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7 Human and Ecological Health Effects of select PFAS

This section discusses both the information related to assessing health effects of PFAS in humans (Section 7.1) and the adverse effects on ecological (nonhuman) species (Section 7.2). Section 7.1 provides information on human biomonitoring and exposure, toxicokinetics, toxicology in mammalian species, and human epidemiology for long-chain and short-chain PFAAs and the fluorinated ether carboxylates (FECAs) commonly known as the GenX chemical HFPO-DA and ADONA. The section is supplemented by additional material on each of these topics, which is included as Section 17.2. Section 7.2 is organized to include ecological toxicology information on invertebrates (aquatic, benthic, terrestrial), vertebrates (fish, birds, reptiles, amphibians, mammals), and plants. PFAS ecotoxicology data summary tables have been developed as separate Excel spreadsheets.

For further information on the scientific names and carbon chain length of PFAAs addressed in these sections, see ITRC Naming Conventions Fact Sheet (ITRC 2018a) and Section 2.2 of this document. Use of the human health effects information in guidance values is discussed in Section 8.3 and in site risk assessment in Section 9.1.

Section Number	Topic
7.1	Human Health Effects
7.2	Ecological Toxicology

7.1 Human Health Effects

The PFAS discussed in this section and in Section 17.2 include perfluorocarboxylic acids (PFCAs) with 4–14 carbons and perfluorosulfonic acids (PFSAs) with four or more carbons. Also covered are two FECAs: ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate (also known as perfluoro-2-propoxypropanoic acid, PFPrOPrA and as the GenX chemical hexafluoropropylene oxide [HFPO] dimer acid; and 4,8-dioxa-3H-perfluorononanoate, commonly known as ADONA. These FECAs are replacements for PFOA as processing aids in certain fluoropolymer production. They are included because they are of current interest and health effects data are available. There is little or no publicly available health effects information for most of the many other PFAS used in commerce (Section 2.5), including precursors that can be converted to PFAAs in the environment and in the human body.

The best studied PFAAs are PFOS and PFOA, although considerable information is available for some other PFAS, including PFNA, PFHxS, PFBA, PFBS, and the GenX chemical HFPO-DA. Laboratory animal toxicology studies and human epidemiological studies suggest health effects that may occur as a result of long-term exposure to PFOA and PFOS at environmentally relevant levels. Figure 7-1 summarizes current health effects information, the references for which are discussed in this section. The other PFAS mentioned above cause generally similar effects in animal studies, with toxicity generally occurring at higher doses for the short-chain PFAAs than for long-chain PFAAs. These health effects, discussed in more detail in Sections 7.1.3, and 7.1.4 are the basis for current guidance values and regulations for PFOA, PFOS, and several other PFAS. These are available in a separate Excel file published regularly by ITRC on the fact sheets page.

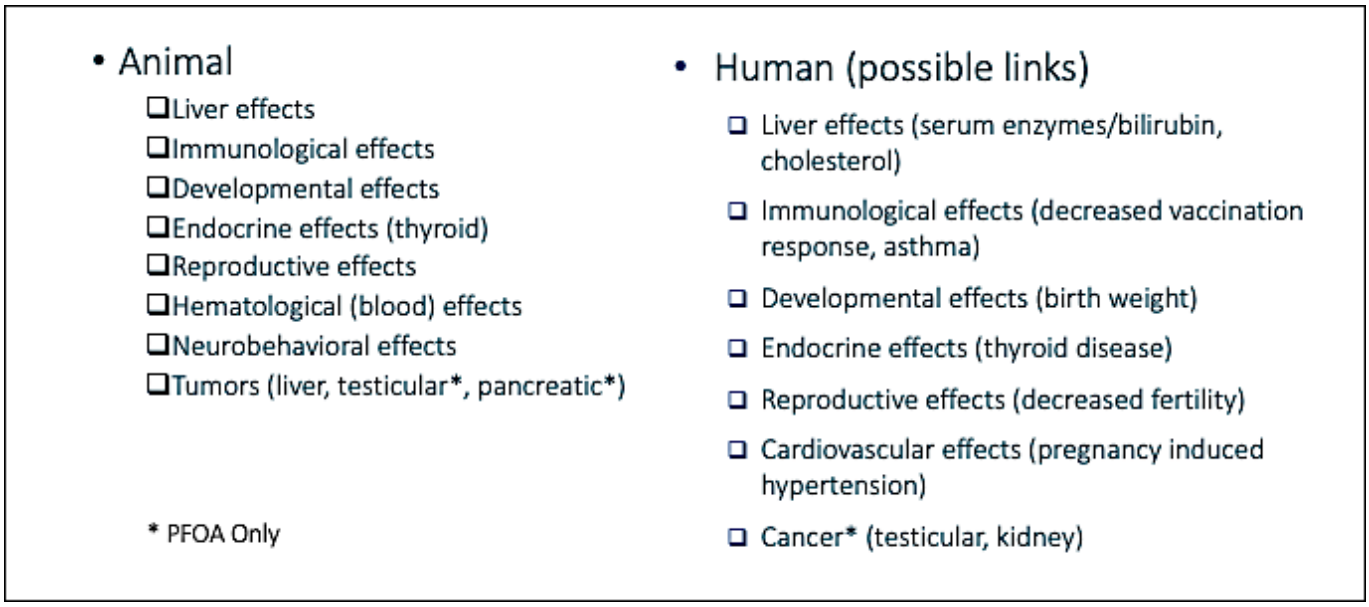

Figure 7-1. Some health effects of PFOA and/or PFOS identified from published studies (not exhaustive).

USEPA has completed draft toxicity assessments for the GenX chemicals and PFBS (USEPA 2018e, d), and USEPA announced in December 2018 that five additional PFAAs (PFNA, PFBA, PFHxA, PFHxS, PFDA) will be reviewed for toxicity assessment through the Integrated Risk Information System (IRIS), but no timeline has been established (USEPA 2019e).

Much of the information presented here is recent, and new studies continue to become available. Additionally, it should be noted that it was not possible to include all relevant citations, particularly for those compounds with large health effects data sets. Further information on the topics in this section can be found in databases such as the National Library of Medicine's PubMed (a database containing citations to relevant peer-reviewed publications), and in reviews such as Kirk (2018) and Lau (2012), and in several chapters of the Agency for Toxic Substances and Disease Registry (ATSDR) draft toxicological profile (ATDSR 2018e), DeWitt (2015), and NICNAS (2018) for PFAS in general; Australian Department of Health Expert Panel, which is a review of systematic reviews since 2013 and key national and international reports since 2015:

- PFOA: Australia Government DOH (2018); USEPA (2016h, 2016d) and NJDWQI (2017c) NJDWQI (2017a)
- PFOS: USEPA (2016g, 2016c) MDH (2019a), and NJDWQI (2018b)
- PFNA: NJDWQI (2015)
- PFBS: MDH (2017c) and USEPA (2018e) (draft)
- PFBA and PFHxS: MDH (2018a, 2019b)
- GenX chemicals: RIVM (2016), Chemours (posted online by (NC DEQ 2018)), and (USEPA 2018g) draft
- Short-chain PFAAs: Buck (2015) and Danish EPA (2015)
- FECAs: Buck (2015)

Human biomonitoring and sources of exposure are addressed in Section 7.1.1. Information on serum levels of long-chain PFAAs from communities with contaminated drinking water is presented in Table 17-6. The unique toxicokinetic properties of PFAS are discussed in Section 7.1.2. Table 17-7 summarizes available data on PFAS elimination half-lives in humans and experimental animals. The numerous reviews of potential epidemiological associations of health endpoints with PFAAs are discussed in Section 7.1.3. Toxicology studies in mammalian species are summarized in Section 7.1.4, and more detailed toxicology information is presented in Section 17.2.5 and Table 17-8 (provided as a separate Excel file).

