Levels, Trends, and Health Effects of Dioxins and Related Compounds in Aquatic Biota

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Abstract The objective of this chapter is to review current knowledge of the levels, trends, and health effects of dioxins and dioxin-like compounds (DLCs) including polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs), polybrominated dibenzo-*p*-dioxins and dibenzofurans (PBDD/Fs), and polychlorinated biphenyls (PCBs) in aquatic biota, with a special focus on high trophic level species. DLCs can be released into the environment through storm runoff, air deposition, wastewater discharge from industrial processes, and leaching from landfills. To characterize their influences in biota, studies examining levels and trends of DLCs from invertebrates to vertebrates from several regions (the Arctic, North America, Asia and Europe) are reviewed. Over several decades, such studies have helped elucidate the accumulation, possible sources, metabolic fate, as well as the potential health effects of dioxins and DLCs in aquatic biota. The trophic transfer of these compounds via bioaccumulation and biomagnification can result in higher concentrations in top predators, and a wide range of toxic effects (e.g., endocrine disruption, developmental and reproductive effects, and immunotoxicity) has been reported in diverse species, especially those occupying high trophic levels, e.g., marine mammals. Because of their high trophic position and widespread distribution, marine mammals are valuable sentinel species for PCB and DLC contamination, providing insights into possible sources, transport pathways, and the distribution of these compounds on a global scale. Population-levels effects related to contaminant-induced reproductive impairment and disease have been reported in wildlife inhabiting polluted regions, and the occurrence of mass mortalities among marine mammal populations has been linked to high body burdens of immunotoxic compounds, notably PCBs. Many affected populations have never recovered to their original levels. For many contaminant-stressed populations, the added stress of climate change is exacerbating the problem, causing shifts in food webs and increasing both the distribution and toxicity of POPs in coastal and oceanic environments. Critical data gaps and future research challenges are highlighted as areas that require further study.

Keywords Aquatic biota, Brominated dibenzo-*p*-dioxins and dibenzofurans, Chlorinated dibenzo-*p*-dioxins and dibenzofurans, Climate change, Dioxin-like PCBs, Immunotoxicity, Marine mammals, Mass mortalities, Polychlorinated biphenyls, Trophic transfer

Contents

1 Introduction

The environmental and human health implications of dioxins and dioxin-like compounds (DLCs) have been of ongoing concern since the mid-1980s. "Dioxins" generally refers to 75 congeners of polychlorinated dibenzo-*p*-dioxins (PCDDs) and 135 congeners of dibenzofurans (PCDFs). Seventeen of these 210 PCDD/Fs congeners have chlorine atoms in the 2, 3, 7, and 8 positions of the molecular structure and exhibit high toxicity [1]. Twelve of the 209 polychlorinated biphenyl (PCBs) congeners, with a similar stereostructure to PCDD/Fs, i.e., PCB-77, -81, -105, -114, -118, -123, -126, -156, -157, -167, -169, and -189, are known as dioxin-like PCBs (dl-PCBs) or DLCs. These 29 compounds can be bound to the aryl hydrocarbon receptor (AhR) and induce the AhR-mediated toxic responses. They also were among the first group of compounds to be included in the toxic equivalency factors (TEFs) scheme by the World Health Organization (WHO) in 1997 [1]. The most toxic congener 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) is used as a reference congener in the TEF scheme with a TEF value defined as 1, and the toxicity of other dioxins and DLC was assigned a value in between 0 and 1 relative to 2,3,7,8-TCDD's TEF. The concepts of TEFs and toxic equivalent (TEQ) concentrations have been introduced to facilitate risk assessments and the regulatory control of dioxin and DLC exposure [1, 2]. Later on, in 2011, a joint WHO and United Nations Environment Programme (UNEP) expert panel evaluated and extended the TEF scheme of dioxin-like compounds to include polybrominated dibenzo-*p*-dioxins (PBDDs), polybrominated dibenzofurans (PBDFs), and certain dioxin-like polybrominated biphenyls (PBBs) [3]. A detailed review of the validity and criteria for inclusion in the TEF concept was recently completed [2, 3]. Although there are a large number of other halogenated compounds (e.g., polychloronaphthalenes, polybrominated naphthalenes, mixed halogenated dibenzo-*p*-dioxins, mixed halogenated dibenzofurans, hexachlorobenzene, and polychloroterphenyls, among others) which meet the inclusion criteria for the TEF scheme, they are not included herein due to the lack of environmental and toxicological data. The chemical structures of PCDD/Fs, PBDD/Fs, PCBs, and related compounds are shown in Fig. 1.

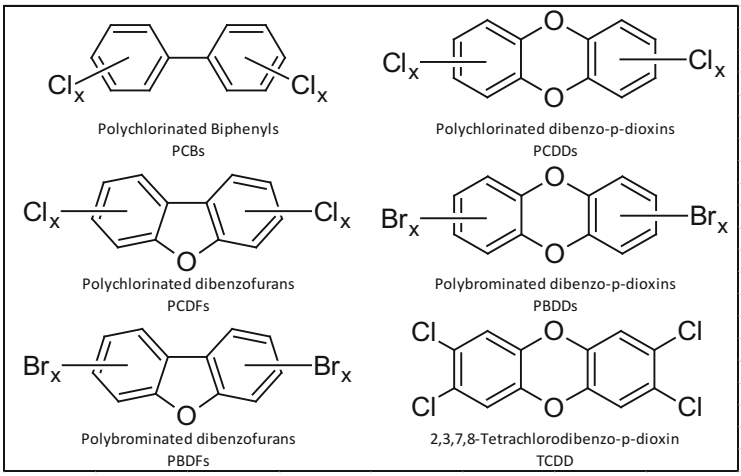

Fig. 1 Structures of dioxin and dioxin-like halogenated compounds

PCDDs and PCDFs are released into the environment from different combustion processes [4–7], and are sometimes present in various chlorinated chemical formulations as byproducts or impurities [8–10]. These compounds can be produced by a wide range of manufacturing processes such as incineration and iron ore sinter plants, as well as from accidental fires. Among the different emission sources, higher levels can be produced by waste treatment processes that use incinerators without proper emission controls [11, 12]. PBDDs and PBDFs have been found in combustion gases (processes) and combustion engines [13–15], and may occur as impurities in commercial PBDE (polybrominated diphenyl ether) mixtures [16, 17]. Large amounts of PBDD/Fs may be formed during fires under uncontrolled combustion conditions in the presence of PBDEs [15, 18–20]. In contrast to the unintended generation of dioxins, PCBs were manufactured for industrial usage and they were typically released from the application or disposal of industrial PCB-containing products. Although the domestic production of PCBs was banned in 1979, PCBs are still used in closed systems such as transformers, capacitors, and other electrical equipment. Four decades later, PCBs can still be detected in the air, water, sediments, soil, and biota. Most PCBs in water are bound to particulates and sediments, and are slowly released over a long period of time (decades). Because of their stability and ongoing inputs, PCBs are subject to recycling in food webs and will remain an environmental concern for the foreseeable future [21].

Because of their lipophilic nature and resistance to metabolism, PCBs, dioxins, and related compounds bioaccumulate and biomagnify in the fatty tissues of animals and humans. PCBs can easily reach higher concentrations in predator species at the upper trophic levels [22, 23] and are the predominant contaminants in most wildlife populations today [24, 25]. High levels of dioxins and PCBs have been detected in dolphins [26–28], harbor seals (*Phoca vitulina*) [25, 29, 30],

northern fur seals (*Callorhinus ursinus*) [31], hooded seals (*Cystophora cristata*) [32], Steller sea lions (*Eumetopias jubatus*) [33], sharks [27, 34], predatory birds [28, 35], and human tissues [28, 36–38]. Toxic responses to DLCs including immunotoxicity, endocrine disruption, and adverse effects on reproduction and development have been observed in diverse species of biota [39–42]. A large amount of data suggests that PCBs and DLCs have adversely affected the health of marine mammals [40, 41, 43–45], and are associated with endocrine-disrupting effects, immune suppression, infertility, skeletal abnormalities, and population declines among seals from the North and Baltic Seas [44, 46–49]. PCBs are also associated with a high prevalence of neoplasms and carcinoma that cause mortality in California sea lions (*Zalophus californianus*) [50]. Reproductive effects resulting in declines in otter (*Lutra lutra*) populations in Europe have been linked to high concentrations of OC contaminants, notably PCBs [44, 51–53].

PCBs and PCDD/Fs have long been suspected to play a role in the recurring epizootics and large-scale mortalities among marine mammals, including US Atlantic coast harbor seals [54, 55] and bottlenose dolphins (*Tursiops truncatus*) [56]; seals in the Baltic and North Seas [57, 58]; Mediterranean striped dolphins (*Stenella coeruleoalba*) [59–61]; Baikal seals (*Phoca sibirica*) [62]; and Caspian seals (*Phoca caspica*) [63], among others. Feeding studies conducted in the mid-1980s and 1990s demonstrated the sensitivity of harbor seals to PCB and PCDD/F exposure and helped establish a threshold level for PCB-related toxic effects in adult marine mammals. Harbor seals fed PCDD/F and PCB-contaminated fish exhibited reproductive impairment [48], reduced plasma thyroid hormone and retinol levels [64], and the suppression of numerous cellular and humoral immune functions [65, 66]. Recent biomarker studies indicate that nursing seal pups with relatively low blubber concentrations of PCBs may be vulnerable to immune- and endocrine disrupting effects during a sensitive window of development [25, 67–70].

The study of temporal trends for PCBs, dioxins, and other DLCs in biota is useful to aid policy makers in developing effective regulatory policies for the protection of public health and the environment. Trend studies provide information that places current environmental inputs and chemical loading into context and helps in the assessment of potential future impacts. This chapter provides an overview of levels, trends, and health effects of PCDD/Fs, PBDD/Fs, and PCBs in aquatic species from invertebrates to vertebrates from different regions, including phytoplankton, zooplankton, shellfish, fish, turtles, seabirds, and marine mammals. Knowledge gaps and potential future research perspectives are highlighted.

2 Sources

2.1 PCDD/Fs and PBDD/Fs

PCDD/Fs and PBDD/Fs are the byproducts of many industrial and combustion processes. Social and scientific concerns regarding PCDD/Fs increased with the detection of TCDD in Agent Orange [71], the herbicide that was widely used during the Vietnam War [71, 72]. Three mechanisms for the formation of PCDD/Fs during incineration have been proposed. These mechanisms include the input of wastes containing unburned PCDD/Fs, combustion processes in the presence of precursors (chlorinated compounds) of PCDD/Fs, and de novo synthesis [73–77]. In accordance with the Stockholm Convention, the USA, Canada, Australia, Japan, and certain European countries have performed nationwide surveys to create an emission inventory of PCDD/Fs in the atmosphere from 1993 to 1997, and these data were intended to identify the potential emission sources of PCDD/Fs [78]. The major emission source of PCDD/F is waste incineration, including municipal, hazardous, and industrial types, which accounted for 69% of the total PCDD/F emissions to the atmosphere. The next highest contributors to the total emissions of PCDD/Fs are the combustion process of iron and steel (10%) and non-ferrous metal processing (8%). Other emission sources of PCDD/Fs are chloralkali processes, the bleaching of pulp and paper, the burning of chlorine–containing fuels, and the production of pentachlorophenols [78–85].

PBDD/Fs are also unintentional by-products of incineration processes, and they have similar physico-chemical properties and anthropogenic sources as PCDD/Fs [86]. An important source of PBDD/F is the incineration of products containing BFRs and the thermolysis of BFR material, e.g., PBDEs during fire events [18–20]. PBDD/Fs can also be formed during thermal processing procedures of PBDEs such as polyeurethane foam extrusion, molding and recycling, and degradation [19, 86, 87] and ultra-violet irradiation of deca-BDE [88]. Additionally, PBDD/Fs are found at trace levels as impurities in commercial BFR products, such as DE-71, DE-79, DE-83, and some deca-BDE products [16, 17, 89].

