REGULATORY TOXICOLOGY AND PHARMACOLOGY **20,** S187–S307 (1994)

Chapter 5: Polychlorinated Biphenyls

CHAPTER SUMMARY

The evaluation of the potential adverse effects of polychlorinated biphenyls (PCBs) on human health and the environment, as summarized in this chapter, is based on an assessment of: (i) the way in which the sources and environmental fate characteristics of PCBs determine their concentrations in various environmental media; (ii) the rates of exposure experienced by various biological systems; and (iii) the potential for the occurrence of adverse effects from these rates of exposure. The potential consequences of the concentrations in environmental media were assessed by comparing the degrees of exposure to various aquatic and terrestrial receptors, including humans, and the exposure limits for PCBs that would not produce adverse effects. The exposure limits were based on current knowledge of the toxic potency of PCBs to various biological systems.

Until recently it was believed that there were no natural sources of PCBs. However, PCBs not associated with anthropogenic activities were identified in ash from the 1980 volcanic eruption of Mt. St. Helens (Pereira *et al.,* 1980), and subunits of PCBs have also been identified as components of two glycopeptides identified from *Amycolatopsis* sp. (Box *et al.,* 1991). Historically, the largest anthropogenic use of PCBs was in the electrical industry (e.g., in transformers and capacitors) where their heat absorbing capacity and electrical insulating properties provided greater safety and equipment reliability compared to alternative materials. Other commercial uses of PCBs included heat exchange fluids, carbonless copy paper, packaging materials, and paint additives. Chemically, the term PCBs denotes a family of 209 isomers consisting of two benzene rings joined by carbon–carbon bonds with chlorine atoms in varying numbers and ring positions. The congener groups range from the three monochlorinated isomers to a fully chlorinated decachlorobiphenyl isomer. The different isomers of PCBs exhibit a wide range of physical/chemical properties. For example, water solubilities range over 5.5 million-fold from the monochloro- to the decachlorobiphenyl, vapor pressures over 100,000-fold (both decreasing with degree of chlorine substitution), and lipid solubilities over 10,000-fold (increasing with degree of chlorine substitution).

Commercial PCBs were mixtures of chlorinated biphenyls with varying percentages of chlorine by weight. For example, the mixtures of PCBs denoted as Aroclor 1242, 1254, and 1260 were 42, 54, and 60% chlorine by weight, respectively.

The differences in physical/chemical properties of the various PCBs are reflected in their distribution and mobility (environmental fate) in the environment. Although generalizations may not be appropriate for a group of chemicals with such widely varying properties, it has been observed that as the chlorine content of PCBs increases, their rate of degradation by environmental systems decreases, resulting in increased persistence. Photodegradation of PCBs occurs in the atmosphere and at water surfaces,

0273-2300/94 $6.00

and photodegradation rates increase as the degree of chlorination increases. Rates of degradation by soil microorganisms and animals, on the other hand, are generally much more rapid for the lesser chlorinated PCBs.

Between the early 1930s and 1972, there were no restrictions on the various commercial uses of PCBs. Their unrestricted use, combined with the physical/chemical properties of some PCBs, has resulted in their widespread distribution throughout the environment. Thus, when analyses for PCBs in the environment were first conducted on a broad scale in the early 1970s, they were found to be ubiquitous in the ecosystem. PCBs have been detected in various tissues (e.g., adipose tissue, liver, blood, human milk) of individuals with no known occupational or unique environmental exposures. Generally, concentrations of PCBs in the tissues are reported to be in the low mg/kg (ppm) ranges in adipose tissues and low μg/kg (ppb) ranges in blood in most human populations. Concentrations of PCBs in various aquatic wildlife (e.g., fish, fish-eating birds) are generally greater than those reported for humans, primarily because of the biomagnification of PCBs in aquatic food chains and the heavy reliance on fish by wildlife, resulting in higher exposures of aquatic wildlife compared to those of humans.

Concentrations of PCBs reported in various environmental media have decreased substantially since their use was controlled in 1972 and production was stopped in 1978. Consistent with the declining concentrations of PCBs in various environmental media, the concentrations of PCBs in tissues and body fluids from humans and aquatic wildlife have also declined substantially since the early 1970s. The rates of decrease of concentrations of PCBs in various environmental media were most rapid in the early 1970s, immediately following restrictions in use. Since the early 1980s, environmental concentrations have continued to decrease, although more slowly than during the 1970s. However, localized areas of higher environmental concentrations remain. Complex mechanisms of environmental mobilization and long-range transport continue to distribute PCBs throughout the environment from large depots in aquatic systems such as the Great Lakes, the Northern Atlantic Ocean, and the Baltic Sea. Since PCBs are no longer produced, environmental concentrations should continue to decline as the PCBs are mobilized from these depots and degraded by natural environmental systems. Active programs are required for the destruction of point sources of PCBs, such as stored old equipment, to eliminate point sources as continuing depots for input into the environment.

Potential Adverse Effects of PCBs in the Environment

As with other chemicals, the potential for adverse effects of PCBs depends on the concentrations that occur in target tissues within organisms. The determination of cause–effect relationships between the potential adverse effects and exposures to PCBs through various environmental media is complicated by at least two factors: (i) the simultaneous occurrence in the environment of a number of other chemicals (some closely related to PCBs) arising from various human activities and natural sources; and (ii) a variety of factors affecting the well being of organisms through changes in habitat quality (e.g., elevated ammonia and decreased oxygen in aquatic systems, and changes in and loss of habitat associated with increased land use for human activity). Laboratory studies, in which these factors can be controlled, demonstrate that PCBs are not particularly potent on a short-term exposure basis; rather, they show a delayed

type of toxicity primarily associated with chronic, long-term exposure. However, a number of toxic effects observed at the upper end of the dose–response curve in laboratory studies may not be relevant to the lower rates of exposure associated with the concentrations of PCBs that typically occur in the environment. All of these factors must be considered in the assessment of potential cause–effect relationships between exposures to the historical, current, and predicted future concentrations of PCBs in the environment and potential adverse effects on the ecosystem, including humans.

The uptake and accumulation of PCBs by animals depend on: (i) the physical/chemical properties of the PCBs, particularly as affected by the degree and pattern of chlorine substitution; and (ii) the rate of exposure resulting from the concentrations of PCBs in environmental media. PCBs with five to seven chlorine atoms have the greatest potential for bioaccumulation and toxicity. The passage of the PCBs through biological membranes is hindered for those with greater than seven chlorine atoms, and those with fewer chlorine atoms are more readily metabolized and excreted. PCBs with chlorine atoms in the *para* and at least one *meta* position (but no *ortho* substitutions) form coplanar structures. These non-*ortho*-substituted PCBs tend to have the greatest potency for enzyme induction and possibly toxic effects in aquatic and likely other organisms.

Based on an evaluation of the available evidence, the toxic effects of most concern from PCBs appear to be associated with the alteration to endogenous enzyme systems important for normal homeostasis of biological systems. Changes in the activity of these enzymes result in a myriad of secondary effects, such as changes in hormone homeostasis, and an array of effects on reproduction, growth and development, and general maintenance of body functions. The coplanar PCBs appear to have greater potential for causing such effects than the nonplanar PCBs. In addition, the coplanar PCBs are believed to act in a manner similar to other polycyclic chlorinated hydrocarbons (PHCs), such as the 2,3,7,8-substituted polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans, and possibly others, regarding the induction of the mixed function oxygenase enzyme systems. However, there are substantial differences in the potency of different PCBs and other PHCs as enzyme inducers. To account for these differences in potency when assessing the potential consequences of the concentrations of these chemicals in the environment, it has been proposed that toxicity equivalency factors (TEFs) be applied to adjust for differences in enzyme induction potency and potentially for toxic effects. Assuming that relative enzyme induction is indicative of toxic potency, the use of TEFs would enable the potential adverse effects of these chemicals to be considered as a group, assuming they act in an additive manner proportional to their 2,3,7,8-tetrachlorodibenzo-*p*-dioxin equivalent (T_4CDD-EQ) concentrations. Although there is considerable evidence supporting this "unified" mechanism of toxic action of these chemicals, the applicability of generalized TEFs with respect to potential toxicity of these chemicals to all species, and the possibility of other mechanisms of action of PCBs that are independent of enzyme induction effects, need to be further addressed before such TEF approaches can be applied to the assessment of potential environmental effects.

As their physical/chemical properties indicate, PCBs tend to accumulate in aquatic sediments. The uptake of PCBs by benthic organisms from such sediments is inversely related to the organic carbon content of the sediments, indicating that the PCBs bound to organic carbon are less bioavailable to these organisms than are PCBs sorbed to noncarbonaceous sediments or extremely low concentrations dissolved in water. Con-

sequently, the bioaccumulation of PCBs occurs primarily through the dietary route of exposure for both terrestrial and aquatic organisms and varies with organism and with the molecular structure of the PCB.

The metabolism and elimination of PCBs vary among life stages, the rates being generally lower at early life stages. During active reproductive stages, female fish eliminate PCBs more rapidly than males, primarily due to distribution to eggs and subsequent elimination from the body. In mammals, including humans, there is a high rate of excretion of PCBs in milk during lactation, associated with milk fat. These factors result in much greater rates of exposures of developing organisms to PCBs than would be expected based simply on concentrations in adult tissues.