Finally, data gaps and research needs are discussed in Section 7.1.5.

7.1.1 Human Biomonitoring and Sources of Exposure

Numerous human biomonitoring studies (such as (CDC 2018, 2019; Olsen et al. 2017)) have demonstrated that certain PFAS, particularly long-chain PFAAs, are present in the blood serum of almost all U.S. residents. Long-chain PFAAs, with half-lives of one to several years, are slowly excreted in humans. Therefore, serum levels are indicators of long-term exposure to long-chain PFAAs and do not fluctuate greatly with short-term variations in exposure. Serum PFAA concentrations originate from direct exposure to the compounds and from metabolism of precursor compounds to PFAAs within the body (reviewed in Kudo (2015)). The largest U.S. general population biomonitoring studies are from the National Health and Nutrition Examination

Survey (NHANES), a nationally representative survey conducted by the Centers for Disease Control and Prevention (CDC), which began monitoring for PFAS in 1999–2000 (Figure 7-2). As can be seen in Figure 7-2, serum PFAS levels in the general population have declined over time, most notably for PFOS. The most recent NHANES monitoring data (2015–2016) include seven PFAAs (PFOA, PFOS, PFNA, PFHxS, PFDA, PFUnDA, PFDoA) and one other PFAS (MeFOSAA); four additional PFAS (PFBS, PFHpA, PFOSA, EtPFOSA) that were infrequently detected in earlier rounds of NHANES were not monitored in 2015–2016 (CDC 2019). Other adult U.S. general population biomonitoring data come from four studies of blood donors in 2000–2015 (Olsen et al. 2017) and the California Environmental Contaminant Biomonitoring Program (CA OEHHA 2011).

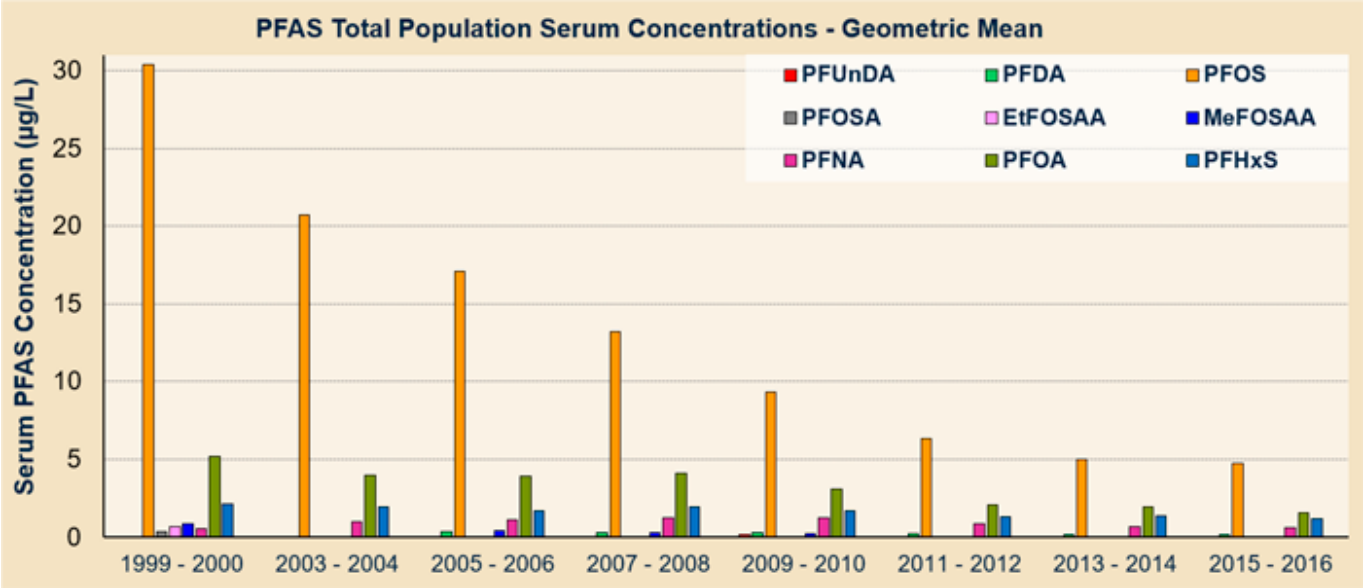

Figure 7-2. Geometric mean serum concentrations (ng/ml) of selected PFAAs (NHANES, 1999-2016).

In the general population, where this is no specific source of PFAS contamination and PFAA concentrations in drinking water and serum are in the typical “background” range, the primary sources of exposure to PFAAs and their precursors appear to be food and food packaging, and consumer products (particularly nonpolymer aftermarket treatments and coatings; Section 2.5), and house dust formed from such consumer products (Trudel et al. 2008; Fromme et al. 2009; Vestergren and Cousins 2009; Beesoon et al. 2012; Gebbink, Berger, and Cousins 2015). PFAS have been detected in air (ATSDR 2018e), and inhalation is therefore an additional potential exposure pathway. Serum levels of PFOS and PFOA documented by NHANES data appear to indicate that the phaseout of production and use of these chemicals in most products has resulted in decreased PFOS and PFOA exposures for the general population from these sources. As this occurs, the relative contribution from drinking water to these PFAAs will increase (where they are present in the drinking water).

In communities near sources of PFAS contamination, exposures that are higher than those in the general population can result from ingestion of contaminated drinking water or consumption of fish from contaminated waters. As PFAS concentrations in drinking water increase, the contribution of drinking water to the total body burden increases and typically dominates an individual’s exposure. Information on serum levels of long-chain PFAAs from communities with contaminated drinking water in several U.S. states and other nations is found in Table 17-6. Finally, occupational exposures to workers can be higher than exposures from environmental media.

Specific considerations and exposure routes relevant to PFAS exposures in the fetus, breast-fed and formula-fed infants, and young children are discussed in Section 17.2. Also see Section 17.2.2 for additional discussion of human biomonitoring and sources of human exposure.

7.1.2 Toxicokinetics

PFAAs have unique toxicokinetic properties as compared to other types of persistent organic pollutants (POPs). Unlike most other bioaccumulative organic compounds (for example, dioxins, PCBs), PFAAs do not have a high affinity for adipose tissue (that is, fat). In contrast, PFAAs are water soluble, have an affinity for proteins, and generally distribute primarily to the liver, blood serum, and kidney (Bischel et al. 2011; Lau 2012, 2015; Kato 2015). PFAAs, GenX chemicals, and ADONA are not metabolized (meaning they do not break down to other PFAS). However, some PFAS that are PFAA precursors can be metabolized to PFAAs within the body.

In general, short-chain PFAS are excreted more rapidly than longer chain PFAS in humans and other mammalian species. The excretion rates for specific PFAS can vary substantially between species, and in some cases between males and females of the same species. Table 17-7 summarizes available data on PFAS elimination half-lives in humans and experimental animals. Half-lives in laboratory animals (rodents and nonhuman primates) generally range from hours to several months for long-chain PFAS, and hours to several days for short-chain PFAS. Human half-lives for PFAS are longer than in other mammalian species, with estimates of several years for long-chain PFAAs and several days to one month for shorter chain PFAAs such as PFBA, PFHxA, and PFBS. Because of the much longer human half-lives, animal-to-human comparisons must account for the much higher internal dose (for example, blood serum level) in humans than in animals from the same administered dose.

