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DDT and Other Organohalogen Pesticides in Aquatic Organisms

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2.1 INTRODUCTION

Organohalogen (OH) compounds are persistent hydrocarbon compounds containing a halogen group, often chlorine or bromine, that substitutes for hydrogen atoms in different positions in the hydrocarbon. They may occur naturally, but this chapter's focus is on synthetically produced compounds, mainly organochlorines, that were produced for use as pesticides. Nine OH compounds (aldrin, chlordane, dichlorodiphenyltrichloroethane [DDT], dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, and toxaphene) are in the top 12 list of particularly toxic and persistent organic pollutants (POPs) identified by the Stockholm Convention treaty implemented in 2004 under the United Nations Environment Program (UNEP). More than 90 countries have signed on to this treaty as Parties. These chemicals became classified as POPs because they may remain in the environment for decades following their use, they accumulate in fatty tissues of exposed organisms, they have a variety of toxic endpoints, and they travel long distances from source areas through atmospheric or aqueous transport.

Synthetic broad-spectrum OH pesticides such as DDT (1,1,1-trichloro-2,2-bis(*p*-chlorophenyl) ethane) became widely used in agriculture beginning in the 1940s. The term total DDT or ∑DDT refers to the sum of DDT and metabolites: 1,1'-(2,2-dichlor-ethenylidene)-bis[4-chlorobenzene] (DDE); and 1,1-dichloro-2,2-bis(4-chlorophenyl)ethane (DDD, also referred to as TDE); and their ortho para (*o,p'* or 2, 4) and para para (*p,p'*, or 4, 4) isomers. Use of these compounds generally consisted of wide-scale spraying and initially was supported by their effectiveness in controlling pest vectors and their apparent low acute toxicity to humans and other mammals. Estimated application amount in 1959 exceeds 450,000 metric tons applied to 5% of the land area in the United States, with cotton growing areas of the southeast United States having high DDT, toxaphene, and lindane applications (Johnson 1968). Rothane, a metabolite of DDT known as DDD (*p,p'* dichlorodiphenyldichloroethane), or TDE (1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane) also was applied as a pesticide in the United States (Schmitt et al. 1990, ATSDR 2002).

DDT's acute toxicity to nontarget aquatic organisms was noted early (Ellis et al. 1944). Effects to fish and invertebrates from aerial spraying were observed in the 1950s with dramatic die-offs from pesticide application (Cope 1961). Shortly after DDT spraying, major fish and benthic invertebrate kills were noted in various locations; such as in the Yellowstone River, Wyoming; in New Brunswick hatchery fish after spruce bud worm spraying; and around Lake George, New York after spraying to control gypsy moths. The persistence in tissue, much higher concentrations in tissue compared to water, development of resistance, and an ability to travel long distances in aquatic systems also were noted early in their use. Public outcry and environmental investigations ensued after the publication of Rachael Carson's book *Silent Spring* (Carson 1962), eventually leading to either a complete ban, or restricted use, in a number of countries. DDT use was banned in Canada and Sweden in 1970, in the United States in 1972 (37 FR 13369, July 7, 1972) and in western European countries in the early 1970s. DDT production continued in some countries even after use was banned. Use of DDT for agriculture was banned in India in 1989, but DDT continues to be manufactured and

have restricted use for public health. Aldrin and dieldrin were banned in the United States in 1974 (39 FR 37246, October 18, 1974), toxaphene in 1983, and chlordane in 1988. Current use of DDT, supported by the World Health Organization since 2006, includes indoor residual spraying of DDT in dwellings as part of a comprehensive program to control malaria epidemics and transmission in African countries such as Zambia, Uganda, Zimbabwe, and Kenya, and some Asian countries. India has used indoor spraying to reduce disease transmission. Recent global DDT use was estimated at 4000–5000 metric tons per year and production occurred in India, China, and the Democratic People's Republic of Korea (UNEP 2008).

After DDT, aldrin, and dieldrin were the next most heavily used pesticides in the United States during the 1960s–1970s. Use was concentrated on corn crops in mid-western states. Dieldrin was used heavily in the northeast United States on a variety of crops, but was also used for pest control such as termites in the southern states. Aldrin also was used on large scale sugar cane crops in Brazil and Australia. Aldrin use continues in some countries; however, once released to the environment, aldrin readily degrades to dieldrin, which is very persistent. After DDT, dieldrin, and aldrin use were restricted, compounds such as endosulfan and toxaphene were used as replacement pesticides.

The National Pesticide Monitoring Program (NPMP) was established in the United States in 1964 to assess regional and national contaminant trends for these widely used compounds. The National Contaminant Biomonitoring Program (NCBP) originated as part of NPMP and was operated by the U.S. Fish and Wildlife Service (USFWS). This program was eventually expanded into the Biomonitoring of Environmental Status and Trends (BEST) program and transferred to the U.S. Geological Survey (USGS) in 1996. Trends in contamination generally have been downward in the United States but continued presence in tissue highlights the extreme persistence of some of these compounds which remain a threat in some areas. Southern California, home to one of the largest DDT manufacturers in the world, still had an estimated 156 metric tons of DDT in shelf sediments. Sampling in 1994 measured DDT in all Pacific and longfin sanddab and Dover sole collected in the area (Schiff and Allen 2000). The Huntsville Spring Branch in Huntsville, Alabama, received over 400 metric tons of DDT from manufacturing at the Redstone Arsenal from 1947 to 1971. More than 35 years after its ban in the United States, the number of DDT fish advisories continues to increase (U.S. EPA 2006). *p,p'*-DDT is ranked 12th on the U.S. Environmental Protection Agency's (EPA) 2007 list of priority hazardous substances, dieldrin is 17th and chlordane is 20th (ATSDR 2007).

Many OH compounds are semivolatile and spread locally and globally via the atmosphere. The wide geographic reach of OH pesticide contamination is highlighted by their elevated concentrations in deep sea fish (Looser et al. 2000) and in higher trophic Arctic organisms (AMAP Assessment 2002). Transport to remote Arctic areas may occur through what is known as "grasshopping," chemicals volatilize and condense, resulting in fractionation, as they are transported atmospherically in step-wise fashion to remote areas. Ocean circulation also transports OH compounds to the Arctic, but more slowly than atmospheric transport for most OH compounds (Lohman et al. 2007).

The high molecular weight chlorinated insecticides (e.g., DDT and dieldrin) are particularly concerning due to their ability to bioaccumulate and persist in tissue. Early studies to understand the significance of tissue residues began with these lipophilic and persistent OH pesticides. Reproductive failure noted in New York lake trout populations as a result of DDT spraying was among the first studies to relate the tissue concentration in egg with mortality (Burdick et al. 1964). The challenge of determining sublethal no-effect concentrations in aquatic organisms was noted early. Researchers at the U.S. EPA Gulf Breeze laboratory (currently known as the Gulf Ecology Division Laboratory) were among the first to conduct laboratory studies measuring tissue-residue concentrations associated with effects, or critical body residues (CBR).

Organochlorine pesticides are grouped into categories, the diphenyl aliphatics, the cyclodienes, hexachlorocyclohexane (HCH), and polychloroterpenes. Properties and uses are summarized briefly in Table 2.1. DDT belongs to the diphenyl aliphatic group. The cyclodienes include aldrin and dieldrin, endrin, chlordane, heptachlor, heptachlor epoxide, and endosulfan. Lindane is the gamma

TABLE 2.1
Organohalogen Compound Properties, Products and Uses

Chemical	Formula	Mol. Wt. g/mole	Metabolites	Isomers	Log K_{ow}[a]	Example Uses
DDT[b]	$C_{14}H_9C_{15}$	354.49	DDE, DDD	*o,p'*, *p,p'*	6.79*	Agriculture, disease vectors
DDD[b]	$C_{14}H_{10}C_{14}$	320.05		*o,p'*, *p,p'*	5.87*	Agriculture
DDE[b]	$C_{14}H_8CL_4$	318.03		*o,p'*, *p,p'*	6.0*	
Aldrin	$C_{12}H_8CL_6$	364.92	Dieldrin		6.75	Agriculture (corn), soil insects (termites)
Chlordane (pure)	$C_{10}H_6CL_8$	409.78	Oxychlordane, heptachlor, chlordene epoxide	Cis, trans	6.22	Corn, citrus, household pests (termites)
Dieldrin	$C_{12}H_8CL_6O$	380.91			5.45	Agriculture, disease vectors
Endrin	$C_{12}H_8CL_6O$	380.91		Dieldrin	5.45	Agriculture, cotton
Endosulfan	$C_9H_6CL_6O_3S$	406.92	Endosulfan sulfate	Alpha, beta	3.5	Agriculture
Heptachlor	$C_{10}H_5CL_7$	373.32	Heptachlor epoxide		5.86	Agriculture, termites only since 1983 in US
Hexachloro-cycohexane (HCH)	$C_6H_6CL_6$	290.83		Lindane (γ-HCH), 7 others	4.26	Ornamentals, soil pests, head lice
Mirex	$C_{10}CL_{12}$	545.55			7.01	Fire ants, flame retardant
Toxaphene (camphechlor)	$C_{10}H_{10}CL_8$ (average of chlorines)	413.82 (component average)	Mixture of polychlorinated terpenes	Numerous	6.79	Agriculture (cotton), fish eradication

[a] Log K_{ow} estimated in EPA EPI Suite KOWWIN v1.67.
[b] Kow for *p,p'* isomers.

isomer of HCH. Toxaphene, a mixture of more than 670 chemicals, is a polychloroterpene and mirex has a caged structure. Several OH pesticides were produced as technical mixtures in addition to pure compounds.

This chapter reviews the tissue residue-effect data available for OH compounds measured frequently in tissues of fish and invertebrates. First we review some issues pertinent to interpreting tissue-residue data such as analytical methods, which have changed over time and are continuing to evolve. We also briefly review factors important to the accumulation and elimination of OH compounds (toxicokinetics), modes of action relevant to the tissue-residue literature, and the importance of lipids and maternal transfer in understanding their toxicodynamics. Most sections of this chapter are divided into separate subsections for fish and invertebrates.

2.2 ANALYTICAL METHOD CONSIDERATIONS

To accurately separate, identify, and quantify the variety of chlorinated hydrocarbon concentrations in tissue, several analytical challenges have to be overcome. These are reviewed here to help understand considerations needed to evaluate both older and recent data.

Due to their persistence and widespread occurrence, OH compounds generally occur as mixtures in the tissues of fish and invertebrates. In addition, environmental degradation and/or transformation within the organism results in various metabolites and isomers of the original forms within the tissue. Measured concentrations often are presented as sums of parent and metabolite compounds, and may represent a complex assortment of related compounds. Chlordane and toxaphene contain many components making quantification very difficult.

OH pesticides have characteristics such as high hydrophobicity and consequently tend to bind to, and concentrate in fatty tissues. The efficient and complete extraction of fat-soluble substances from tissue is therefore an important analytical step. Interference with other compounds and accurate quantification methods can present substantial difficulties potentially causing inaccurate measurements. Compound separation achieved by paper chromatography, an early analytical method, was not always sufficient to estimate individual compound concentrations (Burdick et al. 1964), so measured concentrations may have been biased high. The development of gas–liquid chromatography in the early 1950s was one of the most significant advances to improve the quantification of OH pesticides. When coupled with electron capture detection, developed late in the 1950s, researchers became able to more reliably measure low concentrations of individual OH compounds.

Current analytical methods include lipid extraction with solvents, followed by cleanup techniques to remove coextracted compounds. Lipids typically are removed with liquid-liquid partitioning and Florisil adsorption chromatography. Additional adsorption chromatography columns are used for further cleanup, and supplemental cleanup steps may be included. Analytical standards such as standard reference material should be used to estimate measurement errors.

Past use of packed columns could have resulted in coelution of some additional components and less sensitivity than measurements from capillary columns. For example, differentiating between DDD and *o,p'*-DDT was not always possible with packed columns (Buhler et al. 1969, Jarvinen et al. 1976). Sample cleanup with acid and alkaline treatment overcame some packed column problems (Brevik et al. 1996). Comparison of the two column methods showed similar results even without extra cleanup, although the packed column results were higher for the DDT metabolite. Although the results from packed columns produce different concentrations than capillary columns, the differences may fall within experimental uncertainty (Brevik et al. 1996).

Toxaphene quantification can still be problematic due to the large number of components (Muir et al. 2006). Schmitt (2002a) considers toxaphene residue measurement as approximations, even with the analysis techniques used in this decade.

To circumvent restrictions posed by the typical high costs of analytical chemistry and the detection limits that demand exposure to high concentration in the exposure media, investigations of invertebrate and some fish bioaccumulation and CBRs have resorted to the use of radioactive tracer techniques. The exposure compound radioactivity is measured using liquid scintillation counting (LSC) and its specific activity (Pawlisz and Peters 1993). To identify the compounds providing the source of radioactivity being measured, the thin layer chromatographic (TLC) method typically is used (e.g., Guarino et al. 1974, Lotufo et al. 2000a). All studies reporting DDT invertebrate CBRs derived from radioactivity data (Johnson et al. 1971, Lotufo et al. 2000a, 2000b, 2001a, 2001b), except for Mulsow and Landrum (1995), employed TLC as a compound identity confirmatory tool. The radiotracer technique was also employed for deriving CBRs for DDE (Fisher et al. 1999, Hwang et al. 2004) and endrin (Keilty et al. 1988a, 1988b). Because those compounds are not expected to biotransform in invertebrate tissues, all radioactivity was assumed to be associated with the parent compound.

The cost associated with OH measurement is a major obstacle for understanding distribution and risks in countries that continue to use, or have recently banned these products. Muir and Sverko (2006) review best practice approaches and new advances as they relate to needs in countries with emerging economies.

2.3 ENVIRONMENTAL OCCURRENCE

2.3.1 Water, Sediment, and Air

In the environment, OH pesticides have low aqueous solubility; tend to bind to particulates and organic matter; and bind strongly to sediment where they have long residence times. Consequently, many monitoring programs measure concentrations in sediment and biota for assessing OH contaminant trends. Although dissolved concentrations typically are very low, aqueous measurements do provide OH compound transport and flux information. Several recent studies report aqueous concentrations in areas where OH pesticide use is on-going or recent. For example, in South Africa where DDT is used indoors for malarial control, aqueous ΣDDT concentrations in areas downstream of spraying ranged from below detection (<0.05 μg/L) to 1.1–7.0 μg/L (Barnhoorn et al. 2009). Aqueous ΣDDT ranged from 0.02 to 5.2 ng/L in the Daliao River estuary in China (Tan et al. 2009). Aqueous concentrations for other OH pesticides in this region are also provided in this study.

Surface water sampled for 19 organochlorine pesticides in the Bering and Chukchi Seas measured HCH at the highest concentration (Strachan et al. 2001). ΣDDT in this 1993 study ranged from 0.17 to 0.26 ng/L.

Water column DDT concentrations measured in the United States include locations near former discharges of DDTs such as the Palos Verde shelf in Southern California. Aqueous phase DDT concentrations were measured using solid-phase microextraction (SPME) in 2003–2004. Water column concentrations of DDT ranged from <0.073 to 2.58 ng/L for *p,p'*-DDE and from <0.043 to 0.264 ng/L for *o,p'*-DDE (Zeng et al. 2005). Water column ΣDDT concentrations measured in 1997 from this area ranged from 2.3 to 14.5 ng/L (Zeng and Venkatesan 1999). In San Francisco Bay, aqueous DDT concentrations ranged from 0.16 to 0.657 ng/L; chlordanes from 0.062 to 0.136 ng/L; and dieldrin from 0.028 to 0.067 ng/L (Connor et al. 2007). Water column concentrations of *p,p'*-DDE and *o,p'*-DDE in other parts of the world are summarized in Zeng et al. (2005) and OH compounds in Fowler (1990) for older data.

In their review of toxaphene concentrations in the Great Lakes, Muir et al. (2006) report surface water concentrations are highest in Lake Superior (0.91–1.12 ng/L) and lowest in Lake Ontario and Lake Erie (0.081–0.23 ng/L). In addition to water, toxaphene and HCH are important OH compounds in Great Lakes air and precipitation, especially in late summer and early fall (Muir et al. 2006).

Aqueous concentrations of two current use pesticides (endosulfan and γ-HCH) were studied in Arctic seawater to understand transport patterns and processes (Weber et al. 2006). Air monitoring also is a useful tool for understanding long-range transport and spatial OH compound variation in the Arctic (e.g., Su et al. 2008).

The sea surface microlayer, the thin surface film enriched with organic matter, is another area of study because it may play an important role in OH transport and transfer (García-Flor et al. 2005). Concentrations of organochlorine compounds were enriched in the surface microlayer, sometimes by up to 7 times, compared to concentrations in underlying water.

The extreme persistence of many OH pesticide compounds in freshwater sediments is demonstrated by their continued detection in most U.S. streams measured as part of the USGS NAWQA program (Gilliom et al. 2006). DDE is the metabolite detected most frequently in those areas.

In the marine environment, sediment DDT concentrations on the Palos Verdes shelf from 0.014 to 12.5 mg/kg dw were composed of 92–95% DDE (Zeng and Venkatesan 1999). DDT metabolites may form from aerobic degradation, photochemical decomposition, or abiotic hydrolytic dehydrochlorination. DDE is degraded by reductive dechlorination to DDMU [1,1-dichloro-2,2-bis(4-chlorophenyl)ethylene] under both sulfidogenic and methanogenic conditions. In a study by Eganhouse et al. (2000), DDE concentrations generally comprised 60–70% of the ΣDDT concentrations on the Palos Verde shelf. DDE is very resistant to degradation and only 9–23% of the DDE inventory on the Palos Verdes shelf has been converted to DDMU since releases began in the 1930s (Eganhouse

et al. 2000). Therefore, decreases in DDE concentrations are due mainly to remobilization, not degradation.

Sarkar et al. (2008) report on sediment DDT and HCH concentrations in estuaries and bays of some Asian countries where OH pesticide use has been more recent. DDT was prevalent in sediments along the coast of India and the ratio of *p,p'*-DDT to ΣDDT ranged from 0.36 to 0.75 (Sarkar et al. 2008), consistent with recent use. In China, DDT remains prevalent in coastal sediments, in part due to its use in antifouling paints (Lin et al. 2009). ΣDDT sediment concentrations ranged from 0.009 to 7.35 mg/kg dw in coastal fishing harbors of China with *p,p'*-DDD comprising 64% of the ΣDDT (Lin et al. 2009). Comparison to DDT sediment concentrations in other harbors of the world are provided in Lin et al. (2009).

2.3.2 Tissues

OH compounds in fish tissue have similar patterns of detection compared to sediment, but typically are detected more frequently because they accumulate to higher concentrations (Gilliom et al. 2006). An early study on the prevalence and distribution of DDT in fish tissue from a variety of widely distributed Wisconsin fish measured DDT (0.021–16.2 mg/kg ww or 0.22–534.6 mg/kg lipid) in every fish sampled in that state (Kleinert et al. 1968). Results from this study were consistent with similar programs in other U.S. states for frequency of detection and range of concentrations. More recently, DDE and DDT were detected in fish from 90% and 30%, respectively, of agricultural streams sampled in the United States (Gilliom et al. 2006). Many local, regional, and national programs monitor OH pesticide concentrations in fish and invertebrate tissue. A number of different State and National monitoring programs in the United States generally have measured decreasing concentrations of DDTs and other OH pesticides in fish and invertebrates from many areas during the past several decades since their ban (e.g., Nowell et al. 1999, Gilliom et al. 2006, O'Connor and Lauenstein 2006). In contrast, monitoring programs in countries where DDT has been used more recently have continued to measure stable or increasing concentrations (Wiktelius and Edwards 1997, Tanabe et al. 2000; Ramu et al. 2007). DDT in coastal mussels of Asia were highest in Hong Kong (maximum 0.58 mg/kg), followed by Vietnam (maximum 0.4 mg/kg) and China (maximum 0.18 mg/kg) in the study by Ramu et al. (2007). This study also reports concentrations for HCH and chlordane in green mussels from these areas.

Table 2.2 provides a small subset of DDT residues in marine/estuarine and freshwater organisms from various localities around the world to provide some examples of concentrations measured in a variety of aquatic organisms. Table 2.2 also presents historical and recent DDT concentrations in fish and invertebrates from locations near DDT manufacturers. DDT biota concentrations measured in the past near DDT manufacturing sometimes reached >100 mg/kg. Locations near former DDT manufacturers continue to have elevated DDT concentrations in organisms (Bettinetti et al. 2006, NOAA and EPA 2007, Hinck et al. 2009).

In the marine environment, fish surveys indicated that benthic feeders have higher concentrations of DDT than pelagic feeders (ATSDR 2002, NOAA and EPA 2007). The reverse was observed in a freshwater lake (Kidd et al. 2001).

The USGS National Water-Quality Assessment program measured the following ratios of DDT metabolites and isomers in whole-body field-collected freshwater fish in the United States (1992–1995): 84.5% *p,p'*-DDE, 9.6% *p,p'*-DDD, 4.6% *p,p'*-DDT, 0.6% *o,p'*-DDD, 0.4% *o,p'*-DDE, and 0.3% *o,p'*-DDT (Wong et al. 2000). After uptake, *p,p'*-DDT is metabolized to DDD and to DDE, and therefore their ratios change over time.

For compounds resistant to degradation, environmental half-lives, or the time for the average tissue concentration to decrease by 50%, ranged from 9 to 17.7 years for DDT, 7.7–9.4 years for dieldrin and 1–1.9 years for toxaphene in Great Lakes biota (Hickey et al. 2006). DDT in fish from a Norwegian Lake took 5–7 years for 50% reduction (Brevik et al. 1996).

TABLE 2.2
Environmental DDT Concentrations in Aquatic Organisms from Various Locations Globally and in Locations Near Where DDT Was Manufactured

Species	Tissue	Form	Conc. (Mean/ Median or Range) mg/kg ww	Location	Year(s)	Reference
			Estuarine/Marine			
Fish						
Anchovy	Fillet	DDE	0.009	Adriatic Sea	1997	Bayarri et al. 2001
Mackerel	Fillet	DDE	0.0254	Adriatic Sea	1997	Bayarri et al. 2001
Red mullet	Fillet	DDE	0.0088	Adriatic Sea	1997	Bayarri et al. 2001
Herring	WB	ΣDDT	0.01–0.04	N. Baltic Sea	1991	Strandberg et al. 1998
Herring	WB	ΣDDT	0.116	Gulf of Gdansk	1992	Strandberg et al. 1998
Mullet	Muscle	ΣDDT	0.013[a]	Portugal	2001	Ferreira et al. 2004
Mullet	WB	ΣDDT	0.064	China	2001	Nakata et al. 2005
Goatfish	WB	ΣDDT	0.276	Midway Atoll		Hope and Scatolini 2005
Flounder	Muscle	ΣDDT	0.003[a]	Portugal	2001	Ferreira et al. 2004
Perch	WB	ΣDDT	0.0023–0.0064	N. Baltic Sea		Strandberg et al. 1998
Snapper	WB	ΣDDT	0.37–3.1	Suez Canal	2003	Said and Hamed 2005
Rabbitfish	WB	ΣDDT	0.16–0.56	Suez Canal	2003	Said and Hamed 2005
Fish (19 species)	WB	ΣDDT	0.0003–0.04	Indonesia	2003	Sudaryanto et al. 2007
African lungfish	Muscle	ΣDDT	0.7	Uganda		Ssebugere et al. 2009
Fish (17 species)	WB	ΣDDT	0.0018–0.287	China	2004	Qiu et al. 2009
Dog fish	Muscle	ΣDDT	0.033	India		Pandit et al. 2006
Sturgeon	Muscle	ΣDDT	0.012–0.44	Caspian Sea	2001–02	Kajiwara et al. 2003
Catfish & bass	Fillet	ΣDDT	0.00003–0.002	Gulf of Mexico	1996	Lewis et al. 2002
Chinook salmon	WB	ΣDDT	0.0005–0.041	Pacific NW	1996–01	Johnson et al. 2007a
Fish (7 species)		ΣDDT	0.005–0.061	San Francisco Bay	1997	Greenfield et al. 2005
Invertebrates						
Mussels & Oyster		ΣDDT	0.0026[a]	United States	2003	O'Connor and Lauenstein 2006
Oysters			0.0012[a]	Mexico	2000	Carvalho et al. 2009
Clam		DDE	0.0008	Adriatic Sea	1997	Bayarri et al. 2001
Sea urchin		ΣDDT	0.002	Midway Atoll		Hope and Scatolini 2005
Green mussel		ΣDDT	0.24	China	2001	Monirith et al. 2003
Green mussel		ΣDDT	0.12	Hong Kong	1998	Monirith et al. 2003
Green mussel		ΣDDT	0.0042	India	1998	Monirith et al. 2003
Green mussel		ΣDDT	0.004–0.507	China	2005	Guo et al. 2007
Blue mussel		ΣDDT	0.0035	Japan	1994	Monirith et al. 2003
Green mussel		ΣDDT	0.04	Vietnam	1997	Monirith et al. 2003
Squid		DDE	0.0038	Adriatic Sea	1997	Bayarri et al. 2001
Norway lobster		DDE	0.0012	Adriatic Sea	1997	Bayarri et al. 2001
Prawn		ΣDDT	0.002–0.014	China	2005	Guo et al. 2007
Shrimp	WB	ΣDDT	0.014	China	2001	Nakata et al. 2005
Crab	WB	ΣDDT	0.055	China	2001	Nakata et al. 2005

TABLE 2.2 (continued)
Environmental DDT Concentrations in Aquatic Organisms from Various Locations Globally and in Locations Near Where DDT Was Manufactured

Species	Tissue	Form	Conc. (Mean/ Median or Range) mg/kg ww	Location	Year(s)	Reference
			Freshwater			
Fish						
Predator fish	Fillet	ΣDDT	0.008–1.48	500 U.S. Lakes	2000–03	Stahl et al. 2009
Bottom fish	WB	ΣDDT	0.008–1.76	500 U.S. Lakes	2000–03	Stahl et al. 2009
Game and bottom fish	WB + fillets	*p,p'*-DDE	0.056	U.S. Background	1987	U.S. EPA 1992
Largemouth bass	WB	*p,p'*-DDE	2.7	Gila River, AZ	2003	Hinck et al. 2006a
Largemouth bass	WB	ΣDDT	0.059–0.072	Alabama	2004	Hinck et al. 2009
Walleye	WB	ΣDDT	0.076–0.15	Lake Erie	1991–96	Hickey et al. 2006
Carp	WB	*p,p'*-DDE	0.16–0.58	Idaho	1998	Hinck et al. 2006b
Carp	WB	ΣDDT	0.055	China	2000	Nakata et al. 2005
Lake trout	WB	ΣDDT	0.76–1.6	Lake Michigan	1991–98	Hickey et al. 2006
Fish (4 species)	Muscle	ΣDDT	0.00017–0.0026	Thailand	1997	Kumblad et al. 2001
Trahira	Muscle	ΣDDT	0.027–0.074[a]	Brazil	2005	Miranda et al. 2008
Nile Tilapia	Muscle	ΣDDT	0.051	Uganda		Ssebugere et al. 2009
Tilapia	WB	ΣDDT	0.0781	Indonesia	1998, 2003	Sudaryanto et al. 2007
Catfish	Muscle	ΣDDT	0.0009	Uganda		Ssebugere et al. 2009
Lake trout	Muscle	ΣDDT	0.0615	Arctic	2003	Ryan et al. 2005
Invertebrates						
Zooplankton		ΣDDT	0.00013	NW Territories	1995	Kidd et al. 1998
Chironominae		ΣDDT	0.0015	NW Territories	1995	Kidd et al. 1998
Prawn		ΣDDT	0.0001–0.052	China	2005	Guo et al. 2007
			Near Former DDT Manufacturing			
Fish						
Dover sole	Flesh	ΣDDT	39.7	Palos Verdes, CA	1977	Mearns et al. 1991
White croaker	Flesh	ΣDDT	39.17	Palos Verdes, CA	1975	Mearns et al. 1991
Spiny dogfish	Flesh	ΣDDT	81.2	Palos Verdes, CA	1981	Matta et al. 1986
White croaker	Fillet	ΣDDT	3.18	Palos Verdes, CA	2004	NOAA and EPA 2007
Northern anchovy	WB	ΣDDT	0.061	Southern CA Bight	2004	Jarvis et al. 2007
Largemouth bass	WB		0.24–225	Tennessee River	1978	U.S. EPA 2004
Channel catfish	WB		Up to 411.6	Tennessee River	1978	U.S. EPA 2004
Largemouth bass	WB	ΣDDT	0.42–49.8	Tombigbee River, AL	2004	Hinck et al. 2009

continued

TABLE 2.2 (continued)
Environmental DDT Concentrations in Aquatic Organisms from Various Locations Globally and in Locations Near Where DDT Was Manufactured

Species	Tissue	Form	Conc. (Mean/ Median or Range) mg/kg ww	Location	Year(s)	Reference
			Near Former DDT Manufacturing			
Landlocked shad		*p,p'*-DDT +DDE	0.458	Lake Maggiori, Italy	1998	Bettinetti et al. 2006
Barbel	Muscle	ΣDDT	0.997	Cinca River, Spain	2002	de la Cal et al. 2008
Bleak	WB	ΣDDT	0.840	Cinca River, Spain	2002	de la Cal et al. 2008
Invertebrates						
Coastal mussels		ΣDDT	3.24	Palos Verdes, CA	1969	Matta et al. 1986
Mussels		ΣDDT	0.092[a]	Palos Verdes, CA	2005	Kimbrough et al. 2008
Mussels		ΣDDT	0.013–0.035	Lake Maggiore, Italy	2003	Binelli and Provini 2003
Zooplankton		ΣDDT	0.387	Palos Verdes, CA	1969	Matta et al. 1986
Penaid shrimp		ΣDDT	4.49	Palos Verdes, CA	1969	Matta et al. 1986
Lobster		ΣDDT	0.562	Palos Verdes, CA	1976	Mearns et al. 1991

[a] Converted from dry-weight using 80% moisture.