PCBs are metabolized by various P450 enzymes. The rate of metabolism depends on the positions of chlorine on the benzene rings. PCBs can induce the various P450 enzymes, thereby influencing the rate of metabolism of endogenous and exogenous chemicals metabolized by these systems, including PCBs. The rate of metabolism of PCBs is inversely proportional to the chlorine content and is also affected by specific isomeric positions of chlorine on the molecules. Those PCBs with lower rates of metabolism tend to accumulate in tissues and bioaccumulate in food chains. It has been suggested that coplanar PCBs show greater bioaccumulation than nonplanar PCBs. However, more recent information suggests that coplanar PCBs do not selectively bioaccumulate.

Mammalian Species

PCBs have relatively little potential for acute toxicity (e.g., LD_{50} values in rats are in the range of 1300 to 11,300 mg/kg, depending on the specific mixtures of PCBs tested). There are marked species differences in the sensitivity to PCBs (guinea pigs are most sensitive, followed by rabbits and rats). The comparative sensitivity of humans to acute effects is not clearly understood. Specific enzyme studies suggest that the sensitivity of humans to enzyme induction by PCBs is in the same range as the rat.

PCBs have been shown to diminish reproductive performance (e.g., decreased fertility and litter sizes) in most animals that have been tested under laboratory conditions; however, teratogenic effects have only been reported in various inbred strains of mice known to be particularly sensitive to birth defects. Developmental effects (e.g., impaired learning, decreased activity, delayed reflex development) have been observed in monkeys and some rodents exposed, during pregnancy, to much greater concentrations of PCBs than those found in the environment. The effects on reproductive performance (and perhaps other systems) are believed to be related to the induction by PCBs of enzyme systems involved in the metabolism of reproductive hormones, thereby altering hormonal homeostasis and affecting reproduction.

Conclusions on the potential carcinogenicity of PCBs are controversial. Most long-term studies of animals indicate that PCBs are not carcinogenic, with the exception of Aroclor 1260, for which laboratory studies suggest that a positive relationship exists between exposures to certain PCBs and incidence of liver cancer. Part of the controversy relates to the designation of hyperplastic lesions that occur in the livers of rodents following exposures to increased (relative to the natural environment) dietary concentrations of PCBs. Although experts on liver toxicology and pathology conclude that these lesions are primarily related to liver toxicity which results in increased cell

proliferation, some researchers have historically classified such lesions as precancerous and indicative of cancer-causing potential. The relevance of these types of hyperproliferative liver lesions to humans is even more speculative because of the differences between humans and rodents in the occurrence of hyperplastic lesions and the occurrence of preinitiated cells in the rat, but not human liver. Considering all the information available from animal and epidemiological studies, including the potential existence of arene oxide metabolites of PCBs, some agencies (e.g., IARC) have classified PCBs as having the potential to cause cancer in humans if rates of exposure were great enough. Other agencies (e.g., EPA, Health Canada) consider that the evidence for carcinogenicity of PCBs in humans is inadequate and consider the potential reproductive effects as the primary hazard of concern.

Most studies on the potential effects of PCBs on genetic material are negative; however, test systems that evaluate chromosomal integrity show positive results following exposures to large concentrations of some specific PCBs. Generally, PCBs are not considered potent genotoxins, and genotoxic effects would not be expected to occur at the low rates of exposure arising from the concentrations of PCBs usually observed in the environment.

Epidemiological studies of populations exposed occupationally to PCBs indicate a variety of skin disorders (e.g., chloracne) and some evidence of abnormal liver function (e.g., hepatomegaly, changes in blood enzymes indicative of liver damage) following extreme rates of exposure (i.e., blood PCBs concentrations generally >200 μg/kg). Based on information on the degree of exposure to PCBs required before adverse effects occurred in such populations, it is unlikely that significant adverse health effects to humans would be associated with the rates of exposure to PCBs from the ambient environmental concentrations observed in the early 1970s in air, water, soils, and fish. Substantial decreases in concentrations of PCBs in the typical human diet in the United States, and corresponding decreases in human exposures through diet, were reported between the early 1970s and the early 1980s. Through the 1980s the concentrations of PCBs in the United States diet continued to decline slowly, such that potential exposures in 1990 were over 100-fold less than those in 1970.

There are concerns regarding potential adverse human health effects from exposures to PCBs that are considerably less than those observed in occupational populations. Lower birth weights and lower head circumferences have been reported in newborn infants born to women consuming large quantities of sport fish relative to populations that did not consume sport fish. People consuming large quantities of sport fish also had greater concentrations of PCBs in their blood (i.e., approximately 21 μg/kg in sport fish consumers compared to 7 μg/kg in populations that did not consume sport fish in 1989). These concentrations of PCBs in blood are within the range reported for the general North American population. Furthermore, no other chemical parameters were measured in these populations, and simultaneous exposures to a variety of other chemicals known to be present in sport fish, together with socioeconomic and lifestyle differences between the sport fish and nonsport fish consumers and poor study design, confound the interpretation of the alleged associations, and preclude the establishment of clear causal relationships of the effects reported and exposures of PCBs. The concentrations of PCBs in blood associated with changes in liver function observed in electrical workers were 10- to 100-fold greater than those reported for populations which consume large quantities of fish. The electrical workers were also exposed simultaneously to other chemicals (e.g., chlorobenzenes which are used as solvents in

PCBs oils); however, other socioeconomic and lifestyle factors were more consistent among the occupational populations studied.

Aquatic and Piscivorous Organisms

The toxic effects of PCBs reported for aquatic organisms are similar to the effects observed in terrestrial mammals. The lethal effects of PCBs are directly proportional to the rate of exposure. Younger animals are more sensitive than adults, and certain lower chlorinated PCBs have greater toxic potency than the more chlorinated PCBs. As with mammals, PCBs are not particularly potent acute toxicants to aquatic organisms. Nonlethal effects, associated with either prolonged exposures or after considerable time periods following short-term exposures, are of primary concern due to their environmental persistence, bioaccumulative potential, and mode of action through alterations of enzyme systems in organisms experiencing sufficient exposures.

Decreased reproductive performance of adults and reduced growth and development of early life stages are considered the most critical toxic endpoints for aquatic organisms and for animals that rely heavily on aquatic environments for food and habitat. The weight of available evidence supports the concept that these effects are directly related to the ability of PCBs to induce various enzyme systems (e.g., mixed-function oxygenase systems involving various P450 enzymes). The primary toxicity and secondary effects result from the increased activity of these enzyme systems on various endogenous chemicals (i.e., reproductive and other hormones) and on the metabolism of many other exogenous chemicals (e.g., polycyclic aromatic hydrocarbons, other chlorinated organic chemicals).

Based on laboratory and field studies, no adverse effects would be expected in aquatic life from exposures to the concentrations of PCBs generally observed in surface waters. However, as with other hydrophobic/lipophilic chemicals, greater exposures of PCBs to aquatic life would occur through diet rather than by direct uptake from water. PCBs have been shown to biomagnify such that greater concentrations occur in aquatic species and fish-eating animals at higher trophic levels. The concentrations of PCBs in higher trophic organisms have declined approximately 10-fold since the early 1970s in predatory fish (e.g., salmonids) and in the eggs of birds that consume fish. Several studies have attributed decreases in populations of fish-eating birds (e.g., herring gulls, double-crested cormorants, bald eagles) between the 1950s and 1970s and their subsequent recoveries since the early 1970s to the presence and subsequent decline in the concentrations of PCBs in these organisms. However, the decline of concentrations of PCBs in aquatic wildlife in the Great Lakes is also coincident with declines in concentrations of hexachlorobenzene, dieldrin, DDE, alkyl mercury, chlorinated dioxins/furans, alkylated lead, and mirex. Few of these studies considered the potential involvement of these or other chemicals.

Recent studies have concluded that the correlations between current concentrations of total PCBs, specific coplanar congeners of PCBs, and total T_4CDD-EQ concentrations in predator fish species (e.g., salmonids) were not sufficiently strong enough to explain decreases observed in egg hatching and fry survival observed in the Green Bay region of Lake Michigan. In addition, the reproductive effects observed in fish-eating and insect-eating birds on the Great Lakes could not be attributed solely to PCBs. Such results indicate that either the ecosystem is recovering and the magnitude of the

responses have decreased to the point where clear causal associations are more difficult to establish, or that other factors, either independently or in combination with PCBs, may be involved in producing the adverse environmental effects. The adverse impacts should continue to decline in the future as the environmental concentrations of PCBs continue to decrease by natural chemical and biological degradation processes, by continued burial through sedimentation, and by appropriate management of specific point sources of PCBs.