Toxicokinetics relevant to developmental exposures to PFAAs are important because developmental effects are considered to be sensitive endpoints for toxicity of long-chain PFAAs, and some human studies have found associations of long-chain PFAAs with decreased fetal growth. PFAAs cross the placenta (reviewed in Lau (2012) and Kudo (2015)) and are present in breast milk (Luebker, Case, et al. 2005; White et al. 2009) (Kato 2015), and long-chain PFAAs have been found in cord blood (for example, (Wang et al. 2019) and amniotic fluid (Stein et al. 2012; Zhang, Sun, et al. 2013). In human infants, exposures from breast milk result in substantial increases in long-chain PFAA serum levels during the first months after birth (Fromme et al. 2010; Mogensen et al. 2015). Exposures to infants from formula prepared with PFAS-contaminated water are also higher than in older individuals due to their higher rate of fluid consumption (USEPA 2011a).

Toxicokinetic factors called clearance factors, which indicate bioaccumulative potential, can be used to relate external doses (mg/kg/day) of PFOA and PFOS to steady-state serum levels (ng/L). When combined with average water ingestion rates (USEPA 2011a), these factors can be used to predict that the expected average increases in the levels of PFOA or PFOS in blood serum from long-term drinking water exposure are 100-fold or greater than the concentration in the drinking water (Bartell 2017; NJDWQI 2017a; Post, Gleason, and Cooper 2017).

Finally, toxicokinetics in rodents (Loveless et al. 2006; De Silva et al. 2009) and humans (Zhang, Beesoon, et al. 2013; Gao et al. 2015; Beesoon et al. 2011) may differ among isomers of the same PFAA.

See Section 17.2.3 for additional discussion of PFAS excretion and excretion rates, toxicokinetics relative to developmental exposure, the relationship of human exposure to serum levels, and isomer-specific toxicokinetics.

7.1.3 Human Epidemiology Studies

The epidemiological database for long-chain PFAAs is more extensive than for many other environmental contaminants. Based on publications available through the National Library of Medicine's PubMed database, well over 100 human studies have examined associations (that is, statistical relationships) between PFAS, primarily long-chain PFAAs, and a wide variety of diseases and health endpoints (NJDWQI 2018a). Some effects, such as changes in serum lipids, liver biomarkers, uric acid levels, thyroid endpoints, vaccine response, and fetal growth, have been evaluated in multiple studies and populations, while only one or a few studies were located for many other effects.

These studies can be categorized based on the type of population evaluated: general population, communities with contaminated drinking water, or occupationally exposed workers. Almost all of these studies were published within the past 10 years, with the exception of a small number of occupational studies from a few years prior to that time.

Although discussion of individual epidemiological studies is beyond the scope of this section and the corresponding appendix section, evidence for associations and/or causality for some PFAAs and certain health effects (for example, increased cholesterol, increased liver enzymes, decreased vaccine response, thyroid disease, and for PFOA, some types of cancer) has been evaluated by various academic researchers and government agencies. The conclusions of some of these evaluations are discussed briefly below, with additional detail provided in Section 17.2.4.

For some health endpoints, there is general consensus for consistent evidence for association with one or more long-chain PFAAs, while conclusions differ among evaluations by different groups of scientists for other endpoints. For additional endpoints, data are too limited to make a conclusion, results are inconsistent, or there is no evidence for an association. The general reviews cited in Section 17.2.4 include detailed discussions of epidemiological data for PFOA, PFOS, and PFNA. In-depth reviews for other individual PFAAs (for example, PFHxS, PFDA, PFUnA) are not available.

As shown in Table 7-1, associations in human epidemiological studies of PFAAs (primarily PFOA and PFOS) for some endpoints (for example, increased liver enzymes, decreased fetal growth, decreased vaccine response) are consistent with animal toxicology studies (Section 7.1.4). For serum lipids (for example, cholesterol), conflicting observations (increases in humans versus decreases in rodents) may be impacted by differences in the fat content in the diets of humans versus

laboratory animals and/or large differences in the exposure levels in human versus animal studies (Tan et al. 2013; Rebholz et al. 2016).

Associations of some health endpoints with certain PFAAs are generally, although not totally, consistent, and some evaluations have concluded that the data for certain effects support multiple criteria for causality. However, risk-based toxicity factors (Reference Doses for noncancer effects and slope factors for cancer risk) developed by most government agencies are based on dose-response relationships from animal data, with the human data used to support the hazard identification component of toxicity factor development. A major factor that has precluded the use of human data in the dose-response component of toxicity factor development is the concurrent exposure to multiple PFAAs in most or all study populations. Because serum levels of co-occurring PFAAs tend to correlate with each other, it is difficult to determine the dose-response relationship for individual PFAAs. Notwithstanding, German Human Biomonitoring Commission (2018) the German Environment Agency (2016) developed Human Biomonitoring Values (serum levels below which adverse effects are not expected) and the European Food Safety Authority (EFSA 2018) developed Tolerable Weekly Intakes for PFOA and PFOS based on human data from the general population. These values are lower than many of the values that are based on toxicity data from animals. It is noted that the approaches and policies used to develop these European human-based values may differ from those used by U.S. agencies in toxicity factor development.

See Section 17.2.4 for additional discussion of epidemiologic studies that have been conducted on PFAS.

7.1.4 Animal Toxicology Studies

This section focuses on the most notable toxicological effects in mammalian studies of certain PFCAs, PFSAs, and FECAs. All PFAS covered in this section for which data are available cause increased liver weight; additional effects common to some of these PFAS include immune system, hematological (blood cell), and developmental toxicity, as well as more severe types of liver toxicity. Of the four PFAS that have been tested for carcinogenicity in rodents, PFOA, PFOS, and the GenX chemical HFPO-DA caused tumors while PFHxA did not.

In general, toxicity is dependent on both intrinsic potency of the compound (Gomis et al. 2018) and its toxicokinetics. Longer chain PFAAs are generally toxic at lower administered doses than shorter chain compounds because their slower excretion results in a higher internal dose from the same administered dose. Similarly, for those PFAS that are excreted much more rapidly in female rats than in males (Section 7.1.2 and Table 17-7), higher doses in females than in males are needed to achieve the same internal dose.

Toxicological data from animal studies are used as the basis for almost all human health toxicity factors (for example, Reference Doses, cancer slope factors) for PFAS, with the few exceptions from Europe that are based on human data (Section 7.1.3); all current PFAS standards and guidance values for environmental media are based on animal toxicology data (also see Sections 8.3 and 9.1). As is the case for toxicology studies in general, the doses used in most of these studies are higher than the doses to which humans are generally exposed from environmental contamination. Conversely, unlike most other environmental contaminants, PFAS have been associated with health effects in humans at much lower exposure levels than the doses used in animal toxicology studies.

Table 17-8 (provided as a separate Excel file)provides information on toxicological effects in mammalian species (hazard identification information) for the following PFAS:

- PFCAs including PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnA, and PFDoA
- PFSAs including PFBS, PFPeS, PFHxS, PFHpS, and PFOS
- FECAs including ADONA and the GenX chemical HFPO-DA.

Section 17.2.5 also summarizes information on systemic effects; reproductive and developmental effects, and chronic toxicity and tumorigenicity of these PFAS.

