9 Site Risk Assessment

This section discusses the specific challenges associated with assessing and characterizing potential risks to human and ecological receptors exposed to PFAS in the environment. This includes challenges associated with quantifying the degree of exposure, assessing the hazard associated with PFAS, quantifying the dose-response relationship, and characterizing risks to support effective risk management decision-making. Generally, the challenges associated with performing a site risk assessment where the release of PFAS to the environment is suspected are not necessarily unique. Like any other chemical for which there is limited information, knowledge, or other technical complexity, working through the steps necessary to complete a risk assessment would be similar.

Section 15.3 provides a case study example illustrating how the New Jersey Department of Environmental Protection used risk assessment science to help support the development of fish consumption advisories for select water bodies in New Jersey. Section 17.3 provides additional information related to PFAS risk assessment, including (1) exposure pathways relevant for different exposure media, (2) considerations when calculating exposure point concentrations, and (3) selecting bioconcentration/bioaccumulation factors.

Section Number	Topic
9.1	Human Health
9.2	Ecological Risk Assessment
9.3	Uncertainty

9.1 Human Health

9.1.1 Toxicity Assessment

The toxicity assessment of a site risk assessment involves (1) hazard identification and (2) dose-response assessment. Hazard identification involves determining whether exposures to a chemical can cause an increased risk of an adverse human health effect; dose-response assessment involves quantifying the relationship between the degree of exposure to the chemical and the incidence or severity of the potential adverse effects. More background on each of these steps is detailed in other guidance (USEPA 1989; ITRC 2015a) and is not repeated here.

This section discusses specific complications that may be encountered in completing the toxicity assessment for a site risk assessment involving PFAS.

9.1.1.1 Availability of Toxicity Values from a Variety of Sources

A toxicity value (for example, oral CSF, systemic inhalation reference concentration) is a numerical expression of the dose-response relationship for a given substance. It is used in combination with estimates of chemical exposure to calculate quantitative estimates of cancer risk or noncancer hazard (USEPA 1989). Several state, national, and international regulatory and advisory agencies have developed human toxicity values for various PFAS that could be potentially used in conducting risk assessments or in support of establishing policies for PFAS risk management. Given this variety of sources, specific complications can be encountered in determining which toxicity values to use in conducting a risk assessment:

- Selection of toxicity values for PFAS is dependent on which PFAS are present at a given site. PFAS identification and quantification may vary based on analytical method.
- Differences among toxicity values for PFAS could arise because agencies may rely on different toxicity value derivation methods, may select critical studies by different criteria, may use different uncertainty factors, and may make different judgments about the prioritization of individual PFAS for toxicity value derivation (Table 9-1).
- Available toxicity values may change over time as the results of new studies become available. Newer toxicity values derived by regulatory agencies may be based on more recent and/or different information, methods, and studies than older values, as well as differences in scientific professional judgment and/or different statutory

policy requirements. These differences are described in more detail in Section 8.3.
- All values may not be relevant to all jurisdictions. For example, toxicity values developed by the USEPA may not be accepted in some states or in other countries.

Table 9-1. Example of variability in derived noncancer RfDs for PFOA and PFOS

	Noncancer Toxicity Values for Human Health Risk Assessment (ng/kg body weight*day)			
Source	***PFOA***	***Basis***	***PFOS***	***Basis***
USEPA (2016c) USEPA (2016d)	20	Delayed bone development and accelerated male puberty in mice (following developmental exposure)	20	Reduced growth rate of offspring (following developmental exposure)
ATSDR (2018e) **DRAFT**	3	Behavioral and skeletal effects in mice (following developmental exposure) Based on a study USEPA did not select for consideration, and a newer study from 2016	2	Used same study, but noted additional effect (delayed eye opening) Added a 10X uncertainty factor to protect for immunotoxicity

There are several options and procedures for selection of toxicity values, as has been described in ITRC guidance (ITRC 2015a). For site risk assessments performed in the United States, USEPA, DOD, and other agencies have recommended a tiered hierarchy (Tier 1–Tier 3) of toxicity value sources to guide selection and use (USEPA 2003a, 2013e); (ECOS-DOD 2007). This recommendation has since been implemented in numerous USEPA OSWER (Currently known as Office of Land and Emergency Management) directives (USEPA 1993, 2003a) that further establish a hierarchy and process for selecting toxicity criteria. For PFAS chemicals as of September 2019:

- Tier 1 values are peer-reviewed toxicity values published on the USEPA's Integrated Risk Information System (IRIS).
    - There are no PFAS chemicals in IRIS with published values.
- Tier 2 toxicity values include Provisional Peer-Reviewed Toxicity Values (PPRTV).
    - Only for PFBS.
- Tier 3 toxicity values include those from additional USEPA and non-USEPA sources. They can include values that may or may not have been peer reviewed. As recommended by USEPA (2003a), in using values from Tier 3 sources, it may be appropriate to prioritize those that are the *most current*, have a *transparent* basis, are *publicly available*, have been *peer reviewed*, and are acceptable to local jurisdictions.
    - Available toxicity values for PFAS chemicals are Tier 3 values.
    - Additional definitions and discussion of PFAS toxicity values that are available for use are provided in Section 7 and Section 17.2.

9.1.1.2 Lack of Toxicological Values for Many PFAS

There are more than 4,700 PFAS that could have been, or may be, on the global market (OECD 2018), although the uses of each of these PFAS may not be known (KEMI 2015b). More information about PFAS in use is included in Section 2. A large number of PFAS are considered bioavailable. However, toxicity values have been developed for only a few PFAS compounds for which sufficient information is available. Because of the lack of hazard and dose-response information for other PFAS and the extensive level of effort needed to develop toxicity values, there are no readily available toxicity values for the majority of PFAS.

This lack of information prevents the establishment of compound-specific risk-based concentrations that can be helpful for a variety of applications, including data screening (used to help guide site investigation) and site-cleanup decision-making. In the absence of toxicity values, regulatory agencies and the regulated community are left with uncertainty regarding the potential risks associated with human exposure to impacted environmental media at sites, technically defensible risk management programs may be difficult to create, and the regulated community cannot be responsive to concerns about environmental risk.

An approach often used in HHRA in the absence of compound-specific toxicity values is to use toxicity values developed for

structurally or chemically similar surrogate compounds with similar biological activity. In the case of PFAS, this would be for PFAS from the same structural subgroup (for example, long-chain perfluorocarboxylic acids). The use of surrogates, however, introduces uncertainty, because surrogates may produce adverse health effects by mechanisms different from the compound of concern, the dose-response curve for a surrogate may be different, and the target organ or toxicity endpoint may be different from the compound of concern. In the absence of chemical-specific toxicity values, preparation of health risk assessments may be limited to qualitative methods and have a higher level of uncertainty as a result.

Further information and guidance are needed to identify appropriate surrogates for PFAS that do not currently have available toxicity values. As part of their PFAS Action Plan (USEPA 2019h), USEPA is working on developing an approach to PFAS toxicity testing that could lead to a methodology for inferring the toxicology of a given PFAS based on the toxicology of a PFAS subset. This involves applying computational and high throughput toxicology tools for PFAS toxicity testing on a larger scale to enable faster understanding of potential toxicity for the universe of thousands of PFAS, most of which have little or no published toxicity data.