2.2 PCBs

From 1929 until their prohibition in 1979, PCBs were in widespread use as closed systems and heat transfer fluids, hydraulic fluids and lubricants, plasticizers, and fire retardants [9]. Over five decades, the USA was responsible for approximately half of the world's production of PCBs and imported 50% of the PCBs produced by other countries [90]. PCBs are still authorized for use in many applications [9]. Fresh sources of PCBs include in-service electrical equipment, transformers, machinery, manufacturing sites, building materials, landfills and scrap yards, and waste and recycling operations, many of which are located in densely populated

urban/industrial centers [9, 91]. Because of evidence of adverse health effects in wildlife and humans, PCB production and use was banned by most developed countries in the late 1970s. However, approximately 1.5 million metric tons were produced worldwide in addition to 650,000 metric tons in the USA, and large volumes of PCBs are still contained in transformer equipment and landfills [92]. Incomplete combustion and industrial processes are also an important source of PCBs [93, 94]. Emerging evidence suggests that non-legacy PCBs are unintentionally present in pigments used for dyes, inks, and paints [95]. It was estimated by the late 1980s that only about 1% of all PCBs had reached the oceans, while about 30% had accumulated in dumpsites and sediments of rivers, coastal zones, and estuaries [96]. Because of fresh inputs (from current permitted uses) and vast environmental reservoirs, PCBs are expected to remain the predominant contaminants in aquatic and marine biota at least until 2050 [21].

3 Levels and Trends in Aquatic Biota

3.1 Invertebrates

Understanding the accumulation of dioxins and DLCs in phytoplankton is essential for assessing the occurrence, transport, and distribution of these contaminants in aquatic environments. Phytoplankton uptake influences the fate and transport of pollutants since it is a key step in the transfer of pollutants from water to fish [97–99]. In addition, phytoplankton uptake and the subsequent transfer to zooplankton result in depositional fluxes of organic pollutants in underlying aquatic environments [100].

Joiris and Overloop [101] determined the concentrations of PCBs in phytoplankton and zooplankton that were collected from the Indian sector of the Southern Ocean in 1987. The PCB concentration in netplankton (200 μm mesh size, primarily zooplankton) was 0.35 μg/g dry weight (dw) or 5.8 μg/g lw, which was about half of that measured in phytoplankton (0.74 μg/g dw) on a dry weight basis and about a third of the phytoplankton level (16.3 μg/g lw) on a lipid weight basis. The difference between phytoplankton and zooplankton was even more extreme when reported on a water volume basis thereby emphasizing the need for consistent units when comparing studies. The PCB levels in this study were similar to those found in North Sea zooplankton (0.7 μg/g dw) [102]. Galbán-Malagón et al. [103] recently reported the concentrations of PCBs and other organochlorines in seawater and phytoplankton from the Southern Ocean during their Antarctic cruises in 2005, 2008, and 2009. The PCB concentrations in phytoplankton from this study ranged from 0.0027 to 0.014 μg/g dw which was 1–2 orders of magnitude lower than the 1987 study. The long-term decreasing trends in PCB levels were also found in seawater from the Southern Ocean, with a half-life of 5.7 years.

Seawater and planktonic copepods (*Calanus glacialis* and *C. hyperboreus*) were collected from the Alaskan and Canadian Arctic regions to investigate the spatial distribution and bioaccumulation of organochlorines (OCs) such as PCBs [104]. The PCB concentrations in Alaskan and western Canadian zooplankton (12.6–33.8 ng/g dw) were comparable to those from northern Baffin Bay (30.2 ng/g dw) but lower than those from Rankin Inlet in central Canada (54.5 ng/g dw).

Okumura et al. [105] reported the bioaccumulation of PCDD/Fs and dl-PCBs in lower trophic level organisms collected from Sendai Bay, Japan. The total concentrations of PCDDs, PCDFs, and dl-PCBs in phytoplankton were 150, 12, and 51 pg/g wet weight (ww), respectively. The PCDD/F concentrations in zooplankton (which are primary consumers) were lower than the levels in phytoplankton (a primary producer), but the dl-PCBs concentrations in zooplankton were higher than the levels in phytoplankton thereby indicating a difference in bioaccumulation between PCDD/Fs and dl-PCBs at the lowest trophic levels.

Wan et al. [106] reported PCDD/Fs and PCBs in a marine food web including the phytoplankton and zooplankton collected from Bohai Bay, China. The concentrations of PCDD/Fs were 28.9 pg/g ww (0.50 pg TEQ/g ww) in phytoplankton and 18 pg/g ww (0.32 pg TEQ/g ww) in zooplankton. Dl-PCB concentrations were 57.8 and 8.4 pg/g ww (0.50 and 0.32 pg TEQ/g ww) in phytoplankton and zooplankton, respectively.

Peltonen et al. [107] reported the concentrations of PCDDs, PCDFs, and PCBs in offshore zooplankton (size from 0.2 to 20 mm) collected in 2001, 2002, and 2010 from the northern and central Baltic Sea. Concentrations of PCDD/Fs were 10.1–21.7 pg/g lw WHO_{2005}-TEQ in 2001/2002 and were 7.2–19.3 pg/g lw WHO_{2005}-TEQ in 2010. Among the PCDD/Fs, the most toxic congeners 2,3,7,8-TCDD, 1,2,3,7,8-PeCDD, 2,3,7,8-TCDF, and 2,3,4,7,8-PeCDF contributed above 80% of the total toxicity of PCDD/Fs. PCB concentrations were 6.0–12.9 pg/g lw WHO_{2005}-TEQ in 2001/2002 and were 3.7–9.1 pg/g lw WHO_{2005}-TEQ in 2010 and few temporal differences were noticed. However, 1,2,3,4,6,7,8-HpCDF and OCDF were found to predominate in 2001–2002, especially in the eastern Gulf of Finland (average concentrations 50 and 89 pg/g lw, respectively). The PCB concentrations were highest in the Gulf of Finland and in the Bothnian Bay, and concentrations of most PCBs were somewhat higher in 2001–2002 than in 2010. Among the dioxin-like PCBs, the concentrations of PCB-77 were highest (271–572 pg/g lw), followed by PCB-126 (32–113 pg/g lw), PCB-169 (5.81–25.5 pg/g lw).

Dynamic bioaccumulation models for these contaminants have been developed by researchers through field surveys of dioxins and DLCs in plankton [98, 108]. Dachs et al. [108] developed dynamic models that couple air–water exchange and the phytoplankton uptake of POPs and then applied them to field PCB measurements. The simulation results suggested that air–water exchange and other atmospheric-derived inputs primarily contribute to the POP concentrations in phytoplankton. In addition, this process suggested a major role in the global cycling

of POPs, with POP atmospheric deposition considered a major contamination source for the world's oceans.

Shellfish are useful sentinel species for studying levels and trends of contaminants in aquatic environments. Diaz [109] measured dioxins in shellfish from the Oakland Bay in Washington State, USA and found that the dioxin concentrations in Manila clams ranged from 0.05 to 0.27 pg/g lw, which were similar to those in Pacific oysters (0.13–0.37 pg/g lw), and lower than those in Kumamoto oysters (0.3–0.6 pg/g lw). In mussels, total dioxin concentration was about 0.17 pg/g lw. Parera et al. [110] analyzed PCDDs, PCDFs, and PCBs in marine shellfish (murex, carpet shell, and mussel) of the Ebro River Delta, Spain and found that PCDD/F concentrations were 0.29–1.17 pg/g ww, and the concentrations of dl-PCBs were 24.6–399 pg/g ww. PCDFs contributed a larger content to WHO-TEQ_{2005} extent than PCDDs. A slight decrease of PCDD/F and dl-PCB concentrations was noticed from 2006 to 2012, which was in agreement with the decrease in PCDD/F and PCB concentrations observed in human serum in Spain [111]. The levels of PCDDs, PCDFs, and PCBs for 123 Spanish commercial oyster, mussel, and clam samples from 1995 to 2003 were determined and there was a significant decrease of dioxin and dl-PCB concentrations since 1995. The decrease of dioxin levels was more obvious than that of dl-PCBs, especially during the early years of the study [112]. Munschy et al. [113] evaluated the levels and temporal trends of PCDD/Fs in archived marine mussels collected between 1981 and 2005 from selected sites along French coasts and noticed a pronounced decrease in PCDD/F concentrations over the 24-year period at most sites, except Toulon on the Mediterranean Sea.

In 2005, PBDDs were identified and reported in blue mussels from the Baltic Sea [114], and the concentration of total triBDD was estimated to be 170 ng/g lw [114]. Haglund et al. [115] measured PBDDs in marine fish, mussels, and shellfish from the Bothnian Bay and Bothnian Sea, the West Coast of Sweden, and the Baltic Proper. They found that the levels of PBDDs were higher in mussels than in other species, and there was an increasing temporal trend of PBDDs in mussels with an average annual increase of 11% from 1995 to 2003 [115]. Mussels, oysters, and scallops in Scotland were analyzed for PCDD/Fs, PBDD/Fs, PCBs, and other compounds [116]. PBDFs predominated over brominated dioxins. Generally, mussels and oysters had relatively higher levels of contamination than scallops, and their levels of contamination in the Southern beaches were greater than those in the north and northwest, which was consistent with Scottish industrial activity levels [116]. Fernandes et al. [117] also investigated PBDD/Fs in Pacific oysters (*Crassostrea gigas*), native oysters (*Ostrea edulis*), mussels (*Mytilus edulis*), scallops (*Pecten maximus*), and cockles (*Cerastoderma edule*) collected between 2006 and 2007 in the UK. PBDFs were detected more frequently and generally at a higher level than PBDDs. Oysters and mussels displayed relatively higher levels of PBDD/Fs. The levels of PBDD/Fs were consistent with the extent of local industrialization with lower levels observed in more remote areas such as the north of Scotland [117].

3.2 Fish

Monitoring environmental levels and trends of contaminants in fish is useful for studies of contamination levels and patterns in aquatic ecosystems, and for assessing potential health risks associated with wildlife and human consumption [118]. Kiviranta et al. [119] analyzed Baltic herring samples caught from the Baltic Sea during the spring periods of 1993–1994 and 1999 for PCDD/Fs and PCBs. Concentrations of some PCDD/F congeners and some PCB congeners in herring measured in 1993–1994 in the Gulf of Finland showed a clear correlation with the age of herring, which is consistent with the bioaccumulation of PCDD/Fs and PCBs. The PCDD/F concentrations ranged from 1 to 27 pg TEQ/g ww, and PCB concentrations reached 32 pg TEQ/g ww. No clear downward concentration trend of PCDD/Fs and PCBs in herring was observed between 1993 and 1994 and 1999. Karl et al. [120] determined PCDD/F and dl-PCB levels in the muscle of herring collected in 2006 and compared them with their previous study conducted at the same location in 1999 from the Western and Central Baltic Sea. The results from the 2006 study showed that PCDD/Fs and dl-PCBs of all herring samples were found to be below the maximum and action levels, and the average concentration was 3.55 pg TEQ/g ww. The comparison between 2006 and 1999 did not reveal obvious change in contamination levels during the 7-year time period. Similarly, PCDD/F and dl-PCB concentrations in Baltic herring (*Clupea harengus*) from the Swedish coast were found to be relatively stable since the mid to late 1990s; however, a general decreasing trend was seen for TEQ_{2005} PCDD, PCDF, and dl-PCB values at all sites, especially in the southern Bothnian Sea since 2001 [121]. It is unknown why concentrations in Baltic herring are not following the decreasing trend observed in other environmental matrices [121]. In Finland, altogether 344 samples of Baltic herring from 1978 to 2009 were collected across the Finnish coast of the Baltic Sea [122]. During the 31-year period, PCDD/F and PCB concentrations decreased about 80%, from 20 to 5 pg TEQ/g ww. The current concentrations of PCDD/Fs and PCBs in Baltic herring are relatively low, and mostly below EU maximum accepted levels, and are expected to continue decreasing [122].