- Largest publicly available toxicological data sets for: PFOA and PFOS
- Considerable data for: PFBA, PFHxA, PFNA, PFDA, PFBS, and the GenX chemicals HFPO-DA and its ammonium salt
- One or a few studies for: PFHpA, PFUnA, PFDoA, PFHxS, and ADONA
- No toxicological data were located for PFPeA, PFTrDA, PFTeDA, PFPeS, PFHpS, PFNS, or PFDS.

Most studies were conducted in rats and mice, with a few studies in nonhuman primates (monkeys) and other species such as rabbits. The National Toxicology Program (NTP 2019b, c) has conducted 28-day studies of seven PFAS (PFHxA, PFOA,

PFNA, PFDA, PFBS, PFHxS, PFOS) in male and female rats that evaluated numerous toxicological endpoints and provided serum PFAA data for each dosed group; results of these studies are included in Table 17-8 (provided as a separate Excel file). Although the doses at which effects occurred are not provided in this section or in the supporting appendix material, it is emphasized that No Observed Adverse Effect Level (NOAELs) and Lowest Observed Adverse Effect Level (LOAELs) vary widely between compounds for a given endpoint, between different endpoints for the same compound, and between species (and sexes in some cases) for the same compound and endpoint. Furthermore, the effects noted may not have been observed in all studies in which they were evaluated.

NTP has also completed a chronic carcinogenicity study of PFOA in rats that assessed the contribution of combined gestational and lactational (perinatal) exposure. The draft report (NTP 2019a)for this study concludes that there was clear evidence of carcinogenic activity in male rats based on the increased incidence of liver tumors and pancreatie acinar cell tumors, and some evidence of carcinogenic activity in female rats based on increased incidence of pancreatic acinar cell tumors, and the peer review panel for this study agreed with these conclusions at a December 2019 meeting.

See Section 17.2.5 for additional discussion of studies in animals that have evaluated the effects of PFAS on noncancer and cancer endpoints.

7.1.5 Data Gaps and Research Needs

Although many studies relevant to health effects of PFAAs have become available in the last few years, important data gaps remain for most of the PFAAs and FECAs discussed here and in Section 17.2, as well as for many additional PFAS used in commerce or found in AFFF. The data gaps (discussed in more detail in Section 17.2.6) include:

- Human half-lives and other toxicokinetic data are not available for some PFAS found in drinking water and other environmental media.
- Currently available data indicate that reactive intermediates may form in the body from the metabolism of PFAA precursors to PFAAs. More studies are needed to understand the toxicologic significance of these intermediates.
- With the exception of PFOA, there is a lack of epidemiologic data from communities exposed to AFFF, PFOS, and/or other PFAS in drinking water.
- Additional toxicology data are needed for some PFAAs found in environmental media, including drinking water. In particular, very little toxicologic data are available for PFHpA, and no information was located for PFPeA. There is also a need for toxicologic studies on the effects of PFAS mixtures.
- Multigeneration studies of the reproductive and developmental effects of additional PFAS are needed.
- Chronic toxicity and carcinogenicity studies are currently available for only four PFAS (PFHxA, PFOA, PFOS, GenX), and are needed for PFHxS, PFNA, ADONA, and other PFAS to which humans may be exposed.
- The majority of the many thousands of PFAS, including those in commercial use, have very limited or no toxicity data. This is a critical data gap in health effects information for PFAS.
- Similarly, current NHANES biomonitoring includes only 11 PFAS, primarily PFAAs. There is limited or no biomonitoring data for many other PFAS produced or used in the United States, some of which are known to be bioaccumulative in humans.

7.2 Ecological Toxicology

This section is organized around currently available toxicity information for invertebrates (aquatic/benthic/terrestrial), vertebrates (fish, birds, reptiles/amphibians, mammals), and plants. Toxicological data were obtained from a general literature review as well as querying of the USEPA Ecotox Database (USEPA 2019c). However, as discussed below, this is an active area of research, and interested readers are encouraged to query the literature for updated research and reviews. PFAS ecotoxicology data summary tables have been developed as a separate Excel spreadsheet. The Excel file includes ecotoxicology data for Table 7-1 aquatic species, Table 7-2 terrestrial species and Table 7-3 mammalian species.

7.2.1 Introduction

Biomonitoring studies across a variety of organisms, habitats, and geographies show that certain PFAS compounds can accumulate in wildlife and that exposures are occurring on a global scale (Reiner and Place 2015; Giesy and Kannan 2001). Therefore, it is important to understand how such exposure and bioaccumulation may manifest in adverse effects, particularly as they relate to ecological communities. Information on bioaccumulation of PFAS is addressed in Section 6.5. Section 7.1 focused on the toxicological effects of PFAS on humans and summarized toxicity data from experimental exposures of laboratory animals. This section provides an overview of available, published toxicological data relating

exposure of PFAS to toxic effects on aquatic, benthic, and terrestrial organisms, with the goal of broadening the reader's understanding of known or potential effects in ecological systems, as well as highlighting areas where more data are needed. This information can also be applied for use in ecological risk assessments (ERAs), particularly in light of the fact that ecological risk of PFAS is currently neither well understood nor uniformly assessed or regulated. However, the reader is encouraged to review the primary source literature from which cited ecotoxicity values have been derived to confirm and understand the basis and assumptions of the cited literature before using this information in an ERA.

This review shows that ecotoxicity data is available for aquatic invertebrates, particularly for PFOA and PFOS. However, no spiked sediment toxicity studies are available for benthic invertebrates. Although there are numerous studies on PFAS exposure in terrestrial vertebrates (for example, mammals, reptiles, birds), and ample toxicological studies in laboratory animals, there is, overall, relatively little to no ecologically relevant toxicity data for terrestrial vertebrates in the wild. Although some mechanistic studies have been conducted with aquatic organisms, little has been done with other organisms and even less has been done with different classes of PFAS in aquatic and terrestrial wildlife.

The focus of most ecotoxicity studies to date has been primarily on PFOS and PFOA. Therefore, most of the data discussed and summarized in this section are for those compounds. However, data for other PFAS compounds, including short-chain PFAS and precursors (Section 2.2), are also presented where available. Given the historical differences among older analytical methods and more recent advances in analyzing PFAS, the focus of the ecotoxicity studies covered in this review is generally on those published from approximately the year 2000 and later.

PFAS ecotoxicology data summary tables have been developed as a separate Excel spreadsheet containing toxicity information for PFAS compounds:

- Table 7-1: aquatic and benthic invertebrates, aquatic plants, and fish
- Table 7-2: terrestrial invertebrates, microorganisms and plants
- Table 7-3: mammalian wildlife

It is important to note that neither this spreadsheet nor this section is intended to represent an exhaustive review of PFAS ecotoxicity studies. Ecotoxicity of PFAS is an area of active research, with new information emerging regularly. Toxicological effects presented and discussed herein are generally those considered most relevant to ecological communities—mainly survival, growth, and reproduction. Both acute and chronic exposure studies are included. Although data have been generated for other toxicological endpoints, these studies are not the focus of this section, but may occasionally be referenced.

In general, studies indicate that PFAS toxicity in invertebrates is chemical-specific and varies with the type of organism and environmental factors. There is a paucity of field studies for avian and mammalian wildlife species, and confounding factors such as the co-occurrence of other stressors (other pollutants, physical stressors, etc.) make it difficult to definitively associate PFAS exposure with adverse outcomes. Only one recent avian study on tree swallow egg hatching outcomes is known to date (Custer et al. 2014), and field-based effects studies on mammals are difficult to find (ECCC 2018). However, laboratory animal studies suggest potential relationships between PFAS tissue concentrations and immunological, hematological, liver, kidney, and reproductive effects (DeWitt 2015; ECCC 2018).