2.4 BIOACCUMULATION

OH compounds readily bioaccumulate in aquatic organisms, especially in lipid-rich tissues. OH uptake occurs through passive diffusion across gills, dermal surfaces, and digestive organs. Uptake and elimination kinetics (toxicokinetics) and related topics are briefly reviewed in this section to help interpret tissue-residue toxicity.

The tendency of OH compounds to partition into lipid is an important factor influencing toxicokinetics and the degree of hydrophobicity is expressed as the n-octanol (octanol) water partition coefficient (K_{ow}). K_{ow} is the ratio of the solute concentration in octanol to water, where octanol acts as a surrogate for lipid, and the K_{ow} gives an indication about the ability or tendency of the compound to transfer between water-lipid phases. K_{ow} is generally expressed as a logarithm (log K_{ow}), and different techniques exist for measuring log K_{ow} so a range of values exist for any one compound (Pontolillo and Eganhouse 2001, Shen and Wania 2005). The OH compounds covered in this chapter and their log K_{ow} predicted using the U.S. EPA EPIweb software are listed in Table 2.1. Arnot and Gobas (2006) review both data availability and considerations for bioconcentration factors (BCFs) and bioaccumulation factors (BAFs) of organic chemicals in aquatic organisms.

Quantitative structure–activity relationship (QSAR) models relate BCFs and log K_{ow} using linear regression (see discussion in Arnot and Gobas 2006). OH compounds generally follow QSAR model

predictions for bioaccumulation. However, BCFs predicted from $\log K_{ow}$ may be over-estimated when the biotransformation rates are high (Oliver and Niimi 1985).

Bioaccumulation is the net result of competing process of chemical uptake into the organism from food and water, and elimination from the organism into the environment. The uptake and elimination of OH compounds is influenced by numerous factors, including exposure temperature and organism size (e.g., Landrum et al. 1992, Lotufo et al. 2000a), therefore influencing net bioaccumulation in an organism. The time to steady-state bioaccumulation is directly proportional to the rate of elimination of a chemical from the organism, the slower the rate the longer the time to steady state.

Elimination of OH compounds occurs through passive diffusion through dermal surfaces, excretion, egestion of feces, and biotransformation of the parent compound. The elimination rate (k_e) and time to approximate steady-state body residues ($3/k_e$) of DDT and its major transformation products varied substantially across compounds and invertebrate species (Table 2.3). Comparison of the elimination of DDT, DDD, and DDE was reported for four invertebrate species. The slowest

TABLE 2.3
Elimination Rate Coefficient (k_e) and Corresponding Time to Achieve 95% of Steady-State Body Residue (95% SS) in Invertebrates Exposed to OH Compounds in Water

Species	k_e (d^{-1})	Time to 95% SS (d)	Reference
		Nereis virens	
DDT	0.024	125	Haya and Burridge 1988
DDT	0.029	102	Kennedy et al. 2010
DDD	0.033	90	Kennedy et al. 2010
DDE	0.073	41	Kennedy et al. 2010
Dieldrin	0.024	125	Haya and Burridge 1988
Endosulfan	0.432	7	Haya and Burridge 1988
		Macoma nasuta	
DDT	0.041	73	Boese et al. 1997
DDD	0.078	38	Boese et al. 1997
DDE	0.030	100	Boese et al. 1997
Dieldrin	0.054	56	Boese et al. 1997
		Hyalella azteca	
DDT	0.113	27	Lotufo et al. 2000a
DDD	0.180	17	Lotufo et al. 2000a
DDE	0.386	8	Lotufo et al. 2000a
		Leptocheirus plumulosus	
DDT	0.48	6.25	Lotufo et al. unpublished
		***Diporeia* spp.**	
DDT	0.017	179	Lotufo et al. 2000a
DDD	0.012	250	Lotufo et al. 2000a
DDE	0.014	208	Lotufo et al. 2000a
		Heteromastus filiformis	
DDT	0.103	29	Mulsow and Landrum 1995
		Acartia erythraea	
DDT	0.01 – 0.05	300–500	Wang and Wang 2005

elimination rates for DDT, DDD, and DDE, and therefore longest time for steady-state, were reported for the Great Lakes amphipods of the genus *Diporeia*, while the fastest were reported for the more widely distributed amphipod *Hyalella azteca* (Lotufo et al. 2000a). The slowest elimination rate for DDT was reported for the copepod *Acartia erythraea*. Few reports on toxicokinetics of other OH pesticides were found for invertebrates. The elimination of endosulfan was much faster than DDT or dieldrin in the polychaete *Nereis virens* (Haya and Burridge 1988), and the elimination rate of dieldrin in the clam *Macoma nasuta* was in the same range as those reported for DDT, DDD, and DDE in the same study (Boese et al. 1997). For fish, the DDT elimination rate constant for the mangrove snapper (*Lutjanus argentimaculatus*) was 0.028 d^{-1} and 0.002 d^{-1} for aqueous and dietary exposure, respectively (Wang and Wang 2005). Elimination of DDT from fish tissue varied by tissue type and was lowest in viscera compared to gills and carcass after aqueous or dietary exposure (Kwong et al. 2008).

Exposure route (aqueous or dietary) may influence tissue distribution and transformation processes (Kwong et al. 2008) but did not influence DDT absorption efficiency (Wang and Wang 2005). The OH compound concentration in the diet may influence assimilation efficiency. DDT contaminant uptake efficiency by fish reported from studies using part per million (mg/kg) range concentrations in diet were 20% in rainbow trout (*Oncorhynchus mykiss*) (Macek et al. 1970), 12–25% in chinook salmon (*O. tshawytscha*), 38–68% in coho salmon (*O. kisutch*) (Buhler et al. 1969) and 17–27% in Atlantic menhaden (*Brevoortia tyrannus*) (Warlen et al. 1977). DDT uptake efficiency by Asian seabass (*Lates calcarifer*) from food containing DDT in the part per billion (μg/kg) range was 98% (Bayen et al. 2005). Assimilation efficiency also may be influenced by prey type, as DDT assimilation in mangrove snappers (*Lutjanus argentimaculatus*) was 72% when clams were the DDT food source and 99% when copepods were the DDT source (Wang and Wang 2005).

Biotransformation is typically an important route of parent compound elimination especially if it results in products that are more water soluble. Metabolic products of endosulfan include endosulfan sulfate, which is not excreted, and alcohol, lactone, and ether, which are excreted. Fifty percent of accumulated dietary endosulfan was estimated to be eliminated by transformation (Berntssen et al. 2008). Endosulfan taken up by striped mullet (*Mugil cephalus*) was metabolized to endosulfan sulfate after 28-day (d) aqueous exposure (Schimmel et al. 1977a). Chlordane metabolizes to oxychlordane and also can be dehydrochlorinated to heptachlor. For DDT, metabolism (chemical reduction) results in reduction of the parent DDT compound in fish and an increase in the more resistant DDE metabolite over the more readily excreted DDD metabolite (Kwong et al. 2008) (Table 2.4). The result is an enrichment of the DDE metabolite in fish tissue after longer exposures. Biotransformation rate data in fish are lacking for most compounds. A QSAR was developed to predict screening level whole-body biotransformation of organic compounds in fish (Arnot et al. 2009).

In invertebrates, the degree and product of the transformation of *p,p'*-DDT varies among species (Table 2.4). Following a 3-d exposure of seven species to DDT in water, the parent compound was present at higher concentration than the sum of the transformation products in five species, and DDE was present at higher concentrations than DDD, which was below detection limit in the tissues of five species (Johnson et al. 1971). The amphipods *Diporeia* spp., exposed for 28 d, transformed only a very small fraction of the DDT entering the tissues to DDD, while most DDT was transformed to DDE in *H. azteca* (Lotufo et al. 2000a). Biotransformation considerations will improve kinetics modeling for compounds subject to transformation, and is especially relevant when parent compound and different metabolites vary in toxic potency.

Variable bioaccumulation of DDT in different tissues and organs is a function of differences in lipid content and biotransformation activity. In catfish (*Heteropneustes fossilis*), concentrations were highest in the liver followed by ovary and brain (Singh and Singh 2007). Holden (1966) noted that DDT distribution in salmon differed under different exposure durations. After acute exposure salmon had higher concentrations in the liver, spleen, and fat, while chronic exposures resulted in liver concentrations similar or lower than muscle concentrations. Organ to whole-body

TABLE 2.4
DDT and Transformation Products Expressed as Percentage of Total Body Residue in Fish and Invertebrates Exposed to Either Technical- or *p,p'*-DDT

Species	DDT	DDE	DDD	Other	Exposure (Days)	Reference
			Fish			
Fathead minnow	7.8	80.3	13.4	0	266	Jarvinen et al. 1976
Brook Trout	45.7	14.8	39.5	0	156	Macek 1968
Goldfish	60.2	34.9	4.8	0	4	Davy et al. 1972
			Invertebrates			
Daphnia magna	73.4	19.7	6.6	0	3	Johnson et al. 1971
Gamarus fasciatus	79.1	20.9	0	0	3	Johnson et al. 1971
Palaemonetes kadiakensis	50.9	13.2	7.2	28.7 (DTMC[a], DBP[b])	3	Johnson et al. 1971
Hexagenia bilineata	14.9	85	0	0	3	Johnson et al. 1971
Ishnura vericalis	39.2	60.2	0	0	3	Johnson et al. 1971
Libellula sp.	56.3	28.4	0	15 (DTMC)	3	Johnson et al. 1971
Chironomus sp.	80.8	19.1	0	0	3	Johnson et al. 1971
Neanthes arenaceodentata	63.5	6.3	4.5	25.7 (polar)	28	Lotufo et al. 2000b
Hyalella azteca	34.4	64.4	0	1.2 (polar)	10	Lotufo et al. 2000a
Diporeia spp.	95.7		4	0.3 (polar)	28	Lotufo et al. 2000a
Leptocheirus plumulosus	83.6	9.7	0	6.7 (polar)	2	Lotufo et al. unpublished

Note: All organisms were exposed in water to *p,p'*-DDT, except brook trout which were exposed to technical DDT and *Neanthes arenaceodentata*, which were exposed to *p,p'*-DDT-spiked sediment.

[a] 1,1,1-trichoro-2,2,-bis(*p*-chlorophenyl)ethanol.

[b] 4,4'-dichlorobenzophenone.

relationships can be difficult to predict and may vary among species, between genders, and by age. DDT concentrations in a variety of whole fish were 4–12 times higher and averaged 10-times higher than the skin-off fillet concentrations (NOAA and EPA 2007). White croaker DDT whole-body to fillet ratio was 7–8 in this study.

The fate of DDT and its transformation products in different organs and tissues was examined in crustaceans. In aqueous exposure to DDT, Crosby and Tucker (1971) reported that a significant proportion of the total body residue in daphnids was adsorbed externally by the exoskeleton. A long-term exposure (56 d) of the pink shrimp, *Farfantepenaeus duorarum* (formerly *Penaeus duorarum*), to spiked water resulted in residues of DDT in the hepatopancreas exceeding those in other tissues by wide factors (e.g., 30, 275, and 550 when compared to residues in the gills, digestive tract, and tail muscle, respectively) (Nimmo et al. 1970). For all organs investigated, DDT transformation products were only approximately 10% of the total residue. Similar findings were reported for the lobster *Homarus americanus* (Guarino et al. 1974). Seven days following a 7-d water exposure, approximately 91% of the administered radioactivity was found in the hepatopancreas, 1% in the gill, 4% in the intestine, 3.2% in the egg masses, and 1% in the tail muscle. Similar distribution among organs and tissues was obtained 7 d following a single dose injection of DDT. The hepatic organ contained large amounts of lipids, 50–60% of the wet weight, explaining in part the high concentration relative to other organs. The identity of the radioactivity in the hepatopancreas, determined 48 h after DDT injection, was 91% parent compound, 6.8% DDD, and 2.6% DDE.

2.4.1 Biomagnification

Biomagnification occurs when the thermodynamic activity of the chemical in an organism exceeds that of its diet (Arnot and Gobas 2006). It is expressed as a factor (biomagnification factor or BMF), which for hydrophobic organics is the ratio of the lipid-normalized residue in the predator divided by the lipid-normalized prey residue. Use of stable isotopes to establish trophic relationships has enabled improved quantification and understanding of factors affecting biomagnification. In addition to lipid content, organism size, dietary sources, and intrinsic toxicokinetic parameters have a role in biomagnification (Banas et al. 2009). Biomagnification was reported for DDT (e.g., Fisk et al. 1998, Kidd et al. 2001, Hu et al. 2010), mirex (Fisk et al. 1998), *p,p′* DDE and chlordane (Strandberg et al. 1998, Ruus et al. 1999), and endosulfan (Berntssen et al. 2008).

Concentrations of some OH compounds biomagnify for specific metabolites. For example, DDT concentrations, in the form of *p,p′* DDE, and chlordane in the form of oxychlordane and trans-nonachlor increase in higher trophic predator species compared to concentrations in prey (Strandberg et al. 1998, Ruus et al. 1999). β-Endosulfan had higher biomagnification than α-endosulfan (Berntssen et al. 2008).

BMFs were determined for mirex and 3 toxaphene congeners (Fisk et al. 1998). BMFs in rainbow trout were 1.8 and 2.9 for mirex at two concentrations in the diet. For the higher chlorinated toxaphene congeners, BMFs ranged from 2.1 to 4.9, depending on concentration in the diet. In this study of laboratory-derived parameters relating to bioaccumulation, Fisk et al. (1998) observed a curvilinear relationship between log K_{ow} and BMFs. BMFs were highest for compounds with high log K_{ow} and low transformation. The BMF for *p,p′*-DDT was 1.7 in a freshwater food web in China (Hu et al. 2010). Trophic position was a key determinant, along with lipid, of DDT body residue in a freshwater food web (Kidd et al. 2001). The relationship between lipid and DDT bioaccumulation is explored in more detail in the next section.

2.4.2 Lipids

OH compounds that have low solubility in water (hydrophobic) will partition into lipids within an organism. Lipid content and lipid dynamics are important considerations for understanding OH tissue-residue effect data. Accumulation, transfer, and toxicity of OH compounds can be affected by lipid quantity and type. Contaminants tend to partition into lipids with similar polarity. Polar lipids are associated with cell membranes, which are the site of baseline toxicity. Nonpolar lipids such as triglycerides, cholesterol, and wax esters serve as energy storage. Triglycerides are an important storage lipid in fish. Contaminants can become associated with these storage lipids and are thereby removed from sites of toxic action. Periods of stress, starvation, migration, and/or spawning can draw on and deplete those lipid reserves. As lipid stores are depleted, organochlorine compounds can move to sites of toxic action within the organism where they become available to exert toxic effects (Jørgensen et al. 2006).

The OH–lipid relationship is complicated by a number of factors, but for many compounds and species, lipid normalization can reduce variability in measured tissue residues. For example, lipid normalization reduced the variability of aqueous lindane toxicity across multiple fish species and toxicity to lindane decreased with increasing lipid content (Geyer et al. 1994). Lipid normalization also reduced DDT and DDD lethal CBR variability between two freshwater amphipods (Lotufo et al. 2000a). However, difference in lipid content did not account for major differences in DDT uptake and elimination kinetics between males and females of the polychaete *Neanthes arenaceodenta*, as steady-state lipid-normalized body residues were three times higher in females than in males (Lotufo et al. 2000b).

Understanding how best to interpret the residue-effect literature, and whether to express residue-effects as wet-weight or lipid-normalized (ww or dw residue divided by % tissue lipid) is still being evaluated and the best approach may differ for different compounds, species, and tissue types. For

hydrophobic compounds, normalization to a specific lipid pool such as storage lipid, may improve the toxicity relationship (Delbeke et al. 1995). Residue effect studies often do not report lipid concentrations, and lipid concentrations vary seasonally, with life stage and gender. Different measurement techniques and solvents used for lipid analysis can also yield different results on the same samples (Randall et al. 1991, 1998). Understanding lipid dynamics is a key issue for OH residue transfer and toxicity, especially as it relates to maternal transfer and dose to developing sensitive life stages. Elskus et al. (2005) review many of the important factors affecting persistent contaminant toxicity in fish in the context of lipids.

2.4.3 Maternal Transfer

The maternal transfer of accumulated OH contaminants to developing offspring is a significant and critical pathway for early life-stage exposure and potential for toxicity to this sensitive life stage. Highly lipophilic compounds may be mobilized from parental stores and transferred into the developing eggs as lipids move from adult storage tissues during oogenesis. Lipophilic OH pesticides tend to concentrate in lipid-rich gonads where they are available to exert toxic effects during early development. During oogenesis, estrogen stimulates the formation of the egg yolk precursor protein known as vitellogenin that serves as nutrient reserves to the developing oocyte in the fish ovary. OH compounds can bind to vitellogenin and other lipoproteins and be transported into the developing oocytes (Ungerer and Thomas 1996). Fish early developmental stages are a period of enhanced sensitivity during the formation of the body's major systems. Maternally transferred OH pesticides may have a stronger influence on toxic effects to fish larvae during the first few weeks of feeding than dietary sources (Westin et al. 1985). Bioaccumulation in fish at early life stages is higher than in juvenile or adult fish because of lower metabolic capacity. In addition, enzyme systems may not be sufficiently developed to reduce the toxicity of accumulated compounds.

2.5 TOXICITY

2.5.1 Modes of Action

Early studies on the effects of OH compounds on aquatic organisms focused primarily on mortality endpoints during short-term exposures. Many researchers noted the rapid death of sensitive individuals at relatively low tissue concentrations and the ability of remaining "resistant" organisms to accumulate high residues. Death from central nervous system (CNS) disruption was considered the primary mode of action for these compounds. The focus of recent literature for DDT and some other OHs has shifted toward understanding sublethal effects, in particular endocrine system disruption in fish. The potency of OH pesticides to act as endocrine disruptors in fish and invertebrates is generally low compared to natural hormones, however environmental OH concentrations may be high enough alone, or in combination with other endocrine disrupting substances, to cause effects. The cumulative effect of endocrine disruptors in the environment is an emerging area of research. The next paragraphs provide a brief overview for several modes or mechanisms of action to help interpret residue-effect endpoints frequently encountered in the fish and invertebrate OH tissue-residue literature.

DDT has been described as a neurotoxin (Bloomquist 1996). Accumulation of OH pesticides within the nerve tissue is the site of toxic action for CNS disruption. DDT and other organochlorines act on the CNS via nerve cell membrane sodium channels. Molecules of OH pesticides bind to the lipid-rich membrane-sheaths of nerve axons where they may interfere with sodium and potassium ion permeability. The passage of "action potential" is disrupted and results in uncontrolled spontaneous discharges along the nerve rather than normal responses to stimulation. Endpoints resulting from this mode of action include seizures and behavioral abnormalities that can result in mortality. Cyclodiene pesticides may act on the nervous system through a different mechanism.

For example, lindane, dieldrin, and endosulfan alter chloride ion flux via the gamma-aminobutyric acid (GABA) receptor leading to excitation and hyperactivity, and afterward, suppression (Narahashi 2000). Reduced activity, also known as hypoactivity or lethargy, may result from this mechanism of action (Ballesteros et al. 2009).

For the neurotoxic mode of action, DDT is expected to promote mortality when whole-body residues reach levels well below those observed for organic compounds that act by general narcosis, or baseline toxicity (McCarty and Mackay 1993). However, given the wide range of lethal CBRs in fish and invertebrates, DDT may have a strong neurotoxic action in some organisms, but only a weak action in others; it may produce mortality mostly by a baseline toxicity mechanism. Neurotoxic effects of DDT were noted as spasms, lack of coordination or swimming ability or immobilization in daphnids (*Daphnia magna*) (Crosby and Tucker 1971), crabs (*Cancer irroratus*) (Neufeld and Pritchard 1979), and amphipods (Lotufo et al. 2000a), and hyperactivity in bluegill (*Lepomis macrochirus*) (Ellgaard et al. 1977). It was noted that the amphipods *Diporeia* spp. exposed to DDT and DDD became sluggish and increasingly immobilized long before death occurred (Lotufo et al. 2000a).

Although DDT and DDD are expected to promote neurotoxicity to varying degrees in invertebrates, that mode of action may be weak or not-exist for the transformation product DDE, which produced mortality at levels considered typical for compounds with a baseline toxicity mode of action (Lotufo et al. 2000a, Hwang et al. 2004).

Some OH pesticides are also endocrine disruptors. The endocrine system controls the activity of hormones in the body and substances that interfere with the modulation of these hormones are known as endocrine disruptors. The endocrine (estrogenic) effects of DDT exposure were identified early when cockerels were noted to have decreased testes size and reduced reproduction (Burlington and Lindeman 1950). The similarity in the molecular structure of DDT to synthetic estrogens was noted at that time, but the field of endocrinology was not well developed. Since about the mid-1990s, endocrine disruption from organochlorine exposure has been a major research area for fish and other vertebrates.

Hormone activity can be disturbed by different mechanisms such as OH interaction with hormone receptors, or alteration of steroid synthesis and metabolism (Garcia-Reyero et al. 2006). Endocrine disruptors can interfere with hormone synthesis in the thyroid gland via a number of mechanisms that are still not well-understood. The thyroid controls a number of physiological functions in fish such as reproductive status and embryogenesis. Sex-steroid hormones control sex-specific gonad differentiation activities such as gonadal recrudescence. Substances that mimic sex hormones are known as estrogens or xenoestrogens if they can bind to estrogen receptors and regulate the activity of estrogen responsive genes. Examples of xenoestrogenic substances are: *o,p′* DDD; *p,p′* DDT and *o,p′* DDT; and endosulfan, as described later. Compounds that interfere with male sex hormones are androgenic. Examples include *p,p′* DDE and *p,p′* DDT. Since the endocrine system controls many reproductive functions, disruption can impact the number and health of offspring produced.

During fish sexual maturation, estrogen stimulates the formation of the egg yolk precursor protein, known as vitellogenin, in the liver of female fish. Female fish livers contain high concentrations of estrogen receptors and can synthesize large quantities of vitellogenin, especially during their reproductive season. Vitellogenin serves as nutrient reserves to the developing oocyte in the fish ovary and concentrations increase dramatically during the reproductive phase to enable female fish to form the many, often thousands, of eggs. In contrast, male fish produce no or extremely small quantities of vitellogenin (Sumpter and Jobling 1995). The concentration of plasma vitellogenin indicates estrogen stimulation (Donohoe and Curtis 1996) and is one way to measure exposure to endocrine disrupting compounds in fish. A number of studies in this chapter report vitellogenin and steroid hormone measurements as an endpoint. Induction of vitellogenin was initially considered a biomarker for exposure to endocrine disrupting compounds; however, its connection to reproductive impairment, especially in female fish is becoming supported by more data (Cheek et al. 2001, Thorpe et al. 2007). Therefore, it will be the focus for endocrine disruptive effects reported here.

Studies investigating altered gene expression connected with hormone synthesis from OH exposure is an active area of research but residues are typically not reported (e.g., Zhang and Hu 2008).

A number of studies have examined endocrine responses from exposure to DDT isomers to fish; however, few have measured tissue residues associated with these effects. The naturally occurring estrogen, 17β-estradiol (E_2) is often used as a positive control to compare the responsiveness of potential estrogenic substances. Studies reporting the dose administered to fish egg/embryo via nanoinjection are included in the DDT residue section below.

Endocrine disruption in invertebrates is an area of increasing research but relationship with residues has not been reported to date. Depledge and Billinghurst (1999) suggested that DDT, endrin, toxaphene, and endosulfan may cause endocrine disruption in invertebrates. Exposure of midges to DDE promoted decreased fecundity in association with body residues 2 orders of magnitude lower than those found to promote mortality (Hwang et al. 2004). The DDE effect on insect fecundity may be attributable to endocrine disruption, although the onset of endocrine disruption of DDE may be mechanistically different in insects and fish (Hwang et al. 2004).