Overall Conclusions on the Potential Consequences of PCBs in the Environment

PCBs and certain other chlorinated organic chemicals were formerly used in large quantities and often in what is now known to be an inappropriate manner. Their physical/chemical properties result in their persistence and bioaccumulation in the environment. This led in the 1960s and 1970s to environmental concentrations sufficient to cause adverse effects resulting in declines in the populations of certain species of wildlife, particularly piscivorous birds of the North American Great Lakes. While the effects observed in wildlife are similar to those reported in controlled laboratory studies of PCBs, the effects in the field cannot be solely attributed to PCBs but are likely due to the combined effect of these and other persistent and bioaccumulative chemicals, such as polychlorinated dibenzo-*p*-dioxins (PCDD), polychlorinated dibenzofurans (PCDF), DDT, dieldrin, and hexachlorobenzene. Changes in habitat quality may also have an impact on wildlife population density. As a result of the introduction of appropriate controls, concentrations of these persistent chlorinated organic chemicals in the environment declined during the 1970s and 1980s. Coincident with this decline, populations of several species of piscivorous birds on the Great Lakes are recovering. However, evidence of adverse effects remains in areas of continuing high concentrations of these chemicals. Subtle biochemical effects considered to be associated with chlorinated organic chemicals continue to be observed in piscivorous birds. The significance of these biochemical effects is unclear but they do not appear to be limiting populations of birds in most areas. Environmental release of PCBs, and likely other persistent bioaccumulative chemicals, is expected to decrease further as remaining sources (e.g., waste storage facilities) are eliminated and quantities currently in the environment gradually dissipate.

1. INTRODUCTION

PCBs were first synthesized in 1881 and commercial production began in the United States in 1929. Since their first commercial production, an estimated 1.2 million tonnes of PCBs have been produced worldwide (Tanabe, 1988). The properties of enhanced chemical stability, low solubility in water, low flammability, and excellent insulating properties, provided many commercial advantages for the use of PCBs as heat transfer fluids (e.g., in electrical transformers and capacitors), flame retardants, lubricating and hydraulic oils, additives in plastics, and a myriad of other applications (Pomerantz *et al.*, 1978). These widespread uses, together with their physical/chemical properties, led to their extensive distribution in the environment when first evaluated in the late 1960s. Within a very short time, PCBs were reported in almost every component of the global ecosystem (Tanabe, 1988). In the 1970s, uses of PCBs in open systems were

discontinued, and their use in closed systems was discontinued in 1978. Since 1978, electrical transformers and capacitors have been manufactured with alternative dielectric fluids, and as older equipment containing PCBs is withdrawn from service or for repair, the PCBs fluids are replaced (Safe, 1989).

Due to the widespread occurrence of PCBs in the ecosystem and concern regarding their potential effects on the ecosystem, including humans, considerable effort has been invested by governments and industry throughout the world to understand how PCBs behave and what potential hazards could arise from their presence in the environment and from exposures of various organisms. This chapter presents an interpretive evaluation (compared to an exhaustive literature review) of potential effects of PCBs by an assessment of: (i) potential exposures through an analysis of sources, environmental fate characteristics, and concentrations in various environmental media through which exposures can occur; (ii) potential hazards from PCBs; and (iii) potential risks to various biological systems by the comparisons between their potential exposure from environmental media and the hazard potential of the chemicals.

2. SOURCES, PHYSICAL/CHEMICAL PROPERTIES, AND ENVIRONMENTAL FATE

2.1. Sources

Commercial PCBs are stable, nonflammable, and heat resistant synthetic compounds that have been used historically in various industrial products (Cairns *et al.,* 1986). Since 1972, the use of PCBs has been restricted to controllable closed systems such as transformers and large capacitors (WHO, 1976; Environment Canada, 1988); however, between 1930 and 1972, PCBs were used without restriction in systems that allowed free dissipation in the environment. Some of the products that included PCBs were lubricating and cutting oils, immersion oils, heat transfer and hydraulic fluids, paints, plastics, rubber, waxes, inks, adhesives, sealants, carbonless copying paper, pesticides, antifouling agents, and electrical equipment (Jensen *et al.,* 1972; WHO, 1976; IARC, 1978; Fischbein and Rizzo, 1987).

Estimates of worldwide production of PCBs have been values in excess of 2×10^9 kg (Hutzinger *et al.,* 1974) and 1.2 million tonnes (2.4×10^9 kg) (Tanabe, 1988). There were no restrictions on the use, release, or disposal of PCBs for the first 40 years of production, and it has been estimated that several hundred million pounds of the PCBs produced have been released into the environment (Hutzinger and Veerkamp, 1981). These use patterns, combined with their great stability in the environment (Everaarts *et al.,* 1991), account for the observation that PCBs are now distributed worldwide throughout all environmental ecosystems.

Principal sources of PCBs released to the environment prior to 1972 included leakage and disposal of industrial and municipal fluids, incineration of waste containing PCBs, and disposal in dumps and landfills. Other sources were accidental spills, vaporization from plasticizers, surface runoff, and the release of PCBs in ventilation and exhaust systems from industrial plants (WHO, 1976; Chou and Griffin, 1986; Fischbein and Rizzo, 1987; Environment Canada, 1988).

Since the use, storage, and disposal of PCBs are presently regulated, the future sources of PCBs to the environment will be largely related to various types of accidents

(e.g., transportation spills, transformer fires), improper disposal procedures, release from poorly maintained electrical equipment, clandestine dumping, and environmental dissipation from sites with elevated concentrations of PCBs (Stout, 1986; Fischbein and Rizzo, 1987; Environment Canada, 1988).

In the past, it was believed that there were no natural sources of PCBs; however, PCBs were identified in ash from the 1980 volcanic eruption of Mt. St. Helens. Controlled studies eliminated the possibility that the PCBs identified were from anthropogenic sources. In addition, the three pentachlorobiphenyl isomers identified would not have been expected from commercial PCB mixtures (Pereira *et al.*, 1980). Subunits of PCBs have also been identified as components of glycopeptides identified from *Amycolatopsis* sp. (Box *et al.*, 1991).

The distribution of PCBs from various human activities and to a minor extent from natural sources has resulted in reservoirs of PCBs in the environment. Examples of such reservoirs are the North Atlantic Ocean, fresh water sediments (Fischbein and Rizzo, 1987), and various soils and sludges (WHO, 1976). Continual environmental transport of PCBs occurs based on their physical/chemical properties (e.g., atmospheric transport in gaseous form and in association with particles, deposition from the air onto land and surface water, revolatilization from land and surface waters into the air, transfer from aquatic systems into sediments, etc.) (Atlas *et al.*, 1986; Chou and Griffin, 1986; Sawhney, 1986; Strachan, 1988). The deposition/volatilization cycle of PCBs accumulated in the environment from past human activities continues to disperse PCBs globally even though their distribution, manufacture, and use are restricted or banned.

2.2. Physical/Chemical Properties

Commercial PCB mixtures were prepared by the chlorination of biphenyl and sold based on the percentage of chlorine by weight. For example, there were lesser chlorinated PCB mixtures, such as Aroclor 1221 (21% chlorine), and more chlorinated PCB mixtures, such as Aroclor 1260 (60% chlorine) (Hutzinger *et al.*, 1974). PCB mixtures manufactured by different companies were sold under different trade names (e.g., Aroclors in the United States, Chlophens in Europe, Kanaclors in Japan). Due to the difference in chlorine content, commercial PCB mixtures had markedly different physical/chemical properties as well as different use patterns.

Chemically, there are 209 chlorinated biphenyls ranging in degree of chlorination from the three monochlorinated isomers to the fully chlorinated decachlorobiphenyl isomer. There is also a wide range in the physical/chemical properties of PCBs both within isomeric groups and between congener families.[1] Table 5-1 summarizes the values that were selected by Mackay *et al.* (1992) to best represent the molecular weight, vapor pressure, solubility, and log octanol/water partition coefficient of the PCB congener groups. All properties were chosen to be representative of those that occur at 25°C.

[1] The use of the terms isomer and congener in this chapter are consistent with their use in the dioxin literature. An isomer is a PCB with a specific pattern of chlorine substitution. A congener refers to a group of PCBs all having the same number of chlorine atoms (e.g., 2,2',4,4',-tetrachlorobiphenyl is an isomer; tetrachlorobiphenyl refers to a congener).

TABLE 5-1

SUMMARY OF SELECTED PHYSICAL/CHEMICAL PROPERTIES OF CONGENERS OF PCBs

Congener Group[a]	Molecular Weight (g/mol)	Vapor Pressure (Pa)	Water Solubility (g/m^3)	Log K_{ow}
Monochlorobiphenyl	188.7	0.9-2.5	1.21-5.5	4.3-4.6
Dichlorobiphenyl	223.1	0.008-0.60	0.06-2.0	4.9-5.3
Trichlorobiphenyl	257.5	0.003-0.22	0.015-0.4	5.5-5.9
Tetrachlorobiphenyl	292.0	0.002	0.0043-0.010	5.6-6.5
Pentachlorobiphenyl	326.4	0.0023-0.051	0.004-0.02	6.2-6.5
Hexachlorobiphenyl	360.9	0.0007-0.012	0.0004-0.0007	6.7-7.3
Heptachlorobiphenyl	395.3	0.00025	0.000045-0.0002	6.7-7
Octachlorobiphenyl	429.8	0.0006	0.0002-0.0003	7.1
Nonachlorobiphenyl	464.2	-	0.00018-0.0012	7.2-8.16
Decachlorobiphenyl	498.7	0.00003	0.000001-0.000761	8.26

Source: Mackay *et al.*, 1992.

[a] Ranges given for physical/chemical properties account for differences in properties between different isomers within a congener group.