The abundance of biomonitoring data suggests that PFAS exposure is occurring in wildlife; however, the lack of toxicity data for this group of organisms represents a significant data gap. This highlights the need for additional study of this class of compounds in general, as well as the need for expansion of toxicity studies to a larger group of PFAS and to a greater variety of taxa, and for field studies that may assess population-level effects.

Relative aquatic toxicity for PFAS is discussed in the following sections using descriptive criteria developed by the USEPA within their Design for the Environment Program for the Alternatives Assessments and the Safer Choice Program. These criteria are expressed as relative toxicity based on effects concentrations ranging from less than 0.1 mg/L (very high toxicity) to greater than 100 mg/L (low toxicity); criteria are provided in Table 7-4.

Table 7-4. Hazard criteria for aquatic toxicity studies from USEPA (in mg constituent/L water)

Toxicity	Very High	High	Moderate	Low	Very Low
USEPA: Aquatic Toxicity (Acute)	<1.0	1–10	>10–100	>100	NA

Toxicity	Very High	High	Moderate	Low	Very Low
USEPA: Aquatic Toxicity (Chronic)	<0.1	0.1–1	>1–10	>10	NA
Note: Refer to the PFAS ecotoxicology data summary Table 7-1 in the separate Excel spreadsheet for toxicological endpoints and values.					

7.2.2 Invertebrates

7.2.2.1 Aquatic

There are more toxicity data available for PFOS than for other PFAS compounds. A summary of the range of acute toxicity to aquatic organisms can be found in Table 7-5. PFAS have a very wide range of toxicities to aquatic organisms under acute exposure scenarios following the USEPA Hazard Criteria (Table 7-4), but overall, they would be classified as having moderate to low toxicity. One exception with this generalization is that of mussel exposures to PFOS and PFOA in the marine environment, where no effect was seen at 0.0001 mg/L but was measured at 0.1 mg/L (Fabbri et al. 2014); this would result in high hazard using the USEPA Hazard Criteria.

Compared to acute studies, there are relatively few chronic studies in aquatic invertebrates. PFAS for which we have chronic effects data include PFOS, PFOA, and PFNA. Life cycle tests with multiple taxa have been conducted to evaluate the chronic toxicity of PFOS to freshwater aquatic invertebrates. The chironomid (*Chironomus tentans*) is currently reported as having the greatest sensitivity to chronic exposure, where effects are seen at concentrations less than 0.0023 mg PFOS/L. In the marine environment, a life cycle toxicity test with the saltwater mysid, yielded a concentration of 0.24 mg PFOS/L based on growth and number of young produced (Drottar and Krueger 2000b). Finally, there was one chronic study available for PFNA in which a 21-day exposure of *Daphnia magna* resulted in significant decrease in growth at 0.04 mg/L (Lu et al. 2015).

Table 7-5. Summary of aquatic invertebrate ecotoxicity data for PFAS

PFAS	Carbon Chain Length	Range of Toxicity Values–EC or LC50 (mg/L)*	References
Acute Studies			
PFBA	4	182–521	(Ding et al. 2012) (Barmentlo et al. 2015)
PFBS	4	2,183	(Ding et al. 2012)
PFHxA	6	1,048	(Barmentlo et al. 2015)
PFOS	8	59–169	(3M Company 2003) (Boudreau et al. 2003)
PFOS-Marine	8	0.0001–9.4	(Fabbri et al. 2014); (Robertson 1986)
PFOA	8	131–477	(Ji et al. 2008; Ding et al. 2012)
PFOA-Marine	8	0.0001–0.1	(Fabbri et al. 2014)
PFNA	9	31–151	(Zheng et al. 2011)
PFDA	10	26–163	(Ding et al. 2012)
PFUnA	11	19–133	(Ding et al. 2012)
PFDoDA	12	28–66.3	(Ding et al. 2012)
Chronic Studies			
PFBS	4	LOEC 4.8	(Sant et al. 2018)
PFOS	8	NOEC <0.0023–94.9	(MacDonald et al. 2004) (Boudreau et al. 2003)
		LOEC 0.0023-42.9	

PFAS	Carbon Chain Length	Range of Toxicity Values–EC or LC50 (mg/L)*	References
PFOA	8	NOEC 3.125– >100	(Li 2010; Ji et al. 2008)
		LOEC 6.25–12.5	
PFNA	9	LOEC 0.04	(Lu et al. 2015)
Note: Refer to the PFAS ecotoxicology data summary Table 7-1 in the separate Excel spreadsheet for toxicological endpoints and values. EC50 = median effective concentration. The concentration of test substance which results in a 50 percent reduction in growth or growth rate LC50 = Concentration that is lethal to 50% of test population LOEC = lowest observed effect concentration NOEC = no observed effect concentration			

Benthic Organisms and Sediment Toxicity

Toxicity to benthic organisms is generally the result of exposure to the chemical in overlying water and/or sediment porewater. Effects levels (for example, LC50, EC50, NOEC) based on sediment concentrations (for example, mg of chemical/kg of sediment) of PFAS were not identified in publicly available studies. Bakke et al. (2010) provided PFOS concentration ranges for sediment quality classified as background, good, moderate, bad, and very bad. The PFOS threshold for "good" sediment, for which no toxic effects are expected, is 0.22 mg/kg; however, no toxicity data are provided to justify this value. A few aquatic toxicity studies have been conducted on benthic organisms for PFAS, with most focusing on PFOS. With so few studies available and with variability in test organisms and testing methods, it is difficult to define PFAS toxicity thresholds for benthic organisms or to determine if benthic organisms are similarly sensitive to PFAS compared to other aquatic invertebrates. Table 7-6 summarizes toxicity ranges for PFOS, PFOA, and PFBS from the limited available information for benthic organisms.

Table 7-6. Summary of benthic invertebrate ecotoxicity data for PFAS

PFAS	# of Effects Conc.*	Range of Toxicity Values (mg/L)	References
Acute (freshwater and saltwater)			
PFOS (acid)	n=5	0.00001 (NOEC) – 59 (LC50)	(Drottar and Krueger 2000b; Fabbri et al. 2014; OECD 2002; MPCA 2007)
PFOA (acid)	n=2	0.00001 (NOEC) – 0.0001 (LOEC)	(Fabbri et al. 2014)
Chronic (freshwater and saltwater)			
PFOS (salt)	n=22	<0.0023 (NOEC) – >0.150 (EC50)	(MacDonald et al. 2004)
PFOA (acid)	n=2	0.0089, 100 (NOEC, chronic)	(MacDonald et al. 2004; Stefani et al. 2014)
PFBS (acid)	n=2	0.0077 (NOEC, chronic)	(Stefani et al. 2014)
Note: Refer to Table 7-1 in the separate Excel spreadsheet for the total number of reported effect and no-effect concentrations (from one or more studies, as well as for toxicological endpoints and values.			