2.6 TISSUE-RESIDUE EFFECTS—FISH AND INVERTEBRATES

Studies reporting organismal-level effects associated with a whole-body residue, including appropriate control treatments, were identified with the aid of the Army Corps of Engineer Environmental Residue Effects Database (ERED) as well as library and internet search engines. For some compounds with little or no whole-body effect data, studies that reported fish organ concentrations were also selected. No-effect and low-effect whole-body residue concentrations and the associated effect were identified from each study. CBR data are reported individually in tables or in text descriptions. CBR data are combined and summarized when data are sufficient. The following sections, organized by OH compound, present CBR data for fish and invertebrates. Unless specified, all residue concentrations are wet-weight.

2.6.1 DDT

The DDT pesticide was applied as a technical mixture. Technical DDT is composed of a mixture of DDT forms, approximately 77% *p,p'*-DDT, 15% *o,p'*-DDT, 4% *p,p'*-DDE, and 0.4% DDD (U.S. EPA 1980). The less persistent DDT analogue methoxychlor was once widely used as a pesticide but is not covered in this review.

The ratios of *o,p'*-isomers to total DDT in the environment can provide information about the DDT source since the form applied as an insecticide was technical DDT enriched in the *p,p'* DDT form. When the *o,p'* DDT to DDT ratio is greater than 20%, the source likely is not insecticidal and could be from either industrial DDT production or storage (Nowell et al. 1999). Early studies with DDT primarily dosed fish with the technical mixture, with a high percentage of *p,p'*-DDT.

The following sections review the residue effect literature for DDT in fish and invertebrates. Sections are grouped by DDT isomer and include literature that has focused on endocrine disruption in fish. Invertebrate CBRs for *p,p'*-DDT, -DDD, and -DDE from specific studies are presented in Table 2.5. ∑DDT fish CBR ranges and medians are summarized in Table 2.6, and invertebrate CBR ranges and medians for DDT isomers are summarized in Table 2.7.

2.6.1.1 *p,p'*-DDT

2.6.1.1.1 Fish

In a previous analysis, Beckvar et al. (2005) examined different approaches for developing protective whole-body DDT residues for fish. Using scientific literature primarily consisting of mortality studies and technical or *p,p'*-DDT exposure, four approaches were explored for analyzing no- and low-observed effect residues from different fish species. Results from the different approaches

TABLE 2.5
Toxicity Associated with DDT, DDD, and DDE in Tissues of Aquatic Invertebrates (mg/kg ww)

Species	No Effect mg/kg	Low Effect mg/kg	Exposure	Effect	Reference
			***p,p'*-DDT**		
Callinectes sapidus	—	0.95	14 d in diet	Mortality	Butler 1969
Callinectes sapidus	0.13	1.0	21 d in diet	Mortality	Leffler 1975
Callinectes sapidus	—	0.30	Single oral dose	Behavior	Neufeld and Pritchard 1979
Penaeus sp.	—	0.26	15 d in diet	Mortality	Butler 1969
Farfantepenaeus duorarum	0.1	0.15	22 d in water	Mortality	Nimmo et al.1970
Hyalella azteca	1.0	2.1	10 d in water	Mortality	Lotufo et al. 2000a
Hyalella azteca	0.5	2.8	10 d in sediment	Mortality	Lotufo et al. 2001b
Diporeia spp.	9	15.6	28 d in water	Mortality	Lotufo et al. 2000a
Diporeia spp.	—	5.9	28 d in sediment	Mortality	Lotufo et al. 2001b
Daphnia magna	128	1150	26 h in water	Mortality	Crosby and Tucker 1971
Leptocheirus plumulosus	1.2	2.7	28 d in sediment	Mortality	Lotufo et al. 2001a
Heteromastus filiformis	3.4	5.9	28 d in sediment	Feeding rate	Mulsow and Landrum 1995
Neanthes arenaceodentata	28	35	28 d in diet	Growth	Lotufo et al. 2000b
			***p,p'*-DDD**		
Hyalella azteca	6.5	15.0	10 d in water	Mortality	Lotufo et al. 2000a
Diporeia spp.	—	93.1	28 d in water	Mortality	Lotufo et al. 2000a
			***p,p'*-DDE**		
Hyalella azteca	30	126.6	10 d in water	Mortality	Lotufo et al. 2000a
Hyalella azteca	—	116.8	10 d in water	Mortality	Landrum et al. 2005
Chironomus riparius	—	60	From 2nd instar to adults in diet	Mortality	Hwang 2000
Chironomus riparius	—	0.8	From 2nd instar to adults in diet	Development delayed, fecundity	Hwang et al. 2004
Lumbriculus variegatus	79.2	178.4	35 d in diet	Mortality	Fisher et al. 1999
Daphnia pulex	—	14	5 d in water	Feeding	Bengtsson et al. 2004

— Not available.

were compared to the mean of the control concentrations from the included studies, and ambient DDT concentrations to determine the reasonableness of the calculated no-effect threshold residues. A concentration of 0.6 mg/kg DDT was calculated as the concentration below which effects (primarily mortality) to juvenile and adult fish were expected to be unlikely. For early life stages a threshold residue of 0.7 mg/kg DDT was calculated from the available literature. Data used in this analysis were mostly older studies reporting lethal effects so the calculated thresholds were considered provisional. Sublethal residue-effect data and data correlating isomer-specific residues with an effect

TABLE 2.6
Summary of CBR Ranges and Medians for OH Compounds in Whole-Body Fish (mg/kg ww)

Chemical	Response	Life Stage	Range	Median[a]	*n*
ΣDDT[b]	Lethal	Juv/adult	0.29–113	2.38	6
ΣDDT[b]	Lethal	ELS[c]	0.89–24	1.27	9
ΣDDT	Sublethal	Egg	0.005–91	0.045	4
p,p'-DDE	↓ Sex steroids	Adult	0.38–0.59		2
o,p'-DDT	Sublethal	Egg	0.02–91	0.07	3
Dieldrin	Lethal	Juv	0.2–5.9		2
Endrin	Lethal	Juv/adult	0.012–1.7	0.88	9
Endosulfan	Lethal	Juv/adult	0.03–0.36	0.27	3
Chlordane	Lethal	Adult	0.7–16.6	11.4	3
Heptachlor	Lethal	Adult	0.33–34	4.1	6
Heptachlor epoxide	Lethal	Adult	0.23–11	1.0	6
Lindane	Lethal	Adult	5.2–79	10.8	4
Toxaphene	Lethal	Adult	1.9–6.1	3.25	4
Toxaphene	Lethal	Fry/juveniles	24.7–46.6	34	4
Toxaphene	Sublethal	Adult	0.4–5.9	1.95	4
Toxaphene	Sublethal	ELS[c]	0.4–10	0.95	6

[a] Up to 100% mortality included for lethal effects.
[b] From studies reporting lethality in Beckvar et al. (2005); primarily technical or *p,p'*-DDT.
[c] ELS, early life stages; egg, embryo, and fry.

TABLE 2.7
Summary of CBR Ranges and Medians for OH Compounds in Invertebrates (mg/kg ww)

		CBR			
Chemical	Response	Min	Max	Median	*n*
p,p'-DDT	Lethal	0.15	1150	2.4	10
p,p'-DDD	Lethal	15	93	—	2
p,p'-DDE	Lethal	60	178	122	4
Dieldrin	Lethal	0.08	2.1	1.05	4
Endrin	Lethal	0.03	358	0.61	7
Endosulfan	Lethal	<0.01	0.21	—	2
Chlordane	Lethal	1.7	9.1	—	2
Heptachlor	Lethal	0.02	3.5	—	2
Mirex	Lethal	0.02	10.4	0.27	11
Lindane	Lethal	0.03	5.2	—	2
Toxaphene	Lethal	0.54	2.7	—	2

were insufficient for analysis. No recent studies using technical or *p,p'*-DDT were found to add to this previously compiled dataset. Using the studies identified in Beckvar et al. (2005), the median effect concentrations for different life stages were calculated and are reported in Table 2.6 to compare with median CBRs from other OH pesticides.

2.6.1.1.2 Invertebrates

The lowest reported lethal CBR (0.15 mg/kg) for *p,p'*-DDT was for the pink shrimp, *F. duorarum*, exposed for 22 d to 0.14 µg/L in water in a bioaccumulation experiment (Nimmo et al. 1970) (Table 2.5). The authors stated that this concentration is lethal to those shrimp after 22 d, but did not report percent mortality. Close to 100% mortality likely occurred by day 28, as bioaccumulation data for that sampling period were not provided. A lethal CBR (0.26 mg/kg) was reported for shrimp (*Penaeus* sp.) fed oysters exposed to *p,p'*-DDT (Butler 1969). After 15 d, mortality was 57% (no statistical comparison provided) and whole-body residue in dead shrimp was 0.26 mg/kg. Mortality in both control shrimp (13%) and DDT treatment groups was partially attributed to cannibalism. The same study reported a lethal CBR of 0.95 mg/kg for crabs (*Callinectes sapidus*) fed DDT-exposed oysters (Butler 1969). After 14 d, mortality (54%) was lower than in control crabs (no statistical comparison provided), where high mortality (38%) was also explained by cannibalism. A later study reported three weekly feedings of 3.2 µg DDT resulting in crab mortality at a body residue of 1 mg/kg (Leffler 1975). The percent mortality associated with this lethal residue was not reported. The study also reported that slightly lower concentration (0.82 mg/kg) caused a significant decrease in ability to regenerate limb and doubled metabolic rate. No effects were associated with a body residue of 0.13 mg/kg. Sublethal effects for adult *C. sapidus* injected with DDT (isomer not specified) targeting 0.3 mg/kg body weight were convulsions and lack of coordination, which disappeared within 24 h (Neufeld and Pritchard 1979).

The lethal CBRs of *p,p'*-DDT for two amphipods commonly used in toxicity testing, the estuarine *Leptocheirus plumulosus* (Lotufo et al. 2001a) and the freshwater *H. azteca* (Lotufo et al. 2000a), were similar and higher than those reported for decapod crustaceans (Table 2.5). The median lethal CBR for *L. plumulosus* (2.7 mg/kg) and *H. azteca* (2.8 mg/kg), measured after a 28-d exposure to spiked sediment, were almost identical. A slightly lower median lethal CBR (2.1 mg/kg) was observed after a 10-d exposure to water only (Lotufo et al. 2000a). In a 10-d sediment exposure, where no supplemental food was provided, exposure to sublethal DDT concentrations significantly enhanced growth in *L. plumulosus* (Lotufo et al. 2001a). No sublethal effects were reported for *L. plumulosus* (reproduction or decreased growth) and *H. azteca* (decreased growth) in the latter studies.

Freshwater amphipods, *Diporeia* spp., which are ecologically relevant benthic organisms in the Great Lakes, were more tolerant to *p,p'*-DDT exposure than *H. azteca* and *L. plumulosus*. In 28-d aqueous exposures, the median lethal CBR was 15.6 mg/kg (0.682 µmol/g lipid) (Lotufo et al. 2000a). Using inability to actively swim on contact stimulus as the effect endpoint for lethargy, a substantially lower median CBR of 4.5 mg/kg was reported for the same exposure. In a 28-d sediment exposure, a lower median lethal CBR was reported (5.9 mg/kg) (Lotufo et al. 2001b), but mortality was reported as unexpectedly high and attributed to low lipid content and higher sensitivity of the batch of field organisms used in the experiment.

The CBRs reported for the water flea, *D. magna* (Crosby and Tucker 1971), were orders of magnitude higher than those for other crustaceans. When exposed to *p,p'*-DDT in water for 26 h, the median lethal CBR was 1170 mg/kg. A substantially lower CBR of 128 mg/kg caused only 4% mortality but promoted immobilization in 64% of the exposed cladocerans. Full recovery of those lethargic animals occurred upon transfer to clean water.

Polychaete worms (*Heteromastus filiformis*) were exposed to increasing spiked sediment concentrations of radiolabeled *p,p'*-DDT (Mulsow and Landrum 1995). Although no significant mortality was reported, the feeding rate was estimated at various time periods as the quantity of fecal pellets produced per individual per unit time. Significantly decreased feeding was associated with mean CBRs of 5.9 mg/kg obtained in the highest sediment treatment group. The growth of another species of polychaete, *Neanthes arenoceodentata*, exposed to *p,p'*-DDT-spiked food (fish flakes), sediment or both was significantly decreased at CBRs of 35 mg/kg (Lotufo et al. 2000b). Body residues as high as approximately 140 mg/kg did not elicit lethal effects in those invertebrates, a no-lethal-effect body residue similar to that reported for *D. magna* (Crosby and Tucker 1971).

The range and median CBRs for *p,p'*-DDT in invertebrate species are summarized in Table 2.7. Several studies reporting body residues of invertebrates exposed to *p,p'*-DDT in bioaccumulation exposures did not report any associated mortality or sublethal effects. For bivalves, body residue as high as 0.88 mg/kg in *Mya arenaria* and 0.13 mg/kg in *Mercenaria mercenaria* did not impact their survival or feeding behavior (Butler 1971). When freshwater invertebrates were exposed to DDT in water for 3 d for the determination of BCFs, highest reported body residues were 0.014 mg/kg for the dragonfly (*Libellula* sp.) 0.047 mg/kg for the crayfish (*Orconectes nais*) 0.075 mg/kg for the damselfly (*Ischnura verticalis*) 0.1 mg/kg for the grass shrimp, *Palaemonetes kadiakensis*, 0.336 mg/kg for the mayfly, *Hexagenia bilineata*, and 0.440 mg/kg for the midge, *Chironomus* sp., (Johnson et al. 1971). No effects were reported at a body residue of 6 mg/kg in the mayfly (*Ephemera danica*) exposed in the lab (Sodergren and Svensson 1973). Longer exposure to DDT would likely have resulted in higher body residues in the above species and until further investigation is conducted, their maximum tolerance to DDT bioaccumulation is unknown. Ingersoll et al. (2003) reported a *p,p'*-DDT body residue of 1.9 mg/kg for the oligochaete, *Lumbriculus variegatus*, exposed in the lab. They did not observe mortality, but did observe less activity and smaller size in DDT-exposed oligochaetes compared to control.

2.6.1.2 *o,p'*-DDT

2.6.1.2.1 Fish

Several recent studies examine the effect of maternally transferred DDT isomers using egg-nanoinjection techniques. For fish, DDT concentrations in the eggs were not measured during most of these experiments. Instead, egg residues were estimated based on the injected dose and the approximate weight of the egg/embryo. In the Edmunds et al. (2000) study described below, DDT embryo concentrations measured by gas chromatography were within 20% of the estimated embryo dose. Therefore, doses reported in nanoinjection studies likely estimate actual residues in fish embryos.

Edmunds et al. (2000) injected five doses of *o,p'*-DDT into d-rR strain medaka (*Oryzias latipes*) embryos 6–8 h after fertilization. Triolein injected and uninjected embryos served as controls and estradiol-injected eggs served as positive estrogenic controls. DDT doses were injected into the yolk of the embryos, not the oil globule, unlike studies with DDE described later. Percent hatch, survival to 14 d posthatch and sex-reversal were measured and followed by breeding trials. Survival decreased with increasing DDT dose with a least squares calculated LD_{50} of 511 ng/egg (or 511 mg/kg based on average egg mass of 1 mg). Male to female sex-reversal occurred in 6 of 7 genetic males injected with 227 ng/egg (or 227 mg/kg) DDT. Breeding success of these sex-reversed fish was about 50% and similar to controls. The authors observed that the DDT oil droplet remained intact throughout hatching, so the amount of DDT exposure is uncertain and may not be related to the injected dose.

Adult female medaka were exposed to aqueous concentrations of *o,p'*-DDT to study maternal transfer and effects to offspring (Metcalfe et al. 2000). Adult females were exposed to a single sublethal concentration of 2.5 µg/L *o,p'*-DDT for 2 weeks. During exposure, medaka maternal tissue residues varied from a maximum of 109.6 mg/kg during exposure and decreased to 0.28 mg/kg after 23 weeks. Lipid-weight (lw) DDT concentrations were similar between eggs and maternal tissues. Median time to hatch was significantly longer in treated groups compared to controls, and ovarian development was increased in offspring of DDT-treated fish. The mean DDT concentration in the treated 3- and 6-week-old eggs was 91.2 mg/kg. In the same study, posthatch medaka treated with aqueous exposures of *o,p'*-DDT experienced altered sex ratios and males with testes-ova (intersex). Tissue residues were not measured but testes-ova induction occurred at exposure to about 2 µg/L mean aqueous concentration, and statistically significant difference in sex ratio occurred at about 5 µg/L mean concentration.

Lowered gonadosomatic index (GSI, gonad weight/body weight × 100) was measured in male-summer flounder (*Paralichthys dentatus*) injected subcutaneously with *o,p'*-DDT using a slow-release solvent (Mills et al. 2001). Liver concentrations were highly variable within a treatment

group but increased in a dose–responsive manner with decreasing GSI after 8 weeks. Gonad alterations were confirmed by histological analysis. Plasma testosterone concentration decreased in a dose–dependent manner. Liver concentrations in *o,p'*-DDT treated fish ranged from 188.0 to 521.3 mg/kg compared to 0.3 mg/kg in control flounder after injection with 30, 60, and 120 mg/kg body weight. No effects on these endpoints were observed when fish were injected with *p,p'*-DDE. Study duration was important as a subset of fish that were followed for 15 weeks showed effects (elevated plasma estradiol) not apparent when the study was concluded at 8 weeks.

Faulk et al. (1999) exposed adult Atlantic croaker (*Micropogonias undulatus*) to *o,p'*-DDT in the diet and tested offspring to behavioral assays representing behaviors needed for survival such as feeding and predator avoidance. Growth differences were not observed between control and treated fish but behavioral alterations such as burst speed were reduced in larvae of treated fish. DDT egg residues were 0.07 mg/kg in the low treatment group and 0.2 mg/kg in the high treatment group and effects were dose-responsive.

2.6.1.2.2 Invertebrates

Studies reporting CBRs for *o,p'*-DDT for invertebrates were not found in the available literature. Insufficient data for *o,p'*-DDT preclude toxicity comparison with *p,p'*-DDT based on exposure water concentration.

2.6.1.3 *o,p'*-DDE, *p,p'*-DDE

2.6.1.3.1 Fish

Villalobos et al. (2003) injected *o,p'*-DDE into fertilized d-rR strain medaka embryos using a triolein carrier solvent with 4 doses separated by tenfold dilution (0.0005–0.5 ng/egg or mg/kg based on 1 mg medaka egg weight). *o,p'*-DDE was injected directly into the oil globule of early gastrula embryos. The oil globule is used by the developing fish before hatching. Uninjected eggs and carrier-only injected eggs served as controls. Survival was followed for 2 months. Mortality was statistically different in the highest treatment group with 56% mortality. Mortality occurred most frequently after early development near the time of hatching. The authors note that the morphological defects noted at death were consistent with effects observed from organochlorine exposure in field populations. The survival-based no-observed adverse effect level (NOAEL) and low-observed adverse effect level (LOAEL) egg residues from these dosing intervals were 0.05 and 0.5 mg/kg, respectively.

Papoulias et al. (2003) injected fertilized embryos of d-rR strain medaka using a triolein carrier solvent with three doses of *o,p'*-DDE (0.005, 0.05, and 0.5 ng/egg, or mg/kg). After injection and hatching, fish were reared until sexual maturity. Reproduction was assessed by quantifying GSI in male and female fish. GSI was significantly reduced in all DDE treatments compared to triolein-injected controls. Histopathic analyses revealed developmental alterations in oocyte formation in the ovaries for all treated females, and reduction of testes size in males at the highest treatment (0.5 ng/egg or mg/kg). Fish in the highest treatment group also weighed significantly more and had the highest mortality (56%). The lowest CBRs for different endpoints from this study were 0.005 mg/kg for reduction in male and female GSI and 0.5 mg/kg for growth (increased) and mortality.

Carlson et al. (2000) injected 21-d postfertilization embryos of rainbow trout and coho salmon using menhaden oil as a carrier. Prior to sexual differentiation and hatching of the fish, but after organ formation, yolks were injected with *o,p'*-DDE and *p,p'*-DDE individually or as a mixture. Both oil-injected and noninjected rainbow trout embryos served as control treatments. The ratio of males to females was statistically different in fish injected with 80 or 160 mg/kg *o,p'*-DDE in one of the experiments, but not in the others. Mortality in oil-injected control rainbow trout was high in two of the experiments and was statistically higher than noninjected control fry in doses greater than 40 mg/kg. Fish that were grown out for several years after injection had normal gonads and spawned successfully. Residues measured in fat at the end of the study were higher in fish injected with the *p,p'* isomer by a factor of 10 compared to the *o,p'* isomer.

Milston et al. (2003) report effects from *o,p'*-DDE exposure on immune function in fall chinook salmon. Fertilized eggs were exposed to aqueous nominal concentrations of 10 and 100 mg/L *o,p'*-DDE for 1 h after fertilization and an additional 2 h after hatch. After treatment, fish were reared in the hatchery for 1 year when the effect on gonad histology and humoral immunity was assessed. Fry with 0.02 mg/kg *o,p'*-DDE whole-body residue had significantly reduced ability to respond to a bacterial antigen. These fry also weighed significantly less than controls at the first sampling event. The authors believed that alteration of gonadal steroids during early development likely caused the immune suppression observed 1 year after exposure, although they could not definitely rule out direct toxicity to *o,p'*-DDE.

Muller et al. (2004) exposed 2-year-old largemouth bass to *p,p'*-DDE spiked food for 30 and 50 d and noted statistically reduced sex-steroid concentrations, 17β-estradiol and 11-ketotestosterone (E_2 and 11-KT), in both female and male fish at whole-body concentrations of about 0.375 mg/kg DDE. No statistically significant difference in GSI of treated fish compared to control fish was noted in these sexually immature fish.

Johnson et al. (2007b) measured sex-steroid concentrations in 2-year-old largemouth bass exposed to *p,p'*-DDE in food for 120 d. Concentrations of E_2 in female bass were significantly reduced compared to controls at 0.589 mg/kg *p,p'*-DDE in female carcass (ovary not included, Johnson 2005). The authors were not able to fit a Hill slope dose–response relationship using the dose in the food (not the tissue residues), and did not report whether the data could be fit to other dose–response models.

Other studies have measured endocrine activity from exposure to *p,p'*-DDE; but did not measure associated residues. For example, mature male guppies exposed to *p,p'*-DDE in food for 30 d demonstrated impacts at cellular through organism level with reduced sperm cell counts, loss in sexual coloration and changes in courtship behavior, and reduction in clutch size (Baatrup and Junge 2001). The sperm count of males fed *p,p'*-DDE at the lowest dose had a hormetic effect, that is, was higher than control fish. Juvenile male guppies exposed to the same concentration in food experienced delayed development time, a skewed sex ratio, reduced sperm cell counts, reduced growth, and altered sexual display coloration (Bayley et al. 2002). Male Japanese medaka exposed to *p,p'*-DDE had reduced GSI and the highest exposure group had intersex (Zhang and Hu 2008).

2.6.1.3.2 Invertebrates

Lethal CBRs for *p,p'*-DDE were similar for a variety of freshwater invertebrates (Table 2.5). Median lethal CBRs were 126.6 mg/kg for *H. azteca* exposed in water for 10 d (Lotufo et al. 2000a), 116.8 mg/kg at day 10 for *H. azteca* exposed in water for 28 d (Landrum et al. 2005), and 178.4 mg/kg for *L. variegatus* exposed via feeding on algae grown in spiked medium (Fisher et al. 1999). For the midge *Chironomus riparius* fed algae exposed to *p,p'*-DDE, a lethal body residue of 60 mg/kg was reported (Hwang 2000). Sublethal effects associated with DDE, were significantly delayed development time in female midges and decreased fecundity occurring at approximately 0.8 mg/kg (Hwang et al. 2004). For midge *Chironomus dilutus* (formerly *C. tentans*), body residues ranging from 10 to 60 mg/kg were reported as causing developmental delay (Derr and Zabik 1972). A body residue of 14 mg/kg for sublethal effect was reported for the cladoceran *D. magna* associated with decreased feeding rate (Bengtsson et al. 2004). No significant mortality occurred in *Diporeia* spp. exposed for 28 d to a water concentration approaching the DDE solubility limit and producing body residues as high as 429 mg/kg (Lotufo et al. 2000a).

Studies reporting CBRs for *o,p'*-DDE for invertebrates were not found in the available literature.

2.6.1.4 *o,p'*-DDD, *p,p'*-DDD

2.6.1.4.1 Fish

o,p'-DDD is often present in tissue either as a metabolite of DDT or from the technical mixture. A high DDD residue may indicate past use of the insecticide rothane. DDD acts on adrenal

steroidogenesis in fish affecting cortisol production but effects have not been associated with residues. No dosing studies could be found that exposed fish to the DDD metabolite and measured residue-effects.

2.6.1.4.2 Invertebrates

The lethal CBR of *p,p'*-DDD was reported for freshwater amphipods exposed to spiked water (Lotufo et al. 2000a) (Table 2.5). Median lethal CBRs were 15 mg/kg for *H. azteca* exposed for 10 d and 93.1 mg/kg for *Diporeia* spp. exposed for 28 d. In that study, a mean body residue of 46.7 mg/kg was associated with paralysis characterized by inability to actively swim on contact stimulus. All amphipods in the lowest exposure treatment were affected. No adverse effects were reported in association with a measured body residue of 60 mg/kg in *L. variegatus* (Ingersoll et al. 2003).

Studies reporting CBRs for *o,p'*-DDD for invertebrates were not found in the available literature.

2.6.2 DDT Discussion

2.6.2.1 Fish

Most of the older literature reporting DDT residues associated with effects to fish focused on lethal body residues from exposure to *p,p'*-DDT alone, or as the predominant form in the technical formulation (Beckvar et al. 2005). Lethal body residues spanned several orders of magnitude for a variety of fish species with CNS the mode of action studied (Table 2.6). Many authors noted behavioral disorders preceded death, early life stages were more sensitive than adults, and smaller, leaner, or more sensitive fish died more quickly. Few studies reported residues associated with sublethal effects during these early investigations.

Recent investigations on effects to fish have focused on effects from specific DDT isomers, mostly related to endocrine disruption. These studies observed effects at concentrations similar to and much lower than those reported in the older literature (0.005–91 mg/kg). The variety of effect endpoints, dosing techniques (nanoinjection), and life stages preclude detailed data analyses using these recent investigations. However some general insights about sublethal effect endpoints and effect ranges for the different isomers can be summarized from these more recent studies.

The studies dosing with *o,p'*-DDT measured endocrine-related effects and mortality at very high egg residues. Doses of *o,p'*-DDT injected into medaka embryos resulted in sex-reversal in males at 227 mg/kg, and survival was reduced by 50% at 511 mg/kg (Edmunds et al. 2000). This study differed from the DDE nanoinjection studies because *o,p'*-DDT was injected into the yolk, not the oil globule of the embryo. *o,p'*-DDT fed to Atlantic croaker was found primarily in the triglyceride-rich oil globule in oocytes (Ungerer and Thomas 1996). The way lipids are used from different parts of the fish egg during early embryonic development may impact the ability of DDT to reach sites of toxic action. DDT and lipid movement within developing embryos were correlated in brook trout (Atchison 1976). Comparison of Edmunds et al. (2000) with the studies that injected DDT into other parts of the embryo may not be appropriate.