9.1.2 Exposure Assessment

The exposure assessment of a site risk assessment involves characterizing the exposure setting, identifying relevant exposure pathways and scenarios, and quantifying the magnitude, frequency, and duration of potential human exposure to chemicals in environmental media. More background on the performance of exposure assessments is detailed in other guidance (USEPA 1989; ITRC 2015a) and is not repeated here.

This section discusses specific complications that may be encountered in completing the exposure assessment for a site risk assessment involving PFAS. It should be recognized that the exposure assessment does not generally account for the presence of all PFAS at a site due to limitations in analytical methods. Therefore, there are uncertainties in the characterization of exposures (and associated risks) at PFAS sites that should be acknowledged in the uncertainty analysis section of the risk assessment.

9.1.2.1 Determining Scenarios for Potential Human Exposure

A site-specific conceptual exposure model should be developed during the planning stage of the HHRA, confirmed by stakeholders, and updated as additional information and data are obtained (Section 3 of the RISK-3 guidance (ITRC 2015a). The specific exposure scenarios that are applicable to an HHRA for PFAS include those that could occur in media at the release area (the site) and in media at distant locations (with the extent depending on PFAS properties and the site setting). In general, an HHRA for PFAS may be complex in comparison to HHRAs for other types of chemicals (for example, due to the persistence of PFAS, the complexities associated with PFAS toxicity, and complexities associated with estimating future concentrations or modeling their fate and transport, and the need to include more media than is typical. Figures 9-1, 9-2 and 9-3 are provided below to illustrate conceptual site models (CSMs) for four sources (two sources are illustrated in Figure 9-3) of PFAS. Section 2.6 discusses potential environmental releases of PFAS. A detailed discussion of fate and transport processes for PFAS and environmental media that may be affected is presented in Section 5.

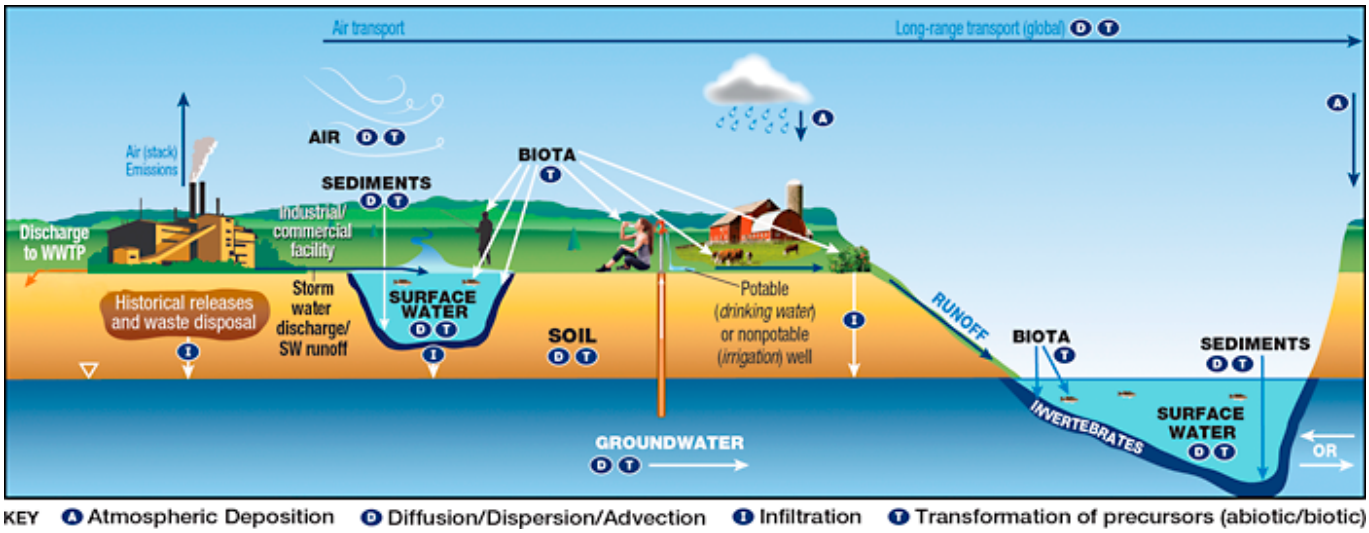

Figure 9-1. CSM for fire training areas.

Source: Adapted from figure by L. Trozzolo, TRC. Used with permission.

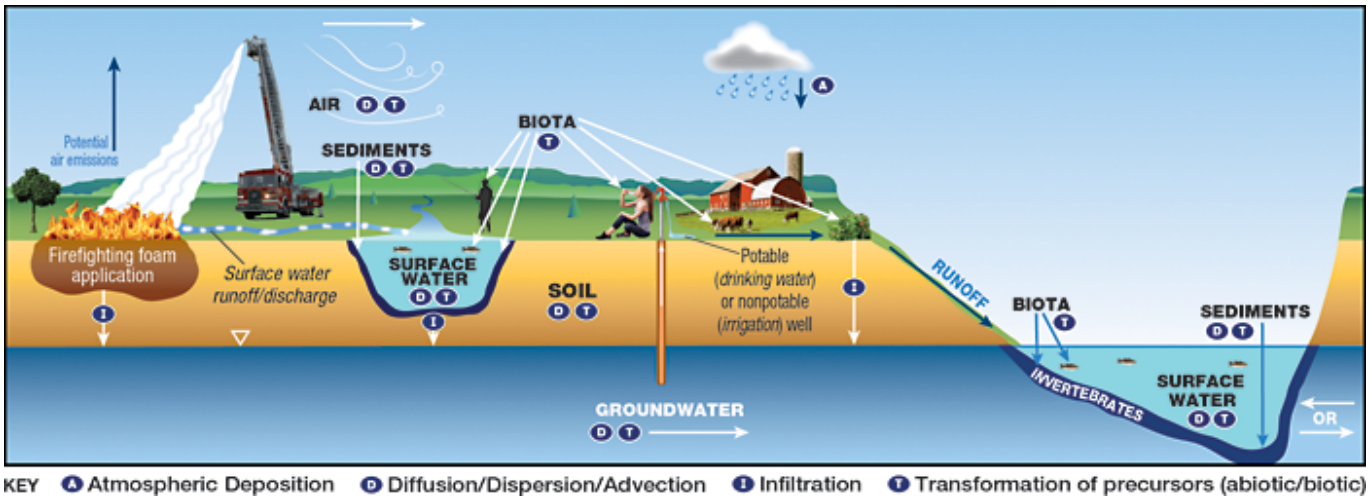

Figure 9-2. CSM for industrial sites.

Source: Adapted from figure by L. Trozzolo, TRC. Used with permission.

