $383 (1987 dollars). Households incurred monthly costs of up to three times normal water bills as a result of behavioral changes such as home water treatment or hauling or purchasing of alternative water sources.

Drinking Water Contamination -- Giardia: The Harrington, et al. study mentioned earlier valued the costs of averting behaviors as well as the costs-of-illness resulting from a giardia contamination episode in Luzerne County, Pennsylvania. Losses due to averting behavior include water hauling or boiling, bottled water purchases, and other actions undertaken to avoid consumption of contaminated water. The study considers the time lost as well as direct expenditures, and is based on survey data (mail and phone) from the affected households. Depending on the costs included in the estimates, the researchers found that the averting behavior losses averaged between approximately $500 and $1,500 per household (1984 dollars).

[45] Agee, Mark D. and Thomas D. Crocker, "Parental Altruism and Child Lead Exposure: Inferences from the Demand for Chelation Therapy," *Journal of Human Resources*, Vol. 31, Summer 1996, pp. 677-691; Abdalla, Charles W., Brian A. Roach, Donald J. Epp., "Valuing Environmental Quality Changes Using Averting Expenditures: An Application to Groundwater Contamination," *Land Economics,* Vol. 68, No. 2, May 1992, pp. 163-169; Abdalla, Charles W., "Measuring Economic Losses From Ground Water Contamination: An Investigation of Household Avoidance Costs," *Water Resources Bulletin*, Vol. 26, 1990, pp. 451-463; Harrington, Winston, Alan J. Krupnick and Walter O. Spofford, Jr., (1989).

3.2.5 Avoided Cost Studies

Avoided cost studies are somewhat similar to the cost-of-illness and averting behavior studies discussed earlier, in that all three methods consider the expenditures averted (or displaced) by reduced exposure to contamination. The term "avoided cost" is generally used when the expenditures would be incurred by private sector or government organizations rather than individuals or households. Such studies often apply a relatively simple approach: they measure the expenditures likely to occur in the absence of the regulation, compare them to the likely expenditures once the regulation is promulgated, and use the difference to estimate benefits.[46] These methods are generally easy to apply and provide useful information for policy analysis. Whether they are a true measure of the value of related benefits depends on whether the researcher considers the effects of these costs on consumers.[47]

The avoided cost method is commonly used to assess material damages that are reduced, prevented, or mitigated by environmental regulations. Some examples include the following:

- If contaminants damage piping or other equipment, regulating the contaminant may reduce the costs of repairing the damages as well as the frequency with which the equipment needs to be replaced.

- If contaminants affect the use of water as a production input (because of the need for purity), regulating the contaminant may reduce industry's water treatment costs.

- If contaminants lead to soiling of items requiring cleansing, regulating the contaminants may reduce the costs and frequency of cleaning.

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[46] For more information on avoided cost methods, see: Adams, Richard M. and Thomas D. Crocker, "Materials Damages," *Measuring the Demand for Environmental Quality* (J.B. Branden and C.D. Kolstad, eds.), Elsevier Science Publishers: The Netherlands, 1991, pp. 271-303.

[47] As discussed earlier in this chapter, consumers benefit if they are willing to pay more than current prices for a good or service. If, for example, industry costs decline because they no longer need to treat water received from the public water system, firms may pass some of these savings onto consumers in the form of lower prices. These lower prices will increase consumer surplus and may also affect producer surplus. A full treatment of avoided costs would account for these changes in consumer and producer surplus. A more detailed discussion of these issues is provided in: U.S. Environmental Protection Agency, *Handbook for Noncancer Health Effects Valuation (draft),* prepared by Industrial Economics, Incorporated, September 1999.

Examples of this type of study are provided in Exhibit 3-6. As is evident from the examples, such analysis includes only those costs that can be avoided by the regulations and that are not attributable to other causes.

Exhibit 3-6
Examples of Avoided Cost Studies[48]

Corrosion: Many of the treatment techniques used to reduce the concentration of lead in drinking water reduce the water's acidity, and thus reduce corrosion. To support development of EPA's drinking water standards for lead, Levin reviewed the literature on the costs of corrosive damages to distribution systems and residential users and determined the per capita value of these damages. She then calculated the proportion of these damages that could be reduced by water treatment, estimating that $8.50 in costs per capita could be avoided annually. She multiplied this cost by the population likely to be served by systems with corrosive waters, estimating the national value of avoided costs as $525.3 million annually (1985 dollars).

Ground Water Remediation: In the absence of clean-up of hazardous waste sites, contaminants released to ground water may eventually affect drinking water supplies in surrounding areas. Water systems and private well users will then incur costs for treating the water and/or for replacing it with uncontaminated supplies. To support development of EPA's corrective action regulations, researchers reviewed the water treatment and replacement costs that might be incurred at several sample facilities in the absence of site remediation. They assessed the likely impact of these costs on water prices and the resulting change in consumer surplus. They found that only about two percent of the loss in consumer surplus ($4.7 million) would be avoided by clean-up of the site because ground water remediation techniques may be only partially effective and can take several years to significantly reduce contaminant concentrations (1992 dollars).

3.3 Methods for Valuing Mortality, Morbidity, and Other Effects

As discussed earlier, the primary benefits of regulations establishing MCLs are effects on human health. This section provides more detailed descriptions of the particular steps needed to assess reduced mortality, morbidity, and other (non-health) effects, summarizing relevant information provided in EPA's *Guidelines for Preparing Economic Analyses* and other references cited in the footnotes.

3.3.1 Valuing Mortality Risk Reductions

The benefits of mortality risk reductions from environmental regulations are generally assessed using empirical estimates of the value of a statistical life (VSL). The value of statistical life does not refer to the value of an identifiable life, but instead to the value of small reductions in mortality risks in a population. A

[48] Levin, Ronnie, *Reducing Lead in Drinking Water: A Benefits Analysis,* prepared for the U.S. Environmental Protection Agency, 1986; Industrial Economics, Incorporated, "Chapter 9: Averted Water Use Costs," *Draft Regulatory Impact Analysis for the Final Rulemaking on Corrective Action for Solid Waste Management Units*, prepared for the U.S. Environmental Protection Agency, March 1993.

"statistical" life can be thought of as the sum of small individual risk reductions across an entire exposed population.

For example, if 100,000 people would each experience a reduction of 1/100,000 in their risk of premature death as the result of a regulation, the regulation can be said to "save" one statistical life (i.e., 100,000 * 1/100,000). The sum of the individual willingness to pay values for the given risk reduction across the population provide a value per statistical life. Continuing with the previous example, if each member of the population of 100,000 were willing to pay $50 for the risk reduction, the corresponding value of a statistical life would be $5 million (i.e., $50 * 100,000). Note that these estimates rely on studies of relatively small changes in risk; they are not values for saving a specific individual's life.

A variation on this approach involves accounting for the effect of risk reductions on the number of life years remaining.[49] The value of statistical life-year (VSLY) approach assigns a value to each year of life extended. In its simplest form, the VSLY approach translates the value of statistical life into annual values, implicitly assuming a linear relationship in which each discounted life year is valued equally. There is significant controversy over this approach, particularly because the value of remaining life years is likely to vary depending on the age of the individual and other factors.

Exhibit 3-7 presents the value of statistical life estimates applied in EPA's recent report to Congress, *The Benefits and Costs of the Clean Air Act, 1990 to 2010,* updated to 2000 values.[50] These estimates, derived from wage-risk and contingent valuation studies, range from $0.8 million to $17.8 million, with a mean of $6.3 million.[51]

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[49] An emerging literature takes a third approach to valuation, focusing on changes in life expectancy. However, this approach is not yet well enough developed for use in valuation of regulatory programs. See, for example: Johannesson, Magus and Per-Olov Johansson, "The Value of Life Extension and the Marginal Rate of Time Preference: A Pilot Study," *Applied Economic Letters,* Vol. 4, 1997, pp. 53-55.

[50] U.S. Environmental Protection Agency, *The Benefits and Costs of the Clean Air Act, 1990 to 2010*, EPA 410-R-99-001, November 1999.

[51] To allow probabilistic modeling of mortality risk reduction benefits, analysts reviewed common distributions and selected the Weibull distribution as a best fit for the mean values from these studies. Percentile values from this distribution can be used for sensitivity analysis in cases where the analyst is interested in estimating reasonable "high" and "low" values.

Exhibit 3-7
Value of Statistical Life Estimates (Mean Values in 2000 Dollars)

Study	Method	Value of Statistical Life
Kneisner and Leeth (1991 - US)	Wage-Risk	$0.8 million
Smith and Gilbert (1984)	Wage-Risk	$0.9 million
Dillingham (1985)	Wage-Risk	$1.2 million
Butler (1983)	Wage-Risk	$1.4 million
Miller and Guria (1991)	Contingent Valuation	$1.6 million
Moore and Viscusi (1988)	Wage-Risk	$3.3 million
Viscusi, Magat, and Huber (1991)	Contingent Valuation	$3.6 million
Marin and Psacharopoulos (1982)	Wage-Risk	$3.7 million
Gegax et al. (1985)	Contingent Valuation	$4.3 million
Kneisner and Leeth (1991 - Australia)	Wage-Risk	$4.3 million
Gerking, de Haan, and Schulze (1988)	Contingent Valuation	$4.5 million
Cousineau, Lecroix, and Girard (1988)	Wage-Risk	$4.7 million
Jones-Lee (1989)	Contingent Valuation	$5.0 million
Dillingham (1985)	Wage-Risk	$5.1 million
Viscusi (1978, 1979)	Wage-Risk	$5.4 million
R.S. Smith (1976)	Wage-Risk	$6.1 million
V.K. Smith (1976)	Wage-Risk	$6.2 million
Olson (1981)	Wage-Risk	$6.9 million
Viscusi (1981)	Wage-Risk	$8.6 million
R.S. Smith t(1974)	Wage-Risk	$9.5 million
Moore and Viscusi (1988)	Wage-Risk	$9.6 million
Kneisner and Leeth (1991 - Japan)	Wage-Risk	$10.0 million
Herzog and Schlottman (1987)	Wage-Risk	$12.0 million
Leigh and Folson (1984)	Wage-Risk	$12.8 million
Leigh (1987)	Wage-Risk	$13.7 million
Garen (1988)	Wage-Risk	$17.8 million

See Viscusi, W.K., *Fatal Tradeoffs* (Oxford University Press, 1992) or Viscusi, W.K., "The Value of Risks to Life and Health," *Journal of Economic Literature*, Vol. 31, pp. 1912-1946, 1993, for full references for these studies. Values are updated to 2000 dollars using the Consumer Price Index.

EPA analysts currently apply these values in most regulatory analyses due to the substantial research and peer review used to develop this range of estimates. However, EPA staff continue to explore options for refining this approach. An example of this approach is provided in Chapter 5.

Use of these estimates to value the mortality risks of environmental policies is an example of the use of benefit transfer techniques, since the subject of most of the

studies (i.e., job-related risks) differs from the fatal risks reduced by environmental policies (usually associated with various forms of cancer). Benefit transfer is discussed in detail in Chapter 4 of this document. As is the case in any transfer, when applying this range of estimates to a particular rule, analysts consider differences between the scenarios considered in these studies and the risk reductions addressed by the regulations, as discussed below.

Reliable methods for adjusting these values to address potential biases have not yet been fully developed or adequately tested in most cases. More empirical research is needed to determine the appropriate adjustments, and here is substantial disagreement within the economics profession about many of these issues. In addition, several of the potential biases are counterbalancing and adjusting for only some sources of bias may lead to significant over- or underestimates of actual value. At minimum, the existing literature can be used to support a qualitative discussion of the direction and magnitude of these biases and their implications for decision-making.[52]

Sources of bias can be grouped into two general areas, including those related to the *risk characteristics* (risk perception, altruism, baseline risk, and delayed manifestation) and the *population characteristics* (income, age, and health status). Quantitative adjustment for these sources of bias is generally considered only for income and latency. As described briefly below, the other sources are usually discussed qualitatively given the status of related research.

Risk perception. The value that people place on risk reduction appears to depend in part on the nature of the risk. Individuals are likely to place different values on avoiding different types of fatal risks, even if the magnitude of the risks (e.g., a 1/100,000 change in the risk of death) is the same. These differences result, at least in part, from how individuals perceive, or feel about, risks with varying characteristics. A substantial body of literature suggests that there are nine major categories that influence individuals' perception and rankings of risks: (1) voluntariness; (2) controllability; (3) known to science; (4) known to those exposed; (5) familiarity; (6) dread; (7) certainty of being fatal; (8) catastrophic; and (9) immediately manifested.[53] Many of these characteristics are highly correlated with

[52] For a more detailed discussion of each of these sources of bias as well as references to the primary research on these topics see Industrial Economics, Incorporated, *The Use of Benefit-Cost Analysis: Valuing Fatal Risk Reductions,* prepared for U.S. Environmental Protection Agency, Office of Ground Water and Drinking Water (forthcoming), as well as EPA's *Guidelines for Conducting Economic Analyses*.

[53] See, for example, Slovic, P., B. Fischoff, and Sarah Lichtenstein, "Perceived Risk: Psychological Factors and Social Implications," *Proceedings of the Royal Society of London. Series A: Mathematical and Physical Sciences,* Vol. 430, No. 1878, 1981, pp. 17-34.

each other, either directly or inversely. For example, risks with a high degree of dread, such as nuclear accidents, also have a low degree of controllability and voluntariness. As a result, differences in risk ranking can be explained by relatively few of these factors. Researchers have found that one of the most important determinants may be the degree of dread.

Altruism. Another factor to consider is the presence of altruism. The existing literature focuses on individual risk tradeoffs, but there is substantial evidence that people are willing to pay to reduce risks incurred by others (e.g., the current generation may choose to bear the costs of a program that will benefit future generations). However, many researchers advocate caution in attempting to increase value of life estimates to reflect altruism, primarily because of concerns over the potential for double-counting.[54]

Baseline Risk. Willingness to pay for fatal risk reduction may vary depending on the whether the affected individuals are already facing high or low levels of fatal risks. These risks can include both those that are relatively voluntary in nature (e.g., smoking, participating in extreme sports) as well as those that are less so (e.g., hereditary health conditions, other environmental hazards). Available evidence indicates that changes in willingness to pay are only significant when the level of baseline risk varies substantially; differences in baseline risk may have little effect in the case of the relatively modest risk reductions typical of many drinking water regulations.[55]

Delayed Manifestation *(latency and cessation lag)***.** Latency generally refers to the delay between exposure and mortality or manifestation of an adverse health effect. When there is a significant delay between manifestation of an adverse health effect and death (i.e., some cancers), this period may include illness and impaired function. Latent risks are likely to be valued differently from risks that are more immediate. Cessation lag is the time between the cessation or reduction of exposure and a reduction of risk. The existence of a cessation lag implies that the physiological damage caused by the contaminant can be completely or partially repaired over a period of time once exposure ceases, thus decreasing the risk for later disease or death among populations that have already been exposed. The value placed on risks

[54] For more information on altruism, see for example, Jones-Lee, M.W., "Paternalistic Altruism and Value of Statistical Life," *The Economic Journal,* Vol. 102, 1992, pp. 80-90.

[55] Hammitt, James K., "Valuing Mortality Risk: Theory and Practice," *Environmental Science and Technology,* Vol. 34, 2000, pp. 1396-1400; and Miller, Ted R., "The Plausible Range for the Value of Life - Red Herrings Among the Mackerel," *Journal of Forensic Science,* Vol. 3, No. 3, 1990, pp. 17-39.

that decline quickly after cessation of exposure may be different from those that decline slowly or not at all.

Heath risks from latent illnesses, like cancer, introduce additional valuation issues. Current valuation estimates are based on risks of relatively immediate fatality. Reducing the risk of an immediate death is generally valued more highly than reducing the risk of a delayed one, assuming the risks are identical in all other respects. If cessation lag applies to a reduction in risk, the length of the lag will also affect valuation.

Income. The most robust estimates of the value of a statistical life tend to come from samples of middle-aged workers, and the income levels associated with these studies may differ from the mean for individuals affected by most drinking water regulations. In addition, national average income is increasing over time. Making adjustments for income across population subgroups may imply that public policies should favor protection of higher income individuals. This implication clearly raises difficult ethical and legal issues and, as a result, these types of quantitative adjustments are rarely implemented. Adjusting value of statistical life estimates for changes in income over time has also been discussed.[56]

Age. The studies cited in Exhibit 3-7 focus on risks incurred by the working age population, not by very young or very old individuals. Several authors have attempted to address potential differences in the value of statistical life due to differences in the average age of the affected population or the average age at which an effect is experienced. While it may seem intuitive to assume that the value of statistical life is greater for young people than older people, studies of people's willingness to engage in high risk behavior suggest a more complex relationship. For example, Jones-Lee et. al. find that the value of a statistical life for adults follows an "inverted-U" pattern, peaking around the age of 40.[57] Valuation of risks to children presents special problems.

Health Status. Individual health status (i.e., whether a person is currently in good health) also may affect the valuation of mortality risk reduction, particularly because individuals with impaired health are often the most vulnerable to death from environmental causes. Health status is distinct from age (a "quality versus quantity" distinction) but the two factors are clearly correlated and therefore are often addressed jointly.

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[56] EPA's Science Advisory Board has recommended adjusting for income changes over time.

[57] Jones-Lee, Michael W., *The Economics of Safety and Physical Risk,* Basil Blackwell: Oxford, 1989.