The information summarized in Table 5-1 indicates a number of relationships between the degree of chlorination and the physical/chemical properties of PCB congeners. As the degree of chlorination increases, both the vapor pressure and the water solubility decrease while the log K_{ow} increases. The vapor pressure varies over almost 100,000-fold from a value of 2.5 Pa for 2-chlorobiphenyl to 0.0003 Pa for the fully chlorinated decachlorobiphenyl. The variation in the solubilities of the PCBs also ranges over approximately 5 million from the most soluble 2-chlorobiphenyl at 5.5 g/m^3 to 1 $\mu g/m^3$ for decachlorobiphenyl. The log K_{ow} of the PCBs varies over approximately four log units (i.e., 10,000-fold) from a value of 4.3 for 2-chlorobiphenyl to 8.26 for decachlorobiphenyl.

It is expected that most of the PCBs in the environment would primarily associate with the organic components of soils, sediments, and biological tissues, or with dissolved organic carbon in aquatic systems, rather than being in solution in water. Despite the low vapor pressure of PCBs, and partly due to their extreme hydrophobicity, PCBs do volatilize from water surfaces, particularly the less chlorinated isomers (Achman *et al.*, 1993). Consequently, atmospheric transport may be a significant pathway for the dispersion or spreading of PCBs in the environment.

2.3. Environmental Fate

PCBs are highly stable under most environmental conditions, although there are substantial differences in stability among different isomers and congener groups. Individual PCBs differ in solubility and vapor pressure and in susceptibility to biodegradation, factors which influence environmental fate (Strachan, 1988). Partitioning of PCBs between environmental media is influenced by various factors, such as sol-

ubility, total organic content of the media, partition coefficients, and degree of chlorination (Chou and Griffin, 1986).

It has been estimated that several hundred million pounds of PCBs have been released into the environment from human activities (Hutzinger and Veerkamp, 1981) since commercial production of PCBs began in 1929 (Tanabe, 1988). During this time, unknown quantities of PCBs were also produced in the environment by natural processes, such as volcanic eruptions. Due to their thermal and chemical stability, concentrations of PCBs in the environment would be expected to change slowly with time (Chou and Griffin, 1986). Nevertheless, concentrations of PCBs in environmental media from certain locations have shown dramatic decreases since their production ceased in 1978. These decreases are due, in part, to sedimentation leading to removal through burial, volatilization from the surface layer of waters and soils and subsequent redistribution and, to a more limited extent, loss through sequential biodegradation. Long-range atmospheric transport continues to distribute PCBs throughout the environment, particularly the lesser chlorinated isomers, from sources related to losses from storage facilities, inadequate disposal sites, and accidental losses from closed systems.

2.3.1. Air

PCBs in the atmosphere exist primarily in the gaseous form (greater than 90%) with a small amount associated with particulate matter (Atlas *et al.*, 1986; Hoff *et al.*, 1992a,b). The amount of PCBs associated with particles is influenced by temperature, with a greater percentage of PCBs adsorbed to particulates at lower temperatures. For example, assuming oceanic total suspended particle concentration to be 7 $\mu g/m^3$, 3.7% of Aroclor 1254 would be bound at 0°C, while only 0.3% would be absorbed to particles at 20°C. An inverse relationship also exists between particle association and vapor pressure. For example, Aroclor 1242, which has a vapor pressure approximately five times greater than Aroclor 1254, would have one-fifth the amount of particle bound PCBs as Aroclor 1254. Seasonal fluctuations in the atmospheric concentrations of PCBs have been observed and show dependence on the vapor pressures of various isomers and on the ambient temperature (Hoff *et al.*, 1992a,b).

The total quantity of PCBs in the atmosphere has been calculated to be 7.7×10^5 kg, by assuming a uniform distribution of PCBs in the troposphere, to a height of 6 km above the earth's surface, an area of 5.1×10^{14} m^2 for the earth's surface, and a conservative estimate of the average concentration of PCBs in the air of 0.25 ng/m^3. Due to the uncertainty of the calculation, the actual quantity of PCBs in the atmosphere has been estimated to be between 10,000 and 100,000 kg (Atlas *et al.*, 1986). Eisenreich *et al.* (1983a), using parameters outlined by Doskey and Andren (1981), estimated the annual total atmospheric input of PCBs to Lake Superior to be 5000 to 7000 kg/year, representing more than 85% of the inputs of PCBs from all sources. Since PCBs are very stable, they can be transported thousands of kilometers (Atlas *et al.*, 1986; Hoff *et al.*, 1992a,b), as demonstrated by the detection of PCBs in remote regions such as Antarctica (Tanabe *et al.*, 1983) and the Arctic (Gregor and Gummer, 1989; Bidleman *et al.*, 1990). However, point sources, such as electrical transformers used in military radar surveillance installations such as the DEWLINE, must also be considered as contributing sources to the concentrations of PCBs observed in the Canadian arctic (Muir *et al.*, 1990).

Vapor pressures of PCBs are small compared to the more volatile chemicals and the vapor pressures of PCBs decrease as the degree of chlorination increases. Thus, volatilization of lesser chlorinated PCBs occurs to a greater degree as compared to the more chlorinated congeners. Although vapor pressures of PCBs are small, because of their hydrophobic nature (relatively low solubility in water), PCBs readily migrate from surface waters and soils via volatilization processes (Sawhney, 1986; Smith *et al.*, 1988). Volatilization of PCBs is reduced when sorbed to soil or sediment (Sawhney, 1986). Murphy *et al.* (1983) determined, using fugacity modeling (see Section 2.4) that there was a net transfer of PCBs from Lake Michigan to the atmosphere, thus suggesting that in situations in which waterborne PCBs are present in sufficient concentrations, they may serve as a source for atmospheric transport. Hornbuckle *et al.* (1993) indicated that concentrations of atmospheric PCB were greater over areas of Lake Michigan where water PCB concentrations were greater, compared to concentrations over land, and that the PCB enrichment of the air samples was primarily due to the lesser chlorinated congeners. The congener distribution of PCBs in the atmosphere was the same as in the surface water samples.

The composition and physical characteristics of the materials to which PCBs are sorbed also influence the rate of vaporization. For example, after a 4-week period, 60% of Aroclor 1254 was lost from Ottawa sand by vaporization, while vapor loss from Woodburn soil, which has a greater percentage of organic matter, was insignificant (Haque *et al.*, 1974). Mackay and Leinonen (1975) determined a half-life of 10 hr for PCBs in a well-mixed body of water 1 m deep. Factors governing volatilization of PCBs from surface waters include the vapor pressure of the isomers, the depth of water column, the concentrations of PCBs in the water column, wind, and water turbulence (Strachan, 1988). Transfer of PCBs between air and soil onto plants is assumed to occur based on a deposition/volatilization cycle (Strachan, 1988).

PCBs have also been detected in surface waters of oceans (Giam *et al.*, 1978; Tanabe *et al.*, 1982; deLappe *et al.*, 1983). The major mechanisms by which PCBs are transferred from the air to the ocean are gas exchange during dry deposition and partitioning during wet deposition whereby precipitation scavenges the PCBs bound to particulate materials in the air (Atlas *et al.*, 1986). Factors that affect the dry deposition rate include meteorological variables (e.g., aerodynamic surface roughness, friction velocity, wind speed), properties of the chemical (e.g., diameter, density, shape, and size), and surface characteristics (e.g., canopy structure and electrostatic properties) (Sehmel, 1980). Bulk collectors are most often used to measure total deposition (wet plus dry deposition). It is very difficult to measure accurately the dry deposition rates of particles onto natural surfaces (Whelpdale, 1976); consequently, most studies use artificial collecting surfaces. As a result, it is difficult to determine how well such measurements represent actual deposition velocities, and studies using this type of technique should be interpreted with caution (Sehmel, 1980; NRCC, 1981).

Early studies of atmospheric deposition rates of PCBs focused on wet deposition. It is only within the past decade that the importance of dry deposition has been appreciated. Only through dry deposition are airborne substances continually removed near ground level. Removal by wet deposition is not continuous (Sehmel, 1980). In dry climates, dry deposition is generally considered more important than is wet deposition for the total removal of airborne chemicals (Marenco and Fontan, 1976; Sehmel, 1980, 1984); however, the contribution of wet deposition increases with in-

creasing quantities of annual precipitation. The dry deposition velocity of PCBs was estimated by Atlas *et al.* (1986) to be approximately 2.0×10^{-3} m/sec.

2.3.2. Water/Sediment

PCBs are relatively insoluble in water and have a high octanol:water partitioning coefficient (K_{ow}). Generally, the solubility of PCBs in water decreases and the K_{ow} increases as the degree of chlorination increases. PCBs with greater amounts of chlorine, therefore, readily adsorb to particulate matter and are removed from the water column into the sediment. Thus, sorption of PCBs to organic matter of soils, sediment, or dissolved organic matter is the major route, not involving destruction, by which PCBs in aquatic environments are immobilized (Chou and Griffin, 1986; Smith *et al.*, 1988).

Upon introduction to the aquatic environment, PCBs readily partition between the water column and the sediment (Pavlou and Dexter, 1979; Phillips, 1986). Due to their hydrophobicity, PCBs adsorb to dissolved organic material (DOM) and organic carbon of suspended particulates in the water column, DOM in the pore water and organic carbon of the bed sediments, and fatty tissues of aquatic biota. Lesser chlorinated PCBs remain in solution longer (Haque *et al.*, 1974; Haque and Schmedding, 1976) and are expected to be transported further, via advection, than more chlorinated PCBs (Phillips, 1986). This principle was demonstrated in a study by Richardson and Waid (1980), in which the concentrations of PCBs were measured in sediments at varying distances from a shore-based point source. A larger proportion of PCBs with more chlorine was observed in sediments nearer the source of discharge as compared to sediments obtained further offshore.