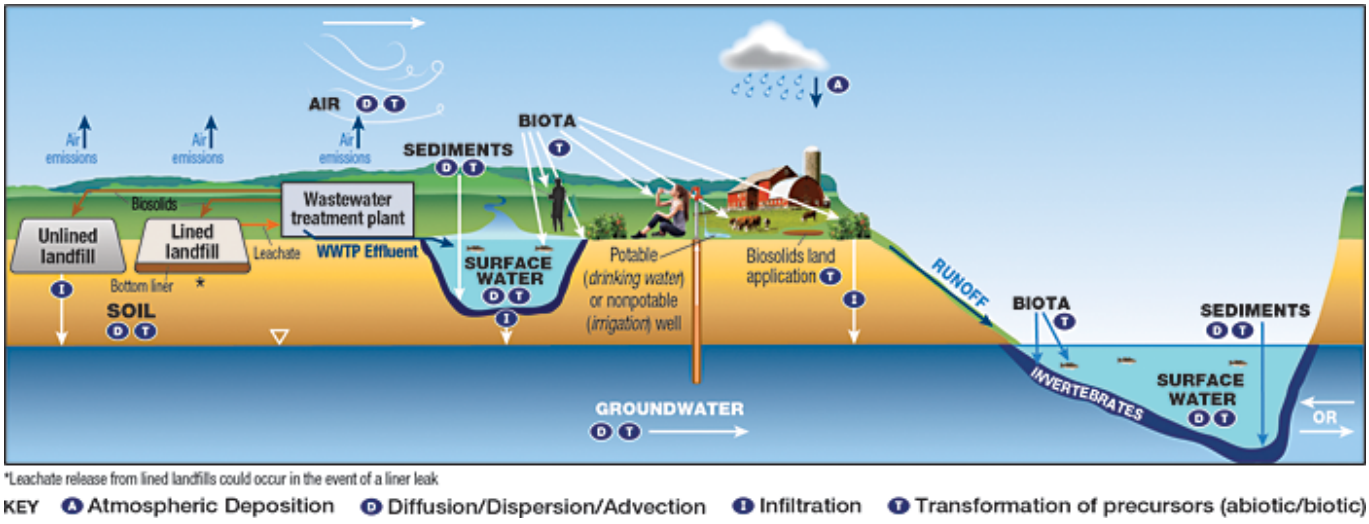

Figure 9-3. CSM for landfills and WWTPs.

Source: Adapted from figure by L. Trozzolo, TRC. Used with permission.

Various exposure scenarios may be possible for a given site, and which specific exposure scenarios should be included in a HHRA is a site-specific decision.

The highest exposures to PFAS can occur during early life stages (ages 0–18) (Winkens et al. 2017). Exposures to infants from breast milk of exposed mothers (Figure 9-4) or formula prepared with contaminated water are higher (on a BW basis) than in older age groups (Fromme et al. 2009; Mogensen et al. 2015; Verner et al. 2016b, a; Post, Cohn, and Cooper 2012). The higher exposures during pregnancy and to infants are of concern because fetuses and infants are sensitive subpopulations for developmental effects of some PFAS, including PFOA and PFOS (USEPA 2016h, g), as discussed in Section 7.1. Therefore, exposure scenarios that include fetuses, infants, children, adolescents, and women of childbearing years should be considered in HHRAs.

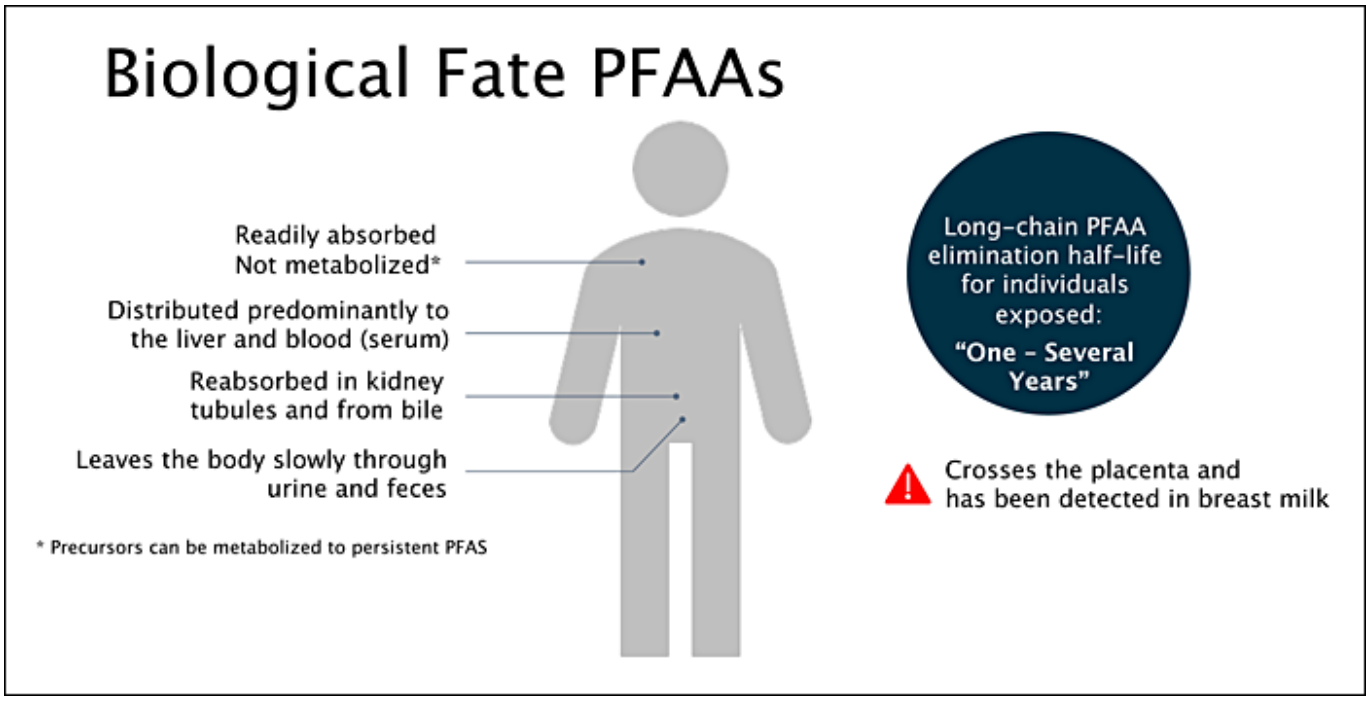

Figure 9-4. Biological fate of long-chain PFAAs.

Figure 9-5 illustrates the predominant exposure pathways. More detailed information about these exposure pathways, as well as other environmental medium-specific issues affecting potential human exposure scenarios, are provided in Section 17.3.1.

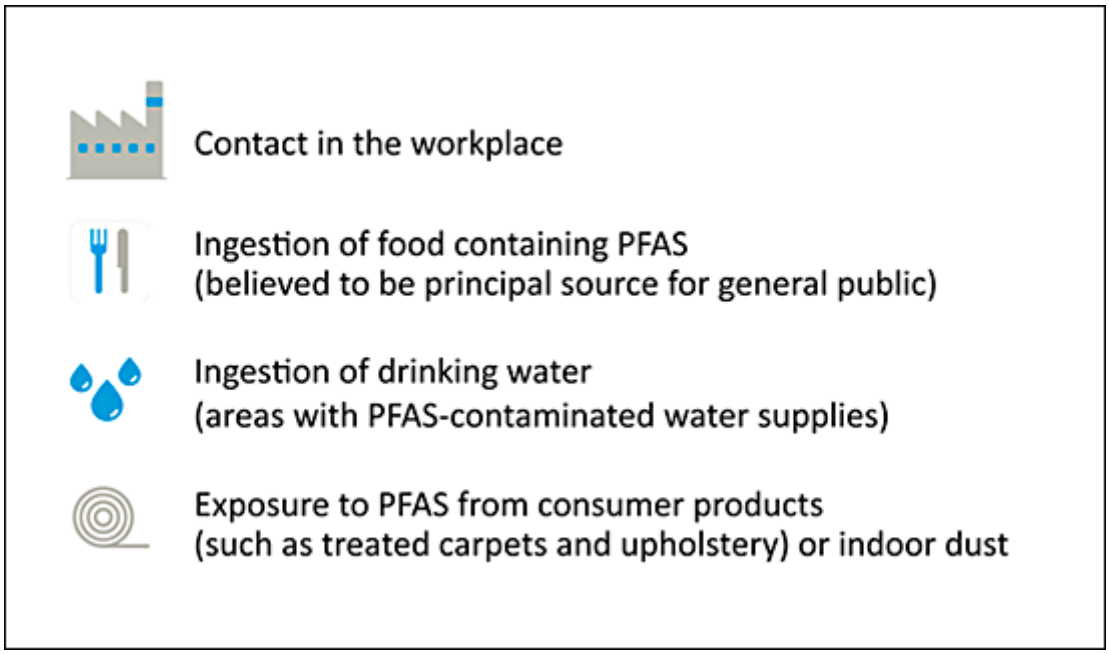

Figure 9-5. Predominant human exposure pathways.