7.2.2.2 Terrestrial Invertebrates

Compared to aquatic invertebrates, there are relatively fewer studies on the effects of PFAS on terrestrial invertebrates. Overall, these few studies indicate a moderate to high toxicity. See Table 7-2 in the separate Excel spreadsheet for available toxicity information for PFOA and PFOS in terrestrial invertebrates. Brignole et al. (2003), as summarized in Beach et al. (2006), summarized results of acute oral and dermal studies of PFOS conducted on the honeybee (*Apis melifera*), although the dose was reported in terms of mass of PFOS per bee, which may not be relevant for evaluating ecological risks. However, these studies, when converted to a dose per kilogram of food (2 mg PFOS per kg sugar solution), suggested that PFOS was highly toxic to honeybees. Mommaerts et al. (2011) identified in a chronic oral dosing study on the bumblebee (*Bombus*

terrestris) an LC50 of 1.01 mg PFOS/L sugar water and noted that PFOS exposure caused detrimental reproductive effects (decreased ovarian size).

Effects on fecundity from exposure to various PFAS compounds have been shown to carry down through multiple generations in the roundworm *Caenorhabditis elegans*. Tominaga Tominaga et al. (2004) conducted a multigenerational study in *C. elegans* exposed to PFOA, PFOS, and PFNA, finding that concentrations orders of magnitude lower than those causing lethality decreased worm abundance, and that effects were observed even in the fourth generation. Other studies have evaluated the mechanisms of PFAS toxicity. Xu et al. (2013) indicated that exposure to PFOS induced oxidative stress and DNA damage in the earthworm, *Eisenia fetida*. Stylianou et al. (2019) evaluated food chain transfer of PFOS-treated *E. coli* to *C. elegans* and noted distinct gene expression profiles associated with development, innate immunity, and stress response.

With regard to soil invertebrate toxicity testing, studies (while few in number) suggest a low to moderate toxicity of PFOS and PFOA, with toxicity generally occurring on a parts per million scale. Table 7-7 summarizes the range of acute and chronic toxicity values identified for various terrestrial invertebrates. These studies have mainly focused on the earthworm *Eisenia fetida*.

Sindermann et al. (2002) conducted a 14-day chronic soil study on *E. fetida* with PFOS and identified a NOEC of 77 mg PFOS/kg soil, a LOEC of 141 mg/kg, and an LD50 of 373 mg/kg. Other chronic earthworm studies indicated toxic concentrations of a similar magnitude, with LC50s ranging from 84 mg/kg–447 mg/kg (Mayilswami 2014) (Zareitalabad, Siemens, Wichern, et al. 2013). The Norwegian Pollution Control Authority NPCA (2006), as reported in Danish Ministry of the Environment (2015), conducted acute soil toxicity tests in *E. fetida*, looking at reproductive endpoints for PFOA, PFOS, and the short-chain 6:2 fluorotelomer sulfonate (6:2 FTS). Results of this study indicated that overall the evaluated PFAS exhibited a moderate-high toxicity. Reproductive effects (decreased number of cocoons, decreased hatchability, and decreased number and weight of juveniles) for PFOS and PFOA were noted. 6:2 FTS toxicity was found to be less than that for either PFOS or PFOA in the same study. Karnjanapiboonwong et al. (2018) conducted a 21-day soil study with *E. fetida* on bioaccumulation, mortality, and weight loss with PFBS, PFHxS, PFNA, and PFHpA and generally observed no effects at soil concentrations below 100 mg/kg, with the exception of PFBS, which resulted in a modest (although statistically significant) decrease in survival at 1 mg/kg.

The limited amount of terrestrial invertebrate data presents a data gap; additional toxicity studies are needed to better characterize ecotoxicological effects in this group of organisms. Additionally, it will be important to understand how field/soil conditions (for example, organic carbon content, pH, etc.) may influence toxicity. For example, Princz et al. (2018) found that PFOS toxicity for two different species of soil invertebrates was approximately two to four times greater when organisms were tested on sandy loam versus clay loam soils.

Table 7-7. Summary of terrestrial invertebrate ecotoxicity data for PFAS

PFAS	Range of Toxicity Values: NOEC, LOEC (mg/kg)	References
Acute Studies		
PFOS	77, 141 (survival)	(Sindermann et al. 2002)
PFBS, PFHxS, PFNA, PFHpA	1, 100 (survival)	(Karnjanapiboonwong et al. 2018)
Chronic Studies		
PFOS	1, 447 (survival) 1 (growth), 233 (reproduction)	(Mayilswami 2014) (Xu et al. 2013; Sindermann et al. 2002) (Princz et al. 2018) (Zhao et al. 2014) (Zareitalabad, Siemens, Wichern, et al. 2013)
PFOA	1 (growth), 84 (survival)	(He, Megharaj, and Naidu 2016) (Zareitalabad, Siemens, Wichern, et al. 2013)
6:2 FTS	30 (reproduction), 566 (growth)	(NPCA 2006)
PFBS, PFHxS, PFNA, PFHpA	100 (weight loss, mortality)	(Karnjanapiboonwong et al. 2018)

PFAS	Range of Toxicity Values: NOEC, LOEC (mg/kg)	References
Note: Refer to Table 7-2 in the separate Excel spreadsheet for toxicological endpoints and values.		

7.2.3 Vertebrates

7.2.3.1 Fish

Table 7-8 summarizes the range of toxicity values observed for fish following PFAS exposures. Acute freshwater LC50 values based on survival for PFOS range from 7.8 to 22 mg/L for Rainbow trout (*Oncorhynchus mykiss*), to 9.1 mg/L for Fathead minnow (*Pimephales promelas*) (Robertson 1986; Palmer, Van Hoven and Krueger 2002).

There are relatively few chronic PFOS studies using PFOS, but (Drottar and Krueger 2000b) calculated a chronic NOAEL based on early life stage mortality to be 0.29 mg/L. Palmer et al. (2002) also calculated an acute NOAEL of 6.3 mg/L for *Oncorhynchus mykiss*. Saltwater acute values based on survival for Oncorhynchus mykiss were calculated to be 13.7 mg/L.

Other than PFOS, there are limited aquatic ecotoxicity data for 'other' PFASs. Within the summary data presented here, acute exposure durations were 6-days. One study was noted that investigated the chronic toxicity of PFNA following a 180-day exposure; the LOEC ranged from 0.01-1 mg/L depending on the endpoint (Zheng et al. 2011).

Table 7-8. Summary of fish ecotoxicity data for PFAS

PFAS	Carbon Chain Length	Range of Toxicity Values: EC or LC50 (mg/L)	References
PFBA	4	2,200 (developmental); >3,000 (survival)	(Ulhaq et al. 2013)
PFBS	4	450 (developmental); 1,500 (survival)	(Ulhaq et al. 2013)
PFOS	8	7.8–22 (survival)	(Robertson 1986; Palmer 2002)
PFOA	8	430 (survival)	(Ulhaq et al. 2013)
PFNA	9	84	(Zhang et al. 2012)
PFDA	10	5 (developmental); 8.4 (survival)	(Ulhaq et al. 2013)
Chronic Studies			
PFOS	8	NOEC 0.29; EC50 7.2	(Drottar and Krueger 2000b; Oakes et al. 2005)
PFNA	9	LOEC 0.01 (growth)	(Zhang et al. 2012)

Note: Refer to Table 7-1 in the separate Excel spreadsheet for toxicological endpoints and values.

7.2.3.2 Amphibians/Reptiles

There are limited toxicity data available for PFAS effects on amphibians, including several studies on various species of frogs; no studies on reptiles were found in the literature search. The data available for PFOS and PFOA show a wide range of effects-based concentrations. Table 7-9 summarizes the range of acute and chronic toxicity data for amphibians.