Haglund et al. [115] determined PBDDs in marine fish from the Bothnian Bay and Bothnian Sea, the West Coast of Sweden, and the Baltic Proper. The levels of PBDDs in littoral fish generally exceeded those of PCDDs in Baltic Proper. Recently, Haglund et al. [123] reported the PBDDs in perch (*Perca fluviatilis*) from a Baltic Sea background contaminated area between 1990 and 2005. Although no temporal trend was found, large variations of PBDD concentrations were observed between consecutive years. Ashizuka et al. [124] measured PBDD/Fs in fish samples from three regions in Japan. 1,2,3,4,6,7,8-HpBDF was the most abundant congener of PBDFs with concentrations of 0.10–25.6 pg/g ww.

Bordajandi et al. [125] determined PCDD/Fs and PCBs in edible fish, namely wedge sole (*Dicologoglossa cuneata*), common sole (*Solea vulgaris*), white seabream (*Diplodus sargus*), sardine (*Sardina pilchardus*), and angler fish (*Lophius*

piscatorius) from the Coast of Huelva, on the Spanish southwest Atlantic coast. Total PCB concentrations were 861–23,787 pg/g ww, while 2,3,7,8-PCDD/Fs concentrations ranged from 0.2 to 1.18 pg/g ww. PCDD/F concentrations ranged from 0.038 to 0.186 pg TEQ/g ww, values well below the maximum concentrations established by the EU. PCBs contributed most to the total TEQ content in most species studied. Gómara et al. [112] also investigated PCDD/F and PCB content of 123 Spanish commercial salmon, tuna fish, and sardine samples from 1995 to 2003. A significant decrease in dioxin and non-ortho PCB concentrations was found over the years. The decrease was greater for dioxins than for non-ortho PCBs, especially during the early years of the study. The high contribution of PCBs to total WHO-TEQs in the fish species investigated suggests that it is important to monitor PCBs in fish products, and they should be included in further research and future legislation [112]. Parera et al. [110] reported the concentration trends of PCDD/F and dl-PCBs during 2006–2012 in marine fish in the Ebro River Delta area (Spain) and found that the concentrations of PCDD/Fs and dl-PCBs ranged from 0.03 to 0.31 pg TEQ/g ww and from 0.02 to 3.15 pg TEQ/g ww, respectively. All levels were below the maximum concentrations established by the EU Regulation. A slight decreasing trend in the levels of PCDD/F and dl-PCBs in fish was found from 2006 to 2012.

Hickey et al. [126] updated earlier reports with data from 1991 to 1998 for lake trout (*Salvelinus namaycush*) (Lake Erie only) and walleye (*Sander vitreus*) from the Great Lakes and quantified contaminant trends using multi-compartment models. As found in the past, fish from Lakes Michigan, Ontario, and Huron had the highest levels of PCBs. In the period after curtailment of chemical use, concentrations rapidly decreased, due to their relatively short half-lives from approximately 1 to 9 years. For dioxin-like PCBs, levels have not been decreasing during the 5-year period (1994 to 1998) [126]. Bhavsar et al. [127] measured concentrations of the seventeen 2,3,7,8-PCDD/Fs in lake trout (*S. namaycush*) or lake whitefish (*Coregonus clupeaformis*) collected in 1989–2003 from the Canadian Great Lakes. 2,3,7,8-TCDD, 2,3,7,8-TCDF, 1,2,3,7,8-PeCDD, 1,2,3,7,8-PeCDF, and 2,3,4,7,8-PeCDF were the most dominant congeners. The highest TEQs were from Lake Ontario lake trout (22–54 pg/g) while the TEQs for the other Canadian Great Lakes were 60–95% lower. A linearly decreasing trend for PCDD/Fs in lake trout from Lakes Ontario and Huron was found. There was no monotonously increasing or decreasing trend found for Lake Superior lake trout.

Brown et al. [128] measured PCDD/Fs and dl-PCBs in fish collected from San Francisco Bay in 2000 and from the California coast in 2001. The samples were composites of only the edible portions of the fish (skin on, skin off, or whole body minus head and guts) of comparable size and from distinct geographical areas. For all fish of all species, the mean PCDD/F was 33.1 pg TEQ/g lw. The mean for PCB-77, -126, and -169 was 109 pg TEQ/g lw. The highest concentrations of PCDD/F and dl-PCBs were found in the highly populated areas of San Francisco Bay, the Los Angeles area, and San Diego Bay.

3.3 Turtles

Snapping turtles (*Chelydra serpentina*) have been commonly used to evaluate the extent of organic chemical contamination and trends in the Great Lakes [129–139] and the Hudson River of New York [140, 141] since the 1970s. Snapping turtle eggs are also excellent bioindicators of the health conditions in wetlands and the bioavailability of organic contaminants. Snapping turtle eggs provide comprehensive information concerning the temporal and spatial trends of PCDD/Fs and PCBs [134, 136, 139]. Bonin et al. [142] compared the OCP and PCB levels in 39 snapping turtle clutches collected from ten sites along a highly polluted stretch of the St. Lawrence River in Canada. The results showed a high inter-site variability in PCB concentrations, which was consistent with those found by Bishop et al. [130] and Struger et al. [139]. De Solla et al. [135] reported a significant correlation between PCB concentrations in snapping turtle eggs and the industrial use of specific technical PCB mixtures in these areas. Hong et al. [143] reported the occurrence of planar, mono- and di-ortho PCBs in the fat tissues of snapping turtles that were collected in 1988 from rivers in the USA. The highest concentrations of PCBs (1,010 μg/g ww) and TEQs (106,000 pg TEQ/g ww) were found in snapping turtles from the Grasse River in northern New York, where extensive PCB and PCDF contamination was associated with the aluminum industry. Relatively higher PCBs (258 μg/g ww) and TEQs (47,000 pg TEQ/g ww) were also found in snapping turtles from the Snye Marsh of the St. Lawrence River, which is contaminated by large point sources. Dabrowska et al. [132] measured the TEQ concentrations of dl-PCBs in the fat tissue, eggs, and plasma of snapping turtles from the Ohio Basin of Lake Erie, USA. The TEQ concentrations, which were based on mammal-specific TEFs, ranged from 1.4 to 6.9 pg/g ww and from 21 to 582 pg/g ww in plasma and eggs, respectively. Significant correlations were found for PCB concentrations among fat tissues, eggs, and plasma from snapping turtles.

In comparison with PCBs, few studies are available on the PCDD/F concentrations in snapping turtle eggs or tissues. Most studies have reported the predominance of 2,3,7,8-TCDD for PCDDs and 2,3,4,7,8-PeCDF and 2,3,7,8-TCDF for PCDFs in snapping turtle eggs, depending on various factors such as the metabolism and the specific source of these contaminants [129, 134, 139]. Similar to the occurrence of PCDD/F congeners in eggs, the fat and liver tissues of snapping turtles from the St. Lawrence River, USA, were also dominated by 2,3,7,8-TCDD and 2,3,4,7,8-PeCDF [137].

Sea turtles are relatively sedentary, long-lived reptiles containing large fat bodies for POP accumulation [143–146]. Although known to be robust to physical damage, sea turtles are surprisingly very susceptible to chemical contaminants [147]. Following a long (10-year) open-water pelagic developmental phase, juvenile turtles settle in near-shore environments and forage on seagrass and algae close to land-based contaminant sources. All seven species of marine turtles worldwide are currently threatened or endangered, thus, sea turtles are important bioindicators of the levels and trends of chemical contamination in near-shore marine biota

[145, 146, 148–152]. Keller et al. [145] investigated PCBs and OCPs and their possible health effects on loggerhead sea turtles (*Caretta caretta*) from Core Sound, North Carolina by associating their concentrations with clinical health assessment data, including hematology, plasma chemistry, and body condition. They found that PCBs and other OC contaminants might affect the health of loggerhead sea turtles even though sea turtles, with an herbivorous diet, tend to accumulate lower concentrations of POPs compared with other wildlife.

Storelli et al. [146] measured PCBs including coplanar PCBs in loggerhead sea turtles (*C. caretta*) from the eastern Mediterranean Sea. Concentrations of PCBs in loggerhead turtles ranged from 4.65 to 52.3 ng/g ww, and the estimated toxic equivalents of non- and mono-ortho PCBs ranged from 1.54 to 5.86 pg TEQ/g ww. Alava et al. [148] measured PCBs in the loggerhead sea turtle egg yolk from North Carolina, eastern Florida, and western Florida, USA. The concentrations of PCBs ranged from 1.54 to 3,500 ng/g lw. PCB concentrations were higher in North Carolina egg samples than those in other regions, and an increasing gradient along the southeast coast around the Florida peninsula to North Carolina was found, likely due to the foraging site selection of the nesting females.

Stewart et al. [152] measured PCBs in fat and blubber of leatherback turtles (*Dermochelys coriacea*), and established baselines in blood and eggs in nesting turtles. Concentrations of PCBs in fat, blubber, blood, and egg were 4.87–188, 1.52–106, 0.162–6.54, and 0.441–19.1 ng/g ww, respectively. PCBs were found to be significantly and positively correlated between blood and eggs, suggesting maternal transfer. Camacho et al. [153] determined PCBs in green sea turtles (*Chelonia mydas*) and hawksbills (*Eretmochelys imbricata*) from the Boa Vista island, Cape Verde, Portugal. Higher concentrations of PCBs were detected in green turtles (∑PCBs 0.73 ng/g ww) than in hawksbills (0.19 ng/g ww).

Hermanussen et al. [154] investigated levels of PCDD/Fs in green sea turtles from Moreton Bay, Queensland, Australia and found higher concentrations and TEQs in turtles foraging in close proximity to river inputs. The highest levels (PCDD/Fs 580 pg/g lw and TEQs 2.7–160 pg/g lw) were elevated compared to levels reported in other higher trophic level wildlife, including seals from Greenland, Mediterranean dolphins, and Baikal seals. The results indicate that certain populations of green sea turtles that forage in close proximity to land-based secondary sources may be among the higher risk groups in terms of sensitivity to and metabolism of PCDD/Fs. Given the endangered status of many populations, future studies are needed to investigate sensitivity to and metabolism of PCDD/Fs in sea turtles.

3.4 Seabirds and Bird Eggs

3.4.1 Polar Region

Dioxins and DLCs were examined in seabirds from the Canadian Arctic (Prince Leopold Island, Lancaster Sound) [155]. Black-legged kittiwakes (*Rissa tridactyla*) collected in 1993 contained 119 pg/g lw of ∑PCDDs, 651 pg/g lw of ∑PCDFs, and 7,436 pg/g lw of non-ortho PCBs (∑NO-PCBs) in the liver. Comparable concentrations were observed in thick-billed murre (*Uria lomvia*), i.e., 169 ng/g pg lw of ∑PCDDs, 431 pg/g lw of ∑PCDFs, and 5,066 pg/g lw of ∑NO-PCBs, and northern fulmar (*Fulmarus glacialis*) contained elevated concentrations, i.e., 2,456, 7,218, and 24,067 pg/g lw of ∑PCDDs, ∑PCDFs, and ∑NO-PCBs, respectively. The ∑TEQ values were 1,117, 719, and 8,192 pg/g lw in kittiwake, murre, and fulmar, respectively. The predominant PCDD/F congener in all species was 2,3,4,7,8-PeCDF. Of the measured non-ortho PCBs, PCB-126 occurred in the highest concentrations and contributed the majority of non-ortho PCB-TEQ in all three species. Braune and Simon [155] also investigated concentration changes from 1975 to 1993, and they found that the concentrations of most PCDD/Fs decreased in the fulmars and kittiwakes but increased in the murres. Various metabolic capacities for PCDD/Fs and different migratory habits may result in those trends among species. Braune et al. [156] examined the liver tissues of northern fulmars collected in 2003 from Prince Leopold Island. The mean ∑PCDD, ∑PCDF, and ∑NO-PCB concentrations were 47.3, 154, and 519 pg/g lw, respectively, which were generally 1–2 orders of magnitude lower than the concentrations from the same species that were collected in 1993 [155]. Consequently, the ∑TEQs declined from 1975 to 2003 in northern fulmars.