Extensive public health literature exists on "quality adjusted life years" (QALY). This approach provides a health state scale for quality of life based on expert medical opinions and/or survey research. It involves determining, for example, that a year with a particular condition is equivalent to a specific percentage of a full year in good health. This approach is designed for use in assessing the cost-effectiveness of alternative medical treatments, and often considers levels of activity rather than the values individuals place on changes in health status.

3.3.2 Valuing Morbidity Risk Reductions

Many regulations establishing MCLs will reduce the risks of incurring nonfatal cancers or other human health effects, including both acute (short-term) and chronic (long-term) illnesses and other effects. One method sometimes used for valuing morbidity risk reductions is the cost of illness (COI) method. However, as discussed earlier, this method has several limitations. Cost-of-illness studies often include medical expenses and lost work time, but may exclude lost leisure time or unpaid work time (e.g., for those who work in the home). Willingness to pay to avoid pain and suffering and reduce future risks are also not addressed by cost-of-illness estimates. As a result, cost-of-illness estimates are usually thought to understate willingness to pay, which is the theoretically correct measure of value and captures the effects not addressed by the cost-of-illness method.[58]

If available, analysts prefer to rely on estimates of willingness to pay rather than cost of illness estimates. However, analysts may at times wish to present both cost-of-illness and total willingness to pay estimates because of limitations in the available literature. Willingness to pay studies are available for only a few types of health risks and in some cases may have methodological problems (such as reliance on surveys using very small samples). Whether benefit transfer techniques (discussed in Chapter 4) can be used to address the limitations in the willingness to pay literature will depend on the effect of concern. Cost-of-illness studies provide estimates of avoided costs that generally can be interpreted as a lower bound on willingness to pay; the willingness to pay estimates may be less certain (depending on study quality and applicability) but more consistent with the theoretically correct definition of value.

Available research suggests that willingness to pay may be two to 79 times higher than cost-of-illness; this multiplier varies significantly for different illnesses.[59] For example, a study of the health effects of ozone shows that the ratio of willingness to

[58] A more detailed discussion of estimating morbidity values and benefits transfer is available in EPA's *Guidelines for Preparing Economic Analyses*.

[59] U.S. Environmental Protection Agency, *Handbook for Noncancer Health Effects Valuation (Draft)*, prepared by Industrial Economics, Incorporated, September 1999.

pay to cost-of-illness estimates may range from a factor of about two to four, while a study of minor health effects shows ratios as high as 79.[60]

Because of the variety of nonfatal health effects that may be addressed and the variation in the availability of suitable studies, whether and how to address potential biases and sources of uncertainty will depend on the characteristics of the particular analysis. At a minimum, analysts usually discuss qualitatively any significant differences between the effects of the regulations and the effects addressed by the valuation studies used. Where significant differences exist and quantitative adjustments or sensitivity analysis is possible, the effects of the differences may be quantified. EPA's *Handbook for Noncancer Health Effects Valuation* provides more information on these topics, along with several valuation case studies. An example of morbidity valuation is also provided in Chapter 5 of this document.

3.3.3 Valuing Other Benefits

In addition to effects on morbidity or mortality, drinking water regulations may affect the aesthetic qualities of public water supplies (taste, odor, color) or the damages they cause to materials (corrosion, soiling, build-up, impurities). The typical approach to assessing these types of effects generally involves using avoided cost methods (described above), which often are interpreted as providing a lower bound estimate of willingness to pay to avoid these effects. The actual approach will depend on the particular effect of concern, and will usually include comparing costs in the absence of the rule to the costs assuming alternative MCLs or treatment requirements are established. In some cases, studies of individual willingness to pay for these benefits (e.g., using contingent valuation) may also be available.

Some regulations establishing MCLs will provide benefits other than those specifically addressed in this document. For example, a regulation establishing an MCL or treatment requirements may improve consumer confidence in water quality, affect the health of livestock or pets, or enhance crop production. Alternatively, source water protection measures may lead to ecological benefits. These benefits are usually explored in the context of the individual rulemaking. In some cases, they may be too small to warrant quantitative assessment, and may be discussed qualitatively when presenting the results of the analysis. To quantify these types of impacts, analysts generally apply the same concepts and types of methods as discussed above, tailored to the effects of concern for the particular rulemaking.

[60] Dickie, Mark and Shelby Gerking, "Willingness to Pay for Ozone Control: Inferences from the Demand for Medical Care," *Journal of Environmental Economics and Management,* Vol. 21, 1991, pp. 1 - 16; Berger, M.C., et al., (1987).

CONDUCTING BENEFIT TRANSFERS CHAPTER 4

EPA analysts often use the benefit transfer technique to value the benefits of drinking water and other regulations. This technique involves using estimates from existing research (based on the methods described in Chapter 3) to value the benefits of the regulatory options under consideration.[61] Existing studies usually assess effects that differ in some respects from the effects of a particular regulation. Analysts thus review the applicability, as well as the quality, of the available studies to determine whether and how to apply them to a specific regulatory scenario. EPA analysts frequently use benefit transfer techniques when estimating the value of effects on human health and the environment, and may also apply this approach when assessing effects on aesthetic properties or material damages.[62]

Benefit transfer is considered a "secondary" methodology because it does not involve collecting primary valuation data. Rather, benefit transfer is a process for reviewing and adjusting existing data to arrive at valuation estimates for the subject under consideration. The study that is the source of existing data is typically called the "study case" and the subject under consideration is called the "policy case." The main advantage of benefit transfer is that the process is less expensive and time consuming than primary valuation techniques. Thus, benefit transfer is useful when limited time and resources preclude conducting primary research to inform policy decisions. It can also be used as part of a preliminary or screening analysis to determine whether additional primary research is warranted and to inform the early phases of the regulatory development process.

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[61] For general information on benefit transfer techniques, see: U.S. Environmental Protection Agency, *Guidelines for Preparing Economic Analyses,* EPA 240-R-00-003, September 2000. *Water Resources Research*, Vol. 28, No. 3, 1992 (an entire issue devoted to benefit transfer); and Desvousges, William H., et al., *Environmental Policy Analysis with Limited Information: Principles and Applications of the Transfer Method,* Edward Elgar Publishing: Northampton, Massachusetts, 1998.

[62] The use of benefit transfer for policies affecting human health is discussed in: U.S. Environmental Protection Agency, *Handbook for Noncancer Health Effects Valuation (draft)*, prepared by Industrial Economics, Incorporated, September 1999. Additional information will be available in EPA's forthcoming *Children's Health Valuation Handbook.* The use of these techniques for natural resource damage assessment is described in: Industrial Economics, Incorporated, *Economic Analysis for Hydropower Project Relicensing: Guidance and Alternative Methods*, prepared for U.S. Fish and Wildlife Service, October 1998.

The overall quality of a benefit transfer relies heavily on the good judgement of the analyst; this chapter describes "best practices" for this type of analysis. Benefit transfer is likely to yield estimates that are less accurate than those that would result from a carefully designed and implemented primary valuation study that directly addresses the effects of concern. Hence the analyst generally presents the implications of the assumptions and uncertainties in the transfer along with the analytic results, so that policymakers can take these implications into account when making regulatory decisions.

This chapter first describes the steps for implementing benefit transfers. Next, it provides a worksheet that analysts can use when assessing the quality, applicability, and transferability of existing studies. Finally, the chapter concludes with a fictional case study that illustrates the benefit transfer technique.

4.1 Implementation Steps

Benefit transfer consists of five steps:

- **Step 1: Describe the Policy Case.** Describe in detail the health or other effects relevant to the proposed regulation, the impacts of these effects, and the demographic characteristics of the affected population.

- **Step 2: Identify Existing Relevant Studies.** Search the economics valuation literature for studies that address similar types of effects.

- **Step 3: Review Existing Studies for Quality and Applicability.** Assess the quality of the identified studies by determining whether they follow generally accepted best practices for the methods used. Assess applicability in terms of: (1) the similarity of the effects; (2) the similarity of the populations experiencing the effects; and (3) the ability to adjust for differences between the study scenario and the policy scenario.

- **Step 4: Transfer the Benefit Estimates.** Conduct the transfer, making any necessary adjustments to existing estimates and applying them to the policy scenario. The transfer may be based on the results of a single study or of several studies.

- **Step 5: Address Uncertainty.** Address uncertainties in the estimates, for example by conducting sensitivity or other types of analysis as appropriate.[63]

Each of these steps is discussed in more detail in the following sections.

4.1.1 Step 1: Describe the Policy Case

To conduct a benefit transfer, the analyst first constructs a detailed description of the contaminant and each effect of concern; i.e., each particular type of health or other effect likely to be reduced by the regulatory options. As discussed in Chapter 1 of this document, regulations establishing Maximum Contaminant Levels (MCLs) or treatment techniques for drinking water generally provide human health benefits, reducing mortality and morbidity from various illnesses. EPA generally uses benefit transfer to value fatal risks, combining the results of several wage-risk and contingent valuation studies as discussed previously in Chapter 3. For non-fatal health effects, estimates of willingness to pay to avoid related risks are available for relatively few effects of concern. Hence, analysts often transfer values from a study of one health effect (the study case) to determine the value of a similar health effect resulting from a particular regulation (the policy case).[64]

Drinking water regulations also may decrease ecological risks (e.g., if they encourage increased source water protection), reduce materials damages (e.g., corrosion of piping and equipment), and provide aesthetic benefits (e.g., improved clarity, taste or odor of drinking water). Benefits transfer may also be useful in assessing some of these other types of effects.

Health Effects

Policy analysts generally rely on health scientists, engineers, and other experts to provide information on the effects of the contaminant. The role of the analyst is to ensure that he or she develops a full understanding of each effect to be assessed, including any uncertainties in its description. This detailed description includes:

- The *physical symptoms* associated with the health effect. For example, for kidney disease, the analyst would describe in detail conditions such as

[63] The economics profession sometimes uses the term "uncertainty" to refer to situations where probabilities are unknowable and "risk" where probabilities are known. In this document, we use the more general definition of uncertainty as "lack of knowledge."

[64] These transferred estimates of willingness to pay may be presented along with cost-of-illness estimates. Cost-of-illness values are often available for the effect of concern and can be interpreted as providing a likely lower bound estimate of willingness to pay, as discussed in Chapter 3 of this document.

impaired mobility, muscle cramps, hypertension and infections, as well as associated lifestyle changes and emotional stresses. Emotional stresses could include effects such as depression or anxiety related to symptoms, prognosis, or other aspects of the illness. The severity of the effects and the extent to which the symptoms curtail normal activities are also considered, as well as information on the fatality rates.

- The *timing and duration* of the effect. An effect may occur immediately upon exposure, or there may be a significant delay between exposure and manifestation of a health effect (i.e., latency). Also there may be a lag (cessation lag) between the cessation or reduction of exposure and a reduction of risk. The health effect may be a short-lived (acute) or a long-term (chronic) condition.

- The *population affected*. Exposure to a contaminant may be more or less likely to lead to adverse effects depending on factors such as age and current health status. The description of the population most likely to be affected by the disease includes the factors that lead to heightened vulnerability such as lifestyle issues (e.g., smoking) or pre-existing conditions (e.g., depressed immune system). It also addresses factors that may affect willingness to pay, such as demographic or socio-economic characteristics including age, sex, geographic location, income level, or race. Analysts also describe the extent to which the health effect is likely to be prevalent, that is, likely to occur in most persons exposed to the contaminant or only in a fraction of the exposed population.

This information is accompanied by a description of the key uncertainties in the health science data related to each of these factors. Uncertainties could, for example, include a lack of knowledge about the physiology of the effect, the emotional stresses of the effect, the risk factors that make individuals or populations susceptible to the effect, or the prevalence of the effect. In addition, uncertainties related to the causative link between a drinking water contaminant and a particular health effect may be significant. It is not unusual to find that uncertainties in the risk assessment far outweigh uncertainties in other aspects of the benefit-cost analysis.

Ecological Effects

Benefit transfer is often used to value ecological effects, for which the literature includes numerous willingness to pay studies. Such a transfer may involve the application of estimates from a studied site to other sites experiencing similar effects, or the combination of values from several studies to estimate the value of such effects in other cases. When combining values for different aspects of an effect from several studies, the analyst is careful to avoid double counting. For example, the value of wildlife viewing may be related to the value of surrounding properties, and

analysts attempt to address the overlap (in quantitative or qualitative terms) if both types of benefits are considered.

The starting point for transferring these types of values is to describe the ecological effects addressed by regulatory standards. The description details the natural resources affected, their current (baseline) condition, and the characteristics and severity of the effects reduced. In addition, the services provided by the resource (such as recreational activities, commercial use, or wildlife viewing) are discussed. The description considers the timing and duration of the effects as well as the potential for natural recovery. The analyst also addresses the characteristics of the human population (for example, recreational anglers, local residents) who may benefit from the ecological improvement. This description guides the subsequent economic analysis, and addresses the characteristics of the ecological effect likely to affect willingness to pay.

Materials and Aesthetic Qualities

In cases where a regulation reduces damages to materials or improves the aesthetic qualities of drinking water, benefit transfer may also be used. For example, a few analyses of averting behavior or avoided costs are available in the literature that could be used to value certain of these types of effects. In such cases, the analyst again begins the transfer process by describing the effect of concern and baseline conditions in detail, including the characteristics and timing of the reduced effect and the population or water systems affected. In some cases, the regulations may alleviate, but not eliminate, adverse impacts, and this concern will need to be taken into account. For example, regulation of a particular contaminant may reduce or delay, but not eliminate, pipe corrosion, or may only partially mitigate taste or odor problems.

4.1.2 Step 2: Identify Existing Relevant Studies

Once the analyst completes the description of the policy case, the next step is to conduct a comprehensive literature search to identify existing valuation literature that focuses on similar effects. The analyst explores journal articles, research reports, dissertations, and published texts identified through a review of databases of environmental, economic, and medical literature, as relevant. There are several bibliographic databases available through Internet services such as Dialog, Lexis/Nexis, and Dow Jones; the databases most pertinent to benefits valuation include: Enviroline, Pollution Abstracts, EconLit (Economic Literature Index), Social SciSearch, SciSearch, Medline, ABI/Inform, IAC Business A.R.T.S, Water Resources Abstracts, and WATERNET.

In addition, for several types of effects, bibliographies of relevant studies are available. For fatal human health effects, the list of studies currently referenced by EPA is provided in Chapter 3 of this document. For nonfatal human health effects, a list of available studies is provided in EPA's *Cost of Illness Handbook* and in

EPA's *Handbook for Non-Cancer Health Effects Valuation.* For ecological effects, analysts may wish to review EPA's Environmental Benefits Database. Studies previously used by various EPA offices are identified in EPA's Environmental Economics Report Inventory.[65] Regardless of the bibliographic source used, analysts typically read the studies themselves, rather than relying on summaries in these sources, because the characteristics that may significantly affect the benefit transfer are not always easy to capture in summary form.

Finally, additional valuation information may be available in unpublished studies or in studies currently underway. To identify these studies, the analyst may contact researchers frequently cited in the published literature, who are likely to be involved in or aware of other sources of valuation estimates. Staff from agencies who frequently support valuation research (such as EPA's National Center for Environmental Economics, the Fish and Wildlife Service, and the National Science Foundation) can provide information on relevant studies. Unpublished studies (which generally have been subject to less review than the published literature) are carefully reviewed to ensure that they are of sufficient quality to support defensible benefits estimates.

4.1.3 Step 3: Review Existing Studies for Quality and Applicability

Assessing the quality of existing research and its applicability to the policy scenario is the third step in benefit transfer. The guidelines in this section can serve as a road map for the analyst to follow in evaluating studies. In addition to reviewing the quality and applicability of existing studies, the analyst considers transferability issues, which are intertwined with the concept of applicability but refer to the steps followed in conducting the transfer. To avoid repetition, these "transferability" concerns are addressed under Step 4 below. A worksheet later in this chapter summarizes the guidelines for quality, applicability, and transferability.

It is not possible to develop absolute standards for assessing a study's quality and applicability. Rather, the analyst considers all of the factors discussed below, and balances the limitations of each study against the value of using it to provide information on the benefits of concern. For those studies ultimately used in the transfer, the analyst discusses the findings of the quality and applicability review when presenting the results. As indicated under Step 5, this discussion describes the extent to which the transfer is likely to overestimate or underestimate the value of the benefits derived from the regulation, given the uncertainties in the original study and in the transfer process.

[65] Available on EPA's website at http://www.epa.gov/economics.

Quality Issues

Quality refers to the appropriateness of the research methodology used, the care with which this methodology was implemented, and the accuracy and reliability of the resulting estimates. Considering these quality issues allows the analyst to identify sources of uncertainty related to the methods used to estimate values, and to weigh these sources of uncertainty in determining whether and how to use each study in a benefit transfer. Assessing quality requires a high degree of judgement in order to separate sound, scientifically valid studies from studies of lesser merit. The importance of particular criteria for assessing quality will vary depending on the type of study and the type of effect. However, there are some general criteria that analysts can apply to most research, which are discussed below.[66]

Opinion of the Professional Community: To a large extent, analysts rely on the opinions of the professional community in assessing the quality of a study. Analysts consider whether the research has been published in a peer-reviewed journal or has undergone other forms of peer review.[67] Analysts may also discuss the study with the original authors, leading researchers in the field, or the study's sponsor to learn more about its strengths and weaknesses and about whether these experts believe that the study conforms with "best practices" as defined by recent research.

Note that some studies that are well-respected in the field (because they explore new issues or apply innovative techniques) may not lead to reliable results in a benefit transfer; for example, if they are pilot studies that use a very small sample. In addition, there will not always be consensus on the merits of each study; analysts will need to take any areas of disagreement into consideration as part of their review and when conducting any subsequent transfer.