It has been proposed that a film exists at the water surface which has a greater concentration of PCBs than does the subsurface water, due to the extreme hydrophobic nature of PCBs. The partitioning of PCBs between water and air would be controlled by relative concentrations of PCBs in water and air, the relationship between water solubility and vapor pressure of PCBs, and the specific characteristics of the water (e.g., dissolved and particulate-form organic carbon content). Concentrations of PCBs at the sediment/water interface in Green Bay, Lake Michigan had an evenly distributed congener profile, but PCBs measured in the vapor phase above the water surface largely consisted of the less chlorinated congeners (Hornbuckle *et al.*, 1993). Quantitatively, the less chlorinated PCBs volatilize from water bodies to a greater extent than the more chlorinated PCBs, and concentrations in air are linearly correlated to concentrations in dissolved water (Achman *et al.*, 1993; Hornbuckle *et al.*, 1993). Congener profiles for both air and dissolved in water consisted of primarily the less chlorinated PCB congener groups. However, since the more chlorinated PCB congeners are persistent in the environment compared to the less chlorinated congeners, even a small amount of volatilization from the water surface would be a significant transport mechanism for these congener groups.

Since PCBs would disperse more rapidly in air than in water, and since it is proposed that their concentrations may be greater in water surface films (Rice *et al.*, 1982, 1983), PCBs in water would tend to volatilize and partition into the atmosphere above the water surface (Raybaud, 1972; Pavlou and Dexter, 1979; Sodergren and Larsson, 1982; Phillips, 1986; Achman *et al.*, 1993; Hornbuckle *et al.*, 1993). These factors may also be important in the volatilization of PCBs from very thin water films on soils and plants.

The partitioning of PCBs between water and air would also be affected by the particulate content of the water. At normal suspended particulate loads, as in coastal waters, less than 20% of PCBs adsorb onto inorganic particulate matter (Pavlou and Dexter, 1979; Phillips, 1986). The bulk of particulate adsorbed PCBs is associated with the organic carbon fraction (Hamelink *et al.,* 1971). Therefore, the partitioning behavior of PCBs would be expected to vary with the dissolved and particulate organic carbon concentrations in water.

Resuspension of PCBs from sediment into the water column (mainly adsorbed to dissolved or particulate-form organic carbon), due to bioturbation by macroinvertebrate fauna, has been demonstrated (Sodergren and Larsson, 1982). Bioturbation promotes a flux system which impedes sedimentation or burial and promotes the retention of PCBs in the aquatic food chain (Krantzberg, 1985). PCBs have a greater affinity for lipid reservoirs of aquatic biota than their water or protein components, and the concentrations of PCBs in aquatic organisms have been reported to be as much as one million times greater than water concentrations (Smith *et al.,* 1988).

2.3.3. Soil

The affinity of PCBs for materials with larger quantities of organic carbon in water and sediment, as discussed in the previous section, is also applicable to soils (Hamelink *et al.,* 1971). In soil–water systems, PCBs partition toward soil particles, and greater quantities of PCBs end up on soil particles rather than the associated water in soils or sediments (Oloffs *et al.,* 1972; Haque *et al.,* 1974; Moein *et al.,* 1976; Paris *et al.,* 1978).

As with the sorption to airborne particles, the degree of soil sorption of PCBs is influenced by the characteristics of the soils, such as organic matter and clay content (e.g., PCBs sorption is greater in Medium Temperature Coal Char followed, in order, by High Temperature Coal Char, Catlin Soil, Montmorillonite Clay, and Ottawa Silica Sand). Also, the amount of PCBs sorbed, regardless of soil type, is less under conditions of low temperature ashing (Tucker *et al.,* 1975; Chou and Griffin, 1986). Lee *et al.* (1979) reported significant correlations between the sorption constant of PCBs and both total organic carbon (TOC) and surface area; however, the magnitude of the coefficients indicated that TOC was the most important soil factor in determining sorption of PCBs.

PCBs with greater amounts of chlorine are preferentially sorbed by soils compared to PCBs with a lesser degree of chlorination (Haque and Schmedding, 1976; Griffin and Chian, 1979; Lee *et al.,* 1979). The extent of sorption varied for individual congeners and was determined to be greatest for hexachlorobiphenyl isomers followed by tetrachlorobiphenyl isomers, and then dichlorobiphenyl isomers (Haque and Schmedding, 1976). However, in situations in which soils/sediments become saturated with PCBs, such as from a spill, the gradual desorption of PCBs into air and water may occur for several years (Veith and Comstock, 1974; Chou and Griffin, 1986). This phenomenon was observed when exposure of oysters to PCBs was attributed to the desorption of PCBs from the sediment into the porewater syphoned by the bivalves (Wilson and Forester, 1978).

Due to their nonpolar characteristics which are largely responsible for their low water solubility, PCBs do not generally leach from soils using water or other aqueous

solutions as leaching agents; however, PCBs are readily mobilized from soils using organic solvents as leaching agents (Griffin *et al.*, 1979). Studies of this phenomenon were conducted using thin-layer chromatography, with the soil as the sorbent phase and various solutions, such as water, landfill leachate, organic solvents, etc., as the mobile phase (Griffin *et al.*, 1979). With this technique it was found that Aroclor 1242 and Aroclor 1254 were immobile in soil materials leached with water or landfill leachate but very mobile in soils leached with the organic solvent, carbon tetrachloride (Griffin and Chian, 1979). Similar results were obtained by Griffin *et al.* (1979) using silica gel and the solvents acetone, methanol, benzene, and carbon tetrachloride. Mobility is related, therefore, to the organic carbon content of the soil and the relative solubility of the PCBs in the leaching solvent (Chou and Griffin, 1986).

Although PCBs have a low degree of mobility in soils leached with water, downward leaching of PCBs in soil may occur to some extent, depending on soil characteristics and the PCB mixture. Moza *et al.* (1976) demonstrated the downward movement of PCBs using 2,2'-dichlorobiphenyl in loamy sand. At the end of the first year, the PCBs had dispersed to a depth of 30 cm. By the end of the second year, small but detectable amounts of PCBs had moved deeper than 40 cm below the soil surface. Since the degree of chlorination influences water solubility and susceptibility to microbial transformation, the lesser chlorinated congeners are more readily leached through soils and more rapidly transformed by soil microbes (Tucker *et al.*, 1975; Suzuki *et al.*, 1977). These factors result in the more resistant PCBs (i.e., those with greater degrees of chlorination) dominating the congener mixtures at soil surfaces (Chou and Griffin, 1986).

As discussed previously, vaporization processes are responsible for the transport of PCBs from soils to the atmosphere; however, the rate of vaporization is also influenced by the adsorption characteristics of soils (Chou and Griffin, 1986). Therefore, the greater vapor loss of Aroclor 1254 from sandy soils, compared to organic soils, would be the result of poor sorption capacity of the sandy soil (Haque *et al.*, 1974). The rate of volatilization of PCBs from soil decreases as the organic content of the soil increases. In addition, the movement of PCBs in soils may occur by vapor phase transport through unsaturated pores within the soil matrix (Chou and Griffin, 1986).

Transport of PCBs from soils to plants may occur. There is a paucity of information concerning the fate of PCBs in plants, and it is unclear whether PCBs are translocated through plants (Sawhney, 1986). Studies of plants growing on soils containing PCBs have demonstrated that their concentrations in plants are inversely related to the degree of chlorination of PCBs present in the soil (Iwata and Gunther, 1976; Suzuki *et al.*, 1977; Sawhney and Hankin, 1984).

It is not known whether PCBs are directly taken up by plant root systems or whether they are associated with the plant only by the soil adhering to the root surface. Several authors have reported residues of PCBs on plant roots and tuberous vegetables grown in soils containing PCBs (Jordan, 1977; Suzuki *et al.*, 1977; Chou and Griffin, 1986). However, Iwata *et al.* (1974) observed that carrots grown in soils containing PCBs had 97% of the Aroclor 1254 on the carrot peel, while 3% was actually translocated into the carrot tissue. In addition, Fries and Marrow (1981) reported that root uptake and translocation of PCBs from soil by soybean plants was not measurable and concluded that the PCBs detected on plant foliage were due to vaporization of PCBs from the soils. However, uptake from dust and soil particles deposited on plants must also be considered.

2.3.3.1. Phototransformation

PCBs undergo photolysis in the presence of ultraviolet (uv) light, and the rate of photolysis depends on the degree of chlorination and on the isomeric position of the chlorine on the PCBs. Laboratory experiments using mercury lamps, high energy uv radiation, or uv fluorescent lamps have demonstrated that photolytic dechlorination of PCBs occurs primarily through reductive dechlorination (C–Cl bond cleavage) (Safe and Hutzinger, 1971; Sawhney, 1986), although photo-induced isomerization and condensation of PCBs may also occur (Sawhney, 1986). The rate of photochemical degradation of PCBs increases with increasing degree of chlorination (Hannan *et al.*, 1973; Hutzinger *et al.*, 1974; Ruzo *et al.*, 1974; Bunce *et al.*, 1978) and is more rapid for *ortho*-substituted chlorine, followed by *meta* and then *para* substitution (Ruzo *et al.*, 1974; Bunce *et al.*, 1978).