In another temporal study in the Canadian Arctic (Seymour Island), ivory gull (*Pagophila eburnea*) eggs exhibited concentration declines from 1976 to 2004 [157]. ∑PCDD concentrations decreased from 207 to 55 pg/g lw, and ∑PCDF and ∑NO-PCB concentrations decreased from 61 to 24 pg/g lw and from 6,970 to 2,220 pg/g lw, respectively. The ∑TEQ also decreased from 697 to 193 pg/g lw. The ∑TEQ concentrations were greater than the no observed adverse effect level (NOAEL) (10 pg/g ww) on reproduction reported in herring gulls [158]. In the far northwestern region of Russia, peregrine falcon eggs collected from 1987 to 2001 on the Kola Peninsula contained ∑TEQ levels of 86–640 pg/g ww [159]. In Sweden, the ∑TEQ concentrations ranged from 180 to 230 pg/g lw (7.5–8.4 pg/g ww) for PCDD/Fs and from 960 to 2,000 pg/g lw (50–100 pg/g ww) for co-planar PCBs [160].

Penguin blood was tested for dioxins and DLCs in Antarctica [161]. The mean ∑PCDD and ∑PCDF concentrations ranged from 6.5 to 22 and from 2.5 to 50 pg/g ww, respectively. PCDD/Fs were generally higher in males than in females for Gentoo (*Pygoscelis papua*) and Chinstrap penguins (*Pygoscelis antarctica*), which was likely related to the partial detoxification that occurred in females during egg formation [161]. The mean ∑NO-PCB concentrations ranged from 200 to 720 pg/g

ww in three species, including Adélie (*Pygoscelis adeliae*), Chinstrap, and Gentoo penguins. PCB-126 occurred at the highest concentrations among the four measured non-ortho PCBs. The total TEQs were 21, 12, and 62 pg/g ww in Adélie, Chinstrap, and Gentoo penguins, respectively.

3.4.2 North America

Custer et al. [162] investigated PCDD/Fs and PCBs in eggs from the piscivorous belted kingfisher (*Ceryle alcyon*) from the upper Hudson River, New York, USA, and compared them with concentrations in omnivorous spotted sandpipers (*Actitis macularia*) and insectivorous tree swallows (*Tachycineta bicolor*). Total PCB concentrations in swallow eggs (with a geometric mean of 6.8 μg/g ww) were approximately half of those present in kingfishers (11.7 μg/g ww) or sandpipers (12.6 μg/g ww). However, the $\sum TEQ_{PCB}$ values were higher in swallows (1,790 pg/g ww) than in the other two species (776 and 881 pg/g ww). Sum PCDD/F concentrations and $\sum TEQ_{PCDD/F}$ values were also higher in the swallows than the other species. The authors suggested that metabolic pathway differences in the respective food chains of these three species likely accounted for the differences in the observed TEQ concentrations.

A site-specific exposure assessment of belted kingfisher was conducted in the Tittabawassee River floodplain, Midland, Michigan (USA), where the soil and sediments exhibited some of the highest levels of dioxin contamination ever reported [163]. PCDD/F concentrations were greater in belted kingfisher eggs and nestlings nesting along the Tittabawassee River when compared with those from upstream sites. The geometric mean ∑PCDD/F concentrations were 130 and 200 pg/g ww in eggs and nestlings, respectively.

Tissues from eight bald eagles (*Haliaeetus leucocephalus*) found dead in the Upper Peninsula of Michigan, USA, in 2000 were examined for contaminants [164]. Their liver PCDD/F concentrations ranged from 23 to 4,500 pg/g ww. The total TEQs ranged from 100 to 9,100 pg/g ww, of which NO-PCBs accounted for 68–88%. Some of the TEQ values were greater than the LD_{50} threshold levels reported in white leghorn chickens (115 pg/g ww) or in double-crested cormorant embryos (550 pg/g ww) [165, 166]. Eagles with elevated TCDD or total PCB concentrations tended to have high TCDD/TCDF or PCB-126/PCB-77 ratios, which may suggest an induction of cytochrome P450 enzymes and the subsequent metabolism of TCDF and PCB-77. The TEQ concentrations generally exceeded the toxicity thresholds suggested for other avian species. Bald eagles from British Columbia, Canada (1989–1994), exhibited a mean ∑TEQ of 600 pg/g ww in the liver tissues [167]. Birds with higher 2,3,7,8-TCDD concentrations tended to have low concentrations of 2,3,7,8-TCDF, indicating a hepatic cytochrome P4501A-type induction by TCDD and the subsequent metabolism of TCDF.

Great blue heron (*Ardea herodias*) eggs were collected from 1983 to 1998 along the coast of British Columbia, Canada and were evaluated for temporal changes in PCDD/Fs and PCBs [168]. The ∑TEQ-TCDD/F concentrations declined markedly

in the early 1990s, e.g., from 136 pg/g ww (1983) to 19 pg/g ww (1998) in colonies located at the University of British Columbia. The authors attributed these declines to pulp mill changes from molecular chlorine bleaching to alternative bleaching technologies and the restricted use of chlorophenolic wood preservatives and anti-sap stains. The strong positive correlation between prey fish and heron egg contaminant levels suggested that local dietary uptake was an important route of exposure for herons.

The biomagnification factors (BMFs) of PCDDs, PCDFs, and non-ortho PCBs were investigated in the fish to osprey (*Pandion haliaetus*) egg food chain in the Willamette River, Oregon [169]. The BMFs ranged from no biomagnification to 174 (OCDD). The ∑TEQ concentrations in the eggs ranged from 6 to 78 pg/g ww for PCBs, from 2 to 24 pg/g ww for PCDDs, and from 10 to 99 pg/g ww for PCDFs. The eggs of ospreys (1999–2005) nesting along the lower portion of the Columbia River, USA, exhibited a geometric mean ∑TEQ (including PCDDs, PCDFs, and PCBs) of 43.8 pg/g ww, which was significantly lower than the concentrations (mean 62.5 pg/g ww) observed in eggs collected in 1997–1998 from the same region [170]. Similar trends have also been found for many other organochlorine pesticides in osprey eggs from the studied watershed. Double-crested cormorant (*Phalacrocorax auritus*) eggs collected from the Great Lakes of North America in 1989 exhibited similar ∑PCDD/F levels across various colonies, i.e., 1,720–2,740 pg/g lw [171]. Eggs collected in 1991 from Lake Ontario contained elevated concentrations, i.e., 4,190 pg/g lw.

Dioxin-like toxic potency was also evaluated in Forster's tern (*Sterna forsteri*) eggs from Green Bay, Lake Michigan, in North America [172]. The average ∑TEQs were 214.5 and 23.4 pg/g ww from Green Bay and Lake Poygan, respectively. These data suggest that dioxin-like effects were responsible for the intrinsic reproductive problems noted in Forster's terns from Green Bay, Lake Michigan. Notably, the reported NOAEL value for reproduction in Forster's tern was 200 pg/g ww [173].

3.4.3 Europe

Jiménez et al. [174] investigated dioxins in osprey eggs collected in Spain from 1994 to 2000. The ∑PCDD/F and ∑NO-PCB concentrations ranged from 2.6 to 14 pg/g ww and from 170 to 1,390 pg/g ww, respectively. The total TEQs ranged from 16 to 140 pg/g ww. Fifty-seven percent of examined eggs contained total PCB concentrations greater than the 4 μg/g ww, NOAEL for reduced hatchability, embryo mortality, and deformities in bald eagles [175]. Eggs from yellow-legged gulls (*Larus michahellis*) and Audouin's gulls (*Larus audouinii*) collected in 2010 from the Ebro Delta Natural Park (Spain) contained ∑PCDD/Fs of 160 and 84 pg/g lw and ∑NO-PCBs of 3,100 and 6,460 pg/g lw, respectively. The mean ∑TEQ concentrations were 290 and 540 pg/g lw in these two gull species, respectively [176].

PCDD/Fs and dl-PCBs in herring gull eggs from the North Sea and Baltic Sea were analyzed [177]. The PCDD/F concentrations were 99–366 pg/g lw, and the dl-PCB concentrations were 726–2,085 ng/g lw. A general decreasing trend of PCDD/F and dl-PCB concentrations in eggs was seen between 1988 and 2003 in both locations but the relative contaminant abundance was different. In eggs from the Baltic Sea island Heuwiese, the PCDD/F concentrations were somewhat lower than those from the North Sea islands, but dl-PCBs showed higher levels in the Baltic Sea island [177]. PCB, DDTs, and several other compounds were analyzed annually in guillemot eggs from the Baltic as part of the Swedish Environmental Monitoring Program [178]. The PCB concentrations varied among species and sites; however, they had decreased temporally by approximately 5–10% per year since the end of the 1970s [178]. For example, the mean ∑PCB concentration in guillemot eggs was approximately 300 μg/g lw in 1969 and 8.7 μg/g lw in 2011 ($n = 430$). Dioxins have been retrospectively analyzed in guillemot eggs, and significant decreasing trends were observed for TCDD, TCDF, and PCDD/Fs (1970–2011), with a decreasing rate from 1.2 to 5.1% annually. However, no trend was observed between 1990 and 2011 for TCDFs. The TEQs were calculated by using the WHO_{98} TEF [1], and the geometric mean value was estimated to be approximately 2,500 pg TEQ/g lw in 1969 and 800 pg TEQ/g lw in 2011 [178].

White-tailed sea eagle (*Haliaeetus albicilla*) eggs collected along the Swedish coast of the Baltic Sea from 1992 to 2004 contained ∑PCDD, ∑PCDF, and ∑NO-PCB concentrations of 0.4–4.1, 1.2–5.3, and 180–970 ng/g lw, respectively [35], compared to ranges of 0.11–0.16, 0.22–0.33, and 57–83 ng/g lw, respectively, in the Greenland population. Non-ortho PCBs were the major contributors to the total TEQs. No evidence was found to link the reproductive impairment in eagles to the DLC concentrations in their eggs. Another study on white-tailed sea eagle eggs from Sweden reported time trends for DDTs and ∑PCBs over four decades [44]. The estimated mean concentrations of ∑PCBs decreased in sea eagle eggs from 955 μg/g lw in 1965 to 275 μg/g lw in 2010. Eggs from Audouin's gull (*L. audouinii*) and yellow-legged gull (*Larus cachinnans*) that were collected from the western Mediterranean in 1992 were evaluated for DLCs [179]. The ∑NO-PCB and ∑PCDD/F concentrations were 4,100 and 140 pg/g dw in Audouin's gull, respectively, and they were 300 and 79 pg/g dw in yellow-legged gull. The ∑TEQ concentrations were 2,955 and 126 pg/g dw in these two species, respectively. The TEQ value in Audouin's gull was much greater than the NOAEL (10 pg/g ww) for reproduction in herring gulls [158], and was comparable to the LD_{50} (550 pg/g ww) in double-crested cormorant embryos [166].