In some cases, the age of a study may affect its usefulness for benefit transfer due to concerns about changes in willingness to pay over time. However, use of older, well reviewed studies may be preferable to use of newer studies that have been subject to less scrutiny in some cases. Because of the need to balance these types of concerns, it is not possible to develop a universally applicable threshold for the age of studies. Rather, analysts will need to address this issue along with the other concerns discussed in this chapter.

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[66] For more specific information on assessing the quality of studies using particular valuation methods, see the references noted in the beginning of this chapter as well as the discussion in Chapter 3 of this document.

[67] For peer review standards, see: U.S. Environmental Protection Agency, *Peer Review Handbook*, January 1998.

Methods and Data Sources: When considering the quality of the methods used for the study, the analyst considers the appropriateness of the approach for valuing the effect of concern, as well as the extent to which the method is likely to yield accurate estimates of willingness to pay. For example, cost of illness methods may be used to value changes in health risks, but may not represent (or may understate) an individual's actual willingness to pay to avoid these risks. The extent to which different methods will yield conceptually correct measures of the value of benefits is discussed in Chapter 3 of this document.

When reviewing data sources, the analyst considers the accuracy, reliability, and completeness of the underlying records or information. For example, researchers using the wage-risk method have employed a multitude of data sources for information on compensation and job-related risks, and these data sources vary in terms of accuracy and completeness.[68] In addition, data sources that were developed many years ago may no longer reflect values held today. In the case of survey techniques, the appropriateness of the population sampled is considered in terms of location, age, and other characteristics that may influence willingness to pay. Literature review or survey articles provide professional opinions on these data quality issues and can assist analysts in assessing these concerns.

Sampling and Survey Administration: Many studies take a statistical sample of either data records or individuals. In these cases, analysts generally prefer studies that use probability sampling and sample sizes that are large enough to allow extrapolation to the underlying population with a reasonable level of confidence. Probability sampling allows the researcher to compute the chance that any particular individual within the population would be included in the sample and to develop appropriate weighting factors for extrapolating from the sample to the total population. While statistical measures of sampling error should be used to provide a more rigorous indicator of appropriate sample size, a rough guideline is that samples of less than 200 observations may result in unreliable estimates.[69]

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[68] See Viscusi, Kip, *Fatal Tradeoffs: Public and Private Responsibilities for Risk* (New York: Oxford Press, 1992) for an assessment of various data sources for wage-risk analyses.

[69] For contingent valuation surveys, Mitchell and Carson suggest that at least 600 useable responses are needed; the Water Resources Council recommends a sample size of 200. See: Mitchell, Robert Cameron and Richard D Carson, *Using Surveys to Value Public Goods: The Contingent Valuation Method,* Washington, DC: Resources for the Future, 1989; and U.S. Department of the Interior, Water Resources Council, *Economic and Environmental Principles and Guidelines for Water and Related Land Resources Implementation Studies,*1983.

Analysts consider the response rate (for surveys) or the extent to which complete records are available (for other types of studies). In the case of surveys, the response rate will vary depending on the method of survey administration: well-designed studies using personal interviews may achieve an 80 to 90 percent response rate, phone interviews may achieve an 85 percent response rate, and mail surveys may achieve a 60 to 75 response rate.[70] However, many surveys achieve lower response rates, and such rates will need to be considered along with other factors affecting the quality and applicability of a study when determining whether to use it for benefit transfer.

"Best practices" for survey development and administration, when contingent valuation or other survey methods are used, are discussed in the references provided in Chapter 3 of this document. In particular, extensive pre-testing of the survey instrument is generally needed to ensure that it is well understood and believable. Analysts interested in applying the results may wish to examine the survey instrument themselves to ensure that it is asking appropriate questions for valuation of the effect of interest and for control of confounding factors.

Data Analysis: Once the data are collected, researchers often analyze them using econometric or other statistical techniques.[71] Key concerns may include whether the theoretically correct variables are included in the analysis, the measures (or specification) of each variable, and the functional form of the equations or calculations employed.

If the original data set is available from the researchers, additional analyses may be conducted as part of the benefit transfer process, both to better understand the data and to adjust the estimates (or equations) for the transfer. For example, if the original study includes data on the age of respondents but does not explicitly assess the effects of this variable on the resulting values, the analyst conducting the transfer may explore these effects.

Evidence of Accuracy and Reliability: Finally, the analyst looks for evidence of the accuracy and reliability of the estimates. Accuracy refers to how precise, or correct, the findings are; for example, how well the sample results mirror the value in the underlying population. Reliability refers to the extent to which the findings can be replicated; for example, whether applying the survey to a second sample would result in the same or similar estimates. At the most basic level, accuracy and reliability may be assessed based on information from the researchers on how they designed the study, checked the data, calculations, and results, and addressed key

[70] Dillman, Don A., *Mail and Telephone Surveys: The Total Design Method,* New York: John Wiley and Sons, 1978.

[71] See, for example: Greene, W.H., *Econometric Analysis, 4th Edition,* New Jersey: Prentice-Hall, 2000.

sources of uncertainty. The analyst may also consider whether the study yields estimates that are in the range found by other studies of similar effects; evidence that study findings have been replicated by other researchers is often the best test of reliability. Finally, the analyst generally assesses whether the results are consistent with general economic theory. For example, he or she may question the quality of a study that found lower values for mitigation of severe adverse effects than for mild effects.

Applicability Issues

In the context of benefit transfer, applicability refers to the extent to which the existing research (the study case) matches the policy case. Applicability therefore involves comparing the effect studied to the description developed under Step 1 above, which again requires a high degree of judgement on the part of the analyst. Three main areas of concern are the similarity of the effect, the population, and the baseline conditions.

Similarity of Effect: The similarity of the effect can be determined by an "item-by-item" comparison of the description of the policy case (developed under Step 1) to the description of the case addressed in each existing study. The analyst generally considers the divergence in physical attributes, severity, timing and duration, etc., as well as the magnitude of the differences. For example, if the contaminant in question is associated with developmental effects, and the existing research focuses on the effects of lead, the analyst would consider the extent to which the developmental problems caused by lead are similar to developmental problems caused by the contaminant.

In reviewing the similarity of the effects, analysts generally consider dimensions of risk in addition to the physical manifestation of the effect, such as the following:

- voluntary/involuntary
- ordinary/catastrophic
- delayed/immediate
- natural/man-made
- old/new
- controllable/uncontrollable
- necessary/unnecessary
- occasional/continuous
- acute/chronic

These risk dimensions may affect willingness to pay to reduce different types of risks. For example, individuals may hold different values for reducing lung cancer risk from smoking (e.g., if they perceive it as a personal lifestyle choice) than from environmental causes (e.g., if they perceive these risks as beyond their control).[72] The impact of risk characteristics on the valuation estimates are generally discussed qualitatively because the empirical data needed to adjust for these impacts have not yet been developed.

For certain effects, high quality valuation literature on similar effects may not exist, and the analyst will have to make judgments about the suitability of other valuation studies. For example, EPA recently used data on chronic bronchitis to value the benefits of avoiding non-fatal bladder cancer associated with regulating drinking water disinfectant by-products.[73] The researchers did not find any willingness to pay studies for non-fatal bladder cancers or other similar cancers. They decided to use chronic bronchitis as a proxy effect, on the grounds that chronic bronchitis and bladder cancer have certain commonalities, such as severity and long-term impacts. They compared the resulting willingness to pay values to cost of illness values for non-fatal bladder cancers as a check on the reasonableness of the estimates.

This use of proxy effects that have dissimilar manifestations to the effects of the policy case may provide useful information for decision-making (e.g., by indicating the range or potential magnitude of benefit values). However, this approach is controversial and requires careful consideration of the limitations of the analysis. Decisions regarding whether to use valuation information for dissimilar effects are made on a case-by-case basis because they will depend on the nature of the issues being addressed as well as the available valuation data. In these situations, analysts work to clearly communicate the advantages and drawbacks of using the chosen study case, and the implications of these concerns for related decision-making. For example, analysts may list and compare characteristics of the proxy and the policy effects, and discuss their expected net impact on willingness to pay, when describing the results of the analysis.

Similarity of Population: In addition to reviewing the similarity of the effects, the analyst compares the population studied to the population affected in the policy case. Populations can differ by geographic location as well as by demographic or socio-economic factors such as age, sex, income and race. The analyst generally focuses

[72] Fischoff, B. et al., "How Safe is Safe Enough? A Psychometric Study of Attitudes Towards Technological Risks and Benefits," *Policy Sciences*, Vol. 9, 1978, pp. 127-152.

[73] The Cadmus Group and Science Applications International Corporation, *RIA for the Stage 1 Disinfectants/Disinfection Byproducts Rule,* prepared for the U.S. Environmental Protection Agency, 1998.

on those dimensions that are associated with potentially significant differences in willingness to pay.[74]

In some cases, the analyst can adjust for population-specific factors by including relevant variables in a valuation function or by only using part of a data set (if possible without adversely affecting the statistical validity of the sample). In other cases, such adjustments will not be possible, and the differences between the populations introduce another layer of uncertainty into the benefit transfer process that can be discussed when presenting the results. For example, if the policy case is exploring the effects of a particular contaminant on children's health, and the study case has analyzed adult health values, the analyst considers whether there is a scientifically valid way to adjust for the difference in effects between the two populations. EPA is currently addressing the many complex issues that arise in this case, and is developing guidance focused particularly on valuing children's health effects.

Similarity of Baseline: The third major area to consider is whether baseline health status, or in the case of an ecological effect, environmental quality, is similar between the policy case and the study case. Willingness to pay to avoid health effects may vary depending on whether the individuals affected are in good or poor health, or have a particularly high risk of being affected compared to others exposed.[75] This difference in baseline health status may be particularly important for sensitive populations (such as those with suppressed immune systems, the elderly, or children) who are more vulnerable to the effects of drinking water contaminants. Individuals are also likely to hold different values for ecological effects resulting from a marginal decrease in contamination in routinely polluted waters than for the same decrease in contamination in more pristine areas.

4.1.4 Step 4: Transfer the Benefit Estimates

The fourth step of the benefit transfer process is to derive values from the study case and apply them to the policy case. The researcher can adjust and transfer values in a number of different ways, but the techniques generally fall into three categories: (1) applying a point estimate (i.e., a single value); (2) using a valuation function (an equation that relates values to characteristics of the effect and/or the population affected); or, (3) using meta-analysis or Bayesian approaches (which combine the results of several studies). These approaches are listed in order of increasing complexity, and (all other things being equal), the more complex approaches will often lead to better estimates. However, the available literature may not be sufficient

[74] Addressing some of these factors may be controversial. For example, if willingness to pay appears to vary by income or race, consideration of this variation may raise environmental justice concerns as discussed in previous chapters of this document.

[75] As noted in the discussion of fatal risk valuation in Chapter 3, the consideration of altruistic values is somewhat controversial and should be approached with caution.

to support use of the more sophisticated approaches, and analysts generally assess these transferability issues when reviewing the available studies.

Point Estimate. A point estimate refers to the process of taking a single estimate for a particular value (often the mean or median) and using it to directly approximate the value in the policy case. Reasonable high and low values (e.g., the 10th and 90th percentile of a distribution) may also be used for bounding or sensitivity analysis. In the most simple case, the analyst will take the mean or median value from the study case and multiply it by the number of statistical cases avoided (for health effects) or the population affected (for ecological effects) by the regulations.[76,77] This type of simple transfer may be useful particularly for initial screening analysis, but does not account for any dissimilarities in the nature of the effects, the population characteristics, or the baseline status. Hence its use is generally limited to cases where the underlying research will not permit a more sophisticated approach. In such cases, the differences between the policy case and the study case are usually discussed quantitatively when presenting the results.

A more sophisticated approach involves tailoring point estimates to the particulars of the policy case through simple adjustments; for example, adjusting for changes in income over time. This type of tailoring improves the transferability of the estimates, and may be the only technique an analyst can employ when the valuation function for the study case is not available.

Benefit Function. The benefit function approach is possible when a valuation function is provided in the study case or can be calculated from the data set. For example, the study may include age and income in an econometric equation that predicts willingness to pay. The benefit function approach utilizes the additional information provided by the function and tailors it by substituting values from the policy case into the function. In other words, data on the age and income of individuals affected by a particular regulation can replace the data from the study case to yield an appropriate value or range of values. In some cases, the valuation function provided in the original study will include information not available for the policy case, such as attitudinal variables. In this case the analyst may wish to re-estimate the equation based on the variables for which data are available if appropriate given the nature of the study.

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[76] A statistical case is calculated by multiplying the number of individuals affected by quantified risk factors. An example of this calculation is provided in the discussion of mortality risks in Chapter 3.

[77] When using benefit transfer to value ecological effects, the analyst often addresses difficult issues regarding the population assumed to value the change, referred to by economists as the "extent of market." For example, for recreational benefits, the study case may focus on households located within a set distance of the site, and the analyst conducting the transfer determines whether this assumption is appropriate for the policy case sites, and if not, how to adjust appropriately.

Because the benefits function approach is better tailored to the policy case than the point estimate approach, it can provide an improved estimate of the value of the benefits. However, one potential problem with this approach is its reliance on the equality of coefficients between the study and policy cases. This approach will still involve additional uncertainty if the two cases differ in ways that are not addressed by the valuation function (e.g., if baseline health conditions differ but are not included in the function resulting from the original case).

Meta-Analysis or Bayesian Approaches. The most complex transfers use statistical methods such as meta-analysis or Bayesian approaches, which combine estimates from several studies of similar effects.[78] Meta-analysis can be used to integrate the results when many relevant studies are available; the Bayesian approach includes data on the policy case as well as from existing studies.[79] These approaches have been used more frequently for ecological effects than for health effects because of the availability of larger numbers of applicable studies. Because these approaches draw on more data sources than a single study and use statistical techniques to explore the variation in the results, the resulting estimates may be more accurate and reliable than point estimates or valuation functions. However, meta-analysis and Bayesian approaches require a high level of technical expertise and can be very time consuming to implement. These approaches are also data intensive and may not be feasible for many effects due to the lack of relevant studies. Thus, analysts generally apply these techniques with caution and involve relevant experts in developing and reviewing the analysis.

With all of these transfer techniques, the analyst need to aggregate individual estimates over the population experiencing the effect. The aggregation process may be designed to take into consideration such issues as bias and distributional effects. For example, if separate values are available for a sensitive sub-population and for the remainder of the general population (minus the sensitive sub-population), the total value of the benefits for each group can be calculated separately and then added together to estimate benefits for the entire population.

4.1.5 Step 5: Address Uncertainty

Uncertainty permeates all the steps of the transfer process, from selecting appropriate studies and manipulating data to establishing a range of values. Each of the existing studies used in the transfer will itself contain uncertainties that result both from the

[78] For more information see Desvousges (1998), and Atkinson et al., "Bayesian Exchangeability, Benefit Transfer, and Research Efficiency," *Water Resources Research* 28(3) 715 - 722, March 1992.

[79] For an example of meta-analysis, see Boyle, K.J., G.L. Poe, and J.C. Bergstrom. "What do We Know about Groundwater Values? Preliminary Implications from a Meta-Analysis of Contingent-Valuation Studies," *American Journal of Agricultural Economics,* Vol. 76, pp. 1055-1061, December 1994.

data and analytic approach used as well as from difficulties related to thoroughly understanding the preferences of the individuals studied. However, the presence of uncertainty does not imply that the resulting values are random or indeterminable. By using techniques such as sensitivity analysis or more complex models such as Monte Carlo simulations, the analyst can, to a certain degree, quantify the effects of uncertainties in the estimates used in the benefit transfer.[80] As noted earlier, those uncertainties that cannot be quantified are generally discussed in qualitative terms when presenting the findings of the benefit transfer. In this discussion, analysts describe the relative importance of each source of uncertainty as well as the direction of the possible bias, if known.

4.2 Benefit Transfer Worksheet

The worksheet presented on the next pages summarizes the key questions discussed in the previous sections on quality, applicability, and transferability. Because it is designed as a general tool, the worksheet does not provide a comprehensive framework appropriate for every benefit transfer situation. Rather, it categorizes the most common issues in a format to facilitate further analysis.

[80] For more information on uncertainty analysis, see: Morgan, Granger M., and Max Henrion, *Uncertainty: A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis,* Cambridge University Press: New York, 1990.

Exhibit 4-1
Sample Worksheet For Review of Valuation Studies

GUIDELINE	QUESTIONS TO ASK	COMMENTS
Quality Issues		
Opinion of the Professional Community	Has the study been published in a peer-reviewed journal or been subject to other types of peer review? What are the strengths and weaknesses of the study according to experts in the field?	
Methods and Data Sources	Is the methodology used appropriate for the subject of the study? Has the methodology been widely used in similar studies? What are the strengths/weaknesses of the methodology? Are the study's data sources appropriate for the subject? What are the strengths/weaknesses of the data sources used?	
Sampling and Survey Administration	Does the study use appropriate probability sampling techniques? Is the sample size large enough? Is the response rate reasonably high? If a survey was conducted, was it adequately pre-tested? Was the survey administration technique (mail, phone, or in- person) employed following standard "best practices"?	
Data Analysis	Are the appropriate variables correctly specified and included in the analysis ? Is the appropriate functional form used for the calculations? Is the data set available for further analysis?	