9.1.2.2 Calculating Exposure Concentrations for PFAS via Fate and Transport Models

When using fate and transport models to calculate exposure point concentrations (EPCs) for PFAS, it is important to note that individual PFAS have different chemical properties that affect their fate in the environment (Section 5). Some PFAS are mobile, persistent, and bioaccumulative (in wildlife and humans), and others are not. Perfluoroalkyl acids (PFAAs) are persistent, and long-chain PFAAs bioaccumulate in humans (USEPA 2003b; ATSDR 2018c; NTP 2016; CONCAWE 2016). USEPA has compiled an online resource for PFAS information that includes guidance on environmental behavior and site characterization (USEPA 2017b). The National Groundwater Association (NGWA) has also published a resource on PFAS that includes information about fate and transport (NGWA 2017 (NGWA 2017). Additional information is included in Section

17.3.2.

When using environmental fate and transport models for estimating EPCs in biota, modeling should be focused on the part of the organism that may be consumed either by humans or by ecological receptors. PFAS generally bind to proteins and accumulate in protein-rich tissues, including the blood, liver, and kidneys (ATSDR 2018c). Currently, models for plant uptake are limited, but several studies have documented uptake of PFAS from soil amended with PFAS-contaminated biosolids (Blaine et al. 2013; Blaine, Rich, Sedlacko, Hundal, et al. 2014; Wen et al. 2016). Section 17.3.3 includes information about selecting bioaccumulation and bioconcentration factor values.

Measured concentrations at exposure points may differ from modeled EPCs. This may be due to other sources of PFAS (for example, a nearby site that had a PFAS release to the ground and that subsequently leached to groundwater) also contributing to concentrations at the exposure point and the limitations of the models currently available.

9.1.3 Risk Characterization

The risk characterization of a site risk assessment combines the results of the exposure assessment and the toxicity assessment to provide a quantitative estimate of risk (ITRC 2015a). It also may include a qualitative narrative designed to provide decision makers with information regarding key assumptions, uncertainties, or other issues that would be important to understand when making risk management decisions. More background on the performance of risk characterizations is detailed in other guidance (USEPA 1989; ITRC 2015a) and is not repeated here.

Because risk characterization involves combining the toxicity assessment and exposure assessment, the complexities discussed in Sections 9.1.1 and 9.1.2 manifest themselves in the risk characterization. There are, however, additional specific complications that may be encountered in completing the risk characterization for a site risk assessment involving PFAS. This section discusses those specific complexities.

9.1.3.1 Assessing the Cumulative Effects of Exposure to PFAS

The overall potential for noncancer effects due to human exposure to more than one chemical is estimated using the hazard index (HI), which is computed as the sum of calculated chemical-specific hazard quotients (HQ). As explained by USEPA (1989), “This approach assumes that simultaneous subthreshold exposures to several chemicals could result in an adverse effect. It also assumes that the magnitude of the adverse effect will be proportional to the sum of the ratios of subthreshold exposures to acceptable exposures.” Risk characterizations commonly produce initial estimates of HI by calculating the sum of all HQs. When the HI is estimated to be greater than 1, there may be potential concern for adverse health effects. However, when this initially estimated HI is greater than 1, refinement of the HI estimate by segregating HIs by effect and mechanism of action may be appropriate to support a risk management decision.

For PFAS, as discussed in Section 7.1, there are several possible adverse health effects associated with exposure. Table 9-2 provides a general summary of the possible noncancer adverse health effects associated with various PFAS. The information in this table can be used to segregate HIs by potential adverse effect in the risk characterization when risks associated with exposure to specific PFAS are being evaluated. Table 17-8 (provided as a separate Excel file) includes additional limitations and considerations regarding this information.

Table 9-2. Summary of potential noncancer health effects of various PFAS

Adapted from (ATSDR 2019a) Health Consultation PFAS HC-508.

	# of Carbons	Liver	Develop-mental	Repro-ductive	Immune	Hema-tologic	Thyroid	Neuro-behavioral	Tumors
Perfluoroalkyl Carboxylates									
PFBA	4	■	■	■	□	■	■	□	□
PFPeA	5	□	□	□	□	□	□	□	□
PFHxA	6	■	■	■	□	■	■	□	□ (Negative)
PFHpA	7	■	□	□	□	□	□	□	□
PFOA	8	■	■	■	■	■	■	■	■
PFNA	9	■	■	■	■	■	■	□	□
PFDA	10	■	■	■	■	■	■	■	□
PFUnA	11	■	■	□	■	□	□	□	□
PFDoA	12	■	■	■	■	■	□	■	□
Perfluoroalkyl Sulfonates									
PFBS	4	■	■	■	■	■	■	□	□
PFHxS	6	■	■	□	□	■	■	■	□
PFOS	8	■	■	■	■	■	■	■	■
Per- & Polyfluoroalkyl Ether Replacements									
ADONA	6	■	■	□	□	■	□	□	□
HFPO-DA GenX	6	■	■	■	■	■	■	□	■

■ Effect reported in one or more laboratory animal study
□ Effect was evaluated but not found, or effect has not been evaluated

9.1.3.2 Characterizing Cancer Risk for Exposure to PFAS

As discussed in more detail in Section 7.1, (USEPA 2016h, g, 2018g) described PFOA, PFOS, and GenX as having suggestive evidence for human carcinogenicity. The International Agency for Research on Cancer (IARC) has also classified PFOA as *possibly carcinogenic to humans* (Class 2B). (USEPA 2005a) carcinogen risk assessment guidance provides for development of a slope factor for chemicals with "suggestive evidence" when supported by available data. USEPA (2016d) has developed a CSF for PFOA of 0.07 mg/kg-day based on testicular tumors. In the case of PFOS and GenX chemicals, although USEPA concluded that there is suggestive evidence of carcinogenic potential in humans based upon liver and thyroid impacts observed in chronic rat studies, the results lacked a dose-response relationship. Because of this limitation, USEPA judged the database too limited to support a quantitative assessment of carcinogenicity. Likewise, the NJDWQI (2018b) developed a slope factor for PFOS of 9 x 10^{-6} ng/kg-day for comparison purposes, but concluded that it is too uncertain to use as the basis for a drinking water value.