Two studies using maternal transfer and *o,p'*-DDT measured effects for different endpoints at very different egg concentrations. Eggs from aqueous-exposed adult female medaka contained a mean concentration of 91.2 mg/kg *o,p'*-DDT, and median time to hatch was significantly longer for these offsprings (Metcalfe et al. 2000). Eggs from adult female Atlantic croaker exposed to dietary *o,p'*-DDT had residues of 0.07 mg/kg. At this much lower concentration, larvae demonstrated behavioral alterations. The studies used different species, exposure routes, and effect endpoints, and the relative contribution of these variables on the three order of magnitude difference in egg-effect residues is unknown.

Alterations of sex-steroid hormones were observed in adult fish at residue concentrations from 0.3 to 0.6 mg/kg *p,p'*-DDE (Muller et al. 2004, Johnson 2005). Fish were exposed as adults in these studies, not during sensitive early life stages, so the effect of a life-time exposure is unknown.

Effects associated with *o,p'*-DDE exposure were reported as doses injected into fish embryos. A reasonable assumption is that the injected embryo dose is a good estimate of the embryo residue concentration (Edmunds et al. 2000). Dose–response relationships also support this assumption. Medaka embryo CBRs associated with increased mortality were 0.5 mg/kg (Papoulias et al. 2003, Villalobos et al. 2003), and an embryo dose/residue of 0.005 mg/kg was associated with reduced gonad weights (GSI) in males and females (Papoulias et al. 2003). Immune response in Chinook salmon fry 1 year after aqueous egg exposure to *o,p'*-DDE was reduced at a measured whole-body CBR of 0.02 mg/kg, with growth significantly reduced at the first sampling event (Milston et al. 2003). CBRs for the DDE isomers in fish were less variable than for the DDT isomer, and the lowest effect concentrations for fish embryos in Atlantic croaker for DDT (Faulk et al. 1999) were similar to that observed for DDE in Chinook salmon (Milston et al. 2003).

The results from different isomer experiments report a variable ability for DDT isomers to affect endocrine activity. This variability may be a function of life-stage differences, and the timing and method of dosing in relation to development and sexual maturation of the organism. Species, gender, and other variables among the reviewed studies make direct comparisons about the strength of different DDT isomers as endocrine disruptors uncertain. For the studies reviewed here, the *o,p'*-DDT isomer appeared to require higher concentrations compared to the DDE isomers for endocrine disruption. This result contrasts with effects in rats where the *o,p'*-DDT isomer was observed to have higher potency for endocrine disruption (ATSDR 2002).

The lowest CBR for fish egg/embryo from the isomer-specific DDT studies reviewed were associated with reproduction and behavior endpoints (0.005 mg/kg *o,p'*-DDE and 0.07 mg/kg *o,p'*-DDT, respectively). Residues associated with mortality in fish eggs were 0.5 mg/kg *o,p'*-DDE. Intersex or sex-reversal endpoints were associated with much higher egg DDT CBRs (80–90 mg/kg *o,p'*-DDT).

Reduction in immune function response in 1-year-old fish exposed as eggs (Milston et al. 2003) was the endpoint associated with the lowest whole-body fry residue (0.02 mg/kg *o,p'*-DDE). Residues associated with reductions in sex-steroid concentrations in adult fish (0.3–0.6 mg/kg) were measured at concentrations comparable to residues associated with mortality reported by Beckvar et al. (2005). However, for the sex-steroid endpoints (Muller et al. 2004, Johnson et al. 2007b), DDE exposure was limited to only the adult life stage. Fish exposed throughout their life-time may experience effects at lower residue concentrations.

Few studies are available to compare summary CBR data for DDT isomers in fish (Table 2.6). Generally, median CBRs for fish egg life stage and sublethal effects are one to two orders of magnitude lower than CBRs for fish exposed during older life stages or lethal effects.

Several studies report reproductive effects from DDT exposure associated with concentrations in fish organs. Hose et al. (1989) observed complete absence of spawning in white croaker (*Genyonemus lineatus*) at concentrations greater than 3.8 mg/kg DDT in ovary, and reduction in spawning at ovary concentrations of 2.2 mg/kg. Ovary concentration >0.2 mg/kg and dieldrin >0.1 mg/kg impaired reproductive success in North Sea whiting (*Merlangius merlangus*) (von Westernhagen et al. 1989). These concentrations are within the range of CBRs observed in the DDT isomer effect studies.

2.6.2.2 Invertebrates

Lethal CBRs reported for invertebrates span a wide range, from 0.15 mg/kg for pink shrimp, to 1150 mg/kg for daphnia with a median 2.4 mg/kg (Table 2.7). While most invertebrates investigated appear to be sensitive to the neurotoxic effects of DDT; some such as daphnia and polychaete worms, are apparently mostly tolerant to DDT specific mode of action. Lethal CBRs for the *p,p'* isomers of DDT, DDD, and DDE were compared using two species of freshwater amphipods. Striking differences in the lethal CBRs for those compounds suggest that they may cause mortality via different modes of action. While DDT, and to a lesser degree DDD, likely act via neurotoxicity impairing the normal functioning of voltage-sensitive sodium channels, DDE likely caused amphipod mortality by a combination of baseline toxicity and a weak specific, yet unknown, mode of action

(Lotufo et al. 2000a). Because the lethal CBR for DDE is much higher (lower toxicity) than for DDT in amphipods, biotransformation acts as a protective mechanism against mortality. The DDE lethal body residues in midges and oligochaetes were similar to those for amphipods, suggesting similar mode of action across taxa. Unfortunately the lethal CBRs of DDT and DDD are unknown for those species, and overall broad comparisons on modes of action for parent and transformation products cannot be established. Based on toxicity comparison using water concentrations, DDD and DDE are more toxic than the parent compound to freshwater planarians (Bonner and Wells 1987), suggesting DDT metabolites may also act by specific modes of action associated with low body residues in some invertebrates.

Lethal body residues for amphipods are among the lowest CBRs reported for invertebrates; growth and reproductive effects were not significant for amphipods (Lotufo et al. 2000a, 2001a). Delayed development in female chironomids and reduced fecundity occurred at a relatively low CBR (0.8 mg/kg, Hwang et al. 2004). Sublethal effects were manifested in polychaete worms with relatively high tolerance to the lethal effect of DDT, as both growth (Lotufo et al. 2000b) and feeding rate (Mulsow et al. 2002). These data suggest that for species tolerant to the neurotoxic effects of DDT, other specific modes of action may cause sublethal effects.

2.6.3 Cyclodienes

2.6.3.1 Aldrin and Dieldrin

Aldrin and dieldrin exist as pure compounds or technical mixtures. The technical mixture of aldrin contains not less than 85.5% pure aldrin. Dieldrin technical mixture contains not less than 80.75% pure dieldrin. The toxicity of the pure compound is greater than the formulations in both cases. Aldrin and dieldrin were used extensively in the United States until the 1970s and continue to be used elsewhere to control insects such as termites and tsetse fly (Table 2.1). Aldrin rapidly metabolizes to dieldrin in the environment, so even though toxic, tissue residues are generally measured as dieldrin. Review of the residue literature for aldrin therefore primarily deals with dieldrin in tissue.

2.6.3.1.1 Fish

Even though dieldrin is highly accumulated in fish tissue and widespread, studies for both lethal and sublethal residue-effects are limited (Table 2.6). A dieldrin concentration of 1.21 mg/kg in winter flounder (*Pseudopleuronectes americanus*) eggs was associated with 100% mortality (Smith and Cole 1973). These eggs also contained 0.76 mg/kg DDT. Juvenile rainbow trout exposed to dieldrin in water for 16 weeks had whole-body residues of 0.2 mg/kg and increased mortality compared to control fish, but no statistics were provided (Shubat and Curtis 1986). Juvenile rainbow trout had estimated whole-body dieldrin residues of 5.9 mg/kg in the treatment group with 100% mortality after dietary exposure (Shubat and Curtis 1986). Behavioral effects in goldfish and bluegill (*Lepomis macrochirus*) were noted at whole-body concentrations of approximately 3.7 mg/kg (Gakstatter and Weiss 1967). One study observed 65% mortality at 62.4 mg/kg whole-body dieldrin in sheepshead minnow (*Cyprinodon variegatus*) (Parrish et al. 1974), but residues in the control minnows were 1.1 mg/kg. Therefore, CBRs associated with mortality in sheepshead minnow from pre-exposed fish in this study may be biased high.

Studies reporting sublethal effects observed histological changes and endocrine effects. A whole-body dieldrin residue in spot (*Leiostomus xanthurus*) of 2.9 mg/kg was associated with histological aberrations of lamellae in gill and mucosal epithelium in small intestine after aqueous exposure for 4 d. Circulating sex-steroid levels of E_2 and 11-KT were reduced in largemouth bass (*Micropterus salmoides floridanus*) fed dieldrin in diet compared to control bass (Muller et al. 2004). GSI was not significantly different between treated and control bass; however, according to the authors, bass were sexually immature, possibly due to handling stress. Residues in whole-body bass were

approximately 0.1 mg/kg dieldrin in the treated bass, with fish retaining 30–35% of the 50-d total administered dose. In a similar study, Johnson et al. (2007b, Johnson 2005) exposed 2-year-old male and female largemouth bass to dietary dieldrin for 30 and 120 d. The longer exposure was needed to measure reductions in sex-steroid concentrations in all the treated bass. Whole-body residues at 120 d were similar in control and the lowest treatment group of fish, but sex steroids were significantly reduced in all the treatment groups compared to control fish. Bass had average whole-body dieldrin residues of 0.2 mg/kg in the lowest treatment and control groups. No difference in GSI was noted after 120 d exposure.

2.6.3.1.2 *Invertebrates*

Invertebrate CBRs for aldrin and dieldrin are presented in Table 2.8 and summarized in Table 2.7. For dieldrin, invertebrate lethal body residue was lowest, 0.08 mg/kg, for the pink shrimp, *F. duorarum* (Parrish et al. 1974) exposed in water for 96 h (44% mortality, full survival in the control). Lethal body residues for other invertebrates were higher and within the narrow range of 1–2.1 mg/kg. For the midge, *C. riparius*, mortality (percent not reported) after 1 d exposure was

TABLE 2.8
Toxicity Associated with Cyclodienes in Tissues of Aquatic Invertebrates (mg/kg ww)

Species	No Effect mg/kg	Low Effect mg/kg	Exposure	Effect	Reference
			Aldrin		
Chlamydotheca arcuata	—	1	96 h in water	Mortality	Kawatski and Schmulbach 1971
			Dieldrin		
Chironomus riparius	—	1.1	24 h in water	Mortality	Estenik and Collins 1979
Chlamydotheca arcuata	—	1	96 h in water	Mortality	Kawatski and Schmulbach 1971
Palaemonetes pugio	0.09	2.1	96 h in water	Mortality	Parrish et al. 1974
Farfantepenaeus duorarum	0.016	0.08	96 h in water	Mortality	Parrish et al. 1974
Crassostrea virginica	13.9	20	96 h in water	Growth	Parrish et al. 1974
			Endrin		
Palaemonetes pugio	0.18	0.61	96 h in water	Mortality	Tyler-Schroeder 1979
Palaemonetes pugio	0.02	0.19	96 h in water	Mortality	Schimmel et al. 1975
Farfantepenaeus duorarum	0.01	0.025	96 h in water	Mortality	Schimmel et al. 1975
Pteronarcys dorsata	0.03	0.07	96 h in water	Mortality	Anderson and DeFoe 1980
Crassostrea virginica	0.26	16.4	68 h in water	Mortality	Mason and Rowe 1976
Crassostrea virginica	—	5.8	96 h in water	Growth	Schimmel et al. 1975
Limnodrilus hoffmeisteri	58	358	43 d in sediment	Mortality	Keilty et al. 1988b
Limnodrilus hoffmeisteri	58	148	43 d in sediment	Growth	Keilty et al. 1988b
Limnodrilus hoffmeisteri	58	0.003	43 d in sediment	Sediment reworking	Keilty et al. 1988b
Stylodrilus heringianus	62	118	43 d in sediment	Mortality	Keilty et al. 1988a
Stylodrilus heringianus	—	1.5	43 d in sediment	Sediment reworking	Keilty et al. 1988a

continued

TABLE 2.8 (continued)
Toxicity Associated with Cyclodienes in Tissues of Aquatic Invertebrates (mg/kg ww)

Species	No Effect mg/kg	Low Effect mg/kg	Exposure	Effect	Reference
			Endosulfan		
Palaemonetes pugio	0.065	0.21	96 h in water	Mortality	Schimmel et al. 1977a
Farfantepenaeus duorarum	<0.01	<0.01	96 h in water	Mortality	Schimmel et al. 1977a
Mytilus edulis	1.9	8.1	112 d in water	Spawning	Roberts 1972
			Chlordane		
Palaemonetes pugio	4.8	9.1	96 h in water	Mortality	Parrish et al. 1976
Farfantepenaeus duorarum	0.71	1.7	96 h in water	Mortality	Parrish et al. 1976
Crassostrea virginica	<0.01	27	96 h in water	Growth	Parrish et al. 1976
			Heptachlor (heptachlor and heptachlor epoxide)		
Farfantepenaeus duorarum	—	0.068[a]	96 h in water	Mortality	Schimmel et al. 1976
Farfantepenaeus duorarum	—	0.016[b]	96 h in water	Mortality	Schimmel et al. 1976
Farfantepenaeus duorarum	—	0.21[c]	96 h in water	Mortality	Schimmel et al. 1976
Palaemonetes vulgaris	0.32	3.5[c]	96 h in water	Mortality	Schimmel et al. 1976
Crassostrea virginica	—	8.4[c]	96 h in water	Growth	Schimmel et al. 1976

[a] Sum heptachlor and heptachlor epoxide (exposure to analytical grade heptachlor).
[b] Heptachlor epoxide (exposure to heptachlor epoxide).
[c] Sum heptachlor and heptachlor epoxide (exposure to technical grade heptachlor).
— Not available.

associated with a body residue of 1.1 mg/kg (Estenik and Collins 1979). Mortality (% not reported) in the ostracod, *Chlamydotheca arcuata*, exposed for 48–96 h was associated with body residues less than 1.0 mg/kg (Kawatski and Schmulbach 1971). Parrish et al. (1974) reported a lethal CBR of 2.1 mg/kg in the grass shrimp, the *Palaemonetes pugio*, displaying 20% mortality (full control survival) in a 96-h exposure to dieldrin in water. Dieldrin body residues ranging from 14 to 107 mg/kg were reported as nonlethal to the Eastern oyster, *Crassostrea virginica* (Parrish et al. 1974, Mason and Rowe 1976, Emanuelsen 1978), while this bivalve displayed decreased growth (24%, no decrease reported for control oysters) at 13.9 mg/kg (Parrish et al. 1974). Statistical comparisons for mortality data were not reported in the above studies.

The only lethal CBR for aldrin was reported for *C. arcuata* (Kawatski and Schmulbach 1971) as less than 1 mg/kg. Highest no-effect body residues in invertebrates exposed to aldrin in water ranged from 0.13 to 2.3 mg/kg (Butler 1971, Johnson et al. 1971). The later studies did not indicate whether aldrin was transformed to dieldrin in those invertebrates. The reported body residues are assumed to correspond to the aldrin-only body residue.

2.6.3.2 Endrin

Endrin is the stereoisomer of dieldrin. The technical formulation contains not less than 92% pure endrin (WHO 1992). Endrin was introduced in 1951 and was used to control cotton crop pests in the United States (Table 2.1). Endrin use is banned or highly restricted in many countries. Although

similar in structure to dieldrin, endrin is more rapidly metabolized and accumulates to a lesser degree in lipids.

2.6.3.2.1 Fish

Endrin has high acute aqueous toxicity to fish with a relatively narrow LC50 range. Lethal CBRs for seven fish species ranged from 0.012 mg/kg in largemouth bass fingerlings (Fabacher and Chambers 1976) to 1.7 mg/kg in sailfin mollies (*Poecilia latipinna*) (Schimmel et al. 1975), and 0.9 mg/kg median lethal CBR (Table 2.6). Lethal CBR for fingerling channel catfish (100% mortality) was 1.0 mg/kg (Argyle et al. 1973) and bluegill sunfish LR50 was 0.3 mg/kg (Bennett and Day 1970). Fathead minnow fry CBR (89% mortality) was 0.24 mg/kg (Jarvinen and Tyo 1978). Adult fathead minnow lethal CBR was 1.1 mg/kg (60% mortality), similar to adult sheepshead minnow lethal CBRs (0.88–1.5 mg/kg; Schimmel et al. 1975, Hansen et al. 1977). One study reported hyperactivity in golden shiner (*Notemigonus crysoleucas*) at 0.21 mg/kg sublethal CBR (Ludke et al. 1968). Exposures were acute and chronic duration, and all but one were aqueous exposures. Immune suppression has been noted from endrin exposure, but CBRs were not reported.

2.6.3.2.2 Invertebrates

Invertebrate CBRs for endrin are presented in Table 2.8. Endrin lethal CBRs varied much more widely than those for dieldrin, ranging from 0.025 to 358 mg/kg for eight species. As for dieldrin, the lowest invertebrate lethal CBR, 0.025 mg/kg, was reported for the pink shrimp, *F. duorarum* (Schimmel et al. 1975) exposed to technical grade endrin in water for 96 h (25% mortality, full survival in the control). In that same study, the grass shrimp, *P. pugio* was more tolerant, accumulating 0.19 mg/kg when mortality was 20% (full control survival). The 28-d median lethal CBR for giant black stonefly *Pteronarcys dorsata* (Anderson and DeFoe 1980) was 0.07 mg/kg. Other invertebrates investigated were substantially more tolerant to endrin. High mortality (90%) of the eastern oyster *C. virginica* occurred at a body residue of 16.4 mg/kg after a 7-d exposure (Mason and Rowe 1976). For the latter species, a lower reported residue of 5.8 mg/kg resulted in 40% decrease in growth of juvenile oysters relative to control organisms after 96 h (Schimmel et al. 1975). Statistical comparisons of mortality data were not reported in the above studies.

Keilty et al. (1988a) exposed the tubificid oligochaete, *Limnodrilus hoffmeisteri*, to sediment spiked with endrin to investigate several toxicity endpoints as well as bioaccumulation. In contrast to CBR of 358 mg/kg for significantly decreased survival (44%; 12% in the control) and 148 mg/kg for decreased growth, feeding activity, measured as sediment reworking rate, was significantly decreased at 0.003 mg/kg. Similarly, Keilty et al. (1988b) reported a significant decrease in feeding activity in the oligochaete, *Stylodrilus heringianus*, associated with a CBR (1.5 mg/kg), much lower than the reported lethal body residue (118 mg/kg) following a 43-d exposure to spiked sediment. Endrin body residues as high as 0.62 mg/kg in the bivalves *Mya arenaria* and 0.24 mg/kg in *Mercenaria mercenaria* did not impact their survival or feeding behavior (Butler 1971).

2.6.3.3 Endosulfan

Endosulfan consists of two stereoisomers, alpha and beta, also known as endosulfan I and endosulfan II. The technical grade mixture has alpha and beta isomers in an approximately 70:30 ratio (WHO 1984a), and the isomers have different toxicity. Aquatic toxicity to endosulfan I is generally greater than toxicity from the other isomers, but the sulfate metabolite can have similar or greater toxicity in some species (Knauf and Schulze 1973). Endosulfan is highly toxic to fish and invertebrates and has resulted in kills following aerial spraying (Naqvi and Vaishnavi 1993). Fairly persistent in water, soil, and sediment, endosulfan fish tissue residues declined rapidly after exposure ceased (Schimmel et al. 1977a). Endosulfan use in the United States was reregistered by the U.S. EPA in 2001 (U.S. EPA 2002) but concentrations in fish were not analyzed by the USGS under its National

Water-Quality Assessment (NAWQA) program. Endosulfan use in other countries such as China and India also continues (PAN North American 2009).

2.6.3.3.1 Fish

Few studies have measured whole-body residues and toxicity. After uptake, endosulfan is oxidized to the metabolite endosulfan sulfate. One study reported lethal CBRs after a 96-h exposure to endosulfan. Spot, pinfish (*Lagodon rhomboids*), and striped mullet experienced 35–40% mortality at whole-body total endosulfan concentrations of 0.031, 0.272, and 0.36 mg/kg, respectively (Schimmel et al. 1977a). Most of the endosulfan was endosulfan sulfate. Adult zebra fish exposed to endosulfan accumulated different concentrations of the individual isomers with the alpha isomer measured at the highest whole-body concentration (Toledo and Jonsson 1992). Maximum total endosulfan residue after the 27-d exposure was 0.9 mg/kg and was associated with alterations in gill lamella and zonal necrosis, and lipid accumulation in liver. In Atlantic salmon, β-endosulfan was accumulated more readily and depurated more slowly than α-endosulfan (Berntssen et al. 2008).

Matthiessen et al. (1982) measured whole-body residues in fish that died within 3 d after aerial spraying with 35% endosulfan emulsifiable concentrate for tsetse fly control in Botswana. Concentrations in juvenile fish ranged from 0.07 mg/kg whole body in African catfish (*Clarias* sp.) to 1.08 mg/kg in African cichlid (*Haplochromis* sp.). Adult southern mouthbrooder (*Pseudocrenilabrus* sp.) that died had 1.46 mg/kg whole body. After 12 months, field fish still had detectable residues in their tissue. In lab studies, Matthiessen et al. (1982) measured concentrations in organs associated with mortality and noted that lean fish died more rapidly.

Endosulfan has been reported to have estrogenic properties, although study results are sometimes conflicting (e.g., Smeets et al. 1999, Hemmer et al. 2001, Balasubramani and Pandian 2008). Reduction in cortisol levels in fish has been reported from *in-vitro* studies (Leblond et al. 2001). CBRs associated with endocrine disruptive effects have not been reported.

2.6.3.3.2 Invertebrates

In the only study reporting endosulfan CBRs for invertebrates (Table 2.8), Schimmel et al. (1977a) observed lethal effects (90% mortality, 100% survival in the control) in pink shrimp, *F. duorarum* at water concentrations of 0.076 µg/L resulting in nondetectable residues of endosulfan I and II and endosulfan sulfate (0.01 mg/kg detection limit) after 96 h. The same study reported a lethal residue of 0.21 mg/kg for the grass shrimp, *P. pugio* (35% mortality, 100% control survival), that was 63% endosulfan sulfate, 28% endosulfan I, and 9% endosulfan II (Schimmel et al. 1977a). The same study reported decreased growth (78%), higher than in the control (10%) for *C. virginica*, and no lethal effects were associated with a body residue of 19.9 mg/kg. Statistical comparisons for mortality data were not reported in that study. Endosulfan body residues as high as 8.1 mg/kg in the mussel *Mytilus edulis* did not impact their survival although timing of spawning was affected (Roberts 1972).

2.6.3.4 Chlordane

Chlordane has been used on agricultural crops and for termite control. Pure chlordane consists of cis- and trans-isomers. In its technical form it is a complex mixture of more than 140 related compounds, including isomers, other chlorinated hydrocarbons, and byproducts. The approximate composition of the technical grade chlordane manufactured by Velsicol is 24% trans-chlordane, 19% cis-chlordane, 10% heptachlor, 20.5% chlordenes, 5% trans-nonachlor, and 2.8% cis-nonachlor (Cardwell et al. 1977). The most persistent forms often measured in tissue are trans-nonachlor and cis-chlordane (Schmitt 2002b). Chlordane can be metabolized in the organism to form a number of different metabolites (Table 2.1). The metabolic products such as heptachlor and its metabolite heptachlor epoxide can be more toxic than the parent compound. Chlordane may be reported as the sum of chlordane-related compounds (cis- and trans-chlordane, nonachlors, oxychlordane, and

heptachlor epoxide) (Schmitt 2002b). Chlordane use is either banned or severely restricted in many countries. Use in the United States has been prohibited since 1983.

2.6.3.4.1 Fish

Tissue-residue concentrations of chlordane associated with effects to fish come from one study that used technical chlordane and two studies that used technical heptachlor for dosing. Pinfish lethal CBR was 16.6 mg/kg and sheapshead minnow fry CBR for behavior was 87 mg/kg (Parrish et al. 1976). When exposed to technical grade heptachlor in chronic exposures, the sum of cis- and trans-chlordane was measured in whole body, and heptachlor and heptachlor epoxide were also present in tissues. Chlordane CBRs were 0.71 mg/kg for mortality in whole-body spot, and 3.85 mg/kg for decreased swimming, and 11.1 mg/kg for mortality in whole-body sheepshead minnow (Schimmel et al. 1976, Goodman et al. 1977a).

2.6.3.4.2 Invertebrates

Invertebrate CBRs for chlordane are summarized in Table 2.8. Parrish et al. (1976) reported CBRs of chlordane associated with toxic effects in invertebrates. Lethal CBRs were lower for pink shrimp, *F. duorarum* (1.7 mg/kg associated with 55% mortality), than for grass shrimp, *P. pugio* (9.1 mg/kg associated with 45% mortality), exposed in water to technical grade chlordane; full control survival was observed for both species. For *C. virginica*, decreased growth (41%), higher than in the control (10%), and no lethal effects, were associated with a CBR of 27 mg/kg. Statistical comparisons for mortality data were not reported in that study.

2.6.3.5 Heptachlor and Heptachlor Epoxide

Pure heptachlor was originally isolated from technical chlordane. The technical formulation for heptachlor contains about 65% heptachlor, 22% trans-chlordane, 2% cis-chlordane, and 2% non-achlor (Schimmel et al. 1976). Tissue residues in organisms exposed to technical heptachlor contain these other compounds. Heptachlor epoxide is a metabolic product of analytical heptachlor and is typically measured in tissue residues after exposure.

2.6.3.5.1 Fish

Residue-effect data for four fish species primarily were mortality endpoints from exposure to technical heptachlor (Table 2.9). The lowest CBR was 0.23 mg/kg whole body for heptachlor epoxide in bluegill resulting in death of almost all the fish in the pond after a 16-h exposure (Andrews et al. 1966). Heptachlor was also present at 2.8 mg/kg for a total heptachlor residue of 3.03 mg/kg. Spot were sensitive to heptachlor with a lethal CBR of 2.08 mg/kg for total heptachlor (Schimmel et al. 1976). Low concentrations of trans- and cis-chlordane also occurred in these fish (0.55 and 0.16 mg/kg, respectively). Sheepshead minnow sublethal CBR for embryos and fry exposed to technical heptachlor occurred at a residue three times lower than the residue associated with adult mortality after acute exposure, and two times lower than the residue associated with mortality after chronic exposure of embryo/fry (Table 2.9). Sheepshead minnow exposed to heptachlor as embryos and juveniles had twice the mortality as minnows exposed during only the juvenile stage (Goodman et al. 1977b).