Exhibit 4-1
Sample Worksheet For Review of Valuation Studies

Evidence of Accuracy and Reliability	Is the study well documented? How were data, calculations, and results validated by the researcher? Are the effects of key uncertainties thoroughly described? Was a quantitative uncertainty analysis performed? When compared to other studies, are the findings reasonable? Are the findings consistent with economic theory?	
Applicability Issues		
Similarity of Effect	How does the effect analyzed in the study case compare to the effect of the policy case? What is the magnitude of the difference? Are the timing and duration of the effects similar?	
Population Affected	How does the population addressed in the study case compare to the population addressed by the policy case (e.g., in terms of age, geographic location, income, etc.)?	
Baseline Conditions	How similar is the policy case baseline (e.g., health status or environmental quality) to the study case conditions? Are there any characteristics of the individuals, ecological systems, or water systems in the policy case that render them more or less susceptible to the effect than the subject of the study case?	
Transferability Issues		
Opportunities for Adjustment	Does the data set from the original study contain information that allows for better tailoring of the study case to the policy case? Is a valuation function reported that can be transferred to the policy case? Are enough studies of similar effects available to use meta-analysis or Bayesian approaches to combine the results?	

IMPLEMENTING BENEFITS ANALYSES CHAPTER 5

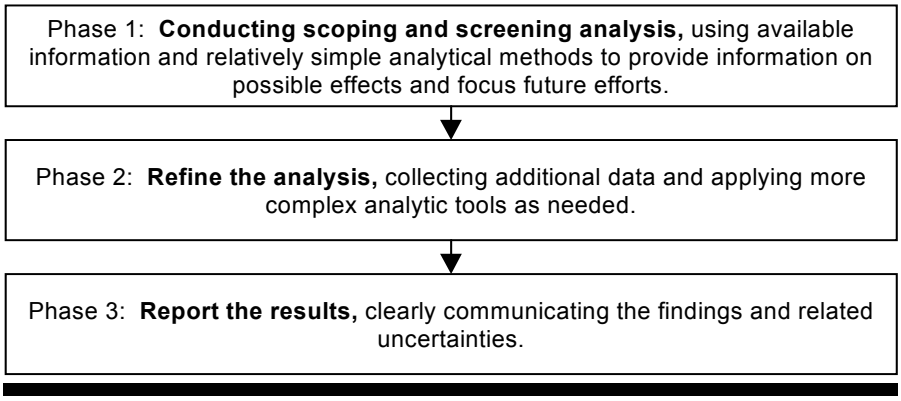
The previous chapters provide information on the requirements and methods for benefits assessment; this chapter discusses considerations related to implementing these types of analysis. It discusses issues related to sequencing the analysis, such as using screening tools to develop preliminary benefits estimates and to focus subsequent research. It also describes the basic steps in conducting benefits analyses, including identifying potential benefits, quantifying physical effects, and determining the monetary value of the effects. It then discusses some issues that relate to both the cost and benefit analyses, such as the definition of the baseline and the selection of discount rates.

5.1 Sequencing The Analysis

The EPA regulatory development process includes several phases of analysis and decision-making that often occur over several months or years depending on the complexity of the rulemaking. Both the internal EPA work group and stakeholder groups involved in developing and evaluating regulatory alternatives often find information on the potential benefits (and costs) of the options under consideration useful in their deliberations throughout this process.

To meet this need for early information on the benefits of different regulatory approaches as well as to focus resources on key issues, analysts generally find it helpful to adopt a sequential approach to data collection and analysis. Under this approach, the analyst begins with available data and relatively simple analyses, then refines the data and analyses as needed. The approach is illustrated in Exhibit 5-1 and discussed in the following sections.

Exhibit 5-1
Phases of the Analysis



Note that while the exhibit identifies reporting the results as a distinct final step for simplicity, the principles discussed below also apply to interim briefings or preliminary reports on earlier phases of the benefits analysis.

A critical advantage of sequential analysis is that it allows analysts and decision makers to apply an informal "value of information" approach to the performance of the benefits assessment, considering whether the time and expense of additional research and data collection are warranted at each stage in the analysis. In some cases, screening analysis alone may prove sufficient to support a regulatory decision. For example, the results of a screening analysis of benefits may be clear, persuasive, and certain enough to justify establishing the MCL at the lowest feasible level without additional analysis. In other cases, the conclusions of the analysis may not clearly support the choice between the lowest feasible level and less stringent alternatives. Analysts can then use the results of a screening study to focus subsequent efforts on those areas where more detailed investigation is most needed. In each stage, analysts work to clearly document the methods used in the analysis, its findings, and related uncertainties.

5.1.1 Conduct Scoping and Screening Analysis

The first step in conducting a benefits assessment is to collect and evaluate readily available information on the nature and extent of potential benefits associated with the proposed regulation. Because this information is typically used to define the scope of the overall assessment, this step is often referred to as "scoping analysis." This stage includes both review of the available literature and informal discussions with other EPA staff and management, outside experts, and stakeholders.

Once the available information has been collected and reviewed, the next step may involve performing a "screening" analysis to develop initial benefits estimates and identify areas where more investigation is needed. Screening analyses will often involve the use of benefit transfer techniques to value selected effects, as discussed in the Chapter 4. The results of these analyses may be used to provide decision-makers with preliminary information on the potential benefits of alternative MCLs or treatment requirements, as well as to define more clearly those areas where additional research is most needed to support decision-making. For example, analysts may find that uncertainties in the risk estimates are substantial and far outweigh uncertainties in the economic valuation data. Additional research could then be focused on refining the risk assessment rather than the valuation estimates.

5.1.2 Collect and Analyze Additional Data as Needed

Following completion of the screening analysis, the next step in the benefits assessment is to collect and analyze additional data that will reduce uncertainties or gaps in the preliminary benefits estimates. The exact steps undertaken will depend

on the nature and importance of the issues to be addressed as well as the time and resources available for the analysis. Options for collecting additional data may include conducting a census or survey, developing case studies, or interviewing pertinent experts.[81] New supporting analysis may also be developed; for example, analysts may commission more primary research on the value of key benefits or use more formal techniques (such as meta-analysis, which uses statistical methods to combine the results of similar studies) in applying the results of available studies. In addition, analysts may attempt to better define areas of uncertainty, either by conducting additional bounding or sensitivity analysis or by applying probabilistic methods (such as Monte Carlo modeling).[82]

Decisions about when to stop the analysis (i.e., when do we have enough information on benefits, with an appropriate level of certainty?) involve interaction between the EPA staff responsible for the cost and benefits analyses and senior managers. The costs and time required for additional analysis is balanced against the likely value of new information for decision-making. Analysts may consider the probability that the new information will significantly reduce uncertainty or improve the ability of decision-makers to select among alternative MCLs or treatment requirements.

5.1.3 Communicate the Results

As the benefits assessment proceeds through the phases described above, analysts are likely to be asked periodically to brief others involved in the regulatory development process (such as Agency management, work group members, and stakeholders) on their findings. In many cases, these audiences may be unfamiliar with the theory and methods of benefits analysis and with the advantages and limitations of various approaches. Communicating effectively to all of these groups involves tailoring the presentation to each audience's level of understanding and interests. An audience composed of EPA economists, for example, is likely to have different interests (as well as a differing level of familiarity with the topics) than would a citizens' group concerned with children's health risks.

[81] All data collection must be conducted in compliance with the Paperwork Reduction Act, under which OMB approval is needed for efforts that pose the same or similar questions to more than nine respondents.

[82] For more information on applying this framework to policy analysis, see: Morgan, Granger M., and Max Henrion, *Uncertainty: A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis,* Cambridge University Press: New York. 1990. For specific guidance on Monte Carlo analysis, see: U.S. Environmental Protection Agency, *Guiding Principles for Monte Carlo Analysis,* March 1997.

Regardless of the background or interests of the audience, analysts generally focus on presenting the results of the benefits assessment in plain English, using simple charts and graphics as appropriate to help communicate key findings. In addition, the presentation may note the uncertainties in the analysis and their implications for decision-making. For example, analysts may both point out the limitations ("the valuation estimates do not include several minor health effects") and to note the implications for decision-making ("these minor impacts may mean that total benefits exceed total costs by a greater amount than indicated by the quantified values").

Text discussions of these concerns are usually accompanied by tables and graphics that summarize key findings. Exhibit 5-2 provides an example of a table that presents analytic results, key uncertainties, and nonquantified effects. This table may be expanded to include costs for comparative purposes, or costs may be presented in a similar, but separate, format.

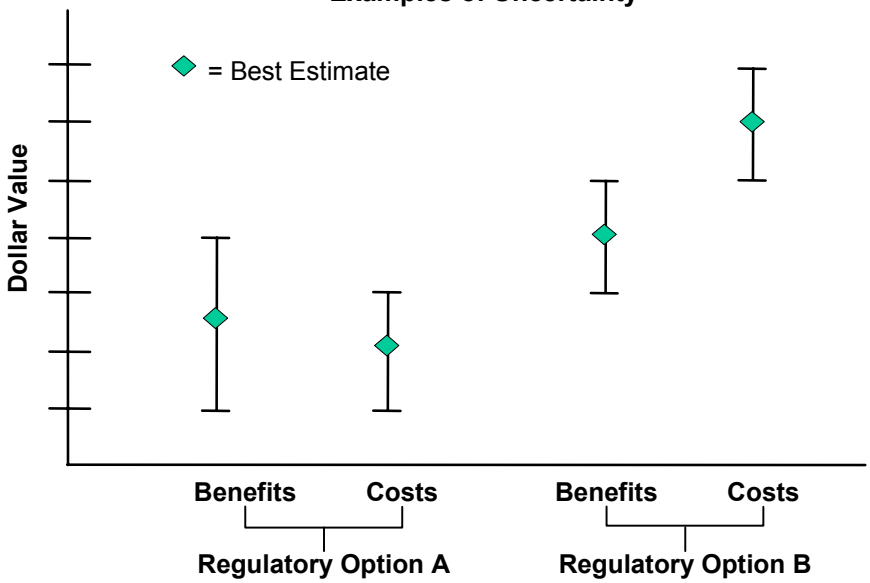
Exhibit 5-2
Sample Summary Table

Regulatory Option	Type of Benefit	Best Estimate	High End Estimate	Low End Estimate
MCL = Xμ/L	Stomach Cancer	$X million	$XX million	$0.X million
	Kidney Disease	$X million	$XX million	$0.X million
	Developmental Effects	Not quantified. Limited available research suggests possible association with low birth weight.		
MCL = Yμ/L	Stomach Cancer	$Y million	$YY million	$0.Y million
	Kidney Disease	$Y million	$YY million	$0.Y million
	Developmental Effects	Not quantified. Limited available research suggests possible association with low birth weight.		

This type of table may be used to report the absolute value of the benefits for the baseline and each regulatory option, and/or the incremental change between options of increasing stringency.

An example of a graphic presentation of the uncertainty in the estimates is presented in Exhibit 5-3.

Exhibit 5-3
Examples of Uncertainty



Note: Nonmonetized costs and benefits should be identified in the notes on the exhibit.

The final results of the analysis are documented as part of the regulatory impact analysis (now generally referred to as the "economic analysis") prepared for the proposed and final regulations and placed in the public docket. This report is written in plain English for a general audience and includes simple tables and graphs that clearly communicate the approach, the results (including nonquantified effects), related uncertainties, and implications. All sources are referenced, and appendices are often used to report detailed analytic results as necessary. In general, the results of the risk assessment are presented separately from the economic valuation of benefits, due both to the importance of the risk data and the complexity of the issues that must be addressed.[83]

5.2 Steps in the Benefits Analysis

In each phase described above, the benefits analysis generally includes three steps: (1) identify the types of benefits; (2) quantify physical effects; and (3) estimate the monetary values of these effects. Exhibit 5-4 illustrates the relationship between the

[83] For more information regarding the presentation of the benefits valuation analysis, see U.S. Environmental Protection Agency, *Guidelines for Preparing Economic Analyses,* EPA 240-R-00-003, September 2000.

phases of the analysis described above and these three steps. We discuss these steps in greater detail below.

Exhibit 5-4

Relationship Between Phases and Steps

Phase 1: Conduct scoping and screening analysis	Step 1: Identify potential types of benefits, including the full range of possible effects.
	Step 2: Quantify physical effects, focusing on key benefits and using available information.
	Step 3: Estimate the dollar value of the effects for key benefits, based on available valuation studies.
Phase 2: Refine the analysis as needed	Step 1: Refine the understanding of potential types of benefits, extending the analysis to include additional types of benefits if relevant.
	Step 2: Refine the estimates of physical effects, collecting additional data and/or performing additional analysis to address key uncertainties.
	Step 3: Refine the estimates of the value of the effects, collecting additional data and/or performing additional analysis to address key uncertainties.
Phase 3: Communicate the results	Step 1: Discuss the process and rationale used to select benefits for analysis, including information on any benefits that were not quantified or monetized.
	Step 2: Describe the methods used to quantify physical effects and the analytic results, including information on related uncertainties.
	Step 3: Describe the methods used to estimate the dollar value of the effects and the analytic results, including information on related uncertainties.

5.2.1 Identify Potential Benefits

In Chapter 1, we introduced three main categories of benefits related to regulations establishing MCLs or treatment requirements: human health effects, aesthetic effects, and effects on materials. Regulations leading to increased source water protection may also have ecological effects. Effects on human health are assessed for all regulations establishing MCLs, and that other effects are generally assessed as relevant to the particular regulation.

The first step in the benefits analysis is to develop a list of the effects in these categories that may be mitigated by the particular regulation, based on review of the relevant literature and consultations with experts. These experts may include risk assessors as well as others knowledgeable about the physical impacts of the contaminants.

In developing this list, analysts generally consider both the types of effects associated with the contaminant and the contaminant concentrations that are necessary to cause the effect. In some cases the regulations will not be sufficient to alter the effect of concern. For example, some health effects may not occur even in the baseline because contaminant concentrations are below the threshold levels for incidence of the effect. In other cases, the difference between baseline concentrations and alternative MCLs may not be sufficient to change the incidence of the health effect. Thus, in addition to identifying the potential effects of the contaminant, this step includes assessing whether each type of effect might be mitigated by the regulatory options under consideration.

At the outset of the analysis, information on baseline concentrations and possible MCLs may be sketchy and presented as broad ranges. Hence the range of possible beneficial effects may be relatively large. For example, the initial list of benefits potentially resulting from controlling a particular contaminant may include several types of fatal and nonfatal health effects, as well as some aesthetic effects. As more information becomes available on baseline and post-regulatory contaminant concentration levels, the list may be trimmed to exclude those types of benefits not likely to accrue.

While it is useful to develop a comprehensive list of possible benefits, some of these benefits may not be subject to detailed assessment. The detailed analysis generally focuses on significant benefits, including those effects that meet one or more of the following criteria: (1) there are likely to be observable changes in the effects when comparing alternative MCLs to each other and to the baseline; (2) the effects may account for a major proportion of the total benefits of the rulemaking; and/or, (3) stakeholders or decision-makers are likely to require information on the effects, even if their magnitude is relatively small. For example, if the contaminant is linked to an illness that particularly affects children, analysts may assess the effect of the regulation on the illness even if the number of cases is relatively small, given the emphasis of SDWA and other mandates on children's health effects. Any benefit categories that are not quantified or valued are discussed qualitatively when presenting the results of the analysis.

5.2.2 Quantify Physical Effects

The next step in the analysis involves quantifying the physical effects of the regulations -- e.g., determining the effect of the regulations on the risks of incurring specific diseases or on the level of corrosion in water system piping. These estimates are generally obtained from health scientists and risk assessors in the case of health effects, and physical scientists or engineers for other types of impacts. EPA's framework for risk assessment and other references provide detailed guidance on risk

assessment; analysts generally review the available literature and consult with relevant experts as needed to determine how to quantify other types of effects.[84]

For health effects, this step results in detailed descriptions of the physical effects likely to be avoided by the regulations -- e.g., the types and severity of the illnesses. For each type of health effect, detailed data are also developed on the change in risk and the change in the number of statistical cases (including mortality rates) attributable to the regulation, the timing of the changes, and the demographics of the affected population. The uncertainty associated with these estimates is also explored.

For example, risk assessors may indicate that a specific MCL will reduce the annual, average individual risk of incurring a particular type of kidney disease by 1/10,000, decreasing the number of statistical cases (given the size of the population affected by the regulation -- in this example, 50,000) by the equivalent of five cases per year. Risk assessors may also note that about half of these cases would be fatal, and that the fatalities reduced by the regulation would primarily be among elderly members of the population. Furthermore, uncertainty analysis may indicate that the number of cases avoided may be understated or overstated by a factor of four.

Analysts generally develop similar types of information for other types of effects. For example, for corrosive contaminants, engineers may be asked to estimate the miles of piping affected, the degree of decrease in corrosion attributable to setting the MCL at different levels, the effect of the decrease on the timing and extent of pipe replacement, and the amount of uncertainty in these estimates.

As noted earlier, some benefits may not be quantified, either because the scientific basis for quantifying them is not well-established (e.g., data are lacking on the link between exposure and disease incidence) or because the time and resources required to perform the analysis outweigh the usefulness of gathering the additional information for decision-making. These benefits are discussed qualitatively when presenting the results of the benefits analysis.

5.2.3 Estimate the Value of the Effects

Once the physical effects of the regulation are quantified, analysts may use the methods described in Chapters 3 and 4 to estimate the dollar value of these effects. Below, we provide simplified examples of this step for mortality, morbidity, and other impacts. These examples are intentionally brief to illustrate the types of

[84] See, for example, U.S. Environmental Protection Agency, *Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A)*, EPA/540/1-89/002, December 1989; U.S. Environmental Protection Agency, *Guidance for Risk Assessment,* prepared by the Risk Assessment Council, November 1991.

approaches that may be used. In reality, assessing these impacts is likely to be substantially more complex due to limitations in the available data and other factors.