Although USEPA and some select states have derived oral CSFs for a select few PFAS, risks associated with PFAS (including derived risk-based values and screening levels) have been primarily based on noncancer effects. CalEPA's OEHHA (2019), however, is unique in that they have issued notification levels for drinking water exposure that are driven by carcinogenicity. This is predominantly because OEHHA applies additional factors in their calculations to reflect what they consider an increased suseptibility of infants and children to carcinogens, and OEHHA derived a CSF for PFOS, which USEPA did not. For site risk assessments, the derived CSFs developed by these agencies could be used (for example, USEPA derived an oral CSF for PFOA of 0.07 mg/kg-day).

Further discussion of the carcinogenicity of PFAS is presented in Section 17.2.4.2 (Carcinogenicity), Section 17.2.5.3 (Chronic Toxicity and Tumorigenicity), and Section 8.2.2.3 (CERCLA).

9.2 Ecological Risk Assessment

9.2.1 Ecological Effects Assessment

Identification of ecological risk-based toxicity thresholds is a challenge for many PFAS. Toxicity data are available as discussed in Section 7.2. Some of these data have been used to establish thresholds as discussed below.

9.2.1.1 Ecological Screening Thresholds

Currently, there are no U.S. federal PFAS guidelines or media screening thresholds available that are ecological risk-based. However, several states have established some criteria that are intended to protect aquatic organisms in their respective surface waters. In Michigan, ambient water quality criteria have been established for PFOS and PFOA based on Rule 57 17 (MI EGLE 2019). This rule is based on the USEPA Great Lakes Initiative (USEPA 1995), which provides procedures and

methodologies to derive numerical criteria that are protective of aquatic ecosystems. Rule 57 presents a two-tiered methodology in which Tier I procedures are essentially the same as the methods used to derive federal national water quality criteria (NWQC) (USEPA 1985) and Tier II can be used to derive values where the full extent of the toxicity data requirements of NWQC are not fulfilled. Rule 57 presents procedures to develop three categories of numeric criteria—final chronic values (FCVs), aquatic maximum values (AMVs), and final acute values (FAVs)—which can be developed under either Tier I or Tier II. Due to the greater uncertainties associated with Tier II values, given the lesser data requirements, these values tend to be more conservative than those derived with Tier I methodologies. The PFOA and PFOS numeric criteria for Michigan are all Tier II values due to the limited amount of peer-reviewed aquatic toxicity data. The final chronic values for the protection of aquatic life (flora and fauna) for PFOA and PFOS were 880 and 140 µg/L, respectively, while aquatic maximum values were 7,700 and 780 µg/L, respectively. In addition, the Michigan Department of Community Health (MDCH 2015) derived provisional PFOS surface water values for mammalian and avian wildlife based on Rule 57 guidance. The surface water avian wildlife value, based on eagles, kingfishers, and herring gull characteristics, was 0.035 µg PFOS/L. The mammalian wildlife value, based on otter and mink characteristics, was 0.084 µg PFOS/L.

The State of Minnesota has also derived several PFAS-based surface water criteria for the protection of aquatic biota. These values were based on guidelines in Minnesota Rules chapter 7050 (MR7050). Continuous chronic criteria for the protection of aquatic biota in surface water are for PFOA (1,700 µg/L) and PFOS (19 µg/L) (Stevens and Coryell 2007b; Stevens and Coryell 2007a). No other surface water values have been derived for PFAS in either state (Michigan or Minnesota) and values for other states are unavailable.

Environment and Climate Change Canada (ECCC, previously known as Environment Canada) has proposed ecological Federal Environmental Quality Guidelines (FEQGs) for PFOS in surface waters, fish tissue, wildlife dietary values, and bird eggs (ECCC 2018). The PFOS threshold for surface waters was derived from a species sensitivity distribution (SSD) based on long-term toxicity data that included data for amphibians, fish, invertebrates, phytoplankton, and macrophytes. The guideline to protect all aquatic life forms for indefinite exposure periods to PFOS in surface waters is 6.8 µg/L, and a fish tissue guideline value of 9.4 mg/kg wet weight (ww) was based on these fish data and bioaccumulation factors for bluegill from Drottar, Van Hoven, and Kruger (2002). The tissue threshold is intended for both freshwater and marine environments. It was not calculated with both food and water (direct media) BAFs, and thus it could be underprotective. However, (Giesy et al. 2010) did use Drottar, Van Hoven, and Kruger (2002) data to calculate an acute no-effect threshold of 87 mg/kg ww. To protect mammalian and avian consumers of aquatic biota, ECCC derived wildlife dietary toxicity reference values (TRVs) using mammalian studies and avian chronic toxicity data. For mammals, the dietary value for PFOS was 4.6 µg/kg ww food while the avian dietary value was 8.2 µg/kg ww food. Based on the avian reproduction studies that were the basis for the dietary values, a guideline of 1.9 µg/g ww whole egg was also derived for PFOS.

Screening level assessment values have also been derived for PFOA (Environment Canada 2012). Environment Canada derived several predicted no-effect concentrations (PNECs) for PFOA for ecological species. PNECs are intentionally conservative concentrations of chemicals designed to represent a concentration at which no adverse effects are likely. These PNECs for PFOA were based on LOAEL values from a limited set of single organism toxicity studies adjusted with uncertainty factors. FEQG values are developed from a distribution of acute and chronic studies conducted on groups of organisms with an intent to be protective of a set percentage of organisms in that category (for example, a 95% protection threshold). Thus, these PFOA PNECs are not equivalent to FEQGs, though they still provide utility for screening level ERA. The PNEC for aquatic organisms, based on a study with the freshwater alga *Pseudokirchneriella subcapitata*, was 20 µg/L; a mammalian wildlife study based on cynomolgus monkey *(Macaca fascicularis)* derived a liver-based PNEC of 158 µg/kg ww. However, given the uncertainties associated with these values, care should be taken in their application to ERA. FEQGs for PFOA are currently under development by ECCC (ECCC 2018).

The Australian and the New Zealand Environment and Conservation Council and Agriculture and Resource Management Council of Australia and New Zealand (ANZECC/ARMCANZ) have established draft protective concentrations for freshwater organisms exposed to PFOS and PFOA. The values, as shown in Table 9-3, were developed by the Cooperative Research Centre for Contamination Assessment and Remediation of the Environment (CRC CARE) (2018). Only the freshwater values have been adopted in the PFAS National Environmental Management Plan (HEPA 2018) for Australia and New Zealand. Instead, the freshwater values have been identified as interim thresholds for marine waters. The values from CRC CARE incorporated multiple studies and were based on SSD for each compound. The 90 and 95% protective thresholds for PFOS are 2.0 and 0.13 µg/L, respectively. These values are within the range of other published values (Giesy et al. 2010; Qi et al. 2011). A 99% protection value for PFOS was also proposed as 0.00023 µg/L, though this may be below ambient concentrations. All three of the PFOS protection values are taken from an SSD that includes studies on the low end that are

well below the majority of other data points. Further, as indicated in table B3 of CRC CARE (2018), data used in the SSD include a mix of effect levels (EC10) and no-effect levels (NOECs). Thus, decisions based on these values should be made with careful consideration.

For PFOA, the 90 and 95% protective thresholds were 632 and 220 µg/L, respectively; these are similar to those derived in Minnesota and Michigan. Marine threshold values for PFOS were 32 and 7.8 µg/L for the 90 and 95% protective levels. For PFOA, the 90 and 95% protective thresholds were 8,500 and 14,000 µg/L, respectively. It is of note that the threshold values for marine species were at least 1–2 orders of magnitude greater than those from freshwater. Thus, one should take care in using freshwater toxicity data or threshold values when evaluating marine and brackish systems, given the apparent differences in species sensitivity between these two environments. Likewise, caution should be used if employing marine values to evaluate other PFAS for which there are no freshwater threshold values.