Similarly, in the environment, PCBs with a high degree of chlorination are also photolyzed more rapidly (Bunce *et al.*, 1978). Based on dissolved concentrations of PCBs in water, Bunce *et al.* (1978) estimated a wide range of loss due to photolysis, ranging between 10 and 1000 g PCBs/km^2/year from natural waters. The proposed larger concentrations of PCBs at water surfaces would facilitate the photolysis of greater amounts of PCBs in surface waters (Bunce *et al.*, 1978; Sawhney, 1986). However, due to the wide variability in surface water characteristics and the wide range in total loss due to photolysis, its contribution to complete degradation of PCBs in the aquatic environment is probably small (Strachan, 1988).

In the atmosphere, direct phototransformation of vaporized PCBs occurs upon absorption of sunlight. PCBs are transformed by dechlorination, hydroxylation, or arylation, with dechlorination (i.e., the cleavage of the C–Cl bond) being the major mechanism of photodegradation. The half-life for 2-chlorobiphenyl and 4-chlorobiphenyl in air was estimated to be approximately 10 to 25 hr of direct noontime summer sunshine, which equates to several days (Bunce *et al.*, 1989). Thus, the PCBs that volatilize into the atmosphere are degraded by uv radiation such that their existence in the atmosphere is limited. Although long-range atmospheric transport has been suggested to be an important transport mechanism for PCBs (Atlas *et al.*, 1986; Hoff *et al.*, 1992a,b), Hornbuckle *et al.* (1993) found that atmospheric PCBs from adjacent industrialized areas had little to no impact on atmospheric PCBs measured over Green Bay, supporting the theory that PCBs are phototransformed in the atmosphere. The significance of atmospheric transport of PCBs may have been masked in this study, however, by the magnitude of Green Bay as a source of atmospheric PCBs.

Photolysis of PCBs can be enhanced by the presence of natural substances or organic compounds, such as suspended materials, humic acids, triethylamine, aliphatic, and aromatic amines, which sensitize the photoreaction in PCBs by creating an excited charge–transfer complex (Ohashi *et al.*, 1973; Nordblom and Miller, 1974; Zepp *et al.*, 1981a,b; Occhiucci and Patacchiola, 1982).

2.3.3.2. Microbial Transformation

Aerobic and anaerobic biogenic degradation of PCBs has been observed in sediments of freshwater lakes and rivers and in soils. Aerobic biotransformation of PCBs has been well studied (Furukawa, 1982, 1986; Abramowicz, 1990; Bedard and Haberl,

1990). Since PCBs in the environment exist as complex mixtures of several different congeners with varying degrees of chlorination, their biogenic degradation requires broad-acting enzyme systems, and specific enzyme systems. Naturally occurring microorganisms, ranging from common soil bacteria to fungi, have been shown to metabolize defined mixtures of PCBs under laboratory conditions. Many of these bacteria have been isolated from soils and sediments from sites with elevated concentrations of PCBs, thereby indicating that PCB-metabolizing microorganisms are quite common in the environment. These organisms tend to demonstrate congener specificity and metabolize individual congeners at different rates. The majority of these aerobic bacteria metabolize only the less chlorinated congeners (e.g., mono- to tetra-substituted) (Ahmed and Focht, 1973; Baxter *et al.*, 1975; Metcalf *et al.*, 1975; Tucker *et al.*, 1975; Furukawa and Matsumura, 1976; Furukawa *et al.*, 1978; Clark *et al.*, 1979; Liu, 1982; Hankin and Sawhney, 1984), although certain bacterial strains have been reported to metabolize a larger range of congeners, including penta-, hexa-, and heptachlorobiphenyls (Furukawa *et al.*, 1978; Bopp, 1986; Bedard *et al.*, 1987a,b).

A study of the effect of chlorine substitution on rate of transformation was conducted by Furukawa *et al.* (1978) in which 33 PCBs were metabolized by the bacterial strains *Alcaligenes* sp. and *Acinetobacter* sp. This study demonstrated not only that the rate at which the PCBs were metabolized decreased as the degree of chlorination increased, but that PCBs containing two chlorines in *ortho* positions were resistant to biotransformation (with the exception of 2,4,6-trichlorobiphenyl) (Furukawa *et al.*, 1978). Furthermore, PCBs with all chlorines on the same ring were metabolized faster than PCBs from the same congener groups but with chlorine substitution on both rings. The authors also reported that tetra- and pentachlorobiphenyls with chlorines at both the 2- and 3-positions of one ring are more susceptible to microbial action than other tetra- and pentachlorobiphenyls, and that ring cleavage primarily occurs with nonchlorinated or lesser chlorinated biphenyl molecules (Furukawa, 1986). These findings are supported by studies showing notable differences between bacterial strains in their relative ability to metabolize mono- and dichlorophenyl groups and in the degree to which the biotransformation was affected by the chlorine substitution pattern on the nonreacting ring (Bedard and Haberl, 1990).

Based on the observations summarized above, it has been proposed that the eight bacterial strains (*Corynebacterium* sp. MB1, *Alcaligenes* strains *A. eutrophus* H850 and *A. faecalis* Pi434, and *Pseudomonas* strains LB400 and H1130, *P. testosterone* H430 and H336, and *P. cepacia* H201) represent four distinct classes of biphenyl/PCBs dioxygenase activity (Bedard and Haberl, 1990). Furthermore, the types of breakdown products were strain independent and were determined primarily by the chlorine substitution pattern on the reacting ring. The major aerobic microbial breakdown products were chlorobenzoic acids and chloroacetophenones (Bedard and Haberl, 1990), which are susceptible to further microbial degradation and complete mineralization.

In general, the aerobic degradation of PCBs involves the addition of O_2 at the 2,3 positions by a dioxygenase enzyme, with subsequent dehydrogenation to the catechol followed by ring cleavage (Abramowicz, 1990). The ring fission product is further metabolized to chlorobenzoic acid (Furukawa *et al.*, 1978). This degradation pathway is the same as that determined for biphenyl and other aromatic hydrocarbons. The genes encoding the PCB degradation have been identified and appear to be similar in otherwise unrelated organisms which also possess this degradation pathway. This find-

ing suggests that horizontal transfer of these genes is occurring in the environment. In addition, recombinant *Escherichia coli* strains capable of degradation of PCBs have been constructed with optimal environmental survival characteristics, a feature that could be advantageous in soil remediation applications (Mondello, private communication; Mondello 1989).

Other routes of metabolism of PCBs may also exist. For example, *A. eutrophus* H850 and *Pseudomonas* sp. LB400 use a novel 3,4-dioxygenase degradation pathway, which results in a *cis*-dihyhrodiol intermediate from 2,5,2′,5′-tetrachlorobiphenyl (Nadim *et al.,* 1987). Although the majority of these aerobic microorganisms do not metabolize PCBs beyond chlorobenzoate, many other common soil microorganism are known to mineralize chlorobenzoates (Dorn *et al.,* 1974; Shelton and Tiedje, 1984).

The filamentous fungus, *Aspergillus niger*, and the wood-decay white-rot fungus, *Phanerochaete chrysosporuim*, have been demonstrated to degrade PCBs, although only at low concentrations (i.e., ppb) (Bumpus *et al.,* 1985; Bumpus and Aust, 1987; Dmochewitz and Ballschmiter, 1988). Complete mineralization of the greater chlorinated PCBs has been demonstrated, including 3,4,3′4′-tetrachlorobiphenyl (Bumpus *et al.,* 1985), 2,4,5,2′,4′,5′-hexachlorobiphenyl (Bumpus and Aust, 1987), and the mixture Aroclor 1254 (Eaton, 1985) by *P. chrysosporium.* Complete mineralization by fungi has only been observed at 250 ppb Aroclor 1254 (Eaton, 1985) and 5.5 ppb 3,4,3′,4′-tetrachlorobiphenyl (Bumpus *et al.,* 1985), in comparison with the activities of bacteria which have been observed at much higher concentrations [10,000 ppb Aroclor 1254 with H850 (Bedard *et al.,* 1987a), 1800 ppb 2,4,5,2′,4′,5′-hexachlorobiphenyl with LB400 (Bopp, 1986) and 15,000 ppb 3,4,3′,4′-tetrachlorobiphenyl with P6 (Furukawa *et al.,* 1979)]. No aerobic microorganisms have been identified that are capable of degrading the greater chlorinated commercial mixtures Aroclor 1260 or Clophen A60 (Abramowicz, 1990).