Example 1: Mortality Valuation. As discussed in Chapter 3, available research provides value of statistical life estimates ranging from $0.8 million to $17.8 million, with a mean value of $6.3 million (2000 dollars).[85] Using a Weibull distribution, the 10th and 90th percentile values are $1.6 million and $12.3 million respectively. These values apply to small changes in the risk of premature mortality among a population; they are not values for saving the life of a particular individual.

In the screening phase of the analysis, these estimates can be simply applied to initial estimates of the number of statistical lives saved to provide a preliminary indicator of the value of these benefits. The results of this analysis, for a regulation that reduces the risks of premature death by the equivalent of five statistical lives per year, would be as follows.

Exhibit 5-5
Example of Screening Analysis for Valuing Mortality Effects
(2000 Dollars)

Low End Estimate (10th percentile value)	Mid-Range Estimate (mean value)	High End Estimate (90th percentile value)
$8.0 million (5*$1.6 million)	$31.5 million (5*$6.3 million)	$61.5 million (5*$12.3 million)

The above example is intentionally simplified and an actual benefits analysis may be significantly more complicated. For example, analysts may perform a sensitivity analysis to account for uncertainty in the risk estimates; e.g., using reasonable upper and lower estimates of the number of statistical lives saved to help bound the benefits estimates, or applying a probabilistic model to estimate the likelihood of different outcomes. In addition, the biases that are introduced by using the available valuation literature (which largely addresses fatalities from work place accidents rather than environmental contaminants) may be addressed qualitatively or quantitatively, as discussed previously in Chapter 3.

Example 2: Morbidity Valuation. As Chapter 3 notes, values for avoiding nonfatal health effects will vary greatly depending on the nature and severity of the effect. Monetary values for several of the health effects associated with drinking water contaminants are provided in EPA's *Cost of Illness Handbook* and *Handbook*

[85] U.S. Environmental Protection Agency, *The Benefits and Costs of the Clean Air Act: 1990 to 2010,* EPA 410-R-99-001, November 1999.

on Noncancer Health Effects Valuation. These estimates include both cost of illness (COI) and willingness to pay (WTP) values; willingness to pay estimates are available for a relatively small number of health effects.

For the purpose of this example, we assume that the regulations will reduce, by 15 statistical cases, a specific type of kidney disease per year. We further assume that available COI estimates indicate that the costs of this illness (medical expenses and lost work time) average about $25,000 per case. In addition, we assume that WTP values for similar (but not identical) illnesses are approximately $45,000 per case. The results of a very simple screening analysis using these estimates is provided in Exhibit 5-6.

Exhibit 5-6
Example of Screening Analysis for Valuing Morbidity Effects
(1999 Dollars)

Cost-of-Illness (COI) Estimate	Willingness to Pay (WTP) Estimate
$375,000 (15*$25,000)	$675,000 (15*$45,000)
Note: The COI estimate is likely to understate the actual value of reducing these health effects, because it does not address pain and suffering or other effects associated with the disease. The WTP estimate accounts for these other effects, but is for a disease similar but not identical to the illness reduced by these regulations.	

In this case, the note in the exhibit would be explained in detail in the text; this discussion could address the likely direction and magnitude of the associated biases to the extent possible. Issues related to the quality, applicability, and transferability of the studies used to develop these estimates may be discussed in detail, as described in Chapter 4. For example, the WTP estimate may understate actual willingness to pay if it is for a less severe form of the illness or for a form with shorter duration. In this example, total benefits would be at least $375,000, but could exceed $675,000 since the WTP estimates probably understate the actual value. Sensitivity or probabilistic analysis could be performed to account for uncertainty in the risk (or valuation) estimates. This simple example does not reflect many of the considerations that might be addressed in an actual analysis, such as the rationale for using a point estimate to value these effects rather than a function that relates this value to the characteristics of the population affected and other determining factors. In subsequent stages of the analysis, this approach to valuation could be refined.

More information on valuing morbidity effects, including several examples, is provided in EPA's *Handbook on Noncancer Health Effects Valuation.*[86]

Example 3: Valuation of Other Impacts. Chapter 3 also describes methods for valuing other types of benefits, such as reduced damages to materials and aesthetic effects. In many cases, the non-health effects of drinking water regulations may be valued using the avoided cost method. This method compares expenditures with and without the regulations to estimate the value of related benefits.

To illustrate this approach, consider a regulation that reduces the corrosion of pipes, which in turn will decrease the frequency of needed repairs and/or replacement. The value of this decreased maintenance and replacement (e.g., per mile of piping) could be estimated by engineers with relevant expertise, then applied to estimates of the length of piping potentially affected by the regulations. As in the mortality and morbidity examples, a simple approach could be applied for screening purposes, then refined if needed to provide better information for decision-making in subsequent phases of the analysis. For example, one refinement would be to consider the extent to which changes in costs would lead to changes in prices, and to re-estimate the benefits values to take into account the resulting change in consumer or producer surplus.

5.3 Cross-Cutting Issues

The previous discussion has focused primarily on issues that relate to the benefits analysis. There are also several cross-cutting issues that are addressed in both the cost and benefits analyses. We discuss two key considerations in more depth — discounting and inflation — and then provide a short overview of several other cross-cutting issues for benefits analyses under SDWA.

5.3.1 Discounting and Inflation

Analyses of the costs and benefits of drinking water regulations may be conducted on an annual basis, or may consider impacts over a number of years. The appropriate time frame for the analysis is determined on a case-by-case basis. In general, the annual approach may be most appropriate in cases where costs and benefits are expected to be relatively constant from year to year once the regulation is implemented. If costs and benefits accrue in different time periods or are likely to change significantly over time, the analysis may cover a multi-year period. For example, if EPA is considering whether to allow water systems to gradually comply with a new standard over a several year period, analysts may wish to compare the

[86] U.S. Environmental Protection Agency, *Handbook on Noncancer Health Effects Valuation (draft),* prepared by Industrial Economics, Incorporated, September 1999.

costs and benefits of the phased approach to the effects of requiring more immediate compliance.

Regardless of the time period selected, analysts are likely to need to work with data on monetary values that were collected at different points in time. For example, recent compliance cost data may be available, but benefits valuation studies may be several years old. Two important factors affect the dollar value of costs and benefits over time — discounting and inflation. These terms apply to two very different concepts. Discounting is a method that accounts for alternative, productive uses of funds over time. Inflation refers to an overall rise in price levels. Below, we discuss each of these factors in more detail and provide an overview of EPA and OMB guidance on selecting a discount rate.

Inflation

Inflation refers to an overall rise in general prices throughout the economy; it is often measured by comparing the average prices of a standard bundle of goods and services across time. Inflation does not reflect a real increase in value; rather it indicates that the same goods and services now command higher prices. Information on inflation rates in available in the *Economic Report of the President*, which is published annually by the Executive Office of the President. This report includes both general inflation rates (the best known of which is the consumer price index or CPI) as well as rates for specific types of goods and services (e.g., the CPI-medical); the appropriate rate depends on the types of goods or services under consideration. These factors can be used to inflate prices incurred in prior years to the present or to decrease (deflate) current prices to a prior level.

For example, if a valuation study reports estimates as 1990 dollars, and an analyst wishes to covert to 1999, dollars using the CPI, he or she would first determine the change in the CPI over this time period. According to the 2000 *Economic Report of the President*, the CPI rose from 130.7 to 166.6 over this time period, or about 127 percent. The analyst would multiply the 1990 value by 1.27 to determine the 1999 equivalent.

To compare costs and benefits through time, analysts remove the effects of inflation from the estimates. Otherwise, it is difficult to disentangle real changes in value from changes that are attributable only to inflation. The OMB guidance recommends deflating benefit and cost estimates that are in nominal dollars by an appropriate inflation index to get constant dollar estimates.[87] In other words, cost and benefit estimates should be presented in real terms based on a specific year. Because of the

[87] U.S. Office of Management and Budget, "Guidelines to Standardize Measures of Costs and Benefits and the Format of Accounting Statements" Appendix 4 in *Report to Congress on the Costs and Benefits of Federal Regulations,* March 22, 2000.

uncertainties related to estimating future inflation, both costs and benefits are generally reported as of the most recent completed year for which inflation rates are available. For example, an analysis completed in 2001 might be reported in 2000 dollars.

Discounting

Discounting differs from inflation in that it measures real changes in value over time. When a water system invests in new treatment technology, or an individual invests in a home water filter, the investment means that the funds are not available for other productive uses. These alternative uses are referred to as "opportunity costs" by economists. In general, individuals prefer to have resources available in the near term rather than in the future, because they can invest the resources and receive a return on their investment. The same is true of consumption, individuals would generally prefer to consume desired goods or services soon rather than waiting.

Discounting is a method for adjusting monetary values to reflect these time preferences. Discounting future costs or benefits involves multiplying the value in each year by a factor that adjusts for both the length of time between the present and when the event occurs and the degree to which current investment (or consumption) is valued over future investment (or consumption). Discounting allows costs and benefits that occur in different time periods to be compared by stating them all in current year terms, referred to as the "net present value." The net present value of a stream of costs and benefits is calculated by multiplying the costs and benefits in each year by a time-dependent weighting factor and summing the results. The rate of change assumed over time is referred to as the "discount rate."

For example, if an analyst wishes to estimate the present (2001) value of costs incurred in year 2002 with an annual seven percent discount rate, he or she would multiply the costs in the year 2002 by 0.93 (the weighting factor for one year at seven percent) to determine the 2001 equivalent.[88]

Both OMB and EPA require that economic analyses discount future costs and benefits to a present value equivalent when presenting the results. While concept of discounting is relatively straightforward, much controversy surrounds the choice of an appropriate discount rate. OMB and EPA currently recommend use of a seven percent discount rate, which "approximates the marginal pretax rate of return on an

[88] Most financial calculators and spreadsheet packages contain the formula for estimating these values, which is expressed as: Net Present Value = $NB_0 + d_1NB_1 + d_2NB_2 + ... + d_nNB_n$, where NB_t is the net difference between benefits and costs that accrue in time period *t* (e.g., 0,1,2...*n*), and *n* is the final period for which the analyst has estimated benefits and costs. The discounting weights (d) are determined by $d_t = 1/(1+r)^t$ where *r* is the discount rate and *t* is the time period (or number of years from the present).

average investment in the private sector in recent years," unless a different rate is clearly justified.[89] This rate essentially assumes that government programs are displacing private investment. EPA suggests that analysts also present the results using a rate of two to three percent, which represents the consumption rate of interest, as discussed in more detail in the EPA *Guidelines for Preparing Economic Analyses.*[90] This rate essentially assumes that the programs are using funds that would otherwise be expended on current consumption. These are "real" discount rates; i.e., net of inflation. Any inflation adjustments needed to bring cost and benefit estimates into the same year are made prior to discounting. Regardless of the discount rate chosen, analysts use the same rate for both the cost and benefit analysis to ensure comparability.

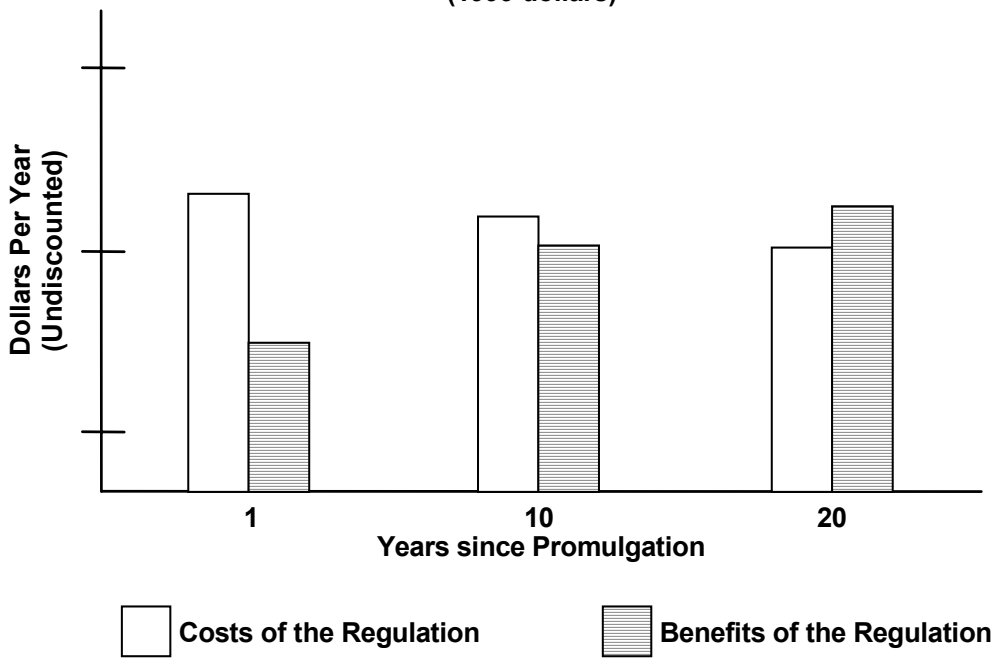
Both OMB and EPA also recommend that analysts present the undiscounted stream of costs and benefits over time. Exhibit 5-7 presents an example of this type of

[89] U.S. Office of Management and Budget, *Guidelines and Discount Rates for Benefit-Cost Analysis of Federal Programs,* October 29, 1992, p. 9.

[90] This suggestion is echoed in the OMB Guidance, which discusses the use of a three percent rate.

graphic

Exhibit 5-7
Example of Distribution of Costs and Benefits Over Time
(1999 dollars)



Note: Nonmonetized costs and benefits should be identified in the notes on the exhibit.

5.3.2 Other Issues

In addition to discounting and inflation, there are several other cross-cutting issues analysts address in both the cost and benefits analyses. We provide a brief overview of these issues below; more information on many of these topics is provided in EPA's *Guidelines for Preparing Economic Analysis.*

Establishing a Baseline. The "baseline" in regulatory analysis refers to conditions now and in the future in the absence of the regulation. The effects of the regulatory options are then compared to this baseline to determine the costs and benefits of each option. Correct specification of the baseline is needed to accurately capture the effects of the regulation; for example, a baseline that exaggerates the deleterious effects of contaminants on the environment without the regulation may overstate the benefits of the regulation, and vice versa. A consistent baseline definition is used in both the cost and benefit analyses to ensure comparable results.

Rule Sequencing. When establishing the baseline conditions from which to assess the benefits of a regulation, another key issue is the sequencing of new regulations. EPA analyses generally assume that the baseline includes the effects of all rules that have been promulgated to date, but do not anticipate the implementation of new rules. However, in cases where several rules with interactive effects are being promulgated jointly, analysts may assess the combined effects of the rules as well as each rule's individual impact.

Risk Trade-Offs: In some cases, techniques to control contamination levels will produce risks. For example, disinfection techniques to control microbial contaminants may create disinfection by-products that pose other risks to human health. Both increases and decreases in various risks may be assessed and presented.[91]

Co-occurring Contaminants: SDWA explicitly requires that analysts consider the effects of co-occurring contaminants [(SDWA, Section 1412(b)(3)(c)(i))]. This issue refers to cases where treatment used to achieve the MCL under consideration also reduces the concentrations of other contaminants. The effects of reducing other contaminant concentrations should be assessed and presented with the overall results. Note, however, that because control of these other contaminants is not required by the regulation, related benefits are generally discussed separately from the benefits

[91] This discussion refers to direct impacts of the regulations on risks. Economists debate whether the effects of regulatory costs on the resources available for other risk-reducing activities (such as health care) are significant and warrant inclusion in these types of analyses. See, for example, Viscusi, W.K., ed., "The Mortality Costs of Regulatory Expenditures," *Journal of Risk and Uncertainty,* Vol. 8, No. 1, 1994 (a special issue devoted to this topic).

associated directly with the MCL, so that decision-makers can consider these impacts independently. This approach is used because the MCL does not require system operators to achieve and maintain the assumed level of removal for the co-occurring contaminants. For example, the level of control of co-occurring contaminants may decrease over time if new treatment techniques are implemented that only target the contaminants for which MCLs are established.

Double-Counting. Throughout the entire analysis, it is important to assess and minimize the extent of double-counting in the benefit and cost estimates. For example, if a rule results in reduced corrosion of water system pipes, it could be assessed as a benefit to the rule. The cost analysis, however, could also assess this impact as a cost savings, resulting in double-counting. In addition, combining certain benefit valuation methods will also lead to double-counting. For example, a property value study may reflect perceived health risks as well as other factors, overlapping with more direct estimates of the value of risk reductions.

Comparing Costs and Benefits. While SDWA requires an assessment of benefits and costs, it does not require EPA to base decisions solely on quantified effects. Rather, it indicates that the quantified and non-quantified benefits must be considered and compared to the costs of the MCL [(SDWA Section 1412(b)(3)(c)(i)]. In many cases, regulatory analyses may include qualitative information for consideration by decision-makers, or may include information on physical effects but no dollar values. In these cases, techniques such as cost-effectiveness analysis or break-even analysis may be used to inform related policy decisions. In a case where the quantified benefits are less than the costs, decision-makers consider whether it is likely that the non-quantified benefits would bridge the gap between costs and benefits, or vice-versa.