The ratio of heptachlor epoxide: heptachlor in the tissues is higher when the exposure duration is longer (Table 2.9). After acute exposure, heptachlor residues in sheepshead minnow were about 4 times higher than heptachlor epoxide residues, probably reflecting less time for metabolites to form (Schimmel et al. 1976). Heptachlor and heptachlor epoxide CBRs in sheepshead minnow whole bodies were similar to each other after chronic exposure to the same technical heptachlor aqueous concentration (Goodman et al. 1977b).

2.6.3.5.2 Invertebrates

Only one study (Schimmel et al. 1976) reported CBRs of heptachlor for invertebrates (Table 2.8). For the pink shrimp, *F. duorarum*, exposure to analytical grade compound resulted in 40% mortality

TABLE 2.9
Toxicity Associated with Heptachlor and Heptachlor Epoxide in Whole-Body Fish (mg/kg ww) after Exposure to Technical Heptachlor

	Heptachlor		Heptachlor Epoxide			
Fish	No Effect	Low Effect	No Effect	Low Effect	Effect, Exposure	Reference
Sheepshead minnow[a]	4.8	10.4	4.2	8.0	Mortality, 25 d	Goodman et al. 1977b
Spot	0.01	1.5	0.016	0.58	Mortality, 96 h	Schimmel et al. 1976
Spot	1.7	5.3	0.64	1.4	Mortality,[b] 96 h	Schimmel et al. 1976
Sheepshead minnow	0.022	20	0.02	6.7	Mortality, 96 h	Schimmel et al. 1976
Pinfish	5.7	34	3.2	11	Mortality, 96 h	Schimmel et al. 1976
Bluegill		2.8		0.23	Mortality, 16 h	Andrews et al. 1966
Bluegill		0.33–6.7		0.23–5.0	Mortality, 84 d	Andrews et al. 1966
Sheepshead minnow[a]	0.038	4.5	0.056	3.6	Behavior, 25 d	Goodman et al. 1977b

[a] Exposed as embryo/fry.
[b] Exposed to analytical grade heptachlor.
No statistically significant differences reported in Schimmel et al. 1976.

and a total heptachlor CBR of 0.068 mg/kg (0.058 mg/kg heptachlor epoxide and 0.010 mg/kg heptachlor), and exposure to heptachlor epoxide resulted in 65% mortality and 0.016 mg/kg CBR. Exposure to technical grade heptachlor resulted in 82% mortality associated with a whole-body CBR of 0.21 mg/kg (0.18 mg/kg heptachlor epoxide and 0.03 mg/kg heptachlor). The same study reported 3.5 mg/kg of total heptachlor (2.5 mg/kg heptachlor epoxide and 1 mg/kg heptachlor) associated with 70% mortality in the grass shrimp, *P. vulgaris*, exposed to technical grade heptachlor. The above exposures were 96 h and did not cause mortality in the control. Sublethal effects in the Eastern oyster (*C. virginica)* exposed to technical grade heptachlor was 33% decreased growth associated with a tissue concentration of 8.4 mg/kg total heptachlor (7.7 mg/kg heptachlor and 0.8 mg/kg heptachlor epoxide, in addition to 6.5 mg/kg trans-chlordane and 0.8 mg/kg cis-chlordane), indicating the higher tolerance of this species. Statistical comparisons for mortality data were not reported.

2.6.4 Cyclodiene Discussion

2.6.4.1 Fish

Dieldrin is frequently measured in tissues of field-collected fish tissue, yet few studies report residues associated with effects investigated in laboratory studies. The lowest whole-body CBR was 0.1 mg/kg for reduced sex steroids in adult largemouth bass (Muller et al. 2004), and 0.2 mg/kg reported for mortality in juvenile rainbow trout (Shubat and Curtis 1986). Reduced production of steroid hormones can lead to reduced reproductive output, but the reviewed dieldrin studies did not provide that link. African catfish exposed to aqueous concentrations greater than 1.5 μg/L dieldrin did not produce eggs, but residues were not measured after the 2-month exposure (Lamai et al. 1999). The dieldrin-exposed fish had significantly less adipose fat reserves than nonexposed fish, which the authors speculate may be related to failure to produce eggs.

Almost all endrin residue-effect studies report fish mortality from aqueous exposures, likely due to its high acute aqueous toxicity. Largemouth bass was the most sensitive species tested with 40% mortality at 0.012 mg/kg CBR. Figure 2.1 compares the trends among fish species for cyclodiene and other OH compounds. Fathead and sheepshead minnow had similar endrin sensitivity.

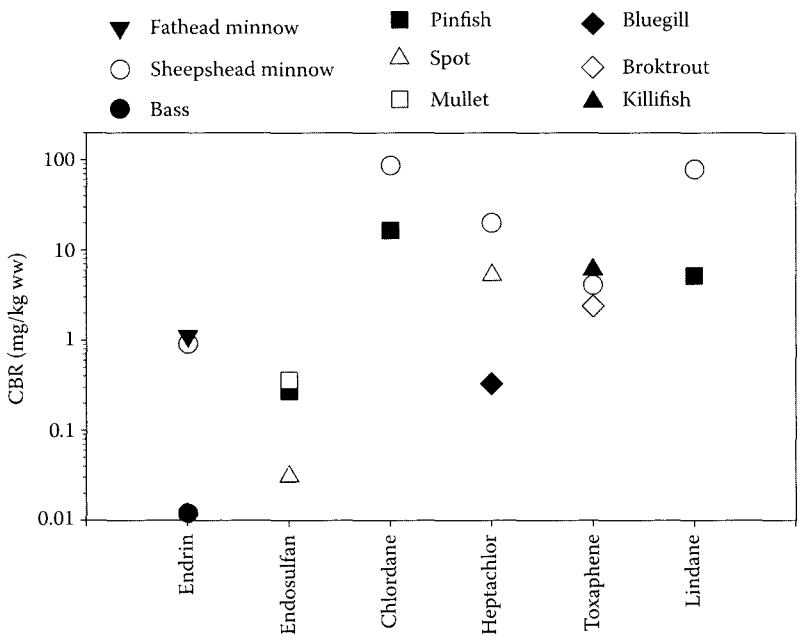

FIGURE 2.1 Comparison of fish critical body residues of select organochlorine pesticides for different species (data reported in text). Mortality endpoints (25–85% mortality) for all species except for sheepshead minnow exposed to chlordane (behavior).

Sublethal endrin CBRs, which would theoretically occur at lower residues, are lacking, possibly as a result of the high acute toxicity of the compound. Only one study reported a sublethal effect for behavior in golden shiner at 0.2 mg/kg (Ludke et al. 1968).

Most of the CBRs for endosulfan are from a single study where residue-effect concentrations ranged over an order of magnitude, and spot were the most sensitive species (Schimmel et al. 1977a) (Figure 2.1). A larger range (0.07–1.5 mg/kg) in species sensitivity was observed during a field application in Africa with African catfish the most sensitive species for mortality (Matthiessen et al. 1982). Species-sensitivity variability in this study was reduced to less than an order of magnitude by lipid normalization (7.4–47.1 mg/kg lipid). Species-sensitivity variability in aquatic toxicity tests for endosulfan ranged up to 4 orders of magnitude (18,000) in saltwater species (Chapman 1983), so the variability in toxicity was reduced when based on residue concentrations.

Fish CBRs from chlordane are too few to make conclusions about species sensitivity or effect ranges, but OH CBRs are highest for this compound (Figure 2.1). Only one study reports residue-effects associated with technical chlordane exposure (Parrish et al. 1976). When present along with heptachlor and heptachlor epoxide, spot lethal chlordane CBRs were close to an order of magnitude lower than sheepshead minnow sublethal and lethal CBRs (Schimmel et al. 1976).

Fish exposed to technical heptachlor had heptachlor, heptachlor epoxide, and often chlordane compounds in their tissue. Most of the studies for heptachlor report mortality and the median lethal CBR for heptachlor was 4.1 mg/kg compared to 1.0 mg/kg median lethal CBR for heptachlor epoxide (Table 2.6).

2.6.4.2 Invertebrates

Similar 96-h water exposures were conducted to assess the effects of dieldrin, endrin, chlordane, and heptachlor on survival of pink shrimp and grass shrimp and (for all but endosulfan) on growth of the Eastern oyster (Parrish et al. 1974, Schimmel et al. 1975, Parrish et al. 1976, Schimmel et al. 1977a).

Table 2.7 reports lowest, highest, and median lethal CBR, and Figure 2.2 compares the trends among invertebrate species for cyclodiene and other OH compounds. The pink shrimp was consistently the species with the lowest lethal CBR, followed by grass shrimp, while much higher residues failed to promote mortality in the Eastern oyster. Endrin and heptachlor were overall the most toxic and chlordane the least toxic cyclodiene for those three marine species.

Endrin lethal CBRs are available for seven species. Freshwater oligochaetes were substantially more tolerant than crustaceans and the sole insect investigated. Therefore, similar to DDT, endrin may be a potent toxicant causing mortality via specific modes of action in some invertebrates, such as pink shrimp and stonefly nymph, while lethal at residues approaching the range typical for nonspecific, baseline-toxicity-type toxicants for other invertebrates, such as oligochaetes. In contrast, endrin sublethal CBRs associated with decreased sediment reworking rates were orders of magnitude lower than lethal body residues for oligochaetes (Keilty et al. 1988a, 1988b), suggesting that physiological impairment by that compound is caused by toxic action other than baseline toxicity.

2.6.5 Mirex, Lindane, and Toxaphene

2.6.5.1 Mirex

Mirex was used mainly for fire ant control in the southeastern U.S., but also as a fire retardant (dechlorane). Application was concentrated in the southern U.S., but manufacturing of mirex resulted in contamination in the Niagara and Oswego Rivers as well as Lake Ontario and the St. Lawrence River. Use of mirex-containing products was cancelled in 1977–1978 in the United States. The technical grade mixture contains about 95% mirex and less than 3% chlordecone (kepone). Due to lower acute toxicity, mirex replaced heptachlor for some uses.

2.6.5.1.1 Fish

In short-term aqueous toxicity tests, mirex did not cause fish mortality even at high concentrations (Tagatz et al. 1975, 1976, Skea et al. 1981). Mirex was not acutely toxic to fathead minnows (*Pimephales promelas*), and percent hatchability and growth of 30-d fry was higher in mirex-exposed

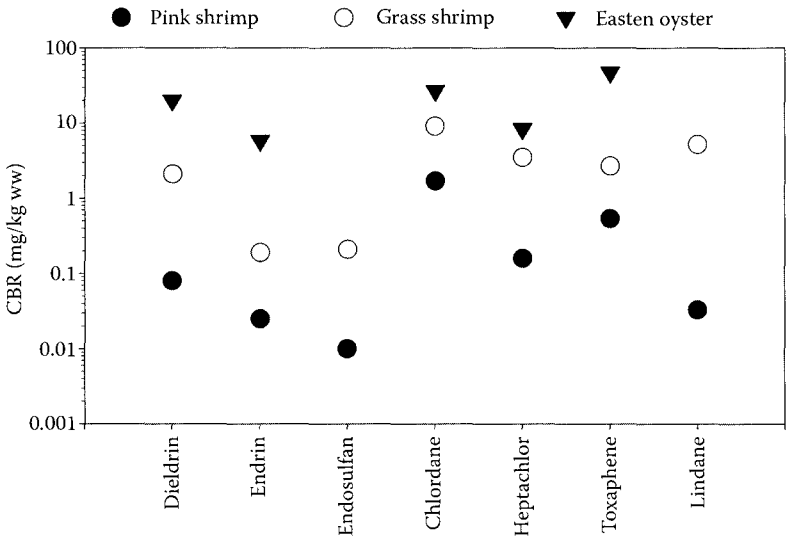

FIGURE 2.2 Comparison of invertebrate critical body residues of select organochlorine pesticides for different species (data reported in Tables 2.7, 2.8, and 2.10). Mortality endpoints for both shrimp species (20–90% mortality), and growth endpoints for Eastern oyster (24–78% reduction in growth).

fish compared to controls (Buckler et al. 1981). The number of spawns by fathead minnow was reduced at a whole-body CBR of 63 mg/kg (Buckler et al. 1981). Histological changes in gill lamellae were observed at whole-body CBR of 0.35–0.94 mg/kg in sheepshead minnow exposed to mirex leached from fire ant bait (Tagatz et al. 1975). Catfish (*Ictalurus punctatus*) survival was reduced in outdoor ponds at 0.015 mg/kg in muscle (Hyde et al. 1974).

Contamination of control fish was a problem in a study of bluegill and goldfish (van Valin et al. 1968). Bluegill fed mirex had reduced growth at whole-body residues that ranged from approximately 15–70 mg/kg from 30 to 160 d, but mirex in control fish ranged from 0.7 to 1.0 mg/kg.

Young juvenile striped mullet exposed to aqueous concentrations of mirex for 96 h experienced 6.4%, 27%, and 32% mortality at whole-body concentrations of 0.18, 0.82, and 3.5 mg/kg, respectively (Lee et al. 1975). The highest-dosed fish, with residues of 22.5 mg/kg experienced no mortality, which the authors could not explain. Older juvenile and adult mullet did not experience mortality after exposure to aqueous concentrations of mirex.

Leatherland and Sonstegard (1979) exposed coho salmon to 50 mg/kg mirex in diet. A mirex concentration in carcass of 9.6 mg/kg was associated with a significant reduction in the lipid content of the carcass after 3 months exposure. The treatment group exposed to 5 mg/kg mirex in diet had 1.6 mg/kg mirex in carcass and had carcass lipid content similar to the control salmon. When PCBs and mirex were combined in the diet, mirex appeared to inhibit the uptake of PCBs by coho salmon.

2.6.5.1.2 *Invertebrates*

Invertebrate CBRs for mirex are summarized in Table 2.10. Mirex lethal CBRs were reported for a variety of estuarine invertebrates in multispecies exposures (Tagatz et al. 1975, 1976). After a 28-d exposure to mirex released to water from ant bait, body residues associated with significant mortality were lowest for the blue crab, *C. sapidus* (0.02 mg/kg), followed by the pink shrimp, *F. duorarum* (0.12 mg/kg), and the grass shrimp, *P. pugio* (0.27 mg/kg) (Tagatz et al. 1975). In a similar experiment conducted for 70 d, lethal body residues were similar for the mud crab, *Panapeus herbstii* (0.22 mg/kg), and the hermit crab, *Clibanarius vittatus* (0.23 mg/kg) (Tagatz et al. 1976). Lethal CBRs were reported for crab by Bookhout and Costlow (1975) in exposure to water throughout its development (0.07 mg/kg) and by Leffler (1975) for a 28-d dietary exposure (0.42 mg/kg). The lowest CBR reported for crayfish juveniles, *Procambarus blandingii*, was 1.45 mg/kg following a 54-h exposure to water contaminated via mirex released from ant bait (Ludke et al. 1971). Various freshwater invertebrates tested in bioaccumulation experiments experienced 100% mortality after 7-d exposures to technical mirex (de la Cruz and Naqvi 1973). Body residues measured after 2 d were 1.06 mg/kg in the crayfish *Orconectes mississippiensis*, 2.56 mg/kg in the amphipod, *H. azteca*, and 10.37 mg/kg in the dragonfly naiad, *Macromia* sp. The highest mirex nonlethal body residues were 2 mg/kg for the ribbed mussel, *Modiolus demissus* and 2.8 mg/kg for the Eastern oyster (Tagatz et al. 1976), as well as 1.92, 5.07, and 4.91 mg/kg for the leeches, *Erpobdella puctata*, *Placobdella rugosa*, and *Glossiphonia* sp., respectively (de la Cruz and Naqvi 1973).

2.6.5.2 Lindane

The compound 1,2,3,4,5,6-HCH has eight isomers and the gamma (γ) isomer is lindane (Table 2.1). Another name used for lindane is benzene hexachloride (BHC). Lindane is not less than 99% pure γ-isomer of HCH (BHC), and is the active insecticide. Product composition varies from different manufacturers. Technical HCH is 65–70% α-HCH, 7–10% β-HCH, 14–15% γ-HCH, and smaller amounts of some additional compounds (WHO 1991).

2.6.5.2.1 *Fish*

The lindane residue-effect literature reports over an order of magnitude difference in species sensitivity from lethal residue data for fish tested under the same conditions. Lethal whole-body CBRs

TABLE 2.10
Toxicity Associated with Mirex, Lindane, and Toxaphene in Tissues of Aquatic Invertebrates (mg/kg ww)

Species	No Effect mg/kg	Low Effect mg/kg	Exposure	Effect	Reference
			Mirex		
Procambarus blandingii	—	1.45	54 h in water	Mortality	Ludke et al. 1971
Callinectes sapidus	—	0.42	28 d in diet	Mortality	Leffer 1975
Callinectes sapidus	0.03	0.07	Throughout development in water	Mortality	Bookhout and Costlow 1975
Callinectes sapidus	—	0.02	28 d in water	Mortality	Tagatz et al. 1975
Palaemonetes pugio	—	0.27	28 d in water	Mortality	Tagatz et al. 1975
Farfantepenaeus duorarum	—	0.12	28 d in water	Mortality	Tagatz et al. 1975
Clibanarius vittatus	—	0.23	70 d in water	Mortality	Tagatz et al. 1976
Panopeus herbstii	—	0.22	70 d in water	Mortality	Tagatz et al. 1976
Macromia sp.	—	10.37	7 d in water	Mortality	de la Cruz and Naqvi 1973
Orconectes mississippiensis	—	1.06	7 d in water	Mortality	de la Cruz and Naqvi 1973
Hyalella azteca	—	2.56	7 d in water	Mortality	de la Cruz and Naqvi 1973
			Lindane		
Farfantepenaeus duorarum	—	0.033	96 h in water	Mortality	Schimmel et al. 1977b
Palaemonetes pugio	—	5.2	96 h in water	Mortality	Schimmel et al. 1977b
Mytilus edulis	—	0.014	7 d in suspended sediment	Feeding	Hermsen et al. 1994
			1,2,3,4,5,6-Hexachlorocyclohexane		
Farfantepenaeus duorarum	—	0.028	96 h in water	Mortality	Schimmel et al. 1977b
			Toxaphene		
Farfantepenaeus duorarum	—	0.54	96 h in water	Mortality	Schimmel et al. 1977c
Palaemonetes pugio	—	2.7	96 h in water	Mortality	Schimmel et al. 1977c
Crassostrea virginica	—	47	96 h in water	Growth	Schimmel et al. 1977c

— Not available.

associated with LC50 data (LR50) after a 96-h exposure were 79 mg/kg for sheepshead minnow and 5.2 mg/kg for pinfish (Schimmel et al. 1977b). Fathead minnow exposed to lindane for 18 months had about 30% reduced survival at 9.5 mg/kg in carcass (Macek et al. 1976). Threespine stickleback mortality was associated with 12 mg/kg ww estimated from whole-body dry-weight (using water content provided in the chapter) (Hansen 1980). In this chapter Hansen (1980) reported that stickleback assimilated about 50% of the lindane in food.

A lindane concentration of 1.07 mg/kg in gudgeon muscle tissue (*Gobio gobio*) was associated with approximately 50% mortality after a 96-h exposure (Marcelle and Thome 1983).

Eyed eggs of rainbow trout were exposed to lindane in sediment for 27 d. Lindane residues in eggs and fry of rainbow trout did not change appreciably during the 27 d continuous exposure.

Sublethal effect residues for fry associated with altered behavior (lethargy) were 0.055–0.1 mg/kg (Ramamoorthy 1985). Rainbow trout egg residues averaged 0.048–0.08 mg/kg in 7-d-old embryos for those fry.

Reduced growth and reproduction in brook trout after exposure to aqueous lindane for 18 months were associated with residues in muscle of 1.2 mg/kg (Macek et al. 1976). Recent sublethal effect studies have measured residues in fat (Pesce et al. 2008) and organs (González de Canales et al. 2009) but not in whole bodies.

Immunosuppression by lindane has also been observed, but residues were not reported. The β-HCH and γ-HCH isomers have been reported to have estrogenic properties (Wester and Canton 1986, Singh and Singh 2007).

2.6.5.2.2 Invertebrates

Lethal effects of lindane (Table 2.10) were reported at body residue of 0.033 mg/kg for the pink shrimp, *F. duorarum*, and a much higher lethal body residue, 5.2 mg/kg, for the grass shrimp, *P. pugio*, following 96 h (Schimmel et al. 1977b). The percent mortality associated with the latter residues was higher than 50%. Lethality to pink shrimp yielded a body residue (0.028 mg/kg) for a mixture of HCH isomers that was similar to the lethal body residue reported for lindane alone in the same study (Schimmel et al. 1977b). Significant sublethal decrease (20%) of the feeding activity in the mussel, *M. edulis*, was associated with a lindane body residue of 0.014 mg/kg (Hermsen et al.1994) (Table 2.10).

2.6.5.3 Toxaphene

Toxaphene (also known as camphechlor) is a complex mixture of compounds and is the technical grade of chlorinated camphene. It contains about 67–69% chlorine (WHO 1984b). Toxaphene was used extensively on cotton crops in the southeastern United States and replaced DDT after DDT use was banned. Toxaphene also has been found in areas where it was never used such as in the Great Lakes (Schmitt et al. 1990) and in the Arctic. Toxaphene use was banned for most purposes in the United States and Canada in 1982. Toxaphene can be difficult to analyze because of coeluting PCBs and other compounds, but use of capillary columns provides good estimates of concentrations (Schmitt 2002a).

2.6.5.3.1 Fish

Toxaphene CBR data exists for six fish species from laboratory studies. Residues in fish contain the more chlorinated toxaphene congeners. Fry and adults had similar accumulation factors.

Toxaphene in adult fish and fry was associated with reduced growth, mortality, and reduced egg viability. The highest CBRs were associated with mortality in fry and juveniles. Lethal body residues ranged from 24.7 to 46.4 mg/kg for longnose killifish (*Fundulus similis*) and sheepshead minnow and were associated with 35–90% mortality. Brook trout and pinfish were more sensitive than both fathead minnow and sheepshead minnow to toxaphene residues but were not represented in the fry and juvenile dataset. Lethal body residues associated in adult fish ranged from 1.9 mg/kg from acute exposure for pinfish to 6.1 mg/kg from chronic exposure for killifish (Schimmel et al. 1977c). The authors note that adult killifish were more sensitive than juveniles. They speculate that the increased sensitivity of adult fish may have been due to their reproductive status, because exposure occurred during their spawning period. Mayer et al. (1975) also noted that adult mortality in brook trout occurred just prior to spawning.

Sublethal effects in adult fish ranged from 0.4 mg/kg for reduced reproduction in brook trout (Mayer et al. 1975) to 5.9 mg/kg for reduced growth in fathead minnow (Mehrle and Mayer 1975a). Sublethal effects in early life-stage fish ranged from 0.4 mg/kg for reduced growth in brook trout fry to 10 mg/kg for abnormal behavior in sheepshead minnow fry (Goodman et al. 1977b).

The lowest CBRs were for sublethal effects to brook trout. Brook trout whole-body residues of 0.4 mg/kg were associated with reduced growth in fry, and in adult tissue, reduced viability

of spawned eggs (Mayer et al. 1975, Mehrle and Mayer 1975b). Fathead minnow fry had reduced growth at 1.0 mg/kg or 17 mg/kg lw, and adult growth was reduced at 3.3 mg/kg or 46.5 mg/kg lw (Mayer et al. 1977). In addition, atrophy and degeneration of cells and tissues in liver, pancreas, and kidney were seen during histological analysis.

Sublethal effects in early life stages were associated with lower whole-body median residues compared to similar effects observed in adult fish (Table 2.6). The opposite was observed for adult residues; median CBRs associated with mortality were lower (3.25 mg/kg) in adult fish compared to median lethal CBRs for juveniles and fry (35.0 mg/kg) (Table 2.6).

Residue effects of toxaphene were examined in a field-based study where wild lake trout and white sucker were injected with a single dose of toxaphene, and along with control fish, monitored for 5 years to assess effects on survival, growth and reproduction (Delorme et al. 1999). White sucker were more sensitive than lake trout to effects of toxaphene when spawning success, using the field-deployed fish, was tested in the laboratory. Adult carcass concentrations of 0.859 mg/kg were associated with reduced fertilization, viability, and survival of embryo and sac fry 3 years after white sucker were injected with toxaphene. White sucker egg concentrations of 0.029 mg/kg experienced an 80% decrease in fertilization success.

2.6.5.3.2 Invertebrates

In the only study reporting toxaphene CBRs for invertebrates (Table 2.10), Schimmel et al. (1977c) reported a 20% decrease in survival associated with 0.54 mg/kg in the pink shrimp, *F. duorarum*, and a 25% decrease in survival at 2.7 mg/kg in the grass shrimp, *P. pugio* (full survival in the control for both species). Growth decreased 34% in the Eastern oyster, *C. virginica*, but no significant effect on survival was observed at a much higher whole-body CBR, 47 mg/kg.

2.6.6 Mirex, Lindane, and Toxaphene Discussion

2.6.6.1 Fish

Mirex is readily accumulated by fish but residue-effects data are insufficient to compare species sensitivity or lethal and sublethal effect concentrations. Mirex is not included in Table 2.6 because endpoints or tissues measured were too dissimilar to combine. The lowest whole-body CBR was 0.82 mg/kg for young juvenile mullet associated with increased mortality after acute exposure (Lee et al. 1975). Statistically significant reduction in catfish survival was associated with 0.015 mg/kg muscle concentration (Hyde et al. 1974) and sheepshead minnow had gill alterations at whole-body residues from 0.35 to 0.94 mg/kg.

The median lethal lindane CBR for four adult fish species was 10.8 mg/kg (Table 2.6). Pinfish were the most sensitive species (Figure 2.1). Altered behavior was also noted in adult fish with high residues. Early life stage sublethal effects were the most sensitive endpoints and were four orders of magnitude lower (0.055–0.1 mg/kg) than the highest LR_{50} adult residues.

Toxaphene has sufficient data to summarize lethal and sublethal CBRs by life stage (Table 2.6). Data within each summarized group is limited to at most three species and therefore likely does not capture the full range of species sensitivities. The early life stages were twice as sensitive to the sublethal effects of toxaphene residues as adult fish. The reverse was true for mortality, as adult fish were more sensitive than juvenile fish. This observation may reflect the species used in the experiments: adult lethal studies included sensitive species such as pinfish and brook trout, early life stage studies included killifish and sheepshead minnow, species typically more tolerant to OH compounds (Figure 2.1).