More amphibian data are available for PFOS, and indicate mortality generally tends to occur at levels of 10 parts per million or higher, whereas nonlethal effects may occur at approximately 1–2 ppm (that is, moderate to high toxicity) (Ankley et al. 2004; Yang et al. 2014).

(Ankley et al. 2004) conducted a 5-week study on PFOS toxicity in the northern leopard frog (*Rana pipiens*) and observed that LC50s decreased with increasing test duration time; LC50s ranged from 12.5 mg/L at 1 week to 6.2 mg/L at 5 weeks. This study also anecdotally noted the presence of kinked tails, as well as a delayed time to initial metamorphosis and differences in limb bud and foot paddle emergence observed in the 1, 3, and 10 mg/L groups. A PFOS study (based on a 3M study reported in OECD, 2002) on another frog species, African clawed frog (*Xenopus laevis*), suggested toxicity at concentrations of similar magnitude to those observed in the Ankley study, and identified inhibition of growth and malformation during development (based on a 3M study reported in OECD, 2002).

Only one amphibian study was identified for PFOA, which suggested moderate aquatic toxicity (Yang et al. 2014).

Table 7-9. Summary of amphibian ecotoxicity data for PFAS

PFAS	Range of Toxicity Values–NOEC/LOEC (mg/L)	References
Acute Studies		
PFOS	3.6–81	(Yang et al. 2014; Stevens and Coryell 2007b) (Ankley et al. 2004; OECD 2002)
PFOA	115 (mortality)	(Yang et al. 2014)
Chronic Studies (EC10)		
PFOS	2 (longevity)	(Yang et al. 2014)
PFOA	5.89 (longevity)	(Yang et al. 2014)
Note: Refer to Table 7-1 in the separate Excel spreadsheet for toxicological endpoints and values.		

7.2.3.3 Birds

There are currently only several published studies available that address PFAS toxicity in avian wildlife species (Newsted et al. 2005; Newsted et al. 2007; Newsted et al. 2008); these studies indicate a low to moderate toxicity in birds. The northern bobwhite quail (*Colinus virginianus*) and the mallard duck (*Anas platyrhynchos*) were exposed to PFOS (Newsted et al. 2005; Newsted et al. 2007) or PFBS (Newsted et al. 2008) via the diet. The LC50s reported following exposure to PFOS are 212 mg/kg-feed and 603 mg/kg-feed for the northern bobwhite quail and the mallard duck, respectively, indicating a moderate toxicity (Newsted et al. 2005); generally, no effects were observed at feed concentrations of 70 mg PFOS/kg-feed or less. In a separate chronic diet study, Newsted et al. (2007) found that that while a feed dose of 10 mg PFOS/kg-feed did not result in mortality, clinical signs of toxicity in quail were observed at 5 weeks of exposure. Mortality in both quail and mallard was observed at feed concentrations of 50–150 mg/kg. The chronic NOAEL and LOAEL for PFOS reported for both species were 10 and 50 mg/kg-feed, respectively (Newsted et al. 2007); the quail appeared to be more sensitive to PFOS than the mallard.

Some egg injection studies suggest exposure to PFOS may adversely affect chick development during incubation. For example, Molina et al. (2006) found that exposure to PFOS lowered the rate of hatching success and caused changes in the liver in the leghorn chicken. However, there is some concern regarding the use of these data in risk assessments due to issues related to the method of exposure and other methodological issues that can influence the outcomes of the studies. Although these studies are useful for evaluating mechanisms and creating structure-activity relationships, they may not be appropriate for direct application in risk assessments.

Quail and mallard appear less sensitive to PFBS. Acute dietary exposure to PFBS resulted in NOAELs of 3,160 and 5,620 mg PFBS/kg-feed for the bobwhite quail and mallard duck, respectively, for the lethal endpoint (Newsted et al. 2008). A NOAEL for bobwhite quail reproduction following dietary exposure to PFBS was reported at 900 mg/kg-feed.

Although there are few PFAS laboratory toxicity studies for birds, there are even fewer field studies. Custer et al. (2012) evaluated PFOS exposure in tree swallows, identifying a negative association between PFOS concentration in eggs and hatching success. One issue with the findings from this field study is that the greatest observed effects on hatching were typically found in areas that also had other significant contamination issues (PCBs, PAHs, mercury); however, the influence of these other contaminants was not addressed in the study. Co-exposure of common environmental contaminants should be taken into consideration when reviewing these types of field studies.

7.2.3.4 Mammalian Wildlife

PFAS exposure to wildlife is occurring on a global scale and across a variety of habitats (Reiner and Place 2015). Sections 5.5.2 and 5.5.3 discussed studies that evaluated bioaccumulation of PFAS. Wildlife may accumulate PFAS from direct exposure to air, dust, water, soil, and sediments, as well as through diet. Maternal transfer of PFAS is also a relevant exposure route, as these compounds have been shown to cross the placenta (Gronnestad et al. 2017; Houde et al. 2006). PFAS have also been shown to biomagnify, so higher trophic level predators have higher PFAS levels in tissues compared with prey items (Reiner and Place 2015). Of the PFAS compounds analyzed in wildlife exposure studies, PFOS is the one most frequently detected, and at the highest concentrations, in tissue samples (Reiner and Place 2015). Concentrations in biotic media have also been observed to vary with age, sex, and species.

Given the widespread occurrence of PFAS in wildlife, it is important to understand if such exposure manifests in adverse effects and ultimately how exposure may impact wildlife populations. Laboratory animal models show that, in general, PFAS compounds are readily absorbed and distributed among protein-rich tissues (liver, serum, kidney) in mammals, and that certain PFAS (particularly long-chain compounds) have a relatively long half-life in the body. Toxicity tests on laboratory mammals (mice, etc.) have shown that exposure to PFAS may result in adverse effects on the hepatic, endocrine, and immune systems; development; and certain types of cancers, as discussed in Section 7.1.4.

Based on the findings from mammalian toxicity studies in laboratory animals, one might expect to find similar effects in mammalian wildlife (at similar exposure levels). Laboratory studies focusing on growth, reproduction, and survival effects on laboratory mammals provide data to support the development of toxicity reference values for use in ERA of wildlife species. Examples of these data are provided Table 7-3 in the separate Excel spreadsheet, but this table is not intended to be exhaustive. NOAELs and LOAELs can be derived from these studies for use in ERA as shown (as further discussed in Section 9.2, Ecological Risk Assessment), but these values should be used with caution and understanding of their associated uncertainty. Many of these studies may have also included other endpoints, such as systemic or metabolic endpoints, that are not typically used for ERA and may demonstrate effects at lower doses than the growth, reproduction, and survival effects.

Although there are numerous studies evaluating toxicity of PFAS in laboratory animals (as discussed in Section 7.1.4), and there are numerous exposure studies in mammalian wildlife, very few studies have evaluated PFAS toxicity with respect to wildlife exposures. The studies that have been conducted typically evaluated relationships between the concentrations of a small number of PFAS compounds in various protein-rich biological media (for example, blood serum, liver) and expression of select biomarkers. One study on sea otters related concentrations of PFOA and PFOS in liver tissue to health condition and. To possible immune effects (Kannan, Perotta and Thomas 2006).

Table 7-10 summarizes these studies.