Table 9-3. Aquatic thresholds developed by CRC CARE (CRC CARE 2018)

Species Protection (%)	PFOS (µg/L)	PFOA (µg/L)
Freshwater		
80	31	1,824
90	2	632
95	0.13	220
99	0.00023	19
Marine		
80	130	22
90	32	14
95	7.8	8.5
99	0.29	3

A number of thresholds for PFOS are also available from the European Union (EU) as described in the Environmental Quality Standards Dossier (EQS) for PFOS (European Union 2011, 2013). These include maximum acceptable quality standards (MAC-EQS) for freshwater and marine ecosystems, and annual average quality standards (AA-EQS) for the same ecosystems. Standards are also available for secondary poisoning (that is, consideration of biomagnification through the consumption of contaminated prey). These values are shown in Table 9-4.

Table 9-4. Environmental quality standards (EQS) for PFOS

Category/Description	Units	Value
Proposed MAC-EQS (freshwater)	µg/L	36
Proposed MAC-EQS (marine)	µg/L	7.1
Pelagic Community AA-EQS (freshwater)	µg/L	0.23
Pelagic Community AA-EQS (marine)	µg/L	0.023
$EQS_{biota,\ sec\ pois}$	mg/kg (ww)	0.033
$EQS_{biota,\ sec\ pois}$ (freshwater)	µg/L	0.002
$EQS_{biota,\ sec\ pois}$ (freshwater)	µg/L	0.00047
MAC-EQS = maximum acceptable environmental quality standard AA-EQS = annual average environmental quality standard Biota, sec pois = secondary poison standard for concentration in fish tissue		

A survey of reports from various regulatory agencies demonstrates that although ecotoxicity data are available for various PFAS, including PFBA, PFBS, and fluorotelomers (including 8:2 FTCA, 8:2 FTUCA, and several FTOHs), to date these typically consider only a few aquatic species that include *D. magna*, a green alga, and perhaps a fish species. Regulations require a robust data set covering several classes of organisms, and due to limitations in the number of classes of organisms represented in the published peer reviewed data, it is difficult to derive ambient surface water quality criteria. Lack of relevant toxicity data is a greater issue for terrestrial wildlife given that the only chronic, reproductive studies that have been conducted to date are in two species, bobwhite quail and mallard duck, with PFOS and PFOA. No ecologically relevant studies have been conducted with mink or an adequate surrogate. As a result, the development of benchmark or threshold concentrations for wildlife and aquatic organisms has been slow and incorporates greater levels of uncertainty in their derivation.

Research on observed effects in benthic invertebrates for direct exposure to sediments contaminated with PFAS is limited. There are no published benchmarks and little published research. Research has focused more on aqueous exposure pathways. Observational data and monitoring have been used in some cases to develop an understanding of what exposure may be associated with effects. A sediment no-effect threshold of 220 µg/kg, a chronic toxicity range of 220–630 µg/kg, and an acute short-term effects range of 630–3,100 µg/kg were established (Bakke et al. 2010) Norwegian Pollution Control Agency NPCA . These sediment thresholds were reported for PFOS concentrations in marine sediments, though they provide some basis for screening level risk decisions for both marine and freshwater. Caution should be observed in using these values because associated effects, if any, are unclear, and the original work is not readily available. Caution should also be used in applying these NPCA sediment values from marine waters to freshwater because the freshwater organisms could be more exposed (as explained in Section 9.1.2) and either more or less sensitive than marine organisms. In its EQSD for PFOS, the European Union (2011) took the position that there is insufficient data available to confirm the need for a sediment quality standard and insufficient data to derive a threshold, thus electing not to develop a value. Similarly, a workgroup in northern Italy concluded that there was no need for a sediment environmental quality standard (EQS) for PFOA, PFBS, PFBA, and PFPeA and that data for a sediment EQS for PFHxA were insufficient (Valsecchi et al. 2017).

For soil, CRC CARE developed soil screening thresholds from SSDs for both PFOS and PFOA. The Canadian Council of Ministers of Environment (CCME 2018) have also developed several draft thresholds for PFOS in soil. A value protective of direct toxicity was developed from an SSD of plant and invertebrate IC25 values (the concentration at which a 25% reduction in a non-lethal biological measurement, such as growth or reproduction, occurs). Food chain models were used to develop values protective of soil and food ingestion by wildlife. CCME (2018) also developed a soil screening value protective of aquatic life for use at sites where off-site migration to nearby surface water bodies may be a concern. These values from CCME were issued draft for public comment, and final FEQGs have not yet been established. Soil threshold values for other PFAS, however, are limited.

9.2.1.2 Ecological Receptor Variability

A second major challenge with toxicity assessment for ERA is accounting for the large number of receptor types and the associated unknown variable sensitivity to PFAS. Although it is commonly understood that sensitivity to contaminants can vary widely across kingdoms or across classes of animals, the challenge for PFAS may be greater due to the lack of knowledge about this family of compounds. Studies have documented the presence of PFAS in various aquatic species since the 1950s (Danish EPA 2015; Giesy and Kannan 2001, 2002)), such as bottle-nosed dolphins (Houde et al. 2006), seals (Butt et al. 2008), squid (Yang et al. 2012), alligators (Bangma et al. 2017), and polar bears (Smithwick, Mabury, et al. 2005; Smithwick, Muir, et al. 2005; Greaves and Letcher 2013). The detection of PFAS within organisms is clear evidence of exposure. Unlike many other commonly detected contaminants, however, the availability of toxicological data for PFAS is limited relative to the broad range of organisms within which PFAS have been detected.

Standard ERA practice includes developing TRVs that consider measures of exposure and effects that could adversely impact populations of wildlife (for example, chronic studies on reproduction, growth, and survival). Mammalian studies on numerous sublethal endpoints (for example, systemic, immunological, developmental, respiratory, cardiovascular, gastrointestinal, ocular, hepatic) have been conducted for PFOS, PFOA, and other PFAS and are well described in the *Draft Toxicological Profile for Perfluoroalkyls* (ATSDR 2018e), but these are less commonly used for TRV development for ERAs. These sublethal, mostly systemic or organ function-based TRVs are really only used for ERAs in the absence of reproduction, survival, or growth data. Mammalian TRVs for the purposes of ERA can be developed for the majority of the Third Unregulated Contaminant Monitoring Rule (UCMR3) PFAS compounds listed in Section 8.2.2.2. Avian oral dosing studies useful for ERA are less available. The dietary acute and chronic studies by Newsted et al. (2005); Newsted et al. (2007) examining PFOS exposure in mallard (*A. platyrhynchos*) and bobwhite quail (*C. virginianus*) may be the only currently published work relevant

to ERA. Newsted et al. (2005) and Molina et al. (2006) have also reported the results of bird egg injection studies using PFOS, while Cassone et al. (2012) and Norden, Berger, and Engwall (2016) have published *in ovo* studies with other PFAS. A caution with interpreting these egg studies is the uncertainty as to whether naturally accumulated concentrations have the same adverse effect as concentrations administered via injection in ovo. There also can be differences when measuring whole egg, yolk, or albumin (Custer, Gray, and Custer 2010). Finally, there is currently not enough data for modeling egg tissue concentration for these chemicals.