3.4.4 Asia

Piscivorous birds of various species from Japan contained dl-PCBs of 61–12,000 ng/g lw and ∑PCDD/Fs of 30–16,000 pg/g lw in the liver [180]. The dl-PCB concentrations among the species were generally in the order of omnivores > piscivores > predators > granivores that were from the same

locations. The ∑TEQ concentrations in aquatic birds ranged from 520 to 28,000 pg/g lw.

Black-tailed gulls (*Larus crassirostris*) were also used as a bioindicator of dioxin contamination in their breeding grounds in Hokkaido, Japan [181]: the mean concentrations of ∑NO-PCBs and ∑PCDD/Fs were 9,150 and 76 pg/g lw in fat and 4,905 and 53 pg/g lw in eggs. The mean ∑TEQ values were 712 and 382 pg/g lw in fat and eggs, respectively. The TEQ values reported in these studies were generally greater than the NOAEL (10 pg/g ww) on reproduction in herring gull but lower than the NOAEL (200 pg/g ww) on reproduction in Forster's tern [158, 173].

PCBs including di-, mono-, and non-ortho PCBs were studied in the livers of common cormorants (*Phalacrocorax carbo*) from Lake Biwa, Japan [182]. The calculated mean ∑TEQ-PCB concentration was 36 ng/g lw and was dominated by PCB-118, followed by PCB-126. A significant increase in ethoxyresorufin-*O*-deethylase (EROD) and pentoxyresorufin-*O*-deethylase (PROD) activities was observed in the studied cormorants, suggesting that the contamination level was sufficient to alter biochemical responses.

Dioxin and DLC concentrations were determined in the eggs, nestlings, and adults of black-footed albatross (BfA; *Diomedea nigripes*) and short-tailed albatross (StA; *Diomedea albatrus*) collected from Torishima Island in Japan in 2002 [183]. The total TEQs ranged from 1,400 to 2,900 pg/g lw in the BfA eggs and from 220 to 2,900 in the StA eggs, nestlings, and adults. The concentrations of PCDDs, with the exception of 1,2,3,7,8-PeCDD and high-chlorinated PCDFs, in 3-month-old BfA nestlings were lower than the concentrations in 1-month-old nestlings, suggesting a developmental dilution for these compounds. The estimated biomagnification factors of the examined compounds were greater in adults than in nestlings, except for 2,3,7,8-TCDF, PCB-77, Hx-CDD/Fs, and Oc-CDD/Fs. The authors hypothesized that this trend might be explained by the preferential metabolism of 2,3,7,8-TCDF and PCB-77 and the lower uptake efficiency of high-chlorinated congeners through the gastrointestinal tract in adults.

The tissue distribution of PCDD/Fs was investigated in piscivorous birds from a heavily contaminated lake (Ya-Er Lake) in China in 1997 [184]. The concentration order of PCDD/F within piscivorous birds was liver > egg ~ heart > muscle ~ stomach > brain. The highest ∑PCDD/F and ∑TEQ concentrations were 1,690 and 552 pg/g lw, respectively, in the liver. PCDD/Fs were also examined in the eggs from eight avian species in Dongting Lake, China [185]. ∑PCDD/F concentrations ranged from 21 to 4,120 pg/g lw, and the ∑TEQ of PCDD/Fs ranged from 2.5 to 17.4 pg/g lw in these species. Although the PCDD/F patterns in the eggs may be influenced by feeding habits, elimination, and metabolism, PCDD concentrations were generally greater than PCDFs in the studied species.

DLCs were examined in the subcutaneous fat of waterbirds from the Nakdong River Estuary (NRE) in Korea [186]. The mean ∑PCDD/F concentration was 396 pg/g lw in black-tailed gull (*L. crassirostris*), a resident bird of the estuary. Resident birds generally contained higher concentrations than migratory species, e.g., 198 pg/g lw in greenshank (*Tringa nebularia*), 90 pg/g lw in common gull

(*Larus canus*) and 47 pg/g lw in common tern (*Sterna hirundo*). These data suggested that the intake of locally contaminated fish near the NRE contributed substantially to the overall burdens of piscivorous birds residing in the estuary. The ∑TEQ values ranged from 34 to 227 pg/g lw in avian species.

3.5 Marine Mammals

As top marine predators, marine mammals accumulate high body burdens of POPs via feeding over a long life span and transfer large amounts to their offspring via placental and lactational transfer. Because they accumulate complex mixtures of POPs and are sensitive to their effects, marine mammals present a "real world" exposure scenario and an early warning signal about chemicals which present the greatest risk to consumers at the top of the food chain, including humans. Marine mammals include cetaceans (whales, porpoises, and dolphins), pinnipeds (phocid seals and otarids), sea otters, sirenians (manatees and dugongs), and polar bears [187]. Apart from the otters, all of these taxa have a thick layer of blubber and spend most of their time in the ocean.

Marine mammals in many parts of the world carry a plethora of POPs in their tissues including PCBs and dioxins, OC pesticides, and compounds of emerging concern such as BFRs, PFASs, PCNs, and others. While emerging contaminants have been increasing in marine mammals [188–190], PCBs remain the predominant POP in lipid tissues and pose the greatest health risks to many populations [24–26, 68, 191]. Over the past four decades, elevated concentrations of endocrine-disrupting POPs have been linked with a number of deleterious effects in marine mammals including hormonal abnormalities, skeletal deformities, reproductive failure, neoplasms, and tumors [44, 46–50, 65, 67, 68, 192, 193]. PCBs and PCDD/Fs have long been suspected to play a role in the recurring epizootics and large-scale mortalities among marine mammals, including the US Atlantic coast harbor seals (*P. vitulina*) [54, 55] and bottlenose dolphins (*T. truncatus*) [56]; seals in the Baltic and North Seas [57, 58]; Mediterranean striped dolphins (*S. coeruleoalba*) [59–61]; Baikal seals (*P. sibirica*) [62]; and Caspian seals (*P. caspica*) [63], among others. Feeding studies conducted in the mid-1980s and 1990s demonstrated the sensitivity of harbor seals to PCB and PCDD/F exposure and helped establish a threshold level for PCB-related immune suppression and other adverse effects in adult marine mammals [43, 48, 64–66]. Recent studies using a biomarker approach indicate that the threshold for PCB-induced immune- and endocrine disrupting effects in nursing seal pups is at least an order of magnitude lower [25, 67–70].

In some cases, restrictions on the production and use of PCBs and other POPs have resulted in decreasing concentrations in marine mammals, but in many parts of the world, these declines have leveled off since the mid- to late 1980s and relatively high levels of these pollutants, especially the PCBs, persist in tissues.

3.5.1 Polar Regions

A review of temporal trends for legacy POPs (PCBs, OC pesticides) in the Arctic included 316 time series in biota from marine, freshwater, and terrestrial ecosystems in Canada, Alaska, Greenland, Iceland, and Norway (including ringed seals and polar bears) [194]. Most time series show decreasing concentrations of POPs, with only a few time-series showing significantly increasing trends.

Riget et al. [195] evaluated the levels and temporal trends of PCDD/Fs and dl-PCBs in ringed seal blubber collected in 1986, 1994, 1999, and 2003 from central East Greenland. The annual median concentrations of PCDDs and PCDFs were 5.4–24.4 pg TEQ/g ww and 2.5–5.1 pg TEQ/g ww, respectively. A decreasing trend was observed for PCDD/Fs and dl-PCBs since 1986, and annual decreases were 5.2% and 5.3% for pg TEQ/g ww of PCDD/Fs and dl-PCB, respectively. In comparison, the levels of PCDD/Fs in 1986 were the highest recorded [195].

Hoguet et al. [196] assessed POP trends in beluga whales (*Delphinapterus leucas*) to determine whether restrictions on legacy POPs have led to concentration declines. PCBs were predominant contaminants in two subpopulations (Cook Inlet, Alaska, and the eastern Chukchi Sea), with median Σ_{80}PCBs concentrations of 2,360 ng/g lw in blubber. $\sum_{32}$PCBs did not change over time; however, tetra-, penta-, and hepta-PCBs decreased by 7.1, 6.8, and 8.5%, respectively, in males, whereas tetra-, penta-, and octa-PCBs declined by 11, 12, and 12.9%, respectively, in females.

Trends in POP concentrations were assessed in adipose tissues of polar bears (*Ursus maritimus*) from East Greenland between 1983 and 2010 [197]. ∑PCBs and PCB congeners (CB-153, -180, and -170/190) showed statistically significant average yearly declines of 4.4% among subadults. Mean ∑PCB concentrations declined from 22,730 ng/g lw in 1983–1986 to 8,473 ng/g lw in 2006–2010, about 2.7-fold. However, the authors concluded that despite declines resulting from international regulations, relatively high levels of these pollutants persist in East Greenland polar bear tissues [197].

McKinney et al. [198, 199] analyzed time trends of POP concentrations in adipose tissues sampled from the western Hudson Bay (WHB) polar bears. Over the 17-year period from 1991 to 2007, concentrations of ΣPCBs and Σchlordane (CHL), the two POPs at the highest concentrations in all years (>1 ppm), showed no distinct trends even when compared to previous data for this subpopulation dating back to 1968; additionally, the PCB metabolites, $\Sigma MeSO_2$-PCBs did not significantly change.

POP concentrations vary within and among circumpolar polar bear subpopulations. McKinney et al. [200, 201] measured geographic variation in PCBs in the adipose tissues of polar bears collected in 2005–2008 from 11 subpopulations in Alaska (AL), Canada including subarctic western and southern Hudson Bay (WHB, SHB), East Greenland (EG), and Svalbard (SV). ∑PCB levels were elevated relative to all other monitored POPs and increased from west to east (subpopulations means ranging from 1,797 to 10,537 ng/g lw).

Recent studies have examined the potential influence of global climate change-linked ecological changes on POP concentrations in polar bears and other arctic marine mammals (reviewed in [202]). McKinney et al. [198] first reported on climate-related changes in diet patterns in WHB polar bears, which altered time trends of POPs. Depleted carbon stable isotope ratios ($\delta_{13}C$) and shifts in fatty acid profiles, as dietary tracers, in years when the sea ice broke up earlier in the summer were proposed to be associated with higher dietary proportions of subarctic seal species (harbor seals *P. vitulina* and harp seals *Pagophilus groenlandicus*) and lower proportions of arctic seals (bearded seals *Erignathus barbatus*). When time trends were compared to those adjusted for the influence of dietary tracers, the diet change resulted in slower rates of decrease of PCBs and faster rates of increase of newer POPs. A long-term study of East Greenland polar bears showed a substantial diet shift over the past three decades, specifically, decreases in Arctic-type ringed seals and increases in subarctic-type harp and hooded seals (*C. cristata*) using a statistical approach known as quantitative fatty acid signature analysis [203]. Higher consumption of subarctic seals occurred in years of warmer temperatures and lower ice extent, as shown by associations between prey consumption and the annual North Atlantic Oscillation (NAO) Index. Climate changes may thus influence the abundance, distribution, and/or accessibility of seal prey, changing polar bear diets. Declines in PCBs were generally faster in East Greenland than in western Hudson Bay polar bears. In addition, adjusting for the proportion of ringed seal in the East Greenland polar bear diet indicated that these POP declines were not as strongly influenced by the diet as observed in western Hudson Bay.

In the Antarctic, Schiavone et al. [204] assessed DLCs in blubber, liver, and muscle of Antarctic fur seal pups. In all seal tissues, PCDF concentrations were greater than PCDDs with total PCDD/F TEQ concentrations of 150, 164, and 89 pg/g ww in blubber, liver, and muscle, respectively. These concentrations were higher than those found in previous studies of pinnipeds from the Antarctic [205, 206] possibly due to local sources on Livingston Island which hosts three permanent scientific bases.