These and other issues mean that benefits analysts generally work closely with other members of the regulatory development team. Coordination is needed to ensure that both the cost and the benefit analyses use consistent assumptions regarding baseline conditions and the effects of different regulatory options. In addition, both cost and benefits analysts need to ensure that they address the issues of concern to work group members, senior EPA managers, and stakeholders. Information from the cost analysis is also required for the analysis of benefits, such as data on the population served by systems likely to be affected by the potential regulatory requirements. Successful efforts often involve weekly or more frequent conversations among lead analysts and regulation managers to discuss the implications of preliminary findings and changes in the options under consideration, supplemented by more formal periodic meetings to report on progress and discuss next steps.

REPORT OF THE BENEFITS WORKING GROUP APPENDIX A

A.1 Introduction

This appendix summarizes the deliberations of the National Drinking Water Advisory Council's (NDWAC's) Benefits Working Group. This group involved a wide variety of stakeholders, including utility company staff, environmentalists, health professionals, state water program staff, an elected official, economists, and members of the general public. Over the course of two meetings and two teleconferences during 1998, the Benefits Working Group discussed issues that arise in developing a new framework for evaluating the benefits of proposed drinking water regulations. This framework is being created by EPA's Office of Ground Water and Drinking Water (OGWDW) as part of the Office's efforts to implement the 1996 Safe Drinking Water Act (SDWA) amendments. The amendments require that EPA fully consider both quantifiable and non-quantifiable benefits that accrue as a result of drinking water regulations, and compare the benefits with the projected costs of the regulations.

The Benefits Working Group was charged with reviewing those quantifiable and non-quantifiable benefits that could be considered when developing drinking water regulations and provide recommendations to the Agency on which benefits should be evaluated in developing its regulations. In addressing the charge, the group considered the following questions:

1. What categories of benefits (qualitative and non-qualitative) should EPA routinely consider in the process of developing its drinking water regulations?

2. How (specifically) should EPA consider qualitative (non-monetizable) benefits in its rulemaking process?

3. How should EPA ultimately compare the results of its benefits evaluations with its cost analysis when developing drinking water regulations?

Numerous other questions and issues pertaining to benefits assessment were also raised for group discussion. Recommendations developed by the Benefits Working Group were presented to NDWAC on November 17, 1998.

This appendix: (1) lists the participants in the Benefits Working Group; (2) provides its recommendations as approved by NDWAC; and (3) includes the report it prepared on its deliberations. Additional information on the activities of the group (including meeting notes and handouts) is available from OGWDW staff.

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Members (continued)

Members (continued)

John Pickle, MSEH

A.3 NDWAC Benefits Analysis Recommendations

On November 17, 1998, the National Drinking Water Advisory Council (NDWAC) approved a series of recommendations for EPA's Office of Ground Water and Drinking Water to consider in its analysis of the benefits of proposed regulations. These recommendations were based upon a report from the NDWAC Benefits Working Group.

The National Drinking Water Advisory Council (NDWAC) recommends that:

(1) EPA should focus its benefits analysis efforts primarily on assessing effects on human health, defining these effects as clearly as possible and using the best available data to value them. It is also recommended that EPA should also consider, where appropriate, taste and odor improvements, reduction of damage to water system materials, commercial water treatment cost reductions, benefits due to source water protection (e.g., ecological benefits and non-use benefits), and benefits derived from the provision of information on drinking water quality (e.g., a household's improved ability to make informed decisions concerning the need to test or filter tap water);

(2) EPA should devote substantial efforts to better understanding the health effects of drinking water contaminants, including the types of effects, their severity, and affected sensitive subpopulations. Better information is also needed on exposures and the effects of different exposure levels, particularly for contaminants with threshold effects. These efforts should pay particular attention to obtaining improved information concerning impacts on children and other sensitive populations;

(3) EPA should clearly identify and describe the uncertainties in the benefits analysis, including descriptions of factors that may lead the analysis to significantly understate or overstate total benefits. Factors that may have significant but indeterminate effects on the benefits estimates should also be described;

(4) EPA should consider both quantified and non-quantified benefits in regulatory decision-making. The information about quantified and non-quantified (qualitative) benefits should be presented together in a format, such as a table, to ensure that decision-makers consider both kinds of information;

(5) EPA should consider incremental benefits and costs, total benefits and costs, the distribution of benefits and costs, and cost-effectiveness in regulatory decision-making. This information should be presented together in a format, such as a table, to ensure its consideration by decision-makers;

(6) Whenever EPA considers regulation of a drinking water contaminant, it should evaluate and consider, along with water treatment requirements to remove a contaminant, source water protection options to prevent such a contaminant from occurring. The full range of benefits of those options should be considered.

A.4 Benefits Working Group

Report to the National Drinking Water Advisory Council

Charge to the Benefits Working Group

The specific charge for the Benefits Working Group was to *"consider the range of quantifiable and non-quantifiable benefits that could be considered when developing drinking water regulations and provide recommendations to the Agency on which benefits should be routinely considered in developing its regulations."* Questions to be addressed by the Working Group in carrying out the charge follow:

- What categories of benefits (both qualitative and quantitative) should EPA routinely consider in the process of developing its drinking water regulations?
- How (specifically) should EPA consider qualitative (non-monetizable) benefits in its rulemaking process?
- How should EPA ultimately compare the results of its benefits assessments with its cost analysis when developing drinking water regulations?

Summary of Benefits Working Group Recommendations

Recommendation #1: Categories of Benefits

The Working Group identified six categories of benefits that can result from drinking water regulations: (1) health risk reductions; (2) taste and odor improvements; (3) reduction of damage to water system materials; (4) commercial water treatment cost reductions; (5) benefits due to source water protection (e.g., ecological benefits and non-use benefits); and (6) benefits derived from the provision of information on drinking water quality (e.g., a household's improved ability to make informed decisions concerning the need to test or filter tap water). The members agreed on the following recommendation:

- EPA should focus its benefits analysis efforts primarily on assessing effects on human health, defining these effects as clearly as possible and using the best available data to value them.

Recommendation #2: Assessing Health Risks and Valuing Benefits

The analysis of health risks is central to EPA's ability to establish the appropriate MCLG and to assess the benefits of alternative levels for the MCL. The Benefits Working Group discussed several concerns related to the valuation of health benefits, and agreed on the following recommendation:

- EPA should devote substantial efforts to better understanding the health effects of drinking water contaminants, including the types of effects, their severity, and affected sensitive subpopulations. Better information is also needed on exposures and the effects of different exposure levels, particularly for contaminants with threshold effects. These efforts should pay particular attention to obtaining improved information concerning impacts on children and other sensitive populations.

Recommendation #3: Addressing Uncertainty

The Benefits Working Group discussed several concerns related to addressing uncertainty in benefits analysis, and agreed on the following recommendation:

- EPA should clearly identify and describe the uncertainties in the benefits and costs analysis, including descriptions of factors that may lead the analysis to significantly understate or overstate total benefits and costs. Factors that may have significant but indeterminate effects on the benefits and costs estimates should also be described.

Recommendation #4: Addressing Non-Quantified Benefits

The Benefits Working Group discussed several issues related to addressing non-quantified benefits, and agreed on the following recommendation:

- EPA should consider both quantified and non-quantified benefits in regulatory decision-making. The information about quantified and non-quantified (qualitative) benefits should be presented together in a format, such as a table, to ensure that decision-makers consider both kinds of information.

Recommendation #5: The Presentation of Information on Benefits and Costs

The Benefits Working Group discussed a number of issues related to the presentation of information on benefits and costs, and agreed on the following recommendation:

- EPA should consider incremental benefits and costs, total benefits and costs, the distribution of benefits and costs, and cost-effectiveness in regulatory decision-making. This information should be presented together in a format, such as a table, to ensure its consideration by decision-makers.

Recommendation #6: Source Water Protection Options

The Benefits Working Group discussed several issues related to addressing increasing source water protection, and agreed on the following recommendation:

- Whenever EPA considers regulation of a drinking water contaminant, it should evaluate and consider, along with water treatment requirements to remove a contaminant, source water protection options to prevent such a contaminant from occurring. The full range of benefits of those options should be considered.

Background and Overview of Working Group Discussions

The Benefits Working Group was established to help shape how EPA should best meet the new benefits analysis requirements that are specified in the 1996 SDWA amendments, as new program regulations are developed over the next few years. Since its inception, EPA has performed benefits analysis, usually as part of a benefit/cost analysis, as one of many sources of information on the potential effects of its regulations. EPA views benefit/cost analysis as a method to organize information in a way that informs the decision. These analyses may contain significant uncertainty and provide only one perspective on the merits of alternative policy choices. Other types of analysis are needed to address concerns about equity, for example.

Several statutes, Presidential Executive Orders, and guidance documents govern the conduct of benefit/cost and related regulatory analyses at EPA. Benefit/cost analyses undertaken by Federal agencies are expected to

adhere to "best practices" as defined by the economics profession. Federal agencies must also address several specific concerns related to imposing costs or other burdens on private industry, state and local government, and other entities, such as avoiding unfunded mandates or requirements that are particularly burdensome for small businesses or local government. Other government-wide requirements focus on protecting certain groups of potentially affected individuals, such as minorities, low income populations and children. In the case of drinking water regulations, SDWA also contains several requirements related to the performance of benefit/cost analysis and its use in decision-making.

I. Categories of Benefits

A. Background

Most drinking water regulations promulgated under SWDA focus on establishing the maximum allowable concentration of a particular contaminant (or group of contaminants) for drinking water supply systems used by the public. For these types of regulations, the "costs" of the standards generally include expenditures on monitoring and treatment (or, in some cases, source water protection) and related market impacts such as the effects on water price increases. The "benefits" include the effects of reducing the concentration of the contaminants in drinking water. Drinking water regulations may also increase the availability of information on water quality.

In 1997, EPA conducted a detailed review of the potential benefits of drinking water regulations, as reported in "*Valuing Drinking Water Quality: Theory, Methods, and Research Needs."* Based on this research, EPA identified four major categories of benefits that may warrant routine consideration for individual rules:

- Reduced health risks, including decreased risks of premature death, illness or other health impacts.
- Improved aesthetic qualities, including tap water taste, odor, and appearance.
- Reduced damages to materials, primarily related to reduced corrosion of water system piping and equipment.

- Improved qualities for commercial and industrial use, for example, in cases where contaminants would adversely affect production processes if not removed by the water supplier.

While effects on health risks are assessed for most drinking water regulations, many of the other categories are considered only when relevant to a particular contaminant. For example, many contaminants do not affect the taste, odor, or appearance of tap water. In addition, some drinking water regulations will address categories not directly included in the above list. For example, regulations requiring increased source water protection may have ecological benefits, such as enhanced recreational fishing and bird-watching opportunities due to improved productivity of the fish and wildlife stock.

B. Working Group Discussion Overview (Recommendation #1: Categories of Benefits)

A key question raised by EPA for the Benefits Working Group was "what categories of benefits should EPA routinely consider in the process of developing its drinking water regulations?" EPA asked the Working Group members to review the potential benefits categories described above, both to determine whether EPA has excluded important categories and to identify which categories are most important to formally assess and quantify. In response to this request, the Working Group identified six categories of benefits that can result from drinking water regulations: (1) health risk reductions; (2) taste and odor improvements; (3) reduction of damage to water system materials; (4) commercial water treatment cost reductions; (5) benefits due to source water protection (e.g., ecological benefits and non-use benefits); and (6) benefits derived from the provision of information on drinking water quality (e.g., a household's improved ability to make informed decisions concerning the need to test or filter tap water). The members agreed on the following recommendation:

- EPA should focus its benefits analysis efforts primarily on assessing effects on human health, defining these effects as clearly as possible and using the best available data to value them.

During the group's discussions of potential benefits categories, the following points were mentioned by at least one member of the group as important considerations for EPA.

- When assessing health-related benefits, EPA should ensure that adequate attention is paid to impacts on vulnerable groups (e.g., children, pregnant women, the elderly, individuals with immune deficiencies, Native Americans). Additional research (and funding) is needed to better understand and value these impacts.

- Benefits categories other than health should be considered in cases where they may affect EPA decision-making, e.g., if the benefits are likely to be significant or if consideration of the benefit category could influence the selection of the MCL.

- The analysis should consider both positive and negative changes in each benefit category.

- EPA should consider all relevant benefits categories in its decision-making regardless of whether the benefits are quantified or valued. However, some members of the group expressed concern that EPA may overemphasize the value of assessing benefits other than health effects.

- Some of the benefits that would be derived from a decrease in health problems for children include less time lost from school, less parental time lost from work, and less family disruption. Children also have more potential years of life to lose, and their earning potential could be affected.

- EPA should conduct retrospective analysis to assess the extent to which predicted benefits are consistent with the actual benefits realized.

- Working Group members agreed that at least six categories of benefits result from drinking water regulations. Of the six, four categories of benefits result from drinking water treatment improvements: health risk reductions, taste and odor improvements,

materials damage reduction (of water systems), and commercial water treatment cost reductions. The other benefits categories arise from source water protection efforts and the provision of information on drinking water quality.

II. Methods for Assessing Health Risks and Valuing Benefits

A. Background

A.1 Assessing Health Risks

EPA requires information on health risks to establish the MCLG, and to assess the benefits of establishing the MCL at or above the “feasible” level. The MCLG is generally set at "zero" for contaminants that pose risks of physiological damage at all doses (i.e., nonthreshold toxicants, including most carcinogens). For threshold toxicants, the MCLG is generally set at the level where there are no observable effects (with a margin of safety).

To estimate the risks associated with particular contaminants, EPA may derive information from epidemiological studies of human populations or from animal studies. Epidemiology generally involves developing statistical relationships between estimates of exposure and the incidence of health effects. The advantage of these studies is that they use data on human effects; the disadvantage is that the results of some studies can be difficult to interpret because of confounding factors such as exposure to other contaminants, and may not provide an understanding of the physiological basis for the effect. Data from animal studies address confounding factors by using a controlled environment, but may be difficult to translate into human terms.

A.2 Methods for Valuing Benefits

From the perspective of economic theory, the appropriate measure of value is willingness to pay for the benefits. Willingness to pay is the maximum amount of money an individual would voluntarily exchange to acquire something or obtain an improvement (e.g. in drinking water quality). An individual’s willingness to pay necessarily includes that individual’s ability to pay because the resources available to any individual are limited. An individual may wish to pay more than the total value of the resources available to him or her, but economic willingness to pay is limited to that amount the individual can actually allocate for the benefit in question. Because “improved drinking water quality” is not directly bought and sold in the marketplace, information on willingness to pay must be derived from the markets for related goods or from surveys or similar data collection efforts.

The particular methods used vary depending on the benefit category assessed. Below, we discuss the approaches used for the major benefit categories discussed by the Working Group: reduced mortality risks, reduced morbidity risks, avoided damages to materials, and effects on commercial and industrial water use.

A.2.1 Valuing Mortality Risks

Drinking water regulations may decrease the risks of contracting a potentially fatal disease, such as certain cancers. The most commonly used approach for valuing these changes in mortality risk focuses on the "value of a statistical life." This term refers to the value of relatively small changes in the risk of death among a population. For example, if 100,000 people are each willing to pay $100 to reduce their own risk of death by 1 in 10,000, then as a group their willingness to pay for a program that would save 10 lives in the population is $10 million, or $1 million per statistical life. This value refers to the sum of individuals' willingness to pay for risk reductions. Presently, the value of statistical life most often used in EPA regulatory analyses includes a best estimate of $5.8 million (in 1997 dollars) per statistical life saved, with a lower bound of $0.7 million and an upper bound of $16.3 million. These values are derived from 26 studies, including 21 wage-risk studies and five contingent valuation studies, and have been subject to substantial peer review.

While this range of values provides the best estimates currently available, applying this range has several limitations. First, there are many differences between the risks addressed by the available studies and the risks associated with environmental regulations. The studies address risks that are incurred voluntarily, and that often accrue from accidents rather than lingering illnesses. Second, drinking water regulations may also affect people with different demographic characteristics than those studied, e.g., different age or income groups, or people whose initial health condition differs.

A.2.2 Valuing Morbidity Risks

The contaminants addressed by drinking water regulations can cause a variety of illnesses, including acute illness, nonfatal cancers, and other chronic diseases, as well as nonfatal reproductive and developmental effects. The most common approach to valuing morbidity is the cost-of-illness method, which derives values from the medical costs and lost work time associated with an illness. While this approach is relatively easy to understand and implement, it is not a complete measure of willingness to pay. The availability of insurance affects people’s willingness to incur these costs, and this approach excludes the value placed on avoiding pain and

suffering and reducing the risk of illness. Under most plausible conditions, cost of illness studies understate total willingness to pay, with the degree of understatement varying depending on the nature and severity of the disease. For many health effects, only cost of illness estimates may be available; studies of total willingness to pay have been undertaken for only some of the health effects of concern.

A.2.3 Valuing Other Effects (avoided damages to materials, and effects on commercial and industrial water use)

The other types of benefits likely to be considered for drinking water regulations include avoided materials damages (e.g., reduced corrosion) and improved water quality for commercial and industrial use. This latter category focuses on water as an input to production processes rather than its use as drinking water, e.g., for cooling or for mixing with other materials. In either case, the method most commonly used to measure the value of related benefits is to assess avoided costs. This approach considers the costs incurred in the absence of the regulation, and assesses the extent to which these costs would be reduced under alternative regulatory levels. These avoided costs may include expenditures on replacing corroded distribution system piping or industrial equipment, or on additional treatment by an industrial plant prior to use.