Reptiles are among the least studied vertebrate taxa in ecotoxicology (Hopkins 2000) Weir, 2010 #1616} despite contamination threatening reptile populations worldwide (Gibbons et al. 2000). To date, there are no published reptile toxicity data available for any PFAS, although studies have shown PFAS tissue concentrations from some reptile species (Wang, Zhang, et al. 2013; Bangma et al. 2017). Amphibian toxicity data are also lacking, with just one study onnorthern leopard frogs (*Rana pipiens*) (Ankley et al. 2004) and one on African clawed frogs (*Xenopus laevis*) (Palmer and Krueger 2001).

For lower trophic-level organisms such as plants and invertebrates, toxicological data are typically generated through studies with direct exposure to spiked media. Studies are available to develop thresholds for use in ERAs, as has been done by both ECCC (2018) and CRC CARE (2017a). Giesy et al. (2010) and ECCC (2018) generated PFOS SSDs for freshwater aquatic organisms, from which thresholds were derived. CRC CARE presented SSDs for PFOS and PFOA for marine waters and for soil to establish their thresholds. Giesy et al. (2010) noted that some guidelines for developing criteria from SSDs rely heavily on the four lowest effect concentrations; thus, results can be skewed if one genus or species is significantly more sensitive than others. In the freshwater SSD for PFOS generated by Giesy et al. (2010), C*hironamous tentans* (a species of midge) were 40 times more sensitive than the next most sensitive species, the fathead minnow (*Pimephales promelas*). However, the ECCC (2018) SSD does not show the same difference in sensitivity with a reported fish 14-day growth LOEC for Japanese rice fish (*Oryzias latipes*) below the *C. tentans* 10-day NOEC. For marine waters, fish are among the most sensitive organisms for both PFOS and PFOA as shown in SSDs (CRC CARE 2017a), but by just an order of magnitude or less. SSDs produced by CRC CARE (2017a) did not use any of the same data and showed lettuce to be more sensitive to PFOS than earthworms, but found the opposite occurred for PFOA.

SSDs have not been published for avian, mammalian, reptilian, or amphibian species. Although SSDs could possibly be generated for laboratory mammalian species, perhaps the most studied organisms for PFAS, there would not be a significant breadth of applicability to wildlife species. Mammalian SSDs would include mostly rat and mouse studies with a few monkey and rabbit studies. Extrapolation to other orders would be required, leaving an uncertainty. Existing data would be more conducive to an effects distribution because the number of species within the class of organisms would be so limited. Insufficient published data are available for a robust SSD or even an effects distribution for avian, reptilian, or amphibian animals.

Available toxicological data clearly do not adequately cover the range of organisms that are exposed to PFAS or within which PFAS have been detected. Nor does the data have much breadth for chemicals beyond PFOS and PFOA. Sensitivity variation for aquatic organisms is evident from the SSDs, and likely sensitivity ranges for untested wildlife leave a clear knowledge gap for some or even most ERAs. However, this problem is not unique to PFAS. As with many other bioaccumulative and biomagnifying compounds, this knowledge gap can be addressed by using available data from surrogate organisms (for example, the closest taxonomic laboratory test species) and making some assumptions. The uncertainty in the potential difference in sensitivity needs to be acknowledged and discussed within ERAs. However, pending the outcome of quantitative analysis, risk conclusions and even risk management decisions are possible on a site-specific basis. Although extrapolations with surrogates is a common practice in ERA, caution should be used and decisions should be made in concurrence with regulatory agencies or other applicable stakeholders.

9.2.1.3 Ecological Toxicity of Mixtures

A third major challenge in effects assessment for PFAS is considering the toxicity of mixtures. At this time there are only limited data available to sufficiently understand the toxicity of more than just a few chemicals with respect to direct toxicity to lower trophic level organisms or exposure to upper trophic level wildlife. Structural and physical properties could be used to relate the toxicity of unknown PFAS to those with known toxicity. Giesy et al. (2010) explored quantitative structure-activity relationships (QSARs) for PFAS with the following conclusions, “Although the analysis given above indicates that structure-activity relationships can be derived from existing data, there are still numerous data gaps that need to be addressed to quantify the toxicity of different classes of perfluorinated compounds and the relative susceptibility of aquatic organisms and plants. When such data are available it will be feasible to develop more sophisticated models to predict the

toxicity of fluorinated compounds to aquatic organisms." There are a number of ongoing research projects investigating multiple PFAS (primarily the UCMR3 chemicals) and their precursors. However, the relative toxicity, additivity, or synergistic effects of PFAS are not fully understood and still uncertain.

9.2.2 Ecological Exposure Assessment

Detections of PFAS in tissues of top predators within both aquatic and terrestrial ecosystems (Section 6.5) points to ongoing exposure from bioaccumulative and possibly biomagnifying PFAS (Section 5.5.3). Thus, accuracy and realism within exposure and risk estimates for PFAS are important to making informed risk management decisions. With the challenges of accounting for multiple exposure pathways, building strong food web and ecological exposure pathway models is an important foundation of PFAS ERAs. Once completed, these models can be used to identify the key receptors and measures of exposure to complete the assessments.

For aquatic ecosystems, published data from laboratory studies and specific field sites are available that include both BCFs, BAFs, and biota-sediment accumulation factors (BSAFs). These values, some of which are discussed and presented in Section 5 and Table 5-1 (provided as a separate Excel file), can be used to model the measures of exposure for aquatic ecosystems. (Larson, Conder, and Arblaster 2018) used such data to conduct food chain modeling in four different avian receptors. Published values for fish are common; however, to date these values are not standardized in how they are reported (for example, wet versus dry weight; organic carbon or lipid normalization). Most importantly, these data are highly variant (Table 5-1); Environment Canada (2006) reported that field BAFs for PFOS in Canadian biota range from 6,300 to 125,000. Burkhard et al. (2012) reported that within published data sources (Giesy et al. 2010; Houde et al. 2006), laboratory and field bioaccumulation metrics usually do not agree. According to Burkhard et al. (2012), field-generated BAFs (wet weight tissue to field water plus some ingestion) for PFOS exceed BCFs (wet weight tissue to lab water) predicted in the laboratory. This is undoubtedly due to the inability or inaccuracy of laboratory models to account for both direct and food ingestion exposure pathways. LaRoe et al. (2017) pointed out that laboratory values include only accumulation across the gill membrane. Thus, ERAs are challenged with attempting to address both pathways. Larsen et al. (2018) demonstrated that using environmentally relevant sediment concentrations with standard food chain models with both BSAFs and BAFs suggested sediment pathways may be underrepresented and studied. Although the combination of direct and ingestion pathways is primarily a challenge for aquatic systems, assessing risk to wildlife exposed to multiple media (for example, amphibians, semiaquatic wildlife) is also problematic.

In addition to fish, accumulation values for benthic organisms (California black worm, *Lumbriculus variegatus*, Higgins (Higgins et al. 2007) and (Lasier et al. 2011); oysters, *Ostrea edulis*, (Thompson et al. 2011) and pelagic invertebrates (*D. magna*, (Dai et al. 2013) have also been reported. Example BSAF values from Lasier et al. (2011) for PFOS, PFOA, PFNA, PFBS, and PFHpA are all fairly low, ranging from 7 to 49.