3.5.2 North America

Trends in PCBs and dioxins have been examined in marine mammals along the US Atlantic coast since the 1970s. Lake et al. [207] reported a decrease in mean ∑PCB concentrations in blubber of harbor seals (*P. vitulina concolor*) from 17,100 ng/g lw in 1980 to 9,500 ng/g lw in 1990–1992, suggesting that PCB levels had declined significantly since the early 1970s when mean blubber concentrations in seals were approaching ~100,000 ng/g lw [208]. Shaw and co-workers [55] reported higher mean PCB concentrations in harbor seal blubber (55,000 ng/g lw in adult males; 43,000 ng/g lw in pups) [55]. Although lower than the 1970s levels, no declines in PCB concentrations in seal tissues were observed during the period 1991–2001, suggesting that the declines in PCB levels had leveled off since in the late 1980s. A similar trend was reported for European seals [209], and may reflect fresh inputs

and/or an equilibrium in environmental cycling. A recent study reported current concentrations of PCBs in liver and blubber in this population [25]. Whereas blubber is the tissue commonly analyzed, liver may be more representative of recent exposure [210]. Hepatic Σ_{30} PCB concentrations in the seals (overall mean 77,000 ng/g lw) exceeded blubber concentrations (overall mean 48,000 ng/g lw). Extremely high liver concentrations (mean 131,000 ng/g lw) were found in male pups, whereas PCB blubber concentrations were higher in the female pups (47,000 ng/g lw) than the males, suggesting possible gender differences in PCB metabolism and accumulation in young seals. Regional trends were suggestive of fresh PCB sources in industrialized, densely populated southern coast of New England versus the rural north. The data suggest that PCB concentrations in northwest Atlantic harbor seals are constant or may even been increasing in industrialized southern parts of the range, most likely due to ongoing inputs from land-based reservoirs and existing (permitted) sources [25].

Kucklick et al. [211] investigated PCBs and OC pesticides in 300 blubber biopsies from coastal and near shore/estuarine male bottlenose dolphins (*T. truncatus*) sampled along the US Atlantic and Gulf of Mexico coasts and Bermuda, and found significant regional differences in concentrations. Mean ∑PCB concentrations in dolphin blubber ranged from 33,000 to 450,000 ng/g lw among the sampling sites with the highest concentrations found in Brunswick, GA, a site heavily contaminated with the commercial PCB mixture Aroclor 1268. PCB-153, a recalcitrant congener associated with non-Aroclor 1268 formulations, was significantly associated with regional human population density, indicating this contaminant came from a general urban PCB source. Johnson-Restrepo et al. [27] examined PCB contamination in a Florida coastal food web. ΣPCB concentrations (lw basis) in biota were in the order: forage fish (silver perch, striped mullet) and Atlantic sting-rays < predator fish (red drum, hardhead catfish, spotted sea trout, spiny dogfish) < Atlantic sharpnose sharks < bull sharks and bottlenose dolphins. PCB concentrations in sharks and dolphins were one to two orders of magnitude greater than those in the lower trophic level fishes. The biomagnification factors (BMFs) for ΣPCBs, calculated as the ratio between lipid-normalized concentrations in predator and prey, ranged, on average, from 3 to 502, indicating a high potential for biomagnification in this food web. The highest BMFs of ΣPCBs were measured from forage fish (silver perch) to bottlenose dolphins and bull sharks (*Carcharhinus leucas*). Bull sharks are apex predators that inhabit estuarine, near-shore, and offshore waters of both the Gulf and the Atlantic coasts of Florida. These sharks are the only shark species to penetrate far into freshwater habitats.

On the US Pacific coast, She et al. [212] measured PCBs and DLCs in harbor seals from the San Francisco, CA area between 1989 and 1998. Overall, PCDD/F concentrations were low in these seals, but concentrations of non-ortho PCBs were relatively high (693 pg/g lw; 68 pg TEQ/g lw). The mean ΣPCB concentration in seal blubber was 71,000 ng/g lw, which is comparable to levels reported for Atlantic coast harbor seals. Pacific killer whales (*Orcinus orca*) living in the waters along the northwest coast of the USA and Canada are among the most contaminated marine mammals in the world. Ross et al. [45] measured PCDD/Fs and PCBs in

blubber biopsies from the northern resident, southern resident, and transient populations of killer whales from the region, and found significant differences in PCB contamination among the three populations. The transient whales had the highest levels (mean adult male: 251,000 ng/g lw) followed by the southern residents (mean AM: 146,000 ng/g lw), with lower levels in the northern residents (mean adult male: 37,000 ng/g lw). Within each population, higher levels were found in the adult males compared with the females. The authors suggest that the contamination difference among the populations may partly be a result of trophic level and dietary differences. Resident populations feed mainly on fish such as salmon, while offshore transient killer whales feed mainly on marine mammals, e.g., sea lions [45].

3.5.3 South America

Dorneles et al. [26] analyzed PCBs and dioxins in blubber of false killer whales (*Pseudorca crassidens*), Guiana dolphins (*Sotalia guianensis*), rough-toothed dolphins (*Steno bredanensis*), and in liver of franciscana dolphins (*Pontoporia blainvillei*) collected from southeast and southern Brazil. Dl-PCBs accounted for over 83% of the total TEQ for all cetaceans. Total DLC concentrations ranged from 36 to 3,006 ng/g lw for franciscana dolphins, and from 356 to 30,776 ng/g for other delphinids. Mean ΣPCB concentrations ranged from 35,000 to 279,000 ng/g lw, indicating that these cetaceans are highly contaminated, on par with the high PCB levels in transient Pacific coast killer whales. The high concentrations found in the study raised concern not only about the conservation of Brazilian coastal cetaceans, but also regarding possible human health risks from consumption of fish from Brazilian estuaries.

3.5.4 Europe

In 1990, the UK started its Cetacean Strandings Investigation Programme to gain greater understanding of contaminant levels in its marine mammal population. In an update on contamination status between 1990 and 2008, Law et al. [191] report sum PCB concentrations in harbor porpoise blubber ranged from 48 ng/g lw to 160,000 ng/g lw. Long term trends show an early decline in PCB concentration that has plateaued since about 1998. Different regions of the UK show somewhat different patterns. PCB concentrations have been steady in the East, variable around Scotland, and steadily decreasing in the West.

Storelli et al. [213] measured PCBs including dl-PCBs in melon, blubber, liver, kidney, lung, heart, and muscle tissue of striped dolphins (*S. coeruleoalba*) from the Eastern Mediterranean Sea (Adriatic Sea). The PCB concentrations ranged from 7 to 69,822 ng/g ww in the organs. Blubber and melon had the highest concentrations (22,000 and 16,400 ng/g ww, respectively) followed by liver (3,600 ng/g ww), and the other organs (mean range 220–725 ng/g ww). Total Dl-PCB TEQ in blubber

was 120,000 pg/g ww, 19,900 pg/g ww, and 21,000 pg/g ww in adult males, adult females, and newborns, respectively. Both the blubber PCB concentrations and the Dl-PCB TEQs exceeded estimated toxic thresholds for adverse effects in harbor seals [43, 45] thereby indicating that this population is likely under stress.

Imaeda et al. [214] investigated PCDD/Fs, PCBs, and dl-PCBs in the blubber of Baikal seals collected in 1992 and 2005. Dl-PCBs were one of the dominant contaminants, with concentrations ranging from 480 to 3,600 ng/g ww. Concentrations of PCDDs and PCBs in males were significantly higher than in females. In males, age-dependent accumulation was observed for PCDDs and mono-ortho PCBs, but PCDFs and non-ortho-PCBs showed no such trends implying that the seals may preferentially metabolize these contaminants or that exposure has been decreasing in recent years. Concentrations of PCDFs and non-ortho PCBs were significantly lower in 2005 than 1992, but no decreasing temporal trend of PCDDs, mono-ortho PCBs, or most non-dioxin like PCBs was observed. In 2005, TEQ levels in 40% of the specimens exceeded the threshold level for adverse effects in harbor seals (209 pg/g ww) [214], which raises concern for the future of the population.

3.5.5 Asia

Moon et al. [215] measured PCDD/Fs and dl-PCBs in the blubber of finless porpoises (*Neophocaena phocaenoides*) collected from Korean coastal waters. Total TEQ concentrations for PCDD/Fs and dl-PCBs were 6.5–31 pg/g lw, which were lower than those of cetaceans and pinnipeds reported from other countries and below the suggested threshold values for adverse health effects in marine mammals. Moon et al. [216] also measured PCDD/Fs and dl-PCBs in liver and blubber of minke whales and long-beaked common dolphins. It showed that PCDF and dl-PCB concentrations in blubber were 3–10 times higher than those in liver, but PCDDs were higher in liver. Concentrations of PCDD/Fs and dl-PCBs in liver and blubber of dolphins were significantly higher than those in whales, due to differences in habitat and diet [216]

Yang et al. [217] determined PCDD/Fs and PCBs in the blubber, liver, kidney, stomach, small intestine, and brains of Yangtze finless porpoises (the sole freshwater subspecies of finless porpoise) from Dongting Lake, China collected from 1998 to 2004. The results showed PCDD/F concentrations ranged from 65 to 1,563 pg/g lw in the organs, and PCBs ranged from 60 to 1,890 ng/g lw.

In 1998, Noël et al. [218] collected blubber biopsy samples from killer whales (*O. orca*) inhabiting the coastal waters around Possession Island, Crozet Archipelago, southern Indian Ocean, for contaminant analyses. The results showed that PCDD concentrations ranged from 5 to 77.1 pg/g lw, PCDFs ranged from 7 to 36.1 pg/g lw, and PCBs ranged from 4.4 to 20,500 ng/g lw. Over 70% of killer whales had blubber PCB concentrations above the PCB threshold established for endocrine disruption and immunotoxicity in young harbor seals, suggesting that PCBs cannot be ruled out as a threat to this declining population [218].

3.5.6 Maternal Transfer

POP concentrations in adult female marine mammals are generally lower than those in adult males due to the transfer of contaminants from females to their offspring during gestation and lactation, except in highly contaminated areas where females maintain higher body burdens due to ongoing exposure [45, 59, 219, 220]. Concentrations of a large suite of POPs were recently examined in the blubber and serum of juvenile and adult Hawaiian monk seals (*Neomonachus schauinslandi*) from the main Hawaiian Island subpopulation [221]. Adult females have the lowest blubber levels of most POPs, whereas adult males have the highest levels [221]. In contrast, a recent study showed that the blubber PCB concentrations in Tasmanian long-finned pilot whales (*Globicephala melas*) decreased with age in males because of growth dilution effect or decreasing levels of PCBs in the environment [222]. POPs were investigated in matched liver samples from five mother–fetus pairs of gray seals (*Halichoerus grypus*) [223], in blubber samples from 20 female sea lions and their fetuses during late pregnancy [224], and in Alaskan harbor seals (*P. vitulina*) [225]. Significant amounts of PCBs and other POPs were transferred from female harbor seals to their fetuses during pregnancy and distributed among the fetal organs [225]. The prenatal transfer of these toxic contaminants may pose health risks to the fetus during early development.

Lactational transfer of PCBs and other POPs was examined in gray seal mother–pup pairs from Scotland [226, 227]. Generally, concentrations of all contaminants increased in the mother and pup tissues from early lactation to late lactation. Mobilization of contaminants from the maternal inner blubber layer to the bloodstream was more efficient for less lipophilic compounds (lower $\log K_{ow}$) than for more lipophilic compounds, leading to selective transfer of lower $\log K_{ow}$ congeners to the pups. Exposure of young marine mammals to toxic contaminants both in utero and during nursing can lead to very high burdens in their developing bodies. Because of their greater sensitivity to developmental toxicity, Mos et al. [68] proposed a much lower toxicity reference value for PCB contamination (1.3 μg/g lw) for pups than had been previously estimated for immunotoxicity in adults (17 μg/g lw [43]).