B. Working Group Discussion Overview (Recommendation #2: Assessing Health Risks and Valuing Benefits)

The analysis of health risks is central to EPA's ability to establish the appropriate MCLG and to assess the benefits of alternative levels for the MCL. The Benefits Working Group discussed several concerns related to the valuation of health benefits, and agreed on the following recommendation:

- EPA should devote substantial efforts to better understanding the health effects of drinking water contaminants, including the types of effects, their severity, and affected sensitive subpopulations. Better information is also needed on exposures and the effects of different exposure levels, for all populations, and especially vulnerable populations, particularly for contaminants with threshold effects.

During the group's discussion on methods for assessing health risks and valuing benefits, the following points were mentioned by at least one member of the group as important considerations for EPA.

- Affordability tends to be the deciding factor in determining whether a customer is willing to pay for a product. EPA should develop clear affordability criteria; for example, by looking at the percentage of disposable income spent on different goods and services.

- As ability to pay and willingness to pay are constrained by income, other kinds of analyses on equitability should be conducted.

- Consumers view water as a non-discretionary product, not consistent with economic principles. The compelling issue is whether WTP is equated with fairness. Affordability is more closely linked to fairness. EPA should consider the consumer's decision-making process for a non-discretionary product and review the available literature on this topic.

- Affordability pertains to equity concerns and WTP to efficiency concerns. Economics tends to ignore equity. Affordability and ability to pay are important for social issues, but not important for cost-benefit analysis which focuses on the most efficient approach to risk reduction. Affordability and WTP involve separate issues, and should be analyzed separately.

- The effects on vulnerable populations, such as fetuses, infants and children, the elderly and the immunosuppressed should be explicitly evaluated.

- Data on health effects should be derived from careful consideration of the quality of available studies, and additional research should be conducted when needed to refine or expand available data.

- EPA should separately evaluate exposure risks to children and other sensitive subpopulations. In the absence of adequate exposure data for these subgroups, EPA should not simply extrapolate from data on the general population.

- The EPA should develop strong working relationships with other components of the Federal Government involved with the collection and study of health information, such as the National Center for Health Statistics and the National Center for environmental health.

- Working Group members disagree on the use of epidemiological studies. Some argue that these studies should not be used as the sole basis for developing regulations if data are lacking on the cause and effect relationship for a particular contaminant and health effect. Others argue that it is reasonable to use the correlations found in well-conducted epidemiological studies when developing regulations.

- Regardless of the particular benefit being valued, EPA should use well-conducted, unbiased studies to estimate the value. While many high quality studies have been conducted in this area, additional research on these values is still necessary. However, the need to address the more significant uncertainties in the health risk data should be a higher priority for EPA.

- EPA should ensure that the approach to valuing morbidity addresses all elements of willingness to pay (not just medical costs), but care should be taken to ensure that the resulting values are not overstated due to difficulties in obtaining estimates for components of willingness to pay such as pain and suffering.

- EPA should support and conduct research to adapt existing methods so that they can be applied to valuing mortality and morbidity risks to children, pregnant women, those with preexisting chronic diseases and the elderly, rather than relying on estimates developed for adults when considering these effects. In considering these groups, one should value the costs to not only the individual involved but to others in their family/social

group as well. A problem in a child usually involves not only the loss of the child's time from school but the parents' time from work. In the case of those with preexisting chronic disease or the elderly, there is often some third party who must also be involved in taking the individual to the doctor or for other services. Most of these costs should be measurable.

III. Methods for Addressing Uncertainty

A. Background

Benefits and costs analyses of drinking water regulations often contain significant uncertainty. The appropriate method for addressing uncertainty depends in part on the source of the uncertainty and on the types of data available. In addition, the method selected will depend on the information needed for decision-making. Simple and inexpensive methods may be adequate for determining appropriate regulatory levels if they clearly support a particular option despite remaining uncertainties (e.g., demonstrate that the benefits analysis clearly supports setting an MCL at the lowest feasible level), or if the value of additional information is outweighed by the costs or time needed to acquire it.

Regardless of the method chosen, EPA believes that uncertainties in the analysis must be clearly stated, with a discussion of the implications for decision-making. The methods and data used in the analysis should be clearly described and justified. The results of the benefits and costs analysis are often best described as a range of values. Benefits and costs that are not quantified, or that are quantified but not assigned a monetary value, also should be included in the presentation of results.

B. Benefits Working Group Discussion Overview (Recommendation #3: Addressing Uncertainty)

The Benefits Working Group discussed several concerns related to addressing uncertainty in benefits analysis, and agreed on the following recommendation:

- EPA should clearly identify and describe the uncertainties in the benefits and costs analysis, including descriptions of factors that may lead the analysis to significantly understate or overstate total benefits and costs. Factors that may have significant but indeterminate effects on the benefits and costs estimates should also be described.

During the group's discussion on methods for addressing uncertainty, the following points were mentioned by at least one member of the group as important considerations for EPA.

- Presentations of quantitative results should be combined with discussions of any benefits that were not quantified or monetized.
- EPA should strive to reduce the uncertainties in health effects studies and exposure data.
- Members disagree about the level at which the MCL should be set in cases where the remaining uncertainty in the analysis does not clearly argue for a particular level. Some believe a stringent level should be selected to be protective, while others argue that a less stringent level is desirable to avoid imposing potentially unwarranted costs.

IV. Cost-benefit Analysis and Qualitative (Non-quantified) Benefits: the Presentation of Information

A. Background

Drinking water regulations often may have benefits that cannot be easily quantified or valued. In some cases, the inability to quantify benefits stems from the status of the underlying scientific research. For example, available studies in the health science literature may suggest that a contaminant is associated with a particular illness, but may not provide data on the relationship between changes in exposure and changes in the incidence of the illness. As a result, it may not be possible to quantify the changes in risk associated with different MCLs (e.g., to determine the number of cases avoided) nor may it be possible to value, in dollar terms, these changes in risk. In other cases, the lack of quantification may result from the need to focus limited time and resources on the most significant issues; EPA may not be able to fund studies of less significant effects especially if they require the use of expensive research techniques over long time periods.

EPA and OMB guidance requires the consideration of non-quantified effects in regulatory analyses, and SDWA explicitly notes that non-quantified benefits should be weighed in determining the appropriate MCL. Information on these effects can be discussed qualitatively using text and graphics to indicate their possible importance in terms of incidence and dollar value. In addition, analysts can use breakeven analysis or measures of cost-effectiveness to provide information on the relationship of the non-quantified

effects to the quantified costs and benefits. For example, analysts can indicate the number of cases that would need to be avoided, or the dollar value per case that would be needed, for the total benefits to equal the total costs associated with alternative MCLs.

B. Benefits Working Group Discussion Overview (Recommendation #4: Addressing Non-Quantified Benefits; also Recommendation #5: The Presentation of Information on Benefits and Costs)

The Benefits Working Group discussed several issues related to addressing non-quantified benefits, and presenting information on costs and benefits, and agreed on the following two recommendations:

- EPA should consider both quantified and non-quantified benefits in regulatory decision-making. The information about quantified and non-quantified (qualitative) benefits should be presented together in a format, such as a table, to ensure that decision-makers consider both kinds of information.

- EPA should consider incremental benefits and costs, total benefits and costs, the distribution of benefits and costs, and cost-effectiveness in regulatory decision-making. This information should be presented together in a format, such as a table, to ensure its consideration by decision-makers.

During the group's discussion of qualitative information, the following points were mentioned by at least one member of the group as important considerations for EPA.

- Information on potential benefits should be presented even in cases where the available evidence is weak or contradictory, to ensure that decision-makers weigh all available information in establishing regulatory levels.

- This information should include calculation of breakeven points or similar measures to indicate the extent to which the non-quantified effects may bridge the gap between costs and benefits, in cases where quantified benefits are less than quantified costs.

- The analysis should clearly indicate the areas where additional research is needed, and explicitly discuss the limitations and uncertainties in the available data. Where possible, additional research should be conducted to increase EPA's ability to quantify the potential benefits of alternative MCLs.

- When health effects cannot be quantified (e.g., the change in risks or in number of cases cannot be determined from available data), EPA should not attempt to assign dollar values to these effects. Monetizing these effects may mask the gaps in the data and is not likely to provide credible results.

V. Consideration of Source Water Protection Options

A. Background

Although the Working Group's main charge was to consider methods for assessing benefits, many members felt that EPA's focus on the process for selecting among alternative MCLs (i.e., on treatment) was too narrow. The members believe that EPA should be considering a wider range of options for addressing contaminants in water supplies. The Working Group indicated that it is particularly important for EPA to focus more attention on options for source reduction, and developed the recommendation discussed below.

B. Benefits Working Group Discussion Overview (Recommendation #6: Source Water Protection Options)

The Benefits Working Group discussed several issues related to addressing increasing source water protection, and agreed on the following recommendation:

- Whenever EPA considers regulation of a drinking water contaminant, it should evaluate and consider, along with water treatment requirements to remove a contaminant, source water protection options to prevent such a contaminant from occurring. The full range of benefits of those options should be considered.

During the group's discussion, the following points were mentioned by at least one member of the group as important considerations for EPA.

- EPA should consider the full range of regulatory and non-regulatory approaches available for addressing drinking water contamination, including improving public education, issuing health advisories, and providing bottled water or filters for household use, as well as protecting water sources from contamination (e.g., cleaning up industrial sites which are contributors to drinking water contamination).

- Approaches to addressing drinking water contamination, other than establishing an MCL or treatment technique, may maximize benefits and/or lower costs.

- The protection of wetland habitats should be considered, as well as point source reduction.

VI. Additional Issues

During the group's discussion of various issues, the following points, which related to additional issues, were mentioned by at least one member of the group as important considerations for EPA.

- EPA should place additional emphasis on ensuring racial and economic diversity when involving stakeholders in its work groups, including more members of minority and low income groups and Indian tribes. Other Working Group members disagreed with this.

- Affordability, for both households and water systems, should be an important consideration in determining

appropriate regulatory levels or alternative technologies.

- The effect of contaminants on sensitive subpopulations should be a key consideration in establishing the MCLG and MCL for threshold toxicants.

- EPA should improve communication regarding the risks associated with drinking water contaminants by working with local public health departments, state public health departments, state and elected officials, regional offices, grassroots organizations, and local communities, including families and health care providers. EPA should develop clearer information on scientific findings, and improve access to this information through the World Wide Web and other media.

- EPA should ensure that regulatory requirements to monitor for the presence of contaminants in drinking water take into account both the costs and benefits of the monitoring effort. In addition, EPA should compile monitoring data in an accessible, computerized format that supports ready analysis of exposure to contaminants, related health risks, and the potential benefits of proposed regulations.

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Attachment 20

Emerging chemical risks in Europe — ‘PFAS’

Emerging chemical risks in Europe — ‘PFAS’

It is currently not possible to perform in-depth environmental and health risk assessments of all chemical substances in use in Europe because of the great variety of chemicals and their diverse uses. New and legacy chemicals continue to be released into Europe’s environment, adding to the total chemical burden on Europe’s citizens and ecosystems. Early identification of emerging risks is one of the activities of the European Environment Agency (EEA). This briefing summarises the known and potential risks to human health and the environment in Europe posed by a group of very persistent chemicals, the per- and polyfluorinated alkyl substances (PFAS).

Key Messages

- Comprising more than 4 700 chemicals, per and polyfluorinated alkyl substances (PFAS) are a group of widely used, man-made chemicals that accumulate over time in humans and in the environment.
- National monitoring activities have detected PFAS in the environment across Europe. The production and use of PFAS in products has resulted in the contamination of drinking water supplies in several European countries. In some highly polluted areas, concentrations of perfluorooctanoic acid (PFOA) and perfluorosulfonic acid (PFOS) in drinking water were above the limit value for individual PFAS proposed in the 2018 recast of the EU Drinking Water Directive (EC, 2017).
- Human biomonitoring has detected a range of PFAS in the blood of European citizens. Though the levels for the most prevalent, studied and regulated PFAS, PFOA and PFOS are decreasing, levels of more 'novel' PFAS are increasing. In some areas, concentrations of PFOA and PFOS in the most exposed citizens were above proposed benchmark levels for adverse effects in humans.
- Due to the large number of PFAS chemicals, a substance-by-substance risk assessment and management approach is not adequate to efficiently prevent risk to the environment and human health from a single PFAS or mixtures of them.
- Taking precautionary risk management actions for groups of chemicals and promoting the use of chemicals that are 'safe-and-circular-by-design' could help to limit future pollution.

What are PFAS and what are they used for?

PFAS are a group of more than 4 700 man-made chemicals (OECD, 2018), the two most well-known of which are perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) (Box 1). PFAS are used in a wide variety of consumer products and industrial applications because of their unique chemical and physical properties, including oil and water repellence, temperature and chemical resistance, and surfactant properties. PFAS have been used in firefighting foams, non-stick metal coatings for frying pans, paper food packaging, creams and cosmetics, textiles for furniture and

outdoor clothing, paints and photography, chrome plating, pesticides and pharmaceuticals. Very limited information is available regarding which specific PFAS are used in which applications and at what levels in Europe.

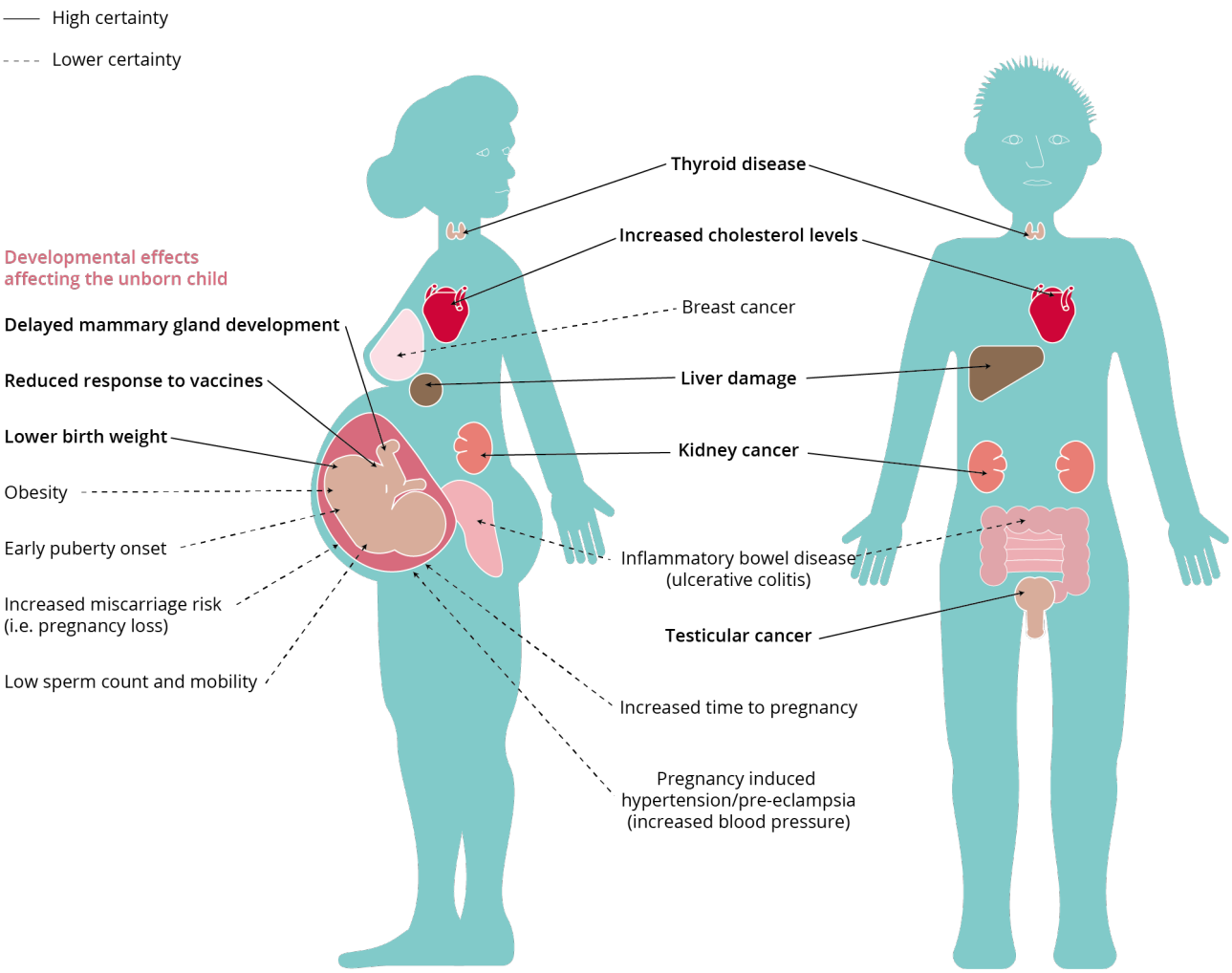
Box 1

PFAS are a group of organic chemicals that contain a stable (unreactive) fluoro-carbon segment. Polyfluorinated PFAS contain both fluoro-carbon and hydro-carbon segments where the non-fluorinated part can degrade and ultimately form perfluorinated PFAS acids, such as PFOA and PFOS. While the long-chain PFAS accumulate in humans, animals and sediment/soil, the short-chain PFAS accumulate in the environment (German EPA, 2017, 2018) due to their persistency and high mobility in air and water. The OECD provides further information on groups of PFAS.

Why are PFAS a concern?

PFAS either are, or degrade to, persistent chemicals that accumulate in humans, animals and the environment. This adds to the total burden of chemicals to which people are exposed (Evans et al., 2016) and increases the risk of health impacts. Of the relatively few well-studied PFAS, most are considered moderately to highly toxic, particularly for children's development. Figure 1 summarises current knowledge of the health impacts of PFAS.