Data for terrestrial systems are limited to primarily plants (agricultural crops) and earthworms, with little available for vertebrate prey tissue. One exception is Müller et al. (2011), which published data for a soil-to-caribou-to-wolf BAF used by ECCC ECCC (2018) in establishing a soil threshold protective of terrestrial carnivores at 2.6 mg PFOS/kg soil. In nearly all cases, these BAFs and BSAFs are available only for PFOS, though the Lasier et al. (2011) study can be used to identify BSAFs for five of the six UCMR3 PFAS.

Caution should be used in applying any of the published bioaccumulation or biomagnification data for desktop exposure estimates that are in turn used to justify remedial action. Several factors and uncertainties are associated with performing desktop food chain modeling with the limited amount of published data. Some of these considerations include the following:

- differences in diets of receptors at investigation sites versus that of studies documented in the published literature: differences in the proportions of prey items; differences in the uptake and elimination rates of PFAS or overall bioaccumulation of PFAS by the prey
- differences in physiology between the site receptors and those in published literature: capacity and magnitude of transformation; metabolism and uptake and elimination rates of PFAS; the amount/composition of protein-containing tissues to which PFAS bind; species home range and migration
- differences in physiochemical properties of the abiotic media containing PFAS between investigation sites and published study sites: bioavailability and uptake of PFAS; environmental processes (photolysis, hydrolysis, microbial aerobic and anaerobic metabolism); the presence of precursors. There is not a sufficient set of bioaccumulation data to date to account for these variations. Such studies were part of the 2019 Statements of Need for Strategic Environmental Research and Development Program (SERDP) grant projects.

These uncertainties are not completely unique to PFAS, as there are many other contaminants for which risk assessments are performed. Though there is some uncertainty with desktop food chain models for PFAS based on abiotic media, quantitative modeling does not need to be avoided. Two conclusions should be reached through food chain modeling with abiotic media and literature based BAFs/BSAFs/BCFs: either concentrations at the site are sufficiently low such that it can be concluded that risk to the environment is negligible and acceptable or concentrations suggest further evaluation by either refined baseline problem formulation or a baseline ecological risk assessment (BERA). Conducting BERAs for sites with PFAS should not be substantially different from BERAs for sites with other chemicals. Either in situ or ex situ direct toxicity tests with representative organisms can and should be performed when exceeding the limited ecological risk thresholds that are available. Likewise, measured concentrations of PFAS in prey should be obtained if desktop food chain modeled exposure exceeds TRVs. But the biggest challenges for measuring PFAS in biota have to do with the unique analytical chemistry method issues (Section 11). Challenges such as selecting the correct biota to sample, matching the prey items to the diets of upper trophic level biota, or obtaining sufficient tissue volume for chemical analysis may exist, but these issues are not unique to PFAS investigations.

9.2.3 Risk Characterization

Some aquatic toxicity data (Table 7-1 provided as a separate Excel file) are available for environmental risk assessment for a few PFAS, but wildlife data are still incomplete. Adequate, though not abundant, data are available for completing wildlife risk assessment, primarily for PFOS. The ability to complete risk assessments for other PFAS regularly analyzed and detected in environmental investigations (Section 6) is limited. However, with the exposure data discussed in Section 5.5 and Section 6.5, and methods discussed in Section 9.2.2, the foundations of a quantitative risk characterization can be completed for PFOS and to an extent, PFOA. Risk assessment for other PFAS can be made with some conservative assumptions and use of PFOS data as a surrogate. Such risk characterizations using nonsite-specific abiotic media, surrogate information, and tools can form the basis of screening level assessments. These screening assessments can be used to make more informed decisions regarding the need for site-specific assessments, including the collection of site-specific tissue data. However, within these screening assessments, discussion of the uncertainties and data gaps and assumptions made should be included to inform the risk management decisions.

9.3 Uncertainty

In performing a site risk assessment, including information and a discussion regarding key factors of uncertainty in the risk characterization can be important. As noted by (USEPA, 1989 #1323@@author-year}, the source and degree of uncertainty associated with the risk characterization is needed to help decision makers (for example, risk managers, stakeholders), with sufficient level of detail to allow them to make informed risk management decisions (National Research Council 2009).

As noted throughout this guidance, while the science of characterizing and evaluating potential risks associated with PFAS exposure continues to develop, there are still uncertainties that arise in conducting site-specific risk assessments for sites with PFAS impacts. This section lists potentially critical uncertainties that, depending on the methodologies and assumptions used in a particular site-specific risk assessment, may warrant a discussion to help decision makers and stakeholders interpret and appropriately use the results of a risk assessment.

9.3.1 Fate and Transport

Site-specific risk assessments typically characterize risks associated with potential contaminant exposure that could occur currently or in the future. To characterize potential future exposures, conservative models are often used as tools to predict the fate and transport of chemicals in the environment. With regard to PFAS fate and transport, uncertainties can be introduced as follows:

- Estimating future environmental concentrations due to airborne wet and dry deposition (Section 5.3.2)
- Estimating the transformation of PFAA precursors to PFAA daughter end products (Section 5.4.2, Section 10.4.4) in the environment
- Modeling groundwater transport considering such factors as chemical-specific retardation (Section 10.4.1) and back-diffusion (Section 10.4.3.3)
- Estimating the bioaccumulation/bioconcentration of PFAS (Section 5.5.2, Section 9.2.1, Section 9.2.2) in a particular animal/plant or via food chain modeling

9.3.2 Human Toxicity

Human health risk assessments typically involve the use of toxicity values that are derived in a manner that is intended to represent a “reasonable conservative estimate” (USEPA 2012a) of the dose-response in humans. All of the toxicity values that have been derived by agencies for PFAS for use in site risk assessments are based upon animal studies with human studies used to support the hazard identification component of the risk assessment (Section 7.1.4). There is also a lack of toxicity values for many PFAS, which with their absence could result in an underestimate of the risks associated with PFAS exposure.

Overall, with regard to PFAS human toxicity, uncertainties in conducting a risk assessment can be introduced as follows:

- Missing dose-response information for site-related PFAS to which receptors could be exposed (Section 7.1, Section 9.1.1.2)
- Using toxicity values for a particular PFAS as a surrogate for another (Section 9.1.1.2)

9.3.3 Ecological Toxicity

As with human health risk assessments, ERAs often use TRVs that are generic and not site-specific. These generic TRVs are conservative by design because they are used for screening purposes (USEPA 2004). Likewise, there is a degree of conservatism incorporated into the derivation of generic criteria (for example, ambient water criteria) to account for uncertainty (Section 9.2.1).

Overall, with regard to PFAS ecological toxicity, uncertainties in conducting a risk assessment stem from using toxicological information from surrogate organism(s) to evaluate potential risks for organisms for which toxicity studies do not exist (Section 9.2.1)

9.3.4 Accounting for Nonsite-Related PFAS

Site-specific risk assessments rely on site characterization information (and as needed, modeling) to help estimate the amount of exposure receptors could be subject to currently or in the future. Given the widespread presence of PFAS in the environment (Section 6), including the potential of upgradient off-site PFAS impacts to migrate onto subject properties (Section 10.5), discerning “background” anthropogenic or off-site PFAS impacts at a site from site-related impacts can be challenging. To streamline risk assessments, it may be conservatively assumed initially that concentrations of PFAS are entirely site-related. Doing so, however, may overestimate the risks associated with site-related releases.

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