Until recently, little was known about the fate of PCBs in anaerobic environments. Alterations in the congener profiles of PCBs, involving the extensive removal of greater chlorinated PCBs congeners with corresponding increases in mono- and dichlorobiphenyls, have been observed in anaerobic river and lake sediments. The most notable study was on Hudson River sediments which were originally contaminated with Aroclor 1242 between 1951 and 1973. Subsurface sediment samples collected in the late 1980s demonstrated a depletion of the tri-, tetra-, and pentachlorobiphenyls present in Aroclor 1242 and a corresponding increase in the proportion of mono- and dichlorobiphenyls (Quensen *et al.,* 1988). Furthermore, the observed degradations appeared to be congener specific with selective removal of chlorine atoms substituted in the *meta* and *para* positions. No known degradation processes could account for these alterations; hence, it was postulated that anaerobic microorganisms present in the sediments were reductively dechlorinating the PCBs (Brown *et al.,* 1984). Reductive dechlorination of aromatics (i.e., chlorinated phenols and chlorinated quinones) by aerobic and anaerobic bacteria has been reported (Abramowicz, 1990). The reductive dechlorination of PCBs in Aroclor 1242 by anaerobic microorganisms from Hudson River sediments was confirmed in the laboratory (Quensen *et al.,* 1988). Rapid dechlorination of PCBs occurred at 700 ppm Aroclor with 53% loss of the total chlorine in 16 weeks and a corresponding increase in the proportion of mono- and dichlorobiphenyls from 9 to 88%. Dechlorination occurred selectively from the *meta* and *para* positions and only congeners with chlorine substitution in the *ortho* position(s) accumulated. A sequential

pathway was observed as follows, with these major transformation products: Penta-(2,3,4,3′,4′-pentachlorobiphenyl) to tetra-(2,4,3′,4′-tetrachlorobiphenyl), tri-(2,4,3′-trichlorobiphenyl), di-(2,3′-dichlorobiphenyl), and mono-(2-monochlorobiphenyl). In general, the anaerobic microorganisms exhibit a broad dechlorination activity on the greater chlorinated PCBs, including those formerly considered recalcitrant in Aroclor 1260 (Abramowicz, 1990).

The most toxic congeners of PCBs contain chlorines in two *para* and at least two *meta* positions; the addition of chlorine in the *ortho* position reduces the toxicity significantly (Safe *et al.*, 1985). Therefore, although the molar concentration of PCBs would remain the same, anaerobic reductive dechlorination would significantly decrease the mammalian toxicity of the residues of PCBs. Furthermore, the removal of chlorine atoms from the *meta* and *para* positions would result in intermediate residues of PCBs that are readily degradable by aerobic bacteria by 2,3-dioxygenase or 3,4-dioxygenase attack. The environmental dechlorination of PCBs has been observed in a number of contaminated anaerobic sediments including the Hudson River, NY, Silver Lake, MA, New Bedford Harbor, MA, Escambia Bay, FL, Woods Pond, MA, the Housatonic River, CT, the Sheboygan River, WI, Waukegan Harbor, IL, and the Hoosic River, MA (Abramowicz, 1990). From these observations it is concluded that the microorganisms capable of the dechlorination of PCBs appear to be widespread and most PCBs can be biodegraded by a sequential anaerobic–aerobic process.

Although PCBs can be transformed by photolysis and microbial activity (Hooper *et al.*, 1990), these processes may be relatively slow in the natural environment; thus, the environmental fate of PCBs is primarily influenced by physical processes such as atmospheric transport and sedimentation.

2.4. Fugacity Modeling

The term fugacity, as discussed by Mackay (1979) and Mackay and Paterson (1981), is described as a measure of the escaping tendency of a chemical in an environmental medium. When introduced to the environment, a chemical is transferred to various media, based on fugacity. At equilibrium, the fugacity of a chemical is equal in all environmental compartments (Murphy *et al.*, 1983).

Several Levels (I, II, and III) of fugacity modeling can be used to predict the partitioning, movement, and behavior of chemicals within different environmental media based on the specific physical properties of chemicals. The results of Level I, II, and III fugacity modeling for some specific polychlorinated biphenyls have been reported by Mackay *et al.* (1992). The reader is referred to this detailed publication for a more comprehensive discussion of PCB fugacity modeling.

Briefly, fugacity Level I results indicate that the lesser chlorinated congeners tend to partition to soil and air, compared to the more chlorinated congeners which tend to partition almost exclusively to the soil. Fish, water, and suspended sediments account for a minor part (less than 0.1%) of the total distribution in terms of number of moles present. However, the total volumes for fish and suspended sediments are small compared to the other four compartments and, as a result, relatively greater concentrations of PCBs could occur in fish and suspended sediments.

The Level II fugacity modeling results reported by Mackay *et al.* (1992) indicates that atmospheric removal processes are significant, particularly for the lesser chlorinated

congener groups, but for the more highly chlorinated congener groups as partitioning into air becomes negligible, reaction in soil dominates the removal processes. Removal by advection (i.e., physical transport of PCBs in environmental media) dominates over removal by reaction (i.e., chemical or biological degradation of the PCB molecule) for virtually all media and isomer/congener types.

The Level III fugacity modeling results demonstrate that the rate of transport between media changes with chlorine substitution. For the less chlorinated PCBs, the rates of transport are greatest to the water, and to a lesser extent, the air. Consequently, the amount of PCBs is greatest in these compartments. For the more chlorinated congeners, the rate of transport is greatest from the water to the sediment; thus, the amount of PCBs is greatest in the sediment compartment.

The behavior of PCBs predicted by fugacity modeling is consistent with their observed behavior in the environment. PCBs tend to accumulate and persist in soils and sediments. The fugacity modeling results for PCBs provide a reasonable prediction of the expected environmental fate of PCBs and are compatible with the information discussed in Section 3 on the concentrations of PCBs in various environmental media. The validation of models for the prediction of the environmental fate of chemicals is important to the utilization of such tools for the prediction of how new organic chemicals will behave in the environment, prior to their commercial production and use. The success of such preproduction and use screening procedures is critical to ensuring that problems, as typified by PCBs, will be avoided in the use of new chemical products in the future.

3. HAZARD ASSESSMENT AND SIGNIFICANCE OF ENVIRONMENTAL CONCENTRATIONS

In the previous section, the various sources that can result in the release of PCBs into the environment and how PCBs partition into various environmental compartments based on their physical/chemical properties were discussed. In this section, environmental concentrations are compared to doses or concentrations that cause adverse effects in humans, aquatic, and terrestrial wildlife. In addition, the concentrations of PCBs in different environmental compartments are compared with environmental concentrations considered not to be associated with adverse effects on the physical environment.

3.1. Environmental Concentrations

PCBs can be found in virtually all environmental media from urban to rural sites. Table 5-2 summarizes some of the published data on the concentrations of PCBs in various environmental media. A temporal trend toward increasing concentrations of PCBs in the environment is evident for the period up to the mid-1970s, after which time the concentrations in most environmental compartments have been decreasing. This trend is most evident in sediment records (one of the major environmental compartments for PCBs and also a medium in which time trends can be more readily determined), and to a lesser extent, it is evident in precipitation records.

TABLE 5-2

CONCENTRATIONS OF POLYCHLORINATED BIPHENYLS BY MEDIA TYPE

Medium	Value	Units	Date	Comments	Reference
Soil	4,400-99,000	μg/g	1981	samples taken from contaminated New England industrial site	Weaver, 1984
	0.015	μg/g	< 1985	Oakville, Ontario	Canviro, 1985
Sediment	11	ng/g	1943	L. Superior	Eisenreich *et al.*, 1983
	17.5		1950		
	22		1955		
	44.8		1961		
	61		1965		
	64		1967		
	88.5		1970		
	109		1972		
	76		1975		
	19.2	ng/g	1971-1981	Dark Lake, Wisconsin	Swackhamer and Armstrong, 1986
	20.4		1962-1971		
	8.8		1948-1962		
	2.2		1935-1948		
	89.0	ng/g	1975-1978	Emrick Lake, Wisconsin	Swackhamer and Armstrong, 1986
	12.8		1971-1975		
	12.7		1963-1971		
	26.3		1954-1963		
	13.3				
	2.6	ng/g	1978-1982	Little Pine Lake, Wisconsin	Swackhamer and Armstrong, 1986
	7.8		1974-1978		
	2.8		1965-1974		
	91.1	ng/g	1964-1980	L. Michigan	Swackhamer and Armstrong, 1986
	54.8		1949-1967		
	42.0		1934-1952		
	18.6		1919-1937		
	7.6		1904-1922		
	0.71-0.81	μg/g	1992	Green Bay, Wisconsin	Ankley *et al.*, 1992
	0.8-0.9	ng/g	1975	Mediterranean surface sediments	Fowler, 1987
	1.5-33		1976		
	0.6-8.9		1977		

3.1.1. Remote Locations

PCBs are present in most environmental media in remote areas throughout the world. Sediment, air, water, and precipitation samples taken at Siskiwit Lake, a remote lake on an island in Lake Superior in Northern Ontario with no point sources of PCBs, show small but measurable concentrations of PCBs (Swackhamer *et al.*, 1988). Concentrations at Siskiwit Lake were reported to be 48 ng/g in sediment, 0.59 to 2.8 ng/m^3 in air, 2.3 ng/liter in surface water, and 13 to 17 ng/liter in precipitation. Snow, air, and water samples from the Canadian Arctic also contained measurable concentrations of PCBs, with concentrations of 0.079 to 7.3 ng/liter in snow, 4 to 16 pg/liter in surface waters, and <9 pg/m^3 in air (Hargrave *et al.*, 1988).