2.6.6.2 Invertebrates

Five marine and estuarine crustacean species had similar sensitivity to the lethal effects of mirex, with lethal CBRs ranging from 0.02 to 0.27 mg/kg (Tagatz et al. 1975, 1976), while four species

of freshwater invertebrates were more tolerant, with lethal CBRs ranging from 1.06 to 10.4 mg/kg (Ludke et al. 1971, de la Cruz and Naqvi 1973). The relatively narrow range of lethal CBRs for mirex, lindane, and toxaphene established with the few existing studies (Table 2.10) suggest less across-species variability for these compounds compared to that for other OH pesticides. Pink shrimp, the most sensitive species for most OH pesticides reviewed in this chapter, was similarly sensitive to the three compounds, while grass shrimp was more sensitive to mirex. Similar to CBRS reported for other OH compounds, the Eastern oyster appears to be more tolerant to other OH pesticides as well (Figure 2.2). The range of invertebrate lethal CBRs for mirex, lindane, and toxaphene is similar to the range associated with potent neurotoxic effects speculated for DDT.

2.7 CONSIDERATIONS

Interpretation of the OH tissue-residue literature has a number of considerations and complexities. Most of the studies were not designed to assess effects from residue concentrations. The differences with species and life stages tested, dosing techniques, dosing concentrations and intervals, and the variety of endpoints increases the difficulty in comparing and contrasting studies. Application of this data to field assessments also has a number of considerations. Single isomer or single chemical exposures rarely occur in field organisms, fish will contain variable amounts of the different OH compounds, their metabolites and isomers, along with other persistent compounds. Aquatic organisms living constantly in contaminated environments typically have life-time exposures. Fish used in laboratory experiments typically have short life spans, and other life-history characteristics such as short time to reproduction, increased frequency but decreased duration of reproduction, and other strategies that may contrast sharply with wild fish living in the field that live much longer, mature more slowly, and possibly stay reproductive for years. Laboratory studies may include effects to life-stages that do not generally have tissue-residue measurement in the field such as fish eggs. Exposure through maternal transfer is an important pathway in the environment, but infrequently considered in laboratory studies. Therefore, applying data from laboratory exposures to concentrations measured in the field has many challenges. These topics are explored further to help with interpretation of the residue data.

2.7.1 Mixtures

One of the greatest challenges to the application of CBRs derived for DDT and other individual OH pesticides is how to interpret residues in field-collected organisms where their concentrations typically co-occur as mixtures. In addition, OH pesticides in the environment typically co-occur in tissues with other hydrophobic compounds such as PCBs and PBDEs. Fifty percent of the streams receiving agricultural or urban runoff had five or more pesticide compounds in fish tissue measured by the USGS NAWQA program (USGS 2008).

Contaminants in a mixture can interact during uptake and excretion, during distribution and metabolism and during action at the receptor site. Interpreting the toxicological consequences of a mixture, its magnitude and nature (noninteraction and synergistic or antagonistic interaction) is an evolving science. The two most common models for noninteraction are dose addition and response addition (Borgert 2007). Response addition assumes that the compounds involved have independent mechanisms of action, in contrast to dose addition, which assumes that the compounds have different potencies with similar mechanism of action. Response addition is typically assumed for risk assessments (Borgert 2007).

The toxic unit (TU) approach calculates the mixture toxicity according to the degree of toxicity for each individual compound. Typically, aqueous mixture TUs are calculated as each compound's aqueous concentration divided by its LC_{50} and summed. When the sum is >1 the TU mixture would predict mortality, or the effect endpoint under consideration. This method assumes response addition, or that the joint toxicity is represented by addition of the individual toxicities.

The use of the TU approach to predict the toxicity of mixtures of DDT, DDD, and DDE in the tissues was validated using freshwater amphipods (Lotufo et al. 2001b). Because substantial differences in lethal body residues occur among those compounds, predicting mortality for a mixture using the toxicity data for a single compound (e.g., DDT) could under- or over-predict mortality. The use of the TU approach assumes that CBRs are independent of the exposure route and that the effects of DDT, DDD, and DDE on survival are additive. Fifty percent mortality was associated with sum TUs of 1.1 for *H. azteca* and 0.53 for *Diporeia* spp., close to the expected value of 1, demonstrating that the assumption of additive effects holds true.

von Westernhagen et al. (1989) used a contamination factor (CF) to scale the relative toxicities of different organochlorine compounds measured in field-collected fish in the mixture, similar to a TU approach. The CFs were developed based on aqueous 96 h LC50 toxicity data and their ratio to PCBs. They scaled each contaminant's LC50 to PCBs because all fish contained PCBs. Residue concentrations for each contaminant were multiplied by its CF and then all the concentrations were summed for each sample. Their CF for endrin was highest and next was α-endosulfan and endosulfan sulfate. Lindane toxicity was lowest of the chlorinated hydrocarbons and closest to PCBs.

Koenig (1977) measured the combined effects of mirex and DDT to the estuarine cyprinodont, *Adinia xenica*. Adult female fish were exposed to either *p,p'*-DDT or mirex separately, or combined at different ratios in diet for 9 d. Mortality of embryo and larval offspring was followed. Embryo concentrations of mirex up to 27.9 mg/kg were not associated with increased mortality. An average *p,p'*-DDT embryo concentration of 8.6 mg/kg had 22% mortality. Embryos exposed to both compounds had 47% mortality with average DDT residue of 8.4 and 2.82 mg/kg mirex. Koenig (1977) estimated that the toxicity of DDT and mirex was more than additive. Another study using mixtures observed that effects in red-eared slider turtle were more than additive when low doses of trans-nonachlor, chlordane and *p,p'*-DDE were combined (Willingham 2004). A mixture of estrogenic compounds (*o,p'* DDT, nonylphenol, octylphenol, arochlor 1221, and bisphenol A) resulted in a higher response (increased vitellogenin synthesis) in male rainbow trout cultured hepatocytes than any of the compounds alone (Sumpter and Jobling 1995).

Monod (1985) measured DDT and PCB concentrations in eggs in Lake Geneva char. PCB and DDT concentrations in eggs were significantly correlated with each other and lipid-normalized concentrations of both were correlated with egg mortality in laboratory rearings. Most DDT measured was DDE, and median concentrations of 20 mg/kg lw DDT and 44.5 mg/kg lw PBCs in eggs correlated with greater than 50% mortality.

Models used to deal with aqueous mixture toxicity may also provide useful concepts for other potential approaches to address residue mixture toxicity (Belden et al. 2007). A more complete discussion about mixture considerations for the tissue-residue approach is available in the discussion in Meador (2006).

2.7.2 Resistance/Pre-Exposure

Resistance, that is, the ability to survive or be less affected by exposure to concentrations that were toxic to naive or earlier generations, has been observed for many invertebrate and fish species exposed to OH pesticides. The development of resistance may be due either to an organism's ability to physiologically acclimate or to genetically adapt. In either case, organisms that develop resistance through short- or long-term processes may respond differently to chemical exposure than naive organisms. For neuroactive OH compounds that target sodium and chloride channels, slight substitutions at the target site can confer resistance to other compounds in the same chemical class, resulting in what is known as cross-resistance (Casida and Quistad 1998).

Resistant fish tolerated aqueous concentrations of toxaphene, aldrin, dieldrin, and endrin that were 36–70 times higher than fish that had not been pre-exposed (Ferguson et al. 1964). Mosquito fish became resistant to insecticides used and the 300-fold resistance to aqueous concentrations persisted for several generations of fish maintained in pesticide-free water (Boyd and Ferguson 1964).

Resistance in mosquito fish pre-exposed to endrin appeared to be related to slower uptake in brain tissues where endrin residues were about half the brain endrin concentration in mosquito fish not resistant to endrin toxicity (Fabacher and Chambers 1976).

Development of resistance has a number of implications. Laboratory studies often employ species with short life spans that have a higher likelihood to develop resistance. OH compounds are present in almost all environments and habitats, whether lab-reared, or field-collected, and some of the studies reviewed for this chapter report elevated OH concentrations in control organisms, indicating pre-exposure. The influence on residue-effect studies is unknown. The potential effect of cross-resistance to other compounds is also unknown. Results from OH studies using field-collected or laboratory-reared organisms may be biased by this pre-exposure. Especially for the older literature reviewed in this chapter, results potentially biased by use of resistant organisms cannot be identified or evaluated. Most researchers have reported an increased ability to withstand exposure which would indicate that tissue residues that used resistant organisms could be biased high. Although recent aqueous toxicity studies continue to report effects resulting from pre-exposure (Brausch and Smith 2009), environmental OH concentrations in the United States have been declining during the past decades so the bias resulting from resistance may be more pronounced in older studies.

2.7.3 Life Stage/Tissue Type

Most of the OH pesticides reviewed here had the lowest effect residues in the egg/embryo and fry stages of fish. These life stages are infrequently measured as part of assessment or monitoring programs. The reproductive cycle in fish may exert important control over organochlorine concentrations in these early and sensitive life stages, and these life stages may provide the best tool for evaluating tissue-residue effects to fish. Several researchers have reported on the transfer of hydrophobic contaminants and noted a relationship between concentration in fish eggs and maternal tissues. A variety of fish species have been shown to have a correlation between organochlorine concentrations in eggs and muscle (Miller 1993, Miller and Amrhein 1995, Fisk and Johnston 1998) and also between liver and oocytes (Serrano et al. 2008). Macek (1968) noted that DDT concentrations in fry were related to the maternal dose. When egg residues are not available for comparison to laboratory studies the following information may provide some guidance on how to assess effects to early life stage when adult tissue has been measured.

Niimi (1983) noted that the percentage of maternal organic contaminants transferred to eggs ranged from about 5% to 30% and that the percentage of lipid in the fish and the percent of that total lipid in the egg significantly influenced contaminant transfer in the five species examined. Russell et al. (1999) reported that the ratio of lipid-normalized organochlorines egg concentrations to lipid-normalized muscle concentrations was approximately one in a variety of fish, with 95% of all the measured ratios within a factor of 2 of the mean ratio (0.56–2.51). Metcalfe et al. (2000) found that the lipid-normalized *o,p'*-DDT concentration in the eggs and the lipid-normalized adult concentration were nearly the same. Serano et al. (2008) found that less than half the contaminant concentration in the liver of sea bream was measured in oocytes.

Residues measured in fish whole body or muscle may be converted to an egg concentration if enough data are collected to make a conversion. Lipid concentration in adult and early life stage tissue is needed to use the relationship explored by Russell et al. (1999).

Burdick et al. (1964) concluded that there was a relationship between maternal and egg DDT concentrations, however, variability in this relationship could be explained by a maternal diet component. Female fish could continue to take up DDT after egg deposition and thereby have a different relationship to the egg concentration than when the oils in the eggs were deposited.

In addition to diet, gender, age, and breeding strategy, influence the uptake, disposition, and elimination of organochlorine compounds. Male pike had significantly higher organochlorine concentrations than the females (Larrson et al. 1993). While oogenesis results in contaminant movement into the ovaries, spawning can result in contaminant loss. Miller (1994) estimated that spawning

eliminated about 28–39% of the *p,p'*-DDE concentration in Lake Michigan Chinook salmon. A negative correlation between age and organochlorine concentration in female pike was explained by the yearly loss of contaminant via deposition of roe (Larsson et al. 1993). For invertebrates, female midges lost 11.6–30.9% of their DDE burden during egg deposition (Derr and Zabik 1972). Therefore, the seasonal reproductive cycle should be a factor considered when sampling tissues for OH compounds.

Summary

OH pesticides remain important global contaminants due to extreme persistence in environmental media, continued use in some countries, and ability to accumulate in tissues of biota. Their widespread occurrence in biota, especially for the hydrophic OH compounds, and their ability to biomagnify, highlights the need for understanding the significance of residue concentrations.

Key processes affecting residue concentrations are elimination rates and biotransformation of parent compounds. DDT and transformation products have slow elimination rates and long time-frames for achieving steady-state concentrations. For some compounds, metabolites may have different toxicities than parent compounds. For instance, the toxicity of DDE to amphipods was much lower than the parent DDT compound, and biotransformation protected against mortality.

For fish, CBR data for OH compounds are supported by a number of studies for DDT, endrin, heptachlor, heptachlor epoxide, and toxaphene (Table 2.6). However, dieldrin and chlordane, which are very persistent in fish tissue, have few studies for discerning residue-toxicity relationships. The same is true for mirex and lindane. More studies are needed to understand the significance of these compounds in fish tissue.

For invertebrates, tissue residue-effect data for OH compounds are supported by a number of studies for *p,p'*-DDT, endrin, and mirex (Table 2.7). Data for chlordane, lindane, toxaphene, heptachlor, and endosulfan are too few to determine residue-toxicity relationships in invertebrates.

Even for OH compounds with multiple studies, data for sublethal effects, long-term exposures, or effects to early life stages are often limited for both fish and invertebrates. Although residue-toxicity relationships have been reported for sublethal effects for some OH compounds, data are generally too few to allow comparison of the same sublethal endpoint for a single compound across different species.

For similar endpoints, species-sensitivity differences sometimes accounted for a one to two order of magnitude difference in CBRs for both fish and invertebrate species (Figures 2.1 and 2.2). Species tended to have similar sensitivity across the different groups of pesticides, but substantial differences in sensitivity among species were observed for most OH pesticides. For fish, sheepshead minnow, fathead minnow, and killifish were less sensitive than bass, spot, pinfish, and bluegill. For invertebrates, pink and grass shrimp were the most sensitive species.

Life stage exposed was an important factor influencing CBRs. The lowest CBRs were reported for egg and embryo life stages in fish, and early development in invertebrates. Sublethal endpoints for early life stages were typically associated with the lowest CBRs.

Comparison between fish and invertebrate CBRs for DDT and endrin are possible with the available datasets (Figures 2.3 and 2.4). DDT lethal residues in fish are within the range of lethal residues for invertebrates with only a slightly narrower range compared to invertebrates (Figure 2.3). In addition, the median lethal *p,p'*-DDT concentrations are about the same for fish and invertebrates (Tables 2.6 and 2.7). The median lethal residues for fish and invertebrates can be compared for the *p,p'*-DDT form since the ΣDDT fish data came primarily from exposure to the *p,p'*-DDT form (Beckvar et al. 2005).

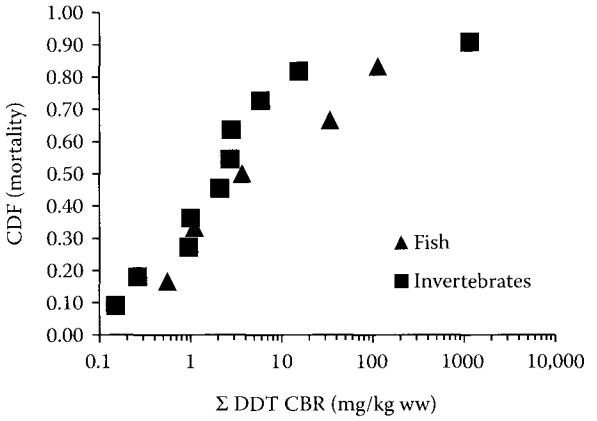

FIGURE 2.3 DDT cumulative distribution function (CDF) for fish and invertebrate lethal CBRs. Solid triangles represent fish species, solid squares invertebrate species. Data for fish from mortality endpoints (35–85% mortality) from adult fish reported in Beckvar et al. (2005). Invertebrate data are mostly LR50 endpoints. Data primarily for *p,p'*-DDT.

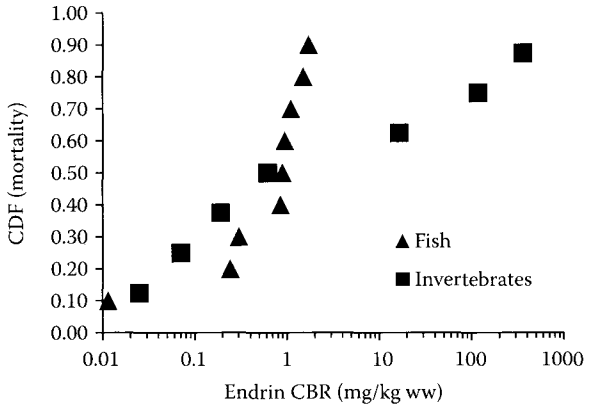

FIGURE 2.4 Endrin cumulative distribution function (CDF) for fish and invertebrate lethal CBRs. Solid triangles represent fish species (data reported in text; 20–100% mortality), solid squares invertebrate species (Table 2.8; 20–90% mortality).

DDT metabolites differed in toxicity for invertebrates. *p,p'*-DDT was clearly more toxic than p,p-DDE, and the two metabolites should be considered separately when metabolite data are available. For fish, lethal residue-effect studies are very limited for the DDE form, so comparing toxicity between metabolites is hampered. CBR for mortality from *o,p'*-DDE tissue residues in medaka eggs (0.5 mg/kg) from one study was comparable to the value derived for fish ELS mortality (0.7 mg/kg) from studies primarily based on *p,p'*-DDT and mortality endpoints (Beckvar et al. 2005). In adult fish, *p,p*-DDE residues (0.4–0.6) were associated with reduced sex-steroid production at concentrations close to the tissue-residue concentration of 0.6 mg/kg derived from mortality studies, primarily the *p,p'*-DDT form, in Beckvar et al. (2005). Sublethal effects from DDE residues in fish may be within the effects range for DDT, but more data are needed to adequately assess that comparison.

For DDT sublethal effects in fish, the median sublethal residue-effect for *o,p'*-DDT in fish eggs was 0.07 mg/kg which is an order of magnitude lower than the threshold no-effect residue concentration of 0.7 mg/kg derived for fish ELS mortality in Beckvar et al. (2005). More studies reporting sublethal effects for this life stage are needed to develop a protective and robust CBR.

DDT sublethal effects reported for invertebrates were limited. For sensitive invertebrate species, strong neurotoxicity appeared to be the primary cause of mortality. Loss of swimming ability or immobilization occurred for both tolerant and sensitive species. Decreased feeding was observed in polychaete species tolerant to the lethal effects of DDT. DDE caused reproductive impacts in midges (0.8 mg/kg), suggesting a potential effect from endocrine disruption. This contrasts with data for other invertebrates which reported no reproductive effects from exposure to the DDT metabolite.

For endrin, variability in fish lethal CBRs is much lower than for invertebrates (Figure 2.4). Mortality of fish at relatively low endrin residues and low variability (range of 0.2–1.7 mg/kg for all but one species) is consistent with toxicity acting via a specific mode of action. Neurotoxic effects in fish may occur through inhibition of the neurotransmitter gamma-aminobutyric acid (GABA) similar to the mechanism in higher vertebrates. In contrast, invertebrate CBRs for endrin were variable, indicating they may experience toxicity through multiple modes of action. Crustaceans, more sensitive (0.025–0.61 mg/kg CBR range) than either bivalves or oligochaetes, had CBRs similar to fish, suggesting that toxicity in crustaceans may also act via a specific mechanism. Feeding reduction in oligochaete occurred at residues similar to lethal endrin CBRs in sensitive invertebrate species. This behavioral alteration may have been caused by a single specific mechanism, such as inhibition of GABA receptor function. Mortality at elevated CBRs in oligochaetes is consistent with baseline toxicity. The combination of rapid metabolism of endrin by fish and sensitivity to neurotoxicity may explain reduced CBR variability in fish compared to invertebrate species.

Limited and inconsistent data preclude robust CBR comparisons between fish and invertebrates for other OH pesticides. However some general observations can be made. Invertebrate lethal CBRs for dieldrin span 2 orders of magnitude (0.08–2.1 mg/kg) and were lower overall than for fish (0.2–5.9 mg/kg). Endosulfan residue effect data were low for both fish (0.03–0.36 mg/kg) and invertebrates (<0.01–0.21 mg/kg) in the results reported from a single study (Tables 2.6 and 2.7).

Chlordane CBRs also span a similar range in both fish (0.7–16.6 mg/kg) and invertebrates (0.7–4.8 mg/kg) for the few species investigated. Heptachlor and the metabolite heptachlor epoxide CBRs span a similar range in fish (0.3–34 mg/kg and 0.2–11 mg/kg, respectively) but the metabolite heptachlor epoxide is more potent than the parent compound. Invertebrate CBRs for heptachlor (0.07–3.5 g/kg) were an order of magnitude lower than CBRs for fish, so invertebrates appear more sensitive.

Fish appear to be less sensitive to the lethal effects of mirex than invertebrates, but fish data are limited and variable. Several studies report no fish mortality from exposure to mirex (van Valin et al. 1968, Tagatz et al. 1975, 1976, Buckler et al. 1981), but increased mortality was observed in catfish at 0.015 mg/kg muscle (Hyde et al. 1974) and in young juvenile striped bass at 0.82 mg/kg (Lee et al. 1975). Invertebrate lethal CBRs for mirex span 2 orders of magnitude (0.03–10.0 mg/kg) with a median lethal residue <0.5 mg/kg. Various crab and shrimp species were very sensitive to the lethal effects of mirex with lethal CBRs for blue crab as low as 0.02 mg/kg.

The lowest invertebrate CBR for lindane (0.033 mg/kg), derived for a sensitive species (pink shrimp) and mortality, is comparable to the lowest fish CBR (0.055 mg/kg) for a sensitive fish species (rainbow trout), life stage (fry), and sublethal endpoint (behavior). The highest fish

lindane CBR, an LR50 (79 mg/kg) for insensitive sheepshead minnow was much higher than the highest invertebrate CBR for grass shrimp (5.2 mg/kg), typically a sensitive species.

Toxaphene studies for invertebrates were very limited compared to data available for fish. The range of toxaphene lethal CBRs were narrower in invertebrates (0.54–2.7 mg/kg) compared to adult fish (1.9–6.1 mg/kg) and compared to the range for sublethal effects in adult fish (0.4–5.9 mg/kg). The reason for the apparent reduced toxaphene sensitivity of juvenile compared to adult fish is not known.

While some species are sensitive to the specific mode of action of OH pesticides (e.g., interference with sodium and potassium ion permeability in axons, endocrine disruption), others (some invertebrates) are affected mostly by the baseline toxicity effect of those compounds. DDT's potency as an endocrine disruptor for invoking complete sex-reversal is weak compared to natural estrogens and would likely require higher residues than typically measured in field-collected fish. DDTs potency for endocrine disruption for other effect endpoints such as reduced reproduction and immune system and behavior alterations is within the range of environmental tissue concentrations. If combined with other endocrine-active compounds, DDT may act additively or synergistically to cause effects. Investigations on mode of action of these compounds using biochemical tools such as gene expression quantification (toxicogenomics) are warranted.

Other important considerations for OH pesticide residues include laboratory to field extrapolation and methods for assessing mixture effects. The use of a TU approach is recommended for DDT compounds in invertebrates. Sublethal toxicity to early life stages through maternal transfer, especially for fish species, should also be considered.

The OH pesticide residue data overall capture a range of species sensitivities and lethal and sublethal effects. Some species were consistently more or less sensitive to OH compounds. For example, within the invertebrate species represented, growth in oysters was typically the least sensitive endpoint and species. Pink and grass shrimp tended to be the most sensitive species for the invertebrates. For fish, sheepshead minnow tended to be one of the least sensitive species. Data for specific compounds often do not have enough species and endpoints represented to fully capture the range of species-sensitivity differences and endpoint differences. If sensitive species or effect endpoints are not represented in a specific OH data set, CBRs developed from that dataset may not be protective of aquatic receptors.

REFERENCES

Anderson, R. L. and D. L. DeFoe. 1980. Toxicity and bioaccumulation of endrin and methoxychlor in aquatic invertebrates and fish. *Environ. Pollut. (Series A)* 22:111–121.

Andrews, A. K., C. C. van Valin, and B. E. Stebbings. 1966. Some effects of heptachlor on bluegills. *Trans. Am. Fish Soc.* 65:297–309.

Arctic Monitoring and Assessment Programme (AMAP). 2002. *Arctic pollution 2002: Persistent organic pollutants, heavy metals, radioactivity, human health, changing pathways.* Arctic Monitoring and Assessment Programme. Oslo, Norway: xii+112.

Argyle, R. L., G. C. Williams, and H. K. Dupree. 1973. Endrin uptake and release by fingerling channel catfish (*Ictalurus punctatus*). *J. Fish. Res. Board. Can.* 30:1743–1744.

Arnot, J. A., et al. 2009. A quantitative structure-activity relationship for predicting metabolic biotransformation rates for organic chemicals in fish. *Environ. Toxicol. Chem.* 28:1168–1177.

Arnot, J. A., and F. A. Gobas. 2006. A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals in aquatic organisms. *Environ. Rev.* 14:257–297.

Atchison, G. J. 1976. The dynamics of lipids and DDT in developing brook trout eggs and fry. *J. Great Lakes Res.* 2:13–19.

ATSDR 2007. Agency for Toxic Substances and Disease Registry. 2007 CERCLA Priority List of Hazardous Substances. http://www.atsdr.cdc.gov/cercla/07list.html (accessed September 30, 2008).

ATSDR 2002. Agency for Toxic Substances and Disease Registry. *Toxicological profile for DDT, DDD, DDE update.* Atlanta, GA: U.S. Department of Health and Human Services, ATSDR.

Baatrup, E., and M. Junge. 2001. Antiandrogenic pesticides disrupt sexual characteristics in the adult male guppy (*Poecilia reticulata*). *Environ. Health. Perspect.* 109:1063–1070.

Balasubramani, A., and T. J. Pandian. 2008. Endosulfan suppresses growth and reproduction in zebrafish. *Curr. Sci.* 94:883–890.

Ballesteros, M. L., G. E. Bianchi, M. Carranza, and M. A. Bistoni. 2007. Endosulfan acute toxicity and histomorphological alterations in *Jenynsia multidentata* (Anablepidae, Cyprinodontiformes). *J. Environ. Sci. Health B* 42:351–357.

Banas, D., et al. 2009. Can we use stable isotopes for ecotoxicological studies? Effect of DDT on isotopic fractionation in *Perca fluviatilis*. *Chemosphere* 76:734–739.

Barnhoorn, I. E. J., M. S. Bornman, C. Jansen van Rensburg, and H. Bouwman. 2009. DDT residues in water, sediment, domestic and indigenous biota from a currently DDT-sprayed area. *Chemosphere* 77:1236–1241.

Bayarri, S., L. T. Baldassarri, N. Lacovella, F. Ferrara, and A. di Domenico. 2001. PCDDS, PCDFs, PCBs and DDE in edible marine species from the Adriatic Sea. *Chemosphere* 43:601–610.

Bayen, S., P. Giusti, H. K. Lee, P. J. Barlow, and J. P. Obard. 2005. Bioaccumulation of DDT pesticide in cultured Asian seabass following dietary exposure. *J. Toxicol. Environ. Health, Part A—Curr. Iss.* 68:51–65.

Bayley, M., M. Junge, and E. Baatrup. 2002. Exposure of juvenile guppies to three antiandrogens causes demasculinization and a reduced sperm count in adult males. *Aquat. Toxicol.* 56:227–239.

Beckvar, N., T. M. Dillon, and L. B. Read. 2005. Approaches for linking whole-body fish tissue residues of mercury or DDT to biological effects thresholds. *Environ. Toxicol. Chem.* 24:2094–2105.

Belden, J. B., R. J. Gilliom, and M. J. Lydy. 2007. How well can we predict the toxicity of pesticide mixtures to aquatic life? *Integr. Environ. Assess. Manag.* 3:364–372.