4 Health Effects and Risk

4.1 Endocrine Disruption

Dioxins and PCBs affect the health of wildlife and their progeny by interfering with their endocrine system, which is responsible for maintaining homeostasis, reproduction, development, and/or behavior [40, 228]. Thus, dioxins and PCBs are known as endocrine disruptors (EDs). The magnitude of adverse effects depends

on the body burden, dosage, frequency, and duration of exposure at different life stages [229]

Thyroid hormones play an important role in growth and development (including somatic and brain development) and in the maintenance of normal physiological status in vertebrates. Dioxins and PCBs can interfere directly with hormone synthesis in the thyroid gland [230–232], and disrupt thyroid hormone receptors and accessory proteins that directly control gene expression through the thyroid hormone responsive element [232]. Additionally, these pollutants competitively bind to thyroid hormone transport proteins in blood, such as transthyretin (TTR), and to membrane-bound transporters of target cells or to intracellular cytosolic thyroid hormone binding proteins, which are thought to act as modulators of nuclear-receptor-mediated transcription [232].

Brar et al. [233] studied thyroid endocrine-related effects and their relationship to accumulated contaminants in two indigenous fish species sampled from San Francisco Bay. Total triiodothyronine (T3) and total thyroxine (T4) levels varied significantly by location, with differing T3/T4 ratios in fish from some locations indicating altered peripheral deiodinase activity. The changes in levels of thyroid endocrine hormone were significantly correlated with hepatic concentrations of certain environmental contaminants. Exposure to a large number of polychlorinated biphenyl (PCB) congeners, both dioxin-like and non-dioxin-like, showed significant inverse correlations with T4 levels in the fish, while in contrast, T3 and T3/T4 ratio were positively correlated with PCB exposures. The positive correlation between T3/T4 ratio and PCB exposure supports the hypothesis that PCBs may alter T4 deiodination.

Similar results were found among northern fulmar (*F. glacialis*) populations from the Canadian Arctic and northern Europe [234]. Hepatic concentrations of dioxins, furans, and DL-PCBs were amongst the highest ever reported in northern seabirds. Hepatic EROD activity and plasma T4 levels were positively correlated with liver organochlorine levels, particularly with the dioxin-like compounds. Additionally, strong negative correlations were found between the dioxin-like compounds and plasma T3 levels. This study provides additional evidence that PCBs, dioxins, and furans may be associated with thyroid disruption [234].

Janz and Bellward [235] examined the effects of *in ovo* TCDD exposure on plasma thyroid hormone concentrations (T3, T4) and body and skeletal growth during the perinatal period in the domestic chicken (*Gallus gallus*), domestic pigeon (*Columba livia*), and great blue heron (*A. herodias*). They found that although hepatic EROD activity was induced 13- to 43-fold above controls in chicken, there was no effect of TCDD exposure on hatchability, body growth, subcutaneous edema, or plasma thyroid hormone levels. For pigeons exposed to TCDD, EROD activity was induced 6- to 15-fold, hatchability was decreased, liver to body weight ratio was elevated, and body and skeletal growth were decreased ($p < 0.01$); but there was no effect of TCDD exposure on plasma thyroid hormone levels. For herons, hepatic EROD activity was induced two- to threefold above control birds, similar to EROD activities measured in heron hatchlings exposed to environmental levels of TCDD and related chemicals in the Strait of Georgia,

British Columbia. But at this level of TCDD exposure, there was no observed effect on plasma thyroid hormone levels or body growth in herons [235].

Field evidence has suggested that plasma PCBs and thyroid hormones are correlated in polar bears, apex predators in the Arctic food web [236]. Amongst females, there were significant correlations between five thyroid hormone variables and plasma PCB levels, but among males, PCBs were related to only two thyroid hormone variables, suggesting that female polar bears may be more susceptible to PCB-related thyroid hormone alterations than are males. In female polar bears from Svalbard, Norway, higher PCB concentrations were positively correlated with increasing plasma progesterone levels, which may indicate possible a defeminizing effect via inhibition of enzymes that convert progesterone to estrogen [237]. In Greenland polar bears, higher PCB and OC levels were negatively correlated with bone mineral density, suggesting a similar anti-estrogenic effect of the compounds [238, 239].

4.2 Developmental/Reproductive Effects

Dioxins, PCBs, and many other DLCs are estrogenic and may adversely affect reproductive functions in diverse species of biota. An abundance of evidence from laboratory and field studies suggests that DLCs can cause infertility [240, 241], reduced hatch rates in fish and birds, and decreased offspring viability in addition to altered hormone levels and adult sexual behaviors [242]. One example is the estrogenic induction of vitellogenin (Vtg) in fish [243]. Vtg is a complex phospholipoglycoprotein synthesized by the liver in response to estrogen stimulation. Vtg is secreted by the liver and transported in the blood to the ovary, where it is sequestered and cleaved into the yolk proteins lipovitellin and phosvitin, which are stored in the yolk and serve as a food reserve for the developing embryo [244]. High Vtg levels in male fish are associated with liver enlargement, feminization, and kidney damage, and are generally accompanied by various degrees of reproductive interference at similar or lower ambient estrogen concentrations [245–248]

Field studies have been conducted to address ecotoxicological concerns regarding PCB exposure in snapping turtles (*C. serpentina*). Eisenreich et al. [140] examined sublethal and lethal responses of juvenile snapping turtles that were exposed maternally and/or through diet to PCBs over 14 months post-hatching. Maternal exposure did not affect embryonic development or hatching success. Dietary PCB exposure reduced the metabolic rates of juveniles in two of the three assays. Kelly et al. [141] reported the accumulation and maternal transfer of PCBs in snapping turtles from the upper Hudson River, NY, USA, by using eggs and blood samples. Significant positive correlations were found between the carapace length and blood PCB concentrations for both sexes in contaminated areas. The results suggest that maternal transfer of PCBs to snapping turtle eggs and high body burdens pose reproductive risks to turtles in the upper Hudson River area.

White-tailed sea eagles had very low population numbers in the 1980s which was linked with high levels of organochlorines (PCBs and DDT) [44, 52, 53]. However, since the banning of DDT and PCBs in the 1970s, reproductive health and population numbers have increased and DDT and PCB concentrations have decreased at fairly similar rates. The mean productivity of sea eagles increased from 0.3 in 1965 to 1.0 in the mid-1990s. Apart from eggshell thinning caused by DDE, PCBs have been correlated with impaired sea eagle reproduction, implying increased embryo mortality in eggs with elevated PCB concentrations [249]. High levels of PCB and DLCs were associated with adverse effects on reproduction and development in other avian predators including Alaskan peregrine falcons, bald eagles from the Aleutian Islands, glaucous gulls from Bjørnøya (Norway), and great black-backed gulls from northern Norway [237, 250].

Organochlorines (primarily PCBs) were suspected to be the underlying cause of reproductive failure in Baltic otters in the 1970s when reproduction plummeted to approximately 2% [52]. Following PCB and DDT bans in the Baltic region, the frequency of adult female otters with signs of reproduction slowly recovered to approximately 67% in 2010 [44, 52].

Similarly, PCBs and DDT were implicated in the widespread reproductive impairment and population declines among seals from northwestern Europe [48, 51, 251, 252] and the disease complex observed in Baltic seals [47, 253]. Because of high hunting pressure, the populations of gray and ringed seals in the Baltic decreased dramatically from 1,900 to approximately 1,950 [254]. Even after their protection, a further decrease followed and a disease complex, including uterine obstructions and tumors (leiomyomas) leading to impaired reproduction, was described [251, 253]. The disease complex was found at high frequencies among gray seals in the 1970–1980s [255], and a high contaminant concentration in their prey was proposed to be the underlying cause. PCBs were indicated as the primary suspect in the reproductive failure [47, 251] and were associated with tumors found in the uteri of older females [256]. Approximately 70% of the females had uterine obstructions in the early 1970s, but the frequency decreased after the end of the 1980s. The pregnancy rate in examined seals increased from close to zero in the late 1970s to close to 100% today. The first signs of recovery were observed approximately 15 years after the ban of PCBs and DDT [44, 52, 53].

An early feeding study conducted by Reijnders [48] reported that reproductive failure in harbor seals from the Wadden Sea was linked to consumption of PCB-contaminated fish. This study was the first to demonstrate a causal relationship between contaminant levels and a physiological response in marine mammals. Subsequent feeding studies conducted in the Netherlands showed that harbor seals that consumed contaminated fish from the Wadden Sea or the Baltic Sea exhibited increased infertility and immunosuppression compared with seals consuming less-contaminated Atlantic fish [48, 64, 65].

4.3 Immunotoxicity

Although dioxins and PCBs are well-studied immunotoxicants in animals [257, 258], little attention was paid to this aspect of their potential toxicity in wildlife until the 1980s when a series of disease outbreaks resulted in mass mortalities among marine mammals, suggesting that the animals were susceptible to disease via PCB-induced suppression of their immune systems [45, 61, 259, 260]. A weight of evidence suggests that PCBs exert immune, endocrine disrupting, and reproductive effects in marine mammals, and PCB toxicity has been strongly implicated in the epizootics that have decimated many populations since the 1980s [43, 45, 68, 261].

Harbor seals in polluted regions of Europe have experienced several virus-induced mortalities, starting with the 1988 morbiilvirus outbreak that resulted in the deaths of 20,000 animals [58, 262]. Similar to European harbor seals, the northwest Atlantic harbor seal population has been susceptible to viral disease outbreaks, as evidenced by a recurrence of epizootics since the late 1970s. In 1979–1980 and again in 1991–1992, viral epizootics resulted in the deaths of approximately 1,000 harbor seals from Maine to New York [54, 263, 264]. Between 2004 and 2009, approximately 2,000 harbor seals died of unknown causes during "Unusual Mortality Events" (UMEs) along the New England coast [265]. The possible contributory role of PCBs and DLCs in these events cannot be ruled out, since the PCB burdens alone in these seals exceed the estimated threshold levels for POP-mediated reproductive and immune system effects in the species [25, 43, 55].

PCB-induced immunotoxicity has been implicated in several dolphin mortalities, rendering the animals susceptible to bacterial, viral, and parasitic infections. In 1987–1988, more than 740 bottlenose dolphins (*T. truncates*) stranded along the northwest Atlantic coast from New Jersey to central Florida [266]. It is estimated that this population may not return to pre-1987 population levels for 100 years [266]. Other similar large-scale dolphin mortalities have been reported in the Gulf of Mexico and in the Mediterranean Sea [60, 267].

Captive feeding studies conducted in the 1990s showed that harbor seals exhibited depressed immune responses if they consumed contaminated fish from the Baltic Sea rather than cleaner fish from the Atlantic Ocean [65, 66, 268]. An impairment of natural killer cell activity, in vitro T-lymphocyte function, antigen-specific in vitro lymphocyte proliferative responses and in vivo delayed-type hypersensitivity and antibody responses to ovalbumin were observed in the seals fed contaminated Baltic fish [65]. Similar feeding studies were conducted in European otters and mink [240, 241, 269, 270]. A study of northern fur seals found that various immune function parameters were negatively correlated to increasing PCB levels, including decreased antibody production after vaccination [271]. In Svalbard polar bears, a significant decrease in antibodies was associated with increased PCB levels [272]. A similar negative correlation was found between IgG levels and increasing PCB levels in the cubs. In the Svalbard/Resolute study, polar bears with high PCB levels exhibited immunosuppression expressed as

reduced IgG production and lowered lymphocyte responses after vaccination [273]. These studies have provided valuable information for establishing a dose–response relation between PCB exposure and adverse health effects for aquatic and marine mammals [43].