Figure 1. Effects of PFAS on human health



Sources: US National Toxicology Program, (2016); C8 Health Project Reports, (2012); WHO IARC, (2017); Barry et al., (2013); Fenton et al., (2009); and White et al., (2011).

People most at risk of adverse health impacts are those exposed to high levels of PFAS, and vulnerable population groups such as children and the elderly. Fewer studies have investigated effects on biota (Land et al., 2018). Throughout life, people and animals accumulate PFAS in their bodies. In 2018, the European Food Safety Authority (EFSA) re-evaluated the multiple lines of evidence of PFOA and PFOS toxicities, which resulted in significantly lower provisional 'safe' limits, known as the 'tolerable weekly intake' (TWI) (EFSA, 2018). The assessment concluded that a considerable proportion of the European population is expected to exceed the TWI due to intake of PFAS from food and drinking water.

Costs to society arising from PFAS exposure are high, with the annual health-related costs estimated to be EUR 52-84 billion across Europe in a recent study (Nordic Council of Ministers, 2019). The study notes that these costs are likely underestimated, as only a limited range of health effects (high cholesterol, decreased immune system and cancer) linked to exposure to a few specific PFAS were included in the estimates. In addition, PFAS pollution also affects ecosystems and generates costs

through the need for remediation of polluted soil and water. Such costs are currently difficult to assess since information on the number and scale of sites contaminated with PFAS in Europe and on how PFAS impact ecosystems is lacking.

What are the main sources of environmental PFAS pollution?

- Production and use of PFAShave been the main sources of PFAS contamination over time (Wang et al., 2014a, 2014b; Hu et al., 2016) for instance from fluoropolymer production installations and from the use of PFAS-containing firefighting foams (Figure 1). Other sources include PFAS produced and applied to textiles and paper and painting/printing facilities (Danish EPA, 2014). Less is known about potential releases of PFAS from other uses such as oil extraction and mining (Kissa, 2001), and the production of medical devices, pharmaceuticals and pesticides (Krafft and Riess, 2015).
- PFAS in consumer products, such as textiles, furniture, polishing and cleaning agents and creams, may contaminate dust and air, while food contact materials can contaminate food (Nordic Council of Ministers, 2019; Danish EPA, 2018). Drugs and medical devices may be other sources.
- Emissions to the environment occur via industrial waste water releases, as well as emissions to air from industrial production sites followed by deposition onto soil and water bodies. Industrial and urban waste water treatment plants are also a significant source of PFAS, via air, water and sludge (Hamid, et al., 2016; Eriksson et al., 2017).
- Reuse of contaminated sewage sludge as fertilisers has led to PFAS pollution of soil (Ghisi et al., 2019) and water in Austria, Germany, Switzerland and the US (Nordic Council of Ministers, 2019). The recycling of PFAS containing materials such as food contact materials and the formation of volatile fluorinated gases during waste incineration (Danish EPA, 2019) are other possible sources of PFAS pollution.

Where are PFAS found in Europe’s environment?

PFAS are ubiquitous in the aquatic environment and organisms (Valsecchi et al., 2013) across Europe, and have been detected in air, soil, plants and biota (Houde et al., 2006). Areas around industrial production, manufacturing and application sites have been found to be particularly contaminated by PFAS. This has led to contaminated drinking water around factories in Belgium, Italy and the Netherlands, and around airports and military bases in Germany, Sweden and the United Kingdom (IPEN, 2018; Hu et al., 2016). The total number of sites potentially emitting PFAS is estimated to be in the order of 100 000 in Europe (Nordic Council of Ministers, 2019).

Generally, regulated PFAS have been substituted with other short-chain and polymeric PFAS.

Regrettably, several of these 'novel' PFAS and their short chain degradation products are also persistent. In particular, short-chain PFAS accumulate in the environment and have been found to contaminate surface, ground- and drinking water (Eschauzier et al., 2012; Sun et al., 2016; Gebbink et al., 2017), and accumulate in plants (Ghisi et al., 2019), which may lead to increases in human dietary exposure.

Novel PFAS are increasingly detected (Xiao, 2017) in European surface waters. PFAS water pollution has been identified in countries across Europe, including Austria, Denmark, France, Germany, the Netherlands and Sweden, as well as outside the EU. Several PFAS are sufficiently volatile to be considered long-range transboundary air pollutants, implying that emissions outside Europe are transported into Europe where they may accumulate in cold areas such as the Arctic (EEA, 2017). The well-known and regularly monitored PFAS (mainly perfluorinated acids) account only for a fraction of the chemical burden from PFAS present in human blood, the environment and wildlife (Koch et al., 2019).

While both well-known and novel PFAS have been detected in drinking water in non-EU countries (Xiao, 2017; Kaboré et al., 2018; Dauchy, 2019), at present there is little monitoring data available in the EU for drinking water. A case study by the World Health Organization (WHO) documents the story of PFAS contamination of the drinking water of 21 municipalities in the Veneto region of Italy. Industrial activity in the area had polluted both surface waters and ground water, as well as the drinking water of approximately 127 000 citizens (WHO, 2017). Monitoring conducted by the authorities of the Veneto Region found PFOS in 63-100 % of the locations sampled and PFOA in 100 % of the sites.

For comparison, the European Commission proposed a limit value of 0.1 µg/L for each individual PFAS in the 2018 recast of the EU Drinking Water Directive. This draft limit value was exceeded by a factor of 130 for PFOS and 66 for PFOA in samples taken in the Veneto Region.

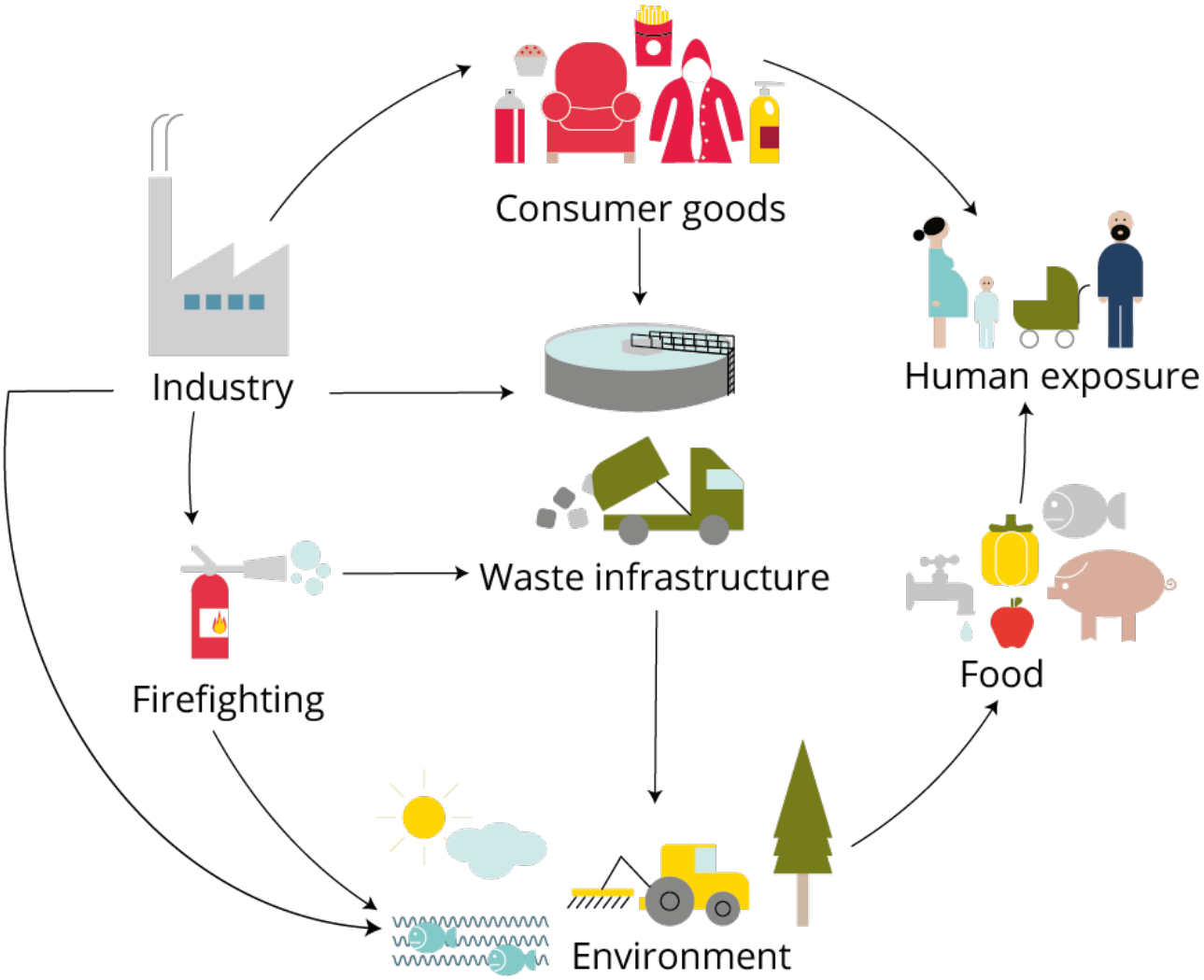
PFOS and their derivatives are included as a priority hazardous substance under the EU Water Framework Directive (EU, 2013), with a much lower Environmental Quality Standard (AA-EQS) limit value of 0.65 ng/L (0.00065 µg/L) in inland surface waters and 0.13 ng/L in seawater. Member States are due to report on compliance with the PFOS EQS by 2021. Samples taken in 2013 in Northern Europe exceeded this EQS in 27 % of river sites and 94 % of Baltic Sea and Kattegat seawater (Nguyen et al., 2017).

What are the main routes of human exposure to PFAS?

The main exposure pathways for human and environmental exposures are shown in Figure 2. For the general population, PFAS sources include drinking water, food, consumer products and dust (EFSA, 2018). In food, fish species at the top of the food chain and shellfish are significant sources of PFAS exposure. Livestock raised on contaminated land can accumulate PFAS in their meat, milk and eggs (Ingelido et al., 2018; Numata et al., 2014). Direct exposure may also come via skin creams and

cosmetics (Danish EPA, 2018; Schultes et al., 2018) or via air from sprays and dust from PFAS-coated textiles. There is little knowledge on uptake via skin and the lungs, which can be severely affected by PFAS (Nørgaard et al., 2010; Sørli et al., 2020). Consumer exposure may also occur via other routes such as via floor, wood, stone, and car polishing and cleaning products. Groups that may be exposed to high concentrations of PFAS include workers and people eating or drinking water and foods contaminated via PFAS treated food contact materials (Susmann et al., 2019). Though PFAS are used in drugs and medical equipment, there is little information on exposure via these routes.

Figure 2: Typical PFAS exposure pathways



PFAS are transferred in the womb from mother to child and unless exposure decreases with age, the PFAS body burden increases due to bioaccumulation (Koponen et al., 2018). Evidence of internal PFAS exposure in humans is available from several national human biomonitoring studies conducted inside and outside Europe. Men generally have higher PFAS body burdens and serum levels (Ingelido et al., 2018) because they excrete fewer PFAS. For the most regulated PFAS, such as PFOA and PFOS, consistent declines have been observed over the past 10-20 years in Europe (e.g. in Belgium, Denmark, Finland, Germany, Spain and Sweden). This decrease in levels in humans is likely to result from reduced exposure as a result of regulatory and non-regulatory action on consumer products, such as food contact materials (Susmann et al., 2019) and textiles (Greenpeace, 2017).

Despite the decreases in long-chain PFAS levels in human blood, concentrations of PFOA and PFOS measured in human blood still exceed the EFSA benchmark dose levels (known as $BMDL_5$). This is particularly true for children and highly exposed sections of the European population (Buekers et al., 2018). The $BMDL_5$ reflect the concentration in blood at which critical effects occur (cholesterol effects for adults and immune-toxicity for children) and are the basis for the provisional TWIs for PFOA and PFOS (EFSA, 2018).

The above mentioned human biomonitoring study in the Veneto Region investigated human exposure to PFOA and PFOS in the period 2015-2016 among 257 Italian residents of contaminated areas and 250 residents of background areas (Ingelido et al., 2018). The PFOA blood concentrations of residents of contaminated areas were 9-64 times higher than those of the background population. For PFOS, the levels were 1.4-1.6 times higher. Levels of PFOA in the highly exposed population were 0.2 to 26 times greater than the EFSA $BDML_5$, while for PFOS, the figure was 0.3-1.3 times. EU research projects, such as Human Biomonitoring for Europe (HBM4EU) (Box 2), are currently working to produce a representative picture of PFAS exposure for the European population, as well as investigating links between exposure and health effects.

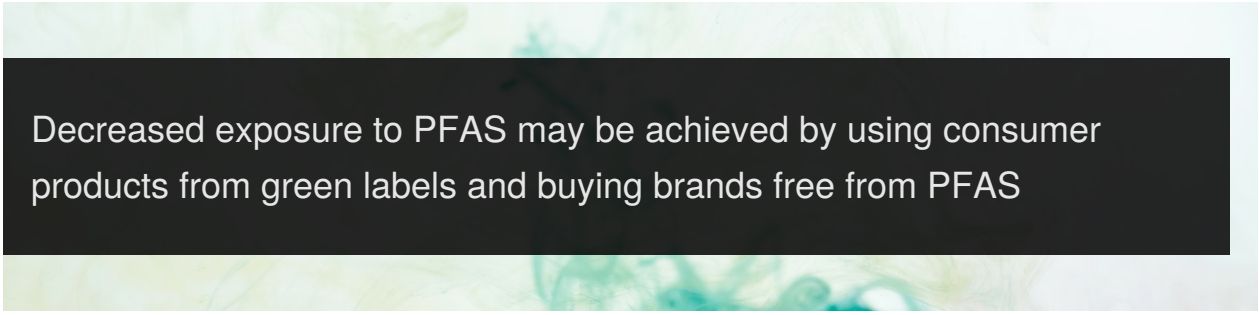
Box 2

The Human Biomonitoring for Europe (HBM4EU) initiative is a 5-year EU Horizon 2020 research programme designed to translate human biomonitoring science into policy-relevant knowledge. A main task within the project is to generate representative chemical exposure data for the European population through harmonised human biomonitoring. PFAS is one of the 18 HBM4EU priority substance groups investigated by HBM4EU to better understand exposure and effects on health.

How can consumers avoid PFAS?

It is difficult for citizens to totally avoid exposure to PFAS. Using PFAS-free personal care products and cooking materials and avoiding direct contact with PFAS-containing products helps to reduce exposure. Decreased exposure to PFAS may be achieved by using consumer products from green labels and buying brands free from PFAS. General and specific guidance to consumers and business on how to find PFAS-free alternatives is provided by consumer organisations and some national

institutions (see Danish EPA, German EPA and Swedish KEMI).



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What is being done in the EU and globally?

Measures to reduce PFAS pollution are in place, mainly addressing well-known PFAS substances and their precursors. PFOS and PFOA are listed under Annex A of the Stockholm Convention on persistent organic pollutants (POPs), implying that parties to the Convention should 'eliminate the production and use' of the chemicals.

At EU level, PFOS is restricted under the EU POPs Regulation (EU, 2019). PFOA and its precursors are currently restricted under the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation (EU, 2006), including their presence in products made or imported into the EU. This will soon be replaced by a new restriction under the POPs Regulation, which will have more limited derogations, following a decision taken at the Stockholm Convention.

A number of other PFAS are on the REACH list of Substances of Very High Concern (SVHCs). In June 2019, GenX (a short-chain PFAS substitute for PFOA in fluoropolymer production) was the first chemical added to the SVHC list on the basis of its persistent, mobile and toxic properties posing a threat to drinking water and the environment. Several PFAS are on the Community Rolling Action Plan for evaluation over the coming years. As mentioned above, PFOA and PFOS are priority hazardous substances under the Water Framework Directive (EC, 2017; EU, 2000).

Across Europe, several countries have been active in monitoring PFAS in environmental media as well as in humans and products. Some countries have set national limit values for water and soil (Denmark, Germany, the Netherlands and Sweden), for textiles (Norway) and for food contact materials (Denmark). Several EU Member States have set drinking water limits for specific PFAS and for groups of PFAS (Dauchy, 2019). In June 2019, Denmark announced a ban on PFAS-treated food contact materials, to enter into force in 2020.

Looking ahead

With more than 4 700 known PFAS, undertaking substance-by-substance risk assessments and

comprehensive environmental monitoring to understand exposure would be an extremely lengthy and resource-intensive process. As a result, complementary and precautionary approaches to managing PFAS are being explored.

This includes the regulation of PFAS as a class, or as subgroups, based on toxicity or chemical similarities. The proposal to establish a new 'group limit' value for PFAS of 0.5 µg/L, in addition to limits for 16 individual PFAS of 0.1 µg/L in drinking water under the recast of the EU Drinking Water Directive is currently under consideration at EU level. Such measures can be supported by cost-effective and targeted monitoring of PFAS in the environment to provide early warning signals of pollution.

In June 2019, the European Council of Ministers (EC, 2019) highlighted the widespread occurrence of PFAS in the environment, products and people, and called for an action plan to eliminate all non-essential uses of PFAS (Cousins et al., 2019).

The move towards zero pollution requires that product life cycles are made safer from the start (Warner and Ludwig, 2016), based on the concept of safe-and-circular-by-design (van der Waals et al., 2019). This approach offers opportunities to protect the health of Europe's citizens and environment at the same time as driving innovation for safer chemicals.

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