Bengtsson, G., L. A. Hansson, and K. Montenegro. 2004. Reduced grazing rates in *Daphnia pulex* caused by contaminants: Implications for trophic cascades. *Environ. Toxicol. Chem.* 23:2641–2648.

Bennett, H. J., and J. W. Day. 1970. Absorption of endrin by bluegill sunfish, *Lepomis macrochirus*. *Pestic. Monit. J.* 3:201–203.

Berntssen, M. H. G., C. N. Glover, D. H. F. Robb, J. V. Jakobsen, and D. Petri. 2008. Accumulation and elimination kinetics of dietary endosulfan in Atlantic salmon (*Salmo salar*). *Aquat. Toxicol.* 86:104–111.

Bettinetti, R., V. Croce, S. Galassi, and P. Volta. 2006. *p,p'*-DDT and *pp'*DDE accumulation in a food chain of Lake Maggiore (northern Italy): Testing steady-state condition. *Environ. Sci. Poll. Res.* 13:59–66.

Binelli, A., and A. Provini. 2003. DDT is still a problem in developed countries: The heavy pollution of Lake Maggiore. *Chemosphere* 52:717–723.

Bloomquist, J. R. 1996. Ion channels as targets for insecticides. *Annu. Rev. Entomol.* 41:163–190.

Boese, B. L., H. Lee, and S. Echols. 1997. Evaluation of a first-order model for the prediction of the bioaccumulation of PCBs and DDT from sediment into the marine deposit-feeding clam *Macoma nasuta*. *Environ. Toxicol. Chem.* 16:1545–1553.

Bonner, J. C., and M. R. Wells. 1987. Comparative acute toxicity of DDT metabolites among American and European species of planarians. *Comp. Biochem. Physiol. Pharmacol. Toxicol. Endocrinol.* 87:437–438.

Bookhout, C. G., and J. D. Costlow Jr. 1975. Effects of mirex on the larval development of blue crab. *Water Air Soil Poll.* 4:113–126.

Borgert, C. J. 2007. Predicting interactions from mechanistic information: Can omic data validate theories? *Toxicol. Appl. Pharmacol.* 223:114–120.

Boyd, C. E., and D. E. Ferguson. 1964. Susceptibility and resistance of mosquito fish to several insecticides. *J. Econ. Entomol.* 57:430–431.

Brausch, J. M., and P. N. Smith. 2009. Pesticide resistance from historical agricultural chemical exposure in *Thamnocephalus platyurus* (Crustacea: Anostraca). *Environ. Pollut.* 157:481–487.

Brevik, E. M., M. Grande, J. Knutzen, A. Polder, and J. U. Skaare. 1996. DDT contamination of fish and sediments from Lake Orsjoen, Southern Norway—Comparison of data from 1975 and 1994. *Chemosphere* 33:2189–2200.

Buckler, D. R., A. Witt, F. L. Mayer, and J. N. Huckins. 1981. Acute and chronic effects of Kepone and mirex on the fathead minnow. *Trans. Am. Fish Soc.* 110:270–280.

Buhler, D. R., M. E. Rasmusson, and W. E. Shanks. 1969. Chronic oral DDT toxicity in juvenile coho and chinook salmon. *Toxicol. Appl. Pharmacol.* 14:535–555.

Burdick, G. E., E. J. Harris, H. J. Dean, T. M. Walker, J. Skea, and D. Colby. 1964. The accumulation of DDT in lake trout and the effect on reproduction. *Trans. Am. Fish Soc.* 93:127–136.

Burlington, H., and V. F. Lindeman. 1950. Effect of DDT on testes and secondary sex characters of white leghorn cockerels. *Proc. Soc. Exp. Biol. Med.* 74:48–51.

Butler, P. A. 1969. The significance of DDT residues in estuarine fauna. In: *Chemical fallout: Current research on persistent pesticides*, ed. M. W. Miller and G. G. Berg, pp. 205–220. Springfield, IL: C.C. Thomas.

Butler, P. A. 1971. Influence of pesticides on marine ecosystems. *Proc. R Soc. Lond. B Biol. Sci.* 177:321–329.

Cardwell, R. D., D. G. Foreman, T. R. Payne, and D. J. Wilbur. 1977. Acute and chronic toxicity of chlordane to fish and invertebrates. Duluth, MN: U.S. Environmental Protection Agency.

Carlson, D. B., L. R. Curtis, and D. E. Williams. 2000. Salmonid sexual development is not consistently altered by embryonic exposure to endocrine-active chemicals. *Environ. Health Perspect.* 108:249–255.

Carson, R. 1962. *Silent Spring*. Boston, MA: Houghton Mifflin.

Carvalho, F. P., J. P. Villeneuve, C. Cattini, J. Rendón, and J. Mota de Oliveira. 2009. Pesticide and PCB residues in the aquatic ecosystems of Laguna de Terminos, a protected area of the coast of Campeche, Mexico. *Chemosphere* 74:988–995.

Casida, J. E., and G. B. Quistad. 1998. Golden age of insecticide research: Past, present, or future? *Annu. Rev. Entomol.* 43:1–16.

Chapman, G. A. 1983. Do organisms in laboratory toxicity tests respond like organisms in nature? In: *Aquatic Toxicology and Hazard Assessment: Sixth Symposium*, eds. W. E. Bishop, R. D. Cardwell, and B. B. Heidolph, pp. 315–327. Philadelphia, PA: American Society of Testing Materials STP 802.

Cheek, A. O., T. H. Brouwer, S. Carroll, S. Manning, J. A. McLachlan, and M. Brouwer. 2001. Experimental evaluation of vitellogenin as a predictive biomarker for reproductive disruption. *Environ. Health Perspect.* 109:681–690.

Connor, M. S., et al. 2007. The slow recovery of San Francisco Bay from the legacy of organochlorine pesticides. *Environ. Res.* 105:87–100.

Cope, O. B. 1961. Effects of DDT spraying for spruce budworm on fish in the Yellowstone River system. *Trans. Am. Fish Soc.* 90:251.

Crosby, D. G., and R. K. Tucker. 1971. Accumulation of DDT by *Daphnia magna*. *Environ. Sci. Technol.* 5:714–716.

Davy, F. B., H. Kleerekoper, and P. Gensler. 1972. Effects of exposure to sublethal DDT on the locomotor behavior of the goldfish (*Carassius auratus*). *J. Fish Res. Board. Can.* 29:1333–1336.

de la Cal, A., E. Eljarrat, D. Raldúa, C. Durán, and D. Barceló. 2008. Spatial variation of DDT and its metabolites in fish and sediment from Cinca River, a tributary of Ebro River (Spain). *Chemosphere* 70:1182–1189.

de la Cruz, A. A., and S. M. Naqvi. 1973. Mirex incorporation in the environment: Uptake in aquatic organisms and effects on the rates of photosynthesis and respiration. *Arch. Environ. Contam. Toxicol.* 1:255–264.

Delbeke, K., T. Teklemariam, E. de la Cruz, and P. Sorgeloos. 1995. Reducing variability in pollution data—the use of lipid classes for normalization of pollution data in marine biota. *Int. J. Environ. Anal. Chem.* 58:147–162.

Delorme, P. D., W. L. Lockhart, K. H. Mills, and D. C. G. Muir. 1999. Long-term effects of toxaphene and depuration in lake trout and white sucker in a natural ecosystem. *Environ. Toxicol. Chem.* 18:1992–2000.

Depledge, M. H., and Z. Billinghurst. 1999. Ecological significance of endocrine disruption in marine invertebrates. *Mar. Poll. Bull.* 39:32–38.

Derr, S. K., and M. J. Zabik. 1972. Biologically active compounds in the aquatic environment: The uptake and distribution of [1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene], DDE by *Chironomus tentans* Fabricius (Diptera: *Chironomidae*). *Trans. Am. Fish Soc.* 101:323–329.

Donohoe, R. M., and L. R. Curtis. 1996. Estrogenic activity of chlordecone, *o,p'*-DDT and *o,p'*-DDE in juvenile rainbow trout: Induction of vitellogenesis and interaction with hepatic estrogen binding sites. *Aquat. Toxicol.* 36:31–52.

Edmunds, J. S. G., R. A. McCarthy, and J. S. Ramsdell. 2000. Permanent and functional male-to-female sex reversal in d-rR strain medaka (*Oryzias latipes*) following egg microinjection of *o,p'*-DDT. *Environ. Health Perspect.* 108:219–224.

Eganhouse, R. P., J. Pontolillo, and T. J. Leiker. 2000. Diagenetic fate of organic contaminants on the Palos Verdes Shelf, California. *Mar. Chem.* 70:289–315.

Ellgaard, E. G., J. C. Ochsner, and J. K. Cox. 1977. Locomotor hyperactivity induced in the bluegill sunfish, *Lepomis macrochirus*, by sublethal concentrations of DDT. *Can. J. Zool.* 55: 1077–1081.

Ellis, M. M., B. A. Westfall, and M. D. Ellis. 1944. Toxicity of dichloro-diphenyl-trichlorethane (DDT) to goldfish and frogs. *Science* 100:477.

Elskus, A. A., T. K. Collier, and E. Monosson. 2005. Interactions between lipids and persistent organic pollutants in fish. *Environ. Toxicol.* 6:119–152.

Emanuelsen, M., J. L. Lincer, and E. Rifkin. 1978. The residue uptake and histology of American oysters (*Crassostrea virginica* Gmelin) exposed to dieldrin. *Bull. Environ. Contam. Toxicol.* 19:121–129.

Estenik, J. F., and W. J. Collins. 1979. *In Vivo* and *in vitro* studies of mixed-function oxidase in an aquatic insect, Chironomus riparius. In: *Pesticide and Xenobiotic Metabolism in Aquatic Organisms*, eds. M. A. Q. Khan, J. J. Lech, and J. J. Menn, pp. 349–370. Washington, DC: American Chemical Society.

Fabacher, D. L. 1976. Toxicity of endrin and an endrin-methyl parathion formulation to largemouth bass fingerlings. *Bull. Environ. Contam. Toxicol.* 16:376–378.

Fabacher, D. L., and H. Chambers. 1976. Uptake and storage of ^{14}C-labeled endrin by livers and brains of pesticide-susceptible and resistant mosquitofish. *Bull. Environ. Contam. Toxicol.* 16:203–207.

Faulk, C. K., L. A. Fuiman, and P. Thomas. 1999. Parental exposure to ortho,para-dichlorodiphenyltrichloroethane Impairs survival skills of Atlantic croaker (*Micropogonias undulatus*) larvae. *Environ. Toxicol. Chem.* 18:254–262.

Ferguson, D. E., D. D. Culley, W. D. Cotton, and R. P. Dodds. 1964. Resistance to chlorinated hydrocarbon insecticides in three species of freshwater fish. *Bioscience* 14:43–44.

Ferreira, M., P. Antunes, O. Gil, C. Vale, and M. A. Reis-Henriques. 2004. Organochlorine contaminants in flounder (*Platichthys flesus*) and mullet (*Mugil cephalus*) from Douro Estuary, and their use as sentinel species for environmental monitoring. *Aquat. Toxicol.* 69:347–357.

Fisher, S. W., S. W. Chordas, and P. F. Landrum. 1999. Lethal and sublethal body residues for PCB intoxication in the oligochaete, *Lumbriculus variegatus*. *Aquat. Toxicol.* 45:115–126.

Fisk, A. T., and T. A. Johnston. 1998. Maternal transfer of organochlorines to eggs of walleye (*Stizostedion vitreum*) in Lake Manitoba and Western Lake Superior. *J. Gt Lakes Res.* 24:917–928.

Fisk, A. T., R. J. Norstrom, C. D. Cymbalisty, and D. C. G. Muir. 1998. Dietary accumulation and depuration of hydrophobic organochlorines: Bioaccumulation parameters and their relationship with the octanol/water partition coefficient. *Environ. Toxicol. Chem.* 17:951–961.

Fowler, S. W. 1990. Critical review of selected heavy-metal and chlorinated-hydrocarbon concentrations in the marine environment. *Mar. Environ. Res.* 29:1–64.

Gakstatter, J. H., and C. M. Weiss. 1967. The elimination of DDT-C^{14}, dieldrin-C^{14}, and lindane-C^{14} from fish following a single sublethal exposure in aquaria. *Trans. Am. Fish Soc.* 96:301–307.

García-Flor, N., et al. 2005. Enrichment of organochlorine contaminants in the sea surface microlayer: An organic carbon-driven process. *Mar. Chem.* 96:331–345.

Garcia-Reyero, N., et al. 2006. Dietary exposure of largemouth bass to OCPs changes expression of genes important for reproduction. *Aquat. Toxicol.* 78:358–369.

Geyer, H. J., et al. 1994. The relevance of aquatic organisms' lipid content to the toxicity of lipophilic chemicals: toxicity of lindane to different fish species. *Ecotoxicol. Environ. Saf.* 28:53–70.

Gilliom, R. J., et al. 2006. The quality of our Nation's waters: Pesticides in the Nation's streams and ground water, 1992–2001. Reston, VA: National Water-Quality Assessment Program, U.S. Geological Survey Circular 1291.

González de Canales, M. L., M. Oliva, and C. Garrido. 2009. Toxicity of lindane (γ-hexachlorocyclohexane) in *Sparus aurata*, *Crassostrea angulata* and *Scrobicularia plana*. *J. Environ. Sci. Health Part B Pestic. Food Contam. Agric. Wastes* 44:95–105.

Goodman, L. R., D. J. Hansen, J. A. Couch, and J. Forester. 1977a. Organochlorine insecticide residues in salmonid fish. *J. Appl. Ecol.* 3:42–53.

Goodman, L. R., D. J. Hansen, J. A. Couch and J. Forester. 1977b. Effects of heptachlor and toxaphene on laboratory-reared embryos and fry of the sheepshead minnow. Proceedings 30th Annual Conference of the SE Fish and Wildlife Agencies, Gulf Breeze Environmental Research Laboratory.

Greenfield, B. K., et al. 2005. Seasonal, interannual, and long-term variation in sport fish contamination, San Francisco Bay. *Sci. Total Environ.* 336:25–43.

Guarino, A. M., J. B. Pritchard, J. B. Anderson, and D. P. Rall. 1974. Tissue distribution of ^{14}C-DDT in the lobster after administration via intravascular or oral routes or after exposure from ambient sea water. *Toxicol. Appl. Pharmacol.* 29:277–288.

Guo, J.-Y., et al. 2007. Organochlorine pesticides in seafood products from southern China and health risk assessment. *Environ. Toxicol. Chem.* 26:1109–1115.

Hansen, P. D. 1980. Uptake and transfer of the chlorinated hydrocarbon lindane (γ-BHC) in a laboratory freshwater food chain. *Environ. Poll. (Series A)* 21:97–108.

Hansen, D. J., S. C. Schimmel, and J. Forester. 1977. Endrin: effects on the entire life cycle of a saltwater fish, *Cyprinodon variegatus*. *J. Toxicol. Environ. Health* 3:721–733.

Haya, K., and L. E. Burridge. 1988. Uptake and excretion of organochlorine pesticides by *Nereis virens* under normoxic and hypoxic conditions. *Bull. Environ. Contam. Toxicol.* 40:170–177.

Hemmer, M. J., et al. 2001. Effects of p-nonylphenol, methoxychlor, and endosulfan on vitellogenin induction and expression in sheepshead minnow (*Cyprinodon variegatus*). *Environ. Toxicol. Chem.* 20:336–343.

Hermsen, W., I. Sims, and M. Crane. 1994. The bioavailability and toxicity to *Mytilus edulis* L. of two organochlorine pesticides adsorbed to suspended solids. *Mar. Environ. Res.* 38:61–69.

Hickey, J. P., S. A. Batterman, and S. M. Chernyak. 2006. Trends of chlorinated organic contaminants in Great Lakes trout and walleye from 1970 to 1998. *Arch. Environ. Contam. Toxicol.* 50:97–110.

Hinck, J. E., R. J. Norstrom, C. E. Orazio, C. J. Schmitt, and D. E. Tillitt. 2009. Persistence of organochlorine chemical residues in fish from the Tombigbee River (Alabama, USA): continuing risk to wildlife from a former DDT manufacturing facility. *Environ. Pollut.* 157:582–591.

Hinck, J. E., et al. 2006a. *Biomonitoring of Environmental Status And Trends (BEST) Program: Environmental Contaminants, Health Indicators, and Reproductive Biomarkers in Fish from the Colorado River Basin.* 119. Reston, VA: U.S. Geological Survey. Scientific Investigation Report 2006–5163.

Hinck, J. E., et al. 2006b. Environmental contaminants and biomarker responses in fish from the Columbia River and its tributaries: spatial and temporal trends. *Sci. Total Environ.* 366:549–578.

Holden, A. V. 1966. Organochlorine insecticide residues in salmonid fish. *J. Appl. Ecol.* 3:45–53.

Hope, B. K., and S. Scatolini. 2005. DDT, DDD, and DDE in abiotic media and near-shore marine biota from Sand Island, Midway Atoll, North Pacific ocean. *Bull. Environ. Contam. Toxicol.* 75:554–560.

Hose, J. E., J. N. Cross, S. G. Smith, and D. Diehl. 1989. Reproductive impairment in a fish inhabiting a contaminated coastal environment off Southern California. *Environ. Pollut.* 57:139–148.

Hu, G., et al. 2010. Concentrations and accumulation features of organochlorine pesticides in the Baiyangdian Lake freshwater food web of North China. *Arch. Environ. Contam. Toxicol.* 58:700–710.

Hwang, H. 2000. Contaminant body residues in *Chironomus riparius* to assess acute and chronic toxic effects of environmental contaminants. PhD dissertation, Ohio State University.

Hwang, H., S. W. Fisher, K. Kim, and P. F. Landrum. 2004. Comparison of the toxicity using body residues of DDE and select PCB congeners to the midge, *Chironomus riparius*, in partial-life cycle tests. *Arch. Environ. Contam. Toxicol.* 46:32–42.

Hyde, K. M., S. Stokes, J. F. Fowler, J. B. Graves, and F. L. Bonner. 1974. The effect of mirex on channel catfish production. *Trans. Am. Fish Soc.* 103:366–369.

Ingersoll, C. G., et al. 2003. Uptake and depuration of nonionic organic contaminants from sediment by the oligochaete, *Lumbriculus variegatus*. *Environ. Toxicol. Chem.* 22:872–885.

Jarvinen, A. W., M. J. Hoffman, and T. W. Thorslund. 1976. Toxicity of DDT food and water exposure to fathead minnows. Duluth, MN: U.S. Environmental Protection Agency 600/3–76–114.

Jarvinen, A., and R. Tyo. 1978. Toxicity to fathead minnows of endrin in food and water. *Arch. Environ. Contam. Toxicol.* 7:409–421.

Jarvis, E., K. Schiff, L. Sabin, and M. J. Allen. 2007. Chlorinated hydrocarbons in pelagic forage fishes and squid of the Southern California Bight. *Environ. Toxicol. Chem.* 26:2290–2298.

Johnson, B. T., C. R. Saunders, H. O. Sanders, and R. S. Campbell. 1971. Biological magnification and degradation of DDT and aldrin by freshwater invertebrates. *Fish Res. Board Can.* 28:705–709.

Johnson, D. W. 1968. Pesticides and fishes—a review of selected literature. *Trans. Am. Fish Soc.* 97:398–424.

Johnson, K. G. 2005. Dietary exposure to organochlorine pesticides *p,p'*-DDE and dieldrin and their effects on steroidogenesis and reproductive success in Florida largemouth bass (*Micropoterus salmoides* floridanus). M.S. Thesis, Gainsville, University of Florida.

Johnson, L. L., et al. 2007a. Contaminant exposure in outmigrant juvenile salmon from Pacific Northwest estuaries of the United States. *Environ. Monit. Assess.* 124:167–194.

Johnson, K. G., et al. 2007b. Influence of seasonality and exposure on the accumulation and reproductive effects of *p,p'*-dichlorodiphenyldichloroethane and dieldrin in largemouth bass. *Environ. Toxicol. Chem.* 26:927–934.

Jørgensen, E. H., M. M. Vijayan, J. E. A. Killie, N. Aluru, O. Aas-Hansen, and A. Maule. 2006. Toxicokinetics and effects of PCBs in Arctic fish: A review of studies on Arctic charr. *J. Toxicol. Environ. Health A* 69:37–52.

Kajiwara, N., et al. 2003. Contamination by organochlorine compounds in sturgeons from Caspian Sea during 2001 and 2002. *Mar. Pollut. Bull.* 46:741–747.

Kawatski, J. A., and J. C. Schmulbach. 1971. Accumulation of insecticide in freshwater ostracods exposed continuously to sublethal concentrations of aldrin or dieldrin. *Trans. Am. Fish Soc.* 100:565–567.

Keilty, T. J., D. S. White, and P. F. Landrum. 1988a. Sublethal responses to endrin in sediment by *Limnodrilus hoffmeisteri (Tubificidae)*, and in mixed-culture with *Stylodrilus heringianus (Lumbriculidae)*. *Aquat. Toxicol.* 13:227–249.

Keilty, T. J., D. S. White, and P. F. Landrum. 1988b. Sublethal responses to endrin in sediment by *Stylodrilus heringianus* (Lumbriculidae) as measured by a 137 cesium marker layer technique. *Aquat. Toxicol.* 13:251–270.

Kennedy, A. J., G. R. Lotufo, J. A. Steevens, and T. S. Bridges. 2010. Determination of steady state tissue residues for invertebrates in contaminated sediment. US Army Engineer Research and Development Center. Vicksburg, MS. ERDC/EL TR-03-2.

Kidd, K. A., R. H. Hesslein, B. J. Ross, K. Koczanski, G. R. Stephens, and D. C. G. Muir. 1998. Bioaccumulation of organochlorines through a remote freshwater food web in the Canadian Arctic. *Environ. Pollut.* 102:91–103.

Kidd, K. A., H. A. Bootsma, R. H. Hesslein, D. C. G. Muir, and R. E. Hecky. 2001. Biomagnification of DDT through the benthic and pelagic food webs of Lake Malawi, East Africa: Importance of trophic level and carbon source. *Environ. Sci. Technol.* 35:14–20.

Kimbrough, K. L., W. E. Johnson, G. G. Lauenstein, J. D. Christensen, and D. A. Apeti. 2008. An assessment of two decades of contaminant monitoring in the Nation's coastal zone. 105 pp. Silver Spring, MD: NOAA Technical Memorandum NOS NCCOS 74.

Kleinert, S. J, P. E. Degurse, and T. L. Wirth. 1968. Occurrence and significance of DDT and dieldrin residues in Wisconsin fish. 43 pp. Madison, WI: Technical Bulletin Number 41, Department of Natural Resources.

Knauf, W., and E. F. Schulze. 1973. New findings on the toxicity of endosulfan and its metabolites to aquatic organisms. Submitted in fulfillment of Pesticide Registration Notice 38: 717–732.

Koenig, C. C. 1977. The effects of DDT and mirex alone and in combination on the reproduction of a salt marsh cyprinodont fish, *Adinia xenica.* In *Physiological Responses of Marine Biota to Pollutants*, eds. F. J. Vernberg, A. Calabrese, F. P. Thurberg, and W. B. Vernberg, pp. 357–376. New York, NY: Academic Press.

Kumblad, L., A. Olsson, V. Koutny, and H. Berg. 2001. Distribution of DDT residues in fish from the Songkhla Lake, Thailand. *Environ. Pollut.* 112:193–200.

Kwong, R. W. M., P. K. N. Yu, P. K. S. Lam, and W.-X. Wang. 2008. Uptake, elimination, and biotransformation of aqueous and dietary DDT in marine fish. *Environ. Toxicol. Chem.* 27:2053–2063.

Lamai, S. L., G. F. Warner, and C. H. Walker. 1999. Effects of dieldrin on life stages of the African catfish, *Clarias gariepinus* (Burchell). *Ecotoxicol. Environ. Saf.* 42:22–29.

Landrum, P. F., H. Lee, and M. J. Lydy. 1992. Toxicokinetics in aquatic systems: Model comparisons and use in hazard assessment. *Environ. Toxicol. Chem.* 11:1709–1725.

Landrum, P. F., J. A. Steevens, M. McElroy, D. C. Gossiaux, J. S. Lewis, and S. D. Robinson. 2005. Time-dependent toxicity of dichlorodiphenyldichloroethylene to *Hyalella azteca. Environ. Toxicol. Chem.* 24:211–218.

Larsson, P., L. Okla, and L. Collvin. 1993. Reproductive status and lipid content as factors in PCB, DDT and HCH contamination of a population of pike (*Esox lucius* L). *Environ. Toxicol. Chem.* 12:855–861.

Leatherland, J. F., and R. A. Sonstegard. 1979. Effect of dietary mirex and PCB (Aroclor 1254) on thyroid activity and lipid reserves in rainbow trout *Salmo gairdneri* Richardson. *J. Fish Dis.* 2:43–48.

Leblond, V. S., M. Bisson, and A. Hontela. 2001. Inhibition of cortisol secretion in dispersed head kidney cells of rainbow trout (*Oncorhynchus mykiss*) by endosulfan, an organochlorine pesticide. *Gen. Comp. Endocrinol.* 121:48–56.

Lee, J. H., J. R. Sylverster, and C. E. Nash. 1975. Effects of mirex and methoxychlor on juvenile and adult striped mullet, *Mugil cephalus* (L.). *Bull. Environ. Contam. Toxicol.* 14:180–186.

Leffler, C. W. 1975. Effects of ingested mirex and DDT on juvenile *Callinectes sapidus* Rathbun. *Environ. Pollut.* 8:283–300.

Lewis, M. A., et al. 2002. Fish tissue quality in near-coastal areas of the Gulf of Mexico receiving point source discharges. *Sci. Total Environ.* 284:249–261.

Lin, T., et al. 2009. Levels and mass burden of DDTs in sediments from fishing harbors: The importance of DDT-containing antifouling paint to the coastal environment of China. *Environ. Sci. Technol.* 43:8033–8038.

Lohmann, R., K. Breivik, J. Dachs, and D. Muir. 2007. Global fate of POPs: Current and future research directions. *Environ. Pollut.* 150:150–165.

Looser, R., O. Froescheis, G. M. Cailliet, W. M. Jarman, and K. Ballschmiter. 2000. The deep-sea as a final global sink of semivolatile persistent organic pollutants? Part II: Organochlorine pesticides in surface and deep-sea dwelling fish of the North and South Atlantic and the Monterey Bay Canyon (California). *Chemosphere* 40:661–670.

Lotufo, G.R., M.D. Duke, and T.S. Bridges. Unpublished. Bioaccumulation of sediment-associated DDT in the amphipod *Leptocheirus plumulosus*. Manuscript in preparation.

Lotufo, G. R., P. F. Landrum, M. L. Gedeon, E. A. Tigue, and L. R. Herche. 2000a. Comparative toxicity and toxicokinetics of DDT and its major metabolites in freshwater amphipods. *Environ. Toxicol. Chem.* 19:368–379.