Based on the data from field and captive feeding studies in marine mammals and mink, Kannan et al. [43] proposed thresholds for immune and reproductive effects of ΣPCBs in marine mammals of 8.7 μg/g lw in the liver and 17 μg/g lw in the blubber. Recent studies have applied these thresholds to estimate potential toxicity of current body burdens of POPs in marine mammals [191, 274]. In UK harbor porpoises with blubber ΣPCB concentrations above 17 μg/g lw, those that died of infectious disease had higher ΣPCB concentrations than those that died of traumatic injury, whereas there was no relationship between PCB concentrations and cause of death for porpoises with PCBs below the threshold [191].

Results of recent biomarker studies of PCB-sensitive endpoints in young free-ranging harbor seals such as decreased immune function, vitamin A, and thyroid hormones suggest that PCB-related adverse effects occur at much lower exposure concentrations in pups than previously demonstrated [67, 68, 70, 192, 275, 276]. Using No Observed Adverse Effect Levels (NOAELs) and allometrically scaled toxicity reference values (TRVs) from rodent studies, Mos et al. [68] proposed new TRVs (consisting of 5% tissue residue concentration and dose) of 1,300 ng/g lw Σ_{154}PCB in the blubber of nursing harbor seal pups. These new TRVs were applied in a recent study of harbor seals along the northwest Atlantic to determine potential PCB-related immunotoxicity and other sublethal effects in the pups [25]. Blubber Σ_{30}PCB concentrations in 87% of the pups exceeded the threshold of 1,300 ng/g lw by an order of magnitude, implying that the majority of these pups may be suffering from PCB-related adverse effects that could diminish their overall fitness and increase their susceptibility to infectious disease during a vulnerable stage of development.

Given the pattern of recurring epizootics among seals and other marine mammal species, current tissue concentrations of PCBs and DLCs may pose a significant immunotoxic threat to the future health of many populations.

4.4 Population Effects

It is difficult to associate a specific compound or class of compounds with a specific health effect in the wild because there are thousands of contaminants in circulation, and many other biotic and abiotic factors may influence animal health. Because of the difficulty in making quantitative observations in the field, it is not easy to identify the types of disturbances that cause wildlife populations to be potentially at risk or reproductively compromised. Any causative mechanisms for altered reproductive parameters or population declines in aquatic biota are likely to be multifactorial and may involve a complex interplay of factors such as contaminant stress, habitat loss, accidents, noise, and climate change [74, 277, 278]. However,

risk assessment can still be reasonably performed using a combination of approaches, including feeding studies, biomarker studies, weight of evidence, and extrapolation across species (e.g., from mink to marine mammals).

Chronic exposure to PCBs and DLCs impacts the fitness and sustainability of many wildlife populations today, especially apex predators such as sea turtles, sharks, and marine mammals [27, 45, 279, 280]. Overall, marine mammal health has been deteriorating over several decades, and trends in marine mammal disease reports are rising [174, 281]. In some regions such as the Baltic where levels of PCBs and OCs have been banned, the reproductive health of seals has gradually improved, and seal population numbers have increased [282]. A similar pattern has been observed for otters and white-tailed sea eagles [44].

The impact of dioxin and dl-PCB contamination on the reproductive health of populations of fish-eating birds including gray herons (*Ardea cinerea*), great cormorants (*P. carbo*), osprey (*Pandion halieaetus*), and kingfishers (*Alcedo atthis*) in the Tokyo Bay area, Japan, has been a concern, although environmental levels have been decreasing [283]. A regional assessment of the ecological risks of dl-PCB exposure was performed to assess the need for risk management measures to protect these populations [283]. Egg mortality risk related to the contamination levels of dl-PCBs in eggs was determined to be relatively low (from <1 to 12%), as were the changes in the population growth rates (lambda) (<1 to 2%), indicating that the current levels of dl-PCB contamination alone are not sufficient to trigger population-level effects.

However, some regions are still highly polluted and populations of high trophic level wildlife continue to suffer from disease and mass mortalities, in some cases, reducing population numbers to levels that cannot be sustained. It is estimated that more than one-third of marine mammals in the North Atlantic and Pacific are in danger of going extinct, according to the International Union for Conservation of Nature (IUCN) [280]. After accidental mortality, pollution is ranked as the prevalent cause of disease and death, affecting up to 60% of all marine mammals. Although it is arguable whether dioxins and PCBs are the primary cause of the mass mortalities affecting marine mammals and other top predators, these compounds have the potential to exacerbate the magnitude of disease outbreaks by compromising normal immune resilience in the animals [45, 284]. For many contaminant-stressed populations, the added stress of climate change is exacerbating the problem, causing shifts in food webs and threatening the survival of species, not only in the Arctic but in temperate oceans as well [280].

Vulnerable species such as polar bears living at the edge of their physiological tolerance range are at extreme risk. Of 19 subpopulations comprising some 25,000 polar bears, at least three are declining rapidly [285]. Canada's Western Hudson Bay (WHB) population has experienced a 22% decline or greater since the early 1980s; the Southern Beaufort Sea population plunged by about 40% over a 10-year period from 2001 to 2010, dropping from about 1,500 bears to 900 bears before stabilizing; and the Baffin Bay population, shared by Greenland and Canada, is in steep decline [286]. The main factor driving these declines is the melting of Arctic sea ice, averaging 10% per decade, displacing the habitats and prey of polar bears,

beluga whales, and walruses. But ironically, climate change alterations in food webs, lipid dynamics, ice and snow melt, organic carbon cycling, and severe storm events are expected to increase both the distribution and toxicity of POPs in coastal and oceanic environments [277]. Many scientists fear that this will trigger even larger-scale catastrophic events among marine mammals. The complex interplay of contaminant stress, climate change, and shifts in food web dynamics on vulnerable populations is an area urgently needing further research.

All seven species of marine turtles have been classified as threatened or endangered, and populations have declined steeply (by almost 95%) in recent years [287]. The causes are unknown, but sea turtles face multiple threats from diverse hazards such as trawler nets, egg poaching, and pollution. Turtles are known to be robust to physical damage, but are surprisingly very susceptible to chemical contaminants [147]. An additional stress on populations is the expansion of fibropapillomas (FP), a benign neoplastic disease associated with a turtle herpesvirus that has increased significantly over the past 20 years [288]. FP is a global disease affecting turtles worldwide including the green sea turtle (*C. mydas*), the loggerhead (*C. caretta*), olive ridley (*Lepidochelys olivacea*), kemp's ridley (*Lepidochelys kempii*), and leatherbacks (*D. coriacea*) [288]. The disease tends to develop after the open-water pelagic developmental phase of approximately 10 years when juvenile turtles arrive and forage on seagrass and algae in nearshore environments with relatively small home ranges. Studies have linked a high prevalence of tumors in turtles to environmentally disturbed habitats, e.g., heavily polluted coasts with high human population density, proximity to river inputs, agricultural runoff, and land-based sources [289]. Immunosuppression is also strongly correlated with FP, but may be a consequence of the development and growth of FP, similar to other virus-induced tumors in other species [288]. The possible role of immunotoxic contaminants such as PCBs and dioxins in sea turtle disease and population declines is not understood and warrants further study.

5 Conclusions

5.1 Data Gaps

From four decades of field and semi-field (feeding) studies, we have a better understanding of the sources, exposure pathways, environmental levels, trends, and health effects of dioxins, PCBs, and related DLCs in aquatic ecosystems. However, data are lacking for many regions, contaminant patterns are changing over time, and large research gaps remain.

- Data are lacking for biota in many highly populated developing countries where the problems of inadequate waste management infrastructure and high volume of waste production are growing larger. Limitations in technical and financial support in these countries may exacerbate the problem. For aquatic biota from

war-torn regions of the Middle East and Africa, contaminant data are non-existent.

- Many developing countries are still establishing contaminant inventories, which are essential before any technologies and measures can be put in place for source reduction. Bridging the data gap between developed and developing countries would provide a clear picture of the needs and options for effectively reducing global contamination.
- The rise of new and emerging persistent pollutants, poses a more complex global threat to both wildlife and humans. While it is known that dioxins and PCBs are linked to cancers, reproductive impairment, and immune system dysfunction in animals, more studies are warranted to understand the extent of the compounded health threat posed by the introduction of emerging POPs.
- Extrapolating from recent trend studies, PCBs remain the predominant contaminants in fish, seabirds, turtles, sharks, and marine mammals, but in certain food webs, bioaccumulation and magnification of PCDD/Fs and dl-PCBs are evident, presenting an increased health risk to marine animals. The synergistic interactions and effects due to exposure to contaminant mixtures in aquatic biota need further investigation.
- Technology has been advancing at an exponential rate, and it is important to use advances in analytical chemistry to advance our science. The evolution of electronic tracking tags might provide an alternative for tracking long-distance migrating species [290].
- Data quality is crucial to decision-making leading to resource management and contaminant regulation. Standardization of sampling, storage, and analytical protocols and harmonization of analytic methods could improve the integrity of collected data across the studies. Additionally, an international, public database for reporting POP levels and mass mortalities in wildlife might facilitate scientific discovery and allow for timely response to warning signals from contaminant-stressed populations.
- Biological effects of dioxins and PCBs are generally first observed in populations with high-level exposure, often accompanied by catastrophic events such as reproductive failure or disease outbreaks. More biomarker studies are needed to advance understanding of the range of health effects associated with moderate to low-level exposure, especially in species and populations in decline, e.g., sea turtles. The possible role of immunotoxic PCBs and dioxins in sea turtle tumors (FPs) and declining numbers worldwide is not understood and warrants further study.
- Climate change alterations in food webs, lipid dynamics, ice and snow melt, organic carbon cycling, and severe storm events are expected to increase both the distribution and toxicity of POPs in coastal and oceanic environments [277]. Many scientists fear that this will trigger widespread, large-scale catastrophic events among marine mammals and other high trophic level wildlife. The complex interplay of contaminant stress, climate change, and shifts in food web dynamics on vulnerable populations such as polar bears is an area urgently needing further research.

5.2 Foresight from Current Knowledge

Dioxins, PCBs, and DLCs are major industrial chemicals that are globally restricted, but still pose a significant health threat to diverse species of aquatic biota, particularly those at high trophic levels. Although PCBs were banned in most developed countries four decades ago, landstocked sources such as old PCB-containing equipment and landfills will remain a reservoir for PCB releases for years to come. Tanabe [291] predicted that most of the PCBs (66%) were stockpiled in products (transformers and capacitors) long after PCBs were banned from production in the 1970s. Trend studies suggest that the amounts of PCBs cycling in aquatic and marine food webs are gradually decreasing, as burial, metabolism, and degradation occur in sediments. However, certain uses of PCBs are still permitted in the USA and Europe, delivering fresh inputs to aquatic food webs. As a result, the large declines observed in PCBs after the bans have plateaued in most developed countries, and in some regions, environmental levels are remaining constant or even increasing. Similarly, regulatory actions aimed at controlling PCDD/Fs and PBDD/Fs have been inefficient, as these compounds continue to be released as by-products of combustion and other industrial and agricultural processes.

With the ongoing challenges associated with POP contamination, continuous efforts are needed to monitor the occurrence, distribution, and health effects in biota with emphasis on highly exposed species with body burdens close to or higher than estimated threshold levels of effect. Thresholds with high uncertainties should be interpreted as warning signals that require more data and further study.

Overall, the future trends for dioxins, PCBs, and related DLCs in aquatic biota are unclear. Given the large reservoir of these compounds in the environment, and ongoing releases and inputs from permitted sources, regulatory controls will do little to impede the continued cycling of these chemicals through aquatic and marine ecosystems for the foreseeable future.

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