TABLE 5-2—*Continued*

Medium	Value	Units	Date	Comments	Reference
			1984	L. Ontario	Oliver and Niimi, 1988
	nd	ng/g		dichl	
	22			tricl	
	200			tetracl	
	180			pentacl	
	93			hexacl	
	48			heptacl	
	22			octacl	
	570			total	
				susp.sed	
	5.4			dichl	
	27			tricl	
	120			tetracl	
	130			pentacl	
	81			hexacl	
	44			heptacl	
	20			octacl	
	440			total	
	0.2-480,000	ng/g	< 1990	Atlantic;	Fowler, 1990
	0.3-7,420			Mediterranean;	
	0.5-2,000			Pacific;	
	11.5-134			North Sea;	
	8.4-212			Baltic Sea; coastal and near shore sediments	
	46-60	ng/g	< 1983	Gulf of Finland;	Perttila, 1985
	5-15			Gulf of Bothnia	
	190-190,000	μg/g	1981	contaminated New England industrial site	Weaver, 1984
	5.32-11.73	ng/g	1986	L. Superior	Baker and Eisenreich, 1989
	1,300-1,900	ng/g	1982-1983	L. Ontario	Oliver *et al.*, 1989
	350-570		1983-1984		
	410-680		1984-1985		
	80-290		1981-1986		
	48	ng/g	1983-1984	Siskiwit Lake (L. Superior)	Swackhamer *et al.*, 1988
	6.9-3,154.9	ng/g	< 1991	Nile Delta sites	El-Gendy *et al.*, 1991
	28	μg/kg	1976-1979	Eastern Adriatic	Picer and Picer, 1991
	23		1980-1983		
	16		1984-1986		
	10		> 1986		

3.1.2. Agricultural Locations

Air concentrations of PCBs in American and Canadian rural areas where agriculture is practiced ranged from 0.19 to 5.4 ng/m^3 (Bidleman and Christensen, 1979; Singer *et al.*, 1983; Canviro, 1985). Concentrations of PCBs in surface water ranged from 1 to 80 ng/liter (Eisenreich and Johnson, 1983; Hargrave *et al.*, 1988). Rain and snow had concentrations ranging from 0.6 to 50 ng/liter (CanViro, 1985; Strachan, 1985).

TABLE 5-2—*Continued*

Medium	Value	Units	Date	Comments	Reference
	2.1-379	ng/g	1988-1989	Finnish Lakes	Paasivirta *et al.*, 1990
	34 (12-51) 29 300 (140-660) 131 (38-190) 91 (37-140)	ng/g	1980	L. Huron; L. St. Clair; western L. Erie; central L. Erie; eastern L. Erie; mean (range)	Oliver and Bourbonniere, 1985
	10.0-530.0	ng/g	1985	St. Lawrence River	Kaiser *et al.*, 1990
	10-600	ng/g	1979	Thunder Bay, Ontario	MOE, 1986
Air	0.17-1.26	mg/m^3	1977	contaminated New England industrial site	Weaver, 1984
	9.63	ng/m^3	< 1985	Toronto, Ontario	Canviro, 1985
	0.44	ng/m^3	< 1979	rural South Carolina	Bidleman and Christensen, 1979
	0.19	ng/m^3	< 1983	rural Ontario	Singer *et al.*, 1983
	0.13-6.2 0.54-5.9 0.19-5.4 0.14-7.6 9.6	ng/m^3	< 1985	urban suburban rural industrial Toronto, Ontario	Canviro, 1985
	2.8 0.59	ng/m^3	1983-1984	summer; winter; Siskiwit Lake	Swackhamer *et al.*, 1988
	670	pg/m^3	1987	urban Germany	Ballschmiter and Wittlinger, 1991
	< 2-9	pg/m^3	1986	Canadian Arctic	Hargrave *et al.*, 1988
Drinking Water	< 20	ng/L	< 1988	Grimsby, Ontario Water Treatment Plant	MOE, 1988
Surface Water	1-10	ng/L	< 1983	Great Lakes	Eisenreich and Johnson, 1983
	0.018 0.150 0.300 0.390 0.160 0.054 0.010 1.100	ng/L	1984	L. Ontario dichl tricl tetracl pentacl hexacl heptacl octacl total	Oliver and Niimi, 1988

3.1.3. Urban Locations

As is the case for most chemicals used in society, the concentrations of PCBs in various environmental media are generally greater in and around urban areas. PCBs in Toronto, Ontario air have been detected at concentrations between the detection limit and 9.6 ng/m^3 (CanViro, 1985).

TABLE 5-2—*Continued*

Medium	Value	Units	Date	Comments	Reference
	40-80	ng/L	< 1984	L. Ontario (nearshore)	Simmons, 1984
	4-16	pg/L	1986	Canadian Arctic	Hargrave *et al.*, 1988
	< 20	ng/L	1988	Grimsby, Ontario Water Treatment Plant; raw water	MOE, 1988
	0.34 (0.2-0.6) 0.63 (0.2-2.3) 0.69 (0.3-1.4) 1.38 (0.3-3.5) 1.41 (0.5-2.6)	ng/L	1986	L. Superior; L. Huron; Georgian Bay; L. Erie; L. Ontario	Stevens and Neilson, 1989
	0.5-2.0 3.2-3.4 0.4-2.1 0.4-7.6 0.9-8.4 0.4-1.9 0.3-6.0 0.3-1.8	ng/L	1978 1979 1980 1978 1979 1980 1979 1980	western L. Superior central L. Superior eastern L. Superior	Eisenreich *et al.*, 1981
	2.3	ng/L	1983-1984	Siskiwit Lake	Swackhamer *et al.*, 1988
	8.28-652.9	ng/L	< 1991	Nile Delta	El-Gendy *et al.*, 1991
	2.46	ng/L	1987	St. Lawrence River	Germain and Langlois, 1988
	nd-950	ng/L	1983	Nipigon Bay, L. Superior	Kirby, 1986
Waste Water	73-400	μg/L	1976	New England industrial discharge	Weaver, 1984
	nd-65	ng/L	1983	Nipigon Bay pulp mill discharge	Kirby, 1986
Precipitation	< 3-24 nd-230 9-32 11-44 13 < 0.6-3.5 12-75 3.65 (1-61) 5.90 (0.6-48) nd-143 nd-17 2.3-8	ng/L	1973-1975 1974-1976 1976 1976-1977 1977-1978 1979 1979-1980 1981 1983 1983-1985 1984 1986	North American and European precipitation	Murray and Andren, 1992

The concentrations of PCBs in indoor air in public buildings and in private residences are generally greater than those reported in outdoor air. The concentrations of PCBs in various buildings ranged from 200 to 240 ng/m^3 for laboratories and 80 to 110 ng/m^3 for offices in an industrial research facility, 210 ng/m^3 for a laboratory in an academic facility, and 44 ng/m^3 for an office in a shopping complex. The concentrations of PCBs in indoor air in residences ranged from 150 to 580

TABLE 5-2—*Continued*

Medium	Value	Units	Date	Comments	Reference
	10-50	ng/L	< 1985	Ontario rain	Canviro, 1985
	13-17	ng/L	1983-1984	Siskiwit Lake	Swackhamer *et al.*, 1988
	79-125	pg/L	1986	Canadian Arctic	Hargrave *et al.*, 1988
	0.6-48	ng/L	1983	L. Superior	Strachan, 1985
	8-40 18-43	ng/L	1976	rain; snow; Great Lakes	Strachan and Hunealt, 1979
	0.02-1.76	ng/L	1984	L. Superior	Strachan, 1988
	1.3-5.0	ng/L	1984	Cree Lake, Saskatchewan	Strachan, 1988
	0.61-17.0	ng/L	1984	Kouchibouguac, New Brunswick	Strachan, 1988
	0.74-7.3	ng/L	1986	Canadian Arctic	Gregor and Gummer, 1989

ng/m^3 in kitchens, 39 ng/m^3 in a living room, 170 ng/m^3 in bedrooms, 120 ng/m^3 in basements, 64 ng/m^3 in garages, and 400 ng/m^3 in libraries (MacLeod, 1981). The indoor air concentrations of PCBs in buildings with electrical transformers containing oils with PCBs averaged 206 ng/m^3 (range: 192 to 215 ng/m^3) for one office, 653 ng/m^3 (range: 448 to 881 ng/m^3) for a second office, and 498 ng/m^3 (range: 355 to 628 ng/m^3) for a laboratory in an office building. The air concentrations of PCBs in buildings without electrical transformers containing oils with PCBs were either similar to the above [average 327 ng/m^3 (range: 202 to 384 ng/m^3) for office 3] or slightly less [117 ng/m^3 (range: 78 to 139 ng/m^3) for office 4, 157 ng/m^3 (range: 114 to 215 ng/m^3) for school 1, and 262 ng/m^3 (range: 220 to 303 ng/m^3) for school 2]. Surface wipe samples demonstrated that PCBs were also present on surfaces within these buildings, with concentrations ranging from 0.1 to 0.8 μg/100 cm^2 for buildings with transformers containing PCBs and 0.09 to 0.37 μg/100 cm^2 for buildings with no transformers containing PCBs (Oatman *et al.*, 1985; Oatman and Roy, 1986). MacLeod (1981) concluded that the concentrations of PCBs measured in the indoor air in various buildings were typically 10-fold greater than the concentrations measured outside the same buildings.

The concentrations of PCBs in the unfiltered surface waters of the Nile delta ranged from less than detection limits to as great as