Table 7-10. Summary of PFAS toxicity studies in mammalian wildlife

Species	Summary of Findings	Reference
Sea otter *Enhydra lutris*	Higher PFOS/PFOA concentrations in liver samples found in diseased otters versus nondiseased group	(Kannan, Perotta and Thomas 2006)
Bottlenose dolphin *Tursiops truncatus*	Significant positive associations between serum total PFAS concentrations and multiple immunological, hematopoietic, renal, and hepatic function endpoints	(Fair et al. 2013)
Wood mouse *Apodemus sylvaticus*	Significant positive relationship between liver PFOS concentration and hepatic endpoints (relative liver weight, microsomal lipid peroxidation level); significant negative association with serum alanine aminotransferase (ALT) activity	(Hoff 2004)
Wild pig *Sus scrofa*	No significant correlation between PFAS liver concentrations and multiple blood, hepatic, and immunological endpoints, whereas significant correlations were observed for other pollutants (for example, dioxin-like compounds, PCBs, organohaline pesticides)	(Watanabe et al. 2010)
Note: Refer to Table 7-3 in the separate Excel spreadsheet for toxicological endpoints and values.		

It is important to note that while certain associations have been observed between PFAS concentrations and various immunological, hematopoietic, renal, and hepatic function biomarkers, these associations are not necessarily indicative of actual impairment to an individual organism or within a larger population.

Perhaps one of the biggest challenges with wildlife toxicity studies is that wildlife are exposed to multiple chemical, biological, and physical stressors, making it difficult to determine whether noted effects are directly related to PFAS, to other stressors, or to a combination of stressors. The accumulation of other types of POPs, such as PCBs, dioxins, and pesticides, and metals such as mercury, in wildlife has been well established and, in some studies, related to effects. Arctic mammal studies have reported relationships between organohalogen exposure and endocrine disruption, reduced immune function, and adverse effects on the liver and other organs (Letcher et al., 2010). Numerous nonchemical environmental factors such as climate change, habitat loss, and seasonal availability of food may also confound toxicity studies, making it difficult for

field studies to discriminate those effects related solely to PFAS. As an example, Watanabe et al. (2010) found no association between PFAS levels and a variety of biomarkers in wild pigs, whereas the study found significant positive associations between these parameters and other types of contaminants (for example, PCBs) that were also detected in liver tissue samples.

Currently, there are few data points available for mammalian wildlife, and the current literature focuses on bioaccumulation and specific endpoints that may not be ecologically relevant, as discussed above. Additionally, studies have traditionally focused on protein-rich tissues such as liver or blood serum, because PFAS preferentially bind to proteins, which can potentially underestimate the total body burden of PFAS. Thus, exposure cannot be fully characterized from these studies, and pinpointing correlations between target organ or whole-body effects and PFAS exposure is not possible at this point in time. A better understanding of mammalian exposures to the broad spectrum of PFAS compounds, precursor compounds, and mixtures of PFAS, as well as other environmental contaminants, is critical in advancing this field of study. Given the challenges with conducting field studies, this information could be obtained in part through more robust dosing studies in mammals that are representative of various wildlife taxa, and on toxicological endpoints that are directly relevant to population-based effects; however, more field studies are also needed to confirm laboratory models. Groups such as the U.S. Department of Defense's Strategic Environmental Research and Development Program (SERDP) and the Environmental Security Technology Certification Program (ESTCP) have recently identified such critical data needs (SERDP-ESTCP 2017).

7.2.4 Plants

7.2.4.1 Aquatic Plants

Data on the toxic effects of PFAS on aquatic plants are limited, with available studies focusing on PFOS included in Table 7-1 in the separate Excel spreadsheet. The acute toxicity (EC50s) of PFOS to aquatic plants generally ranges from roughly 31 to 108 parts per million (mg/L), with NOEC values from the same studies being approximately 7–30 mg/L; (Boudreau et al. 2003; Sutherland and Krueger 2001; Drottar and Krueger 2000a). Chronic effects (EC50s) were found to be similar to acute values, but varied over a wide range, depending on species and endpoint (2–305 mg/L), with NOECs from the same studies ranging from 0.3 to 11.4 mg/L (Hanson et al. 2005; Boudreau et al. 2003; Desjardins et al. 2001a, b, c).

7.2.4.2 Terrestrial Plants

There are limited PFAS toxicity data for terrestrial plants; a review of the literature yielded only a few soil phytotoxicity studies, summarized in the See Table 7-2 in the separate Excel spreadsheet and in Table 7-11 below. Brignole et al. (2003) evaluated PFOS exposure (21 days) on a variety of crop plants (alfalfa, onion, ryegrass, soybean, tomato, flax, and lettuce) using emergence, survival, and shoot height and weight as endpoints, and demonstrated effects occurring at concentrations ranging from 57 mg/kg to over 1,000 mg/kg. Other studies (Li 2009; Zhao et al. 2011) conducted on both PFOS and PFOA on multiple crop plants found a wide range of toxicity among species and also within species for *Brassica rapa chinensis*. The most sensitive species may be *Triticum aestivum* where the 30-day NOEC reported was 1 mg/kg (Zhao et al. 2014). Toxicity may also be moderated by soil characteristics; for example, Zhao et al. (2011) showed that the amount of organic matter in soil significantly influenced toxicity, where higher organic carbon content decreased both accumulation of PFOA and PFOS and phytotoxicity. See the Table 7-2 in the separate Excel spreadsheet for a summary of phytotoxicity information for PFOA and PFOS.

Table 7-11. Summary of terrestrial plant ecotoxicity data for PFAS

PFAS	Range of Toxicity Values–NOEC/LOEC (mg/kg)	References
Acute Studies		
PFOS	<3.9 (growth)– >1,000 (survival)	Qu et al. 2010 ; (Zhao et al. 2014) (Li 2009); (Brignole et al. 2003)
PFOA	103 (growth)–812 (growth)	(Li 2009; Zhao et al. 2011)
Chronic Studies		
PFOS	1 (growth)	(Zhao et al. 2014)
PFOA	30 (growth)	(Zhao et al. 2014)
Note: Refer to Table 7-2 in the separate Excel spreadsheet for toxicological endpoints and values.		

7.2.5 Uncertainties and Conclusions

This section presented ecotoxicological information from an array of studies with the intent of providing the reader with an overview of the types of organisms and ecotoxicity studies available for PFAS compounds in the current literature. This section also presented available information about the ranges of concentrations of PFAS (notably, PFOS) in soil, sediment, and water that have been associated with adverse effects. In summary, ecotoxicity studies demonstrate a wide range of effects concentrations across the various terrestrial and aquatic biota. In general, aquatic invertebrates appear to be more sensitive to PFOS and other PFAS compounds than their terrestrial counterparts. Differences in species sensitivities, analytical methods, environmental substrate, test conditions, and reproducibility of results make it difficult to generalize overall effects, and some species may be more or less sensitive than others.

Although there are numerous studies on the toxicity of select PFAS to aquatic invertebrates, these studies are generally limited to a very small number of PFAS compounds (typically PFOS, and to a lesser extent, PFOA). Because PFAS represent a broad spectrum of compounds, it is important to expand ecotoxicity studies in this field to evaluate additional PFAS, including short-chain and precursor compounds, as well as “next generation” replacement compounds. Furthermore, the available studies indicate a wide range of effects levels for PFAS compounds in aquatic invertebrates, suggesting a level of complexity that has not yet been adequately assessed.

Significantly fewer toxicity studies are available for other groups of aquatic or benthic organisms, and few to no studies are available for avian or mammalian wildlife or plants, presenting a significant gap in our understanding of how the widespread presence of PFAS in the environment may be affecting ecological communities. Additional (or any) data on toxicological endpoints most relevant to community-level effects, such as survival, growth, and reproduction, will be extremely beneficial in understanding potential ecological impacts.

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