Lotufo, G. R., J. D. Farrar, and T. S. Bridges. 2000b. Effects of exposure source, worm density, and sex on DDT bioaccumulation and toxicity in the marine polychaete *Neanthes arenaceodentata*. *Environ. Toxicol. Chem.* 19:472–484.

Lotufo, G. R., J. D. Farrar, B. M. Duke, and T. S. Bridges. 2001a. DDT toxicity and critical body residue in the amphipod *Leptocheirus plumulosus* in exposures to spiked sediment. *Arch. Environ. Contam. Toxicol.* 41:142–150.

Lotufo, G. R., Landrum, P. F., and Gedeon, M. L. 2001b. Toxicity and bioaccumulation of DDT in freshwater amphipods in exposures to spiked sediments. *Environ. Toxicol. Chem.* 20:810–825.

Ludke, J. L., D. E. Ferguson, and W. D. Burke. 1968. Some endrin relationships in resistant and susceptible populations of golden shiners, *Notemigonus crysoleucas*. *Trans. Am. Fish Soc.* 97:260–263.

Ludke, J. L., M. T. Finley, and C. Lusk. 1971. Toxicity of mirex to crayfish, *Procambarus blandingi*. *Bull. Environ. Contam. Toxicol.* 6:89–96.

Macek, K. G. 1968. Reproduction in the brook trout (*Salvelinus fontinalis*) fed sublethal concentration of DDT. *Fish Res. Board Can.* 25:1787–1796.

Macek, K. J., C. R. Rodgers, D. L. Stalling, and S. Korn. 1970. The uptake, distribution and elimination of dietary ^{14}C-DDT and ^{14}C-dieldrin in rainbow trout. *Trans. Am. Fish Soc.* 99:689–695.

Macek, K. J., K. S. Buxton, S. K. Derr, J. W. Dean, and S. Sauter. 1976. Chronic toxicity of lindane to selected aquatic invertebrates and fishes. U.S. Environmental Protection Agency, EPA—600/3–76-046.

Marcelle, C., and J. P. Thome.1983. Acute toxicity and bioaccumulation of lindane in gudgeon, *Gobio gobio* (L.). *Bull. Environ. Contam. Toxicol.* 31:453–458.

Mason, J. W., and D. R. Rowe. 1976. The accumulation and loss of dieldrin and endrin in the Eastern oyster. *Arch. Environ. Contam. Toxicol.* 4:349–360.

Matta, M. B., A. J. Mearns, and M. F. Buchman. 1986. *Trends in DDT and PCBs in U.S. West Coast fish and invertebrates*. Seattle, WA: Ocean Assessments Division, National Ocean Service, NOAA.

Matthiessen, P., P. J. Fox, R. J. Douthwaite, and A. B. Wood. 1982. Accumulation of endosulfan residues in fish and their predators after aerial spraying for the control of testse fly in Botswana. *Pestic. Sci.* 13:39–48.

Mayer, F. L. J., P. M. J. Mehrle, and W. P. Dwyer. 1977. Toxaphene: Chronic Toxicity to Fathead Minnows and Channel Catfish. *Ecological Research Series*, 39. Duluth, MN: U.S. Environmental Protection Agency 600/3–77-069.

Mayer, F. L., Jr., P. M. Mehrle, Jr., and W. P. Dwyer. 1975. Toxaphene effects on reproduction, growth, and mortality of brook trout. Duluth, MN: U.S. Environmental Protection Agency 600/3–75/013.

McCarty, L. S., and D. Mackay. 1993. Enhancing ecotoxicological modeling and assessment. *Environ. Sci. Technol.* 27:1718–1728.

Meador, J. 2006. Rationale and procedures for using the tissue-residue approach for toxicity assessment and determination of tissue, water, and sediment quality guidelines for aquatic organisms. *Hum. Ecol. Risk Assess.* 12:1018–1073.

Mearns, A. J., et al. 1991. Contaminant trends in the Southern California bight: Inventory and assessment. In: *NOAA Technical Memorandum NOS ORCA 62*. Seattle, WA: Office of Ocean Resources Conservation and Assessment, National Ocean Service.

Mehrle, P. M., and F. L. Mayer. 1975a. Toxaphene effects of growth and bone composition of fathead minnows, *Pimephales promelas*. *Fish Res. Board Can.* 32:593–598.

Mehrle, P. M., and F. L. Mayer. 1975b. Toxaphene effects on growth and development of brook trout (*Salvelinus fontinalis*). *Fish Res. Board Can.* 32:609–613.

Metcalfe, T. L., C. D. Metcalfe, Y. Kiparissis, A. J. Niimi, C. M. Foran, and W. H. Benson. 2000. Development and endocrine responses in Japanese medaka (*Oryzias latipes*) exposed to *o,p'*-DDT in water or through maternal transfer. *Environ. Toxicol. Chem.* 19:1893–1900.

Miller, M. A. 1993. Maternal transfer of organochlorine compounds in salmonines to their eggs. *Can. J. Fish Aquat. Sci.* 50:1405–1413.

Miller, M. A. 1994. Organochlorine concentration dynamics in Lake Michigan chinook salmon (*Oncorhynchus tshawytscha*). *Arch. Environ. Contam. Toxicol.* 27:367–374.

Miller, M. A., and J. F. Amrhein. 1995. Maternal transfer of organochlorine compounds in Lake-Superior Siscowet (*Salvelinus namaycush siscowet*) to their eggs. *Bull. Environ. Contam. Toxicol.* 55:96–103.

Mills, L. J., et al. 2001. Effects of estrogenic (*o,p'*-DDT; octylphenol) and anti-androgenic (*p,p'*-DDE) chemicals on indicators of endocrine status in juvenile male summer flounder (*Paralichthys dentatus*). *Aquat. Toxicol.* 52:157–176.

Milston, R. H., et al. 2003. Short-term exposure of chinook salmon (*Oncoryhnchus tshawytscha*) to *o,p'*-DDE or DMSO during early life-history stages causes long-term humoral immunosuppression. *Environ. Health Perspect.* 111:1601–1607.

Miranda, A. L., H. Roche, M. A. F. Randi, M. L. Menezes, and C. A. O. Ribeiro. 2008. Bioaccumulation of chlorinated pesticides and PCBs in the tropical freshwater fish *Hoplias malabaricus*: Histopathological, physiological, and immunological findings. *Environ. Int.* 34:939–949.

Monirith, I., et al. 2003. Asia-Pacific Mussel Watch: Monitoring contamination of persistent organochlorine compounds in coastal waters of Asian Countries. *Mar. Pollut. Bull.* 46:281–300.

Monod, G. 1985. Egg mortality of Lake Geneva charr (*Salvelinus alpinus* l.) contaminated by PCB and DDT derivatives. *Bull. Environ. Contam. Toxicol.* 35:531–536.

Muir, D., and E. Sverko. 2006. Analytical methods for PCBs and organochlorine pesticides in environmental monitoring and surveillance: A critical appraisal. *Anal. Bioanal. Chem.* 386:769–789.

Muir, D., D. Swackhamer, T. Bidleman, and L. Jantunen. 2006. Toxaphene in the Great Lakes. In *Persistent Organic Pollutants in the Great Lakes*, ed. R. A. Hites, pp. 201–265. Berlin Heidelberg: Springer-Verlag.

Muller, J. K., K. G. Johnson, M. S. Sepulveda, C. J. Borgert, and T. S. Gross. 2004. Accumulation of dietary DDE and dieldrin by largemouth bass, *Micropterus salmoides floridanus*. *Bull. Environ. Contam. Toxicol.* 73:1078–1085.

Mulsow, S., P. F. Landrum, and J. A. Robbins. 2002. Biological mixing responses to sublethal concentrations of DDT in sediments by *Heteromastus filiformis* using a 137-Cs marker layer technique. *Mar. Ecol. Prog. Ser.* 239:181–191.

Mulsow, S. G., and P. F. Landrum. 1995. Bioaccumulation of DDT in a marine polychaete, the conveyor-belt deposit feeder *Heteromastus filiformis* (Claparede). *Chemosphere* 31:3141–3152.

Nakata, H., et al. 2005. Concentrations and compositions of organochlorine contaminants in sediments, soils, crustaceans, fishes and birds collected from Lake Tai, Hangzhou bay and Shanghai city region, China. *Environ. Pollut.* 133:415–429.

Naqvi, S. M., and C. Vaishnavi. 1993. Bioaccumulative potential and toxicity of endosulfan insecticide to non-target animals. *Comp. Biochem. Physiol. C: Pharmacol. Toxicol.* 105:347–361.

Narahashi, T. 2000. Neuroreceptors and ion channels as the basis for drug action: Past, present, and future. *J. Pharmacol. Exp. Ther.* 294:1–26.

National Oceanic and Atmospheric Administration (NOAA) and U.S. Environmental Protection Agency (EPA). 2007. 2002–2004 Southern California coastal marine fish contaminants survey. 91 pp. Long Beach, California: U.S. Department of Commerce, National Oceanic and Atmospheric Administration, on behalf of the Natural Resource Trustees, and U.S. Environmental Protection Agency–Region IX.

Neufeld, G. J., and J. B. Pritchard. 1979. An assessment of DDT toxicity on osmoregulation and gill Na, K-ATPase activity in the blue crab. In *Aquatic Toxicology*, eds. L. L. Marking and R. A. Kimerle, pp. 23–34. Philadelphia, PA: American Society for Testing and Materials STP 667.

Niimi, A. J. 1983. Biological and toxicological effects of environmental contaminants in fish and their eggs. *Can. J. Fish Aquat. Sci.* 40:306–312.

Nimmo, D. R., A. J. Wilson, and R. R. Blackman. 1970. Localization of DDT in the body organs of pink and white shrimp. *Bull. Environ. Contam. Toxicol.* 5:333–341.

Nowell, L. H., P. D. Capel, and P. D. Dileanis. 1999. Pesticides in stream sediment and aquatic biota: Distribution, trends, and governing factors. In: *Pesticides in the Hydrologic System Vol. 4.* Boca Raton, FL: Lewis Publishers, CRC Press.

O'Connor, T. P., and G. G. Lauenstein. 2006. Trends in chemical concentrations in mussels and oysters collected along the US coast: Update to 2003. *Mar. Environ. Res.* 62:261–285.

Oliver, B. G., and A. J. Niimi. 1985. Bioconcentration factors of some halogenated organics for rainbow trout: limitations in their use for prediction of environmental residues. *Environ. Sci. Technol.* 19:842–849.

Pandit, G. G., S. K. Sahu, S. Sharma, and V. D. Puranik. 2006. Distribution and fate of persistent organochlorine pesticides in coastal marine environment of Mumbai. *Environ. Int.* 32:240–243.

PAN North American. 2009. http://www.panna.org/campaigns/endosulfan (accessed October 13, 2009).

Papoulias, D. M., S. A. Villalobos, J. Meadows, D. B. Noltie, J. P. Giesy, and D. E. Tillitt. 2003. *In ovo* exposure to *o,p'*-DDE affects sexual development but not sexual differentiation in Japanese medaka (*Oryzias latipes*). *Environ. Health Perspect.* 111:29–32.

Parrish, P. R., J. A. Couch, J. Forester, J. M. Patrick, and G. H. Cook. 1974. Dieldrin: effects on several estuarine organisms. *Proc. 28th Ann. Conf. Southeast Assoc. Game Fish Comm.* 427–434.

Parrish, P. R., S. C. Schimmel, D. J. Hansen, J. M. Patrick, and J. Forester. 1976. Chlordane: Effects on several estuarine organisms. *J. Toxicol. Environ. Health Part A* 1:485–494.

Pawlisz, A. V., and R. H. Peters. 1993. A radioactive tracer technique for the study of lethal body burdens of narcotic organic chemicals in *Daphnia magna*. *Environ. Sci. Technol.* 27:2795–2800.

Pesce, S. F., J. Cazenave, M. V. Monferrán, S. Frede, and D. A. Wunderlin. 2008. Integrated survey on toxic effects of lindane on neotropical fish: *Corydoras paleatus* and *Jenynsia multidentata*. *Environ. Pollut.* 156:775–783.

Pontolillo, J., and R. P. Eganhouse. 2001. The search for reliable aqueous solubility (S_w) and octanol-water partition coefficient (k_{ow}) data for hydrophobic organic compounds: DDT and DDE as case study. 61 pp. Reston, VA: U.S. Geological Survey Water-Resources Investigations Report 01–4201.

Qiu, Y. W., et al. 2009. Current status and historical trends of organochlorine pesticides in the ecosystem of Deep Bay, South China. *Estuar. Coast Shelf Sci.* 85:265–272.

Ramamoorthy, S. 1985. Competition of fate processes in the bioconcentration of lindane. *Bull. Environ. Contam. Toxicol.* 34:349–358.

Ramu, K., et al. 2007. Asian mussel watch program: Contamination status of polybrominated diphenyl ethers and organochlorines in coastal waters of Asian countries. *Environ. Sci. Technol.* 41:4580–4586.

Randall, R. C., H. Lee II, R. J. Ozretich, J. L. Lake, and R. J. Pruell. 1991. Evaluation of selected lipid methods for normalizing pollutant bioaccumulation. *Environ. Toxicol. Chem.* 10:1431–1436.

Randall, R. C., D. R. Young, H. Lee II, and S. F. Echols. 1998. Lipid methodology and pollutant normalization relationships for neutral nonpolar organic pollutants. *Environ. Toxicol. Chem.* 17:788–791.

Roberts, D. 1972. The assimilation and chronic effects of sub-lethal concentrations of endosulfan on condition and spawning in the common mussel. *Mar. Biol.* 16:119–125.

Russell, R. W., F. A. P. C. Gobas, and G. D. Haffner. 1999. Maternal transfer and *in ovo* exposure of organochlorines in oviparous organisms: A model and field verification. *Environ. Sci. Technol.* 33:416–420.

Ruus, A., K. I. Ugland, O. Espeland, and J. U. Skaare. 1999. Organochlorine contaminants in a local marine food chain from Jarfjord, Northern Norway. *Mar. Environ. Res.* 48:131–146.

Ryan, M. J., et al. 2005. Temporal trends of organochlorine contaminants in burbot and lake trout from three selected Yukon lakes. *Sci. Total Environ.* 351–352:501–522.

Said, T. O., and M. A. F. Hamed. 2005. Distribution of chlorinated pesticides in surface water and fish of El Temsah and Bitter Lakes, Suez Canal. *Egyptian J. Aquat. Res.* 31:200–213

Sarkar, S. K., et al. 2008. Occurrence, distribution and possible sources of organochlorine pesticide residues in tropical coastal environment of India: An overview. *Environ. Int.* 34:1062–1071.

Schiff, K., and M. J. Allen. 2000. Chlorinated hydrocarbons in flatfishes from the Southern California, USA, Bight. *Environ. Toxicol. Chem.* 19:1559–1565.

Schimmel, S. C., P. R. Parrish, D. J. Hansen, J. M. Jr. Patrick, and J. Forester. 1975. Endrin: effects on several estuarine organisms. *Proc. 28th Ann. Conf. Southeast Assoc. Game Fish Comm.* 187–194.

Schimmel, S. C., J. M. Jr. Patrick, and J. Forester. 1976. Heptachlor: Toxicity to and uptake by several estuarine organisms. *J. Toxicol. Environ. Health* 1:955–965.

Schimmel, S. C., J. M. Jr. Patrick, and A. J. Wilson Jr. 1977a. Acute toxicity to and bioconcentration of endosulfan by estuarine animals. In: *Aquatic Toxicology and Hazard Evaluation*, eds. F. L. Mayer and J. L. Hamelink, pp. 241–252. Philadelphia, PA: American Society for Testing and Materials STP 634.

Schimmel, S. C., J. M. Jr. Patrick, and J. Forester. 1977b. Toxicity and bioaccumulation of BHC and lindane in selected estuarine animals. *Arch. Environ. Contam. Toxicol.* 6:355–363.

Schimmel, S. C., J. M. Patrick, and J. Forester. 1977c. Uptake toxicity of toxaphene in several estuarine organisms. *Arch. Environ. Contam. Toxicol.* 5:353–367.

Schmitt, C. J. 2002a. Organochlorine chemical residues in fish from the Mississippi River basin, 1995. *Arch. Environ. Contam. Toxicol.* 43:81–97.

Schmitt, C. J. 2002b. Biomonitoring of environmental status and trends (BEST) program: environmental contaminants and their effects on fish in the Mississippi River Basin. USGS/BRD/BSR-2002–0004.

Schmitt, C. J., J. L. Zajicek, and P. H. Peterman. 1990. National contaminant biomonitoring program: residues of organochlorine chemicals in U.S. freshwater fish, 1976–1984. *Arch. Environ. Contam. Toxicol.* 19:748–781.

Serrano, R., M. A. Blanes, and F. J. López. 2008. Maternal transfer of organochlorine compounds to oocytes in wild and farmed gilthead sea bream (*Sparus aurata*). *Chemosphere* 70:561–566.

Shen, L., and F. Wania. 2005. Compilation, evaluation, and selection of physical-chemical property data for organochlorine pesticides. *J. Chem. Eng. Data* 50:742–768.

Shubat, P. J., and L. R. Curtis.1986. Ration and toxicant preexposure influence dieldrin accumulation by rainbow trout (*Salmo gairdneri*). *Environ. Toxicol. Chem.* 5:69–77.

Singh, P. B., and V. Singh. 2007. Exposure recovery response of isomers of HCH, metabolites of DDT and estradiol-17 beta in the female catfish, *Heteropneustes fossilis*. *Environ. Toxicol. Pharmacol.* 24:245–251.

Skea, J. C., H. J. Simonin, S. Jackling, and J. Symula. 1981. Accumulation and retention of mirex by brook trout fed a contaminated diet. *Bull. Environ. Contam. Toxicol.* 27:79–83.

Smeets, J. M. W., I. van Holsteijn, J. P. Giesy, W. Seinen, and M. van den Berg. 1999. Estrogenic potencies of several environmental pollutants, as determined by vitellogenin induction in a carp hepatocyte assay. *Toxicol. Sci.* 50:206–213.

Smith, R. M., and C. F. Cole. 1973. Effects of egg concentration of DDT and dieldrin on development in winter flounder (*Pseudopleuronects americanus*). *Fish Res. Board Can.* 30:1894–1898.

Sodergren, A., and B. J. Svensson. 1973. Uptake and accumulation of DDT and PCB by *Ephermera danica* (Ephemeroptera) in continuous-flow systems. *Bull. Environ. Contam. Toxicol.* 9:345–350.

Ssebugere, P., B. T. Kiremire, M. Kishimba, S. O. Wandiga, S. A. Nyanzi, and J. Wasswa. 2009. DDT and metabolites in fish from Lake Edward, Uganda. *Chemosphere* 76:212–215.

Stahl, L., B. Snyder, A. Olsen, and J. Pitt. 2009. Contaminants in fish tissue from US lakes and reservoirs: A National probabilistic study. *Environ. Monit. Assess.* 150:3–19.

Strachan, W. M. J., D. A. Burniston, M. Williamson, and H. Bohdanowicz. 2001. Spatial differences in persistent organochlorine pollutant concentrations between the Bering and Chukchi Seas (1993). *Mar. Pollut. Bull.* 43:132–142.

Strandberg, B., et al. 1998. Concentrations and spatial variations of cyclodienes and other organochlorines in herring and perch from the Baltic Sea. *Sci. Total Environ.* 215:69–83.

Su, Y., et al. 2008. A circumpolar perspective of atmospheric organochlorine pesticides (OCPs): Results from six Arctic monitoring stations in 2000–2003. *Atmos. Environ.* 42:4682–4698.

Sudaryanto, A., et al. 2007. Levels and distribution of organochlorines in fish from Indonesia. *Environ. Int.* 33:750–758.

Sumpter, J. P., and S. Jobling. 1995. Vitellogenesis as a biomarker for estrogenic contamination of the aquatic environment. *Environ. Health Perspect.* 103:173–178.

Tagatz, M. E., P. W. Borhtwick, and J. Forester. 1975. Seasonal effects of leached mirex of selected estuarine animals. *Arch. Environ. Contam. Toxicol.* 3:371–383.

Tagatz, M. E., P. W. Borthwick, J. M. Ivey, and J. Knight. 1976. Effects of leached mirex on experimental communities of estuarine animals. *Arch. Environ. Contam. Toxicol.* 4:435–442.

Tan, L., M. He, B. Men, and C. Lin. 2009. Distribution and sources of organochlorine pesticides in water and sediments from Daliao River estuary of Liaodong Bay, Bohai Sea (China). *Estuar. Coast Shelf Sci.* 84:119–127.

Tanabe, S., M. S. Prudente, S. Kan-Atireklap, and A. Subramanian. 2000. Mussel watch: Marine pollution monitoring of butyltins and organochlorines in coastal waters of Thailand, Philippines and India. *Ocean Coast Manag.* 43:819–839.

Thorpe, K. L., R. Benstead, T. H. Hutchinson, and C. R. Tyler. 2007. Associations between altered vitellogenin concentrations and adverse health effects in fathead minnow (*Pimephales promelas*). *Aquat. Toxicol.* 85:176–183.

Toledo, M. C. F., and C. M. Jonsson. 1992. Bioaccumulation and elimination of endosulfan in zebra fish (*Brachydanio rerio*). *Pest. Sci.* 36:207–211.

Tyler-Schroeder, D. B. 1979. Use of the grass shrimp (*Palaemonetes pugio*) in a life cycle toxicity test. In: *Aquatic Toxicology*, eds. L. L. Marking and R. A. Kimerle, pp. 159–170. Philadelphia, PA: American Society for Testing and Materials STP 667.

Ungerer, J. R., and P. Thomas. 1996. Role of very low density lipoproteins in the accumulation of *o,p'*-DDT in fish ovaries during gonadal recrudescence. *Aquat. Toxicol.* 35:183–195.

United Nations Environment Programme (UNEP). 2008. Global status of DDT and its alternatives for use in vector control to prevent disease. Stockholm convention of persistent organic pollutants. Geneva, Henk van den Berg, Laboratory of Entomology, Wageningen University and Research Centre, Netherlands: 31.

U.S. Geological Survey (USGS). 2008. Pesticide National Synthesis Project, National Water-Quality Assessment Program, Frequency of Mixtures. http://water.usgs.gov/nawqa/pnsp/pubs/circ1291/show_description.php?chapter=5&figure=6/ (accessed October 26, 2009).

U.S. Environmental Protection Agency (U.S. EPA). 1980. Ambient water quality criteria for DDT. Springfield, VA. U.S. Environmental Protection Agency 440/5-80-038.

U.S. EPA. 1992. National study of chemical residues in fish. Washington, DC: Office of Science and Technology EPA-823-R-92–008.

U.S. EPA. 2002. Reregistration eligibility decision for endosulfan, U. S. Enviromental Protection Agency 738-F-02–012.

U.S. EPA. 2004. Five-year review report. Third five-year review report for Triana/Tennessee River site, Triana, Madison Country, Alabama. 14 pp + 17 attachments. Atlanta, GA: U.S. Environmental Protection Agency.

U.S. EPA. 2006. National Listing of Fish Advisories. General Fact Sheet: 2005/06 National Listing. http://www.epa.gov/waterscience/fish/advisories/2006/index.html (accessed September 30, 2008).

Ungerer, J. R., and P. Thomas. 1996. Role of very low density lipoproteins in the accumulation of *o,p'*-DDT in fish ovaries during gonadal recrudescence. *Aquat. Toxicol.* 35:183–195.

van Valin, C. C., A. K. Andrews, and L. L. Eller. 1968. Some effects of mirex on two warm-water fishes. *Trans. Am. Fish Soc.* 97:185–196.

Villalobos, S. A., et al. 2003. Toxicity of *o,p'*-DDE to medaka d-rR strain after a one-time embryonic exposure by *in ovo* nanoinjection: An early through juvenile life cycle assessment. *Chemosphere* 53:819–826.

von Westernhagen, H., P. Cameron, V. Dethlefsen, and D. Janseen. 1989. Chlorinated hydrocarbons in North Sea whiting (*Merlangius merlangus* L.), and effects on reproduction. 1. Tissue burden and hatching success. *Helgol. Meeresunters* 43:45–60.

Wang, X. H., and W. X. Wang. 2005. Uptake, absorption efficiency and elimination of DDT in marine phytoplankton, copepods and fish. *Environ. Pollut.* 136:453–464.

Warlen, S. M., Wolfe, D. A., Lewis, C. W., and Colby, D. R. 1977. Accumulation and retention of dietary ^{14}C-DDT by Atlantic menhaden. *Trans. Am. Fish Soc.* 106:95–104.

Weber, J., et al. 2006. Endosulfan and γ-HCH in the Arctic: An assessment of surface seawater concentrations and air-sea exchange. *Environ. Sci. Technol.* 40:7570–7576.

Wester, P. W., and J. H. Canton. 1986. Histopathological study of *Oryzias latipes* (medaka) after long-term beta-hexachlorocyclohexane exposure. *Aquat. Toxicol.* 9:21–45.

Westin, D. T., C. E. Olney, and B. A. Rogers. 1985. Effects of parental and dietary organochlorines on survival and body burdens of striped bass larvae. *Trans. Am. Fish Soc.* 114:125–136.

Wiktelius, S., and C. A. Edwards. 1997. Organochlorine insecticide residues in African fauna: 1971–1995. *Rev. Environ. Contam. Toxicol.* 151:1–37.

Willingham, E. 2004. Endocrine-disrupting compounds and mixtures: unexpected dose-response. *Arch. Environ. Contam. Toxicol.* 46:265–269.

Wong, C. S., P. D. Capel, and L. H. Nowell. 2000. Organochlorine pesticides and PCBs in stream sediment and aquatic biota—initial results from the National Water Quality Assessment Program, 1992–1995. Sacramento, CA: Water-Resources Investigations Report USGS 00–4053.

World Health Organization (WHO). 1984a. Environmental health criteria 40—Endosulfan. Published under the joint sponsership of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. Geneva: World Health Organization, International programme on Chemcal Safety.

World Health Organization (WHO). 1984b. Environmental health criteria 45—Camphechlor. Published under the joint sponsership of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. Geneva: World Health Organization, International programme on Chemical Safety.

World Health Organization (WHO). 1991. Environmental health criteria 124—Lindane. Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. Geneva: World Health Organization, International Programme on Chemical Safety.

World Health Organization (WHO). 1992. Environmental health criteria 130—Endrin. Published under the joint sponsership of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. Geneva: World Health Organization, International Programme on Chemical Safety.

Zeng, E. Y., and M. I. Venkatesan. 1999. Dispersion of sediment DDTs in the coastal ocean off southern California. *Sci. Total Environ.* 229:195–208.

Zeng, E. Y., et al. 2005. Distribution and mass inventory of total dichlorodiphenyldichlorothylene in the water column of the southern California Bight. *Environ. Sci. Technol.* 39:8170–8176.

Zhang, Z. B., and J. Y. Hu. 2008. Effects of *p,p'*-DDE exposure on gonadal development and gene expression in Japanese medaka (*Oryzias latipes*). *J. Environ. Sci. (China)* 20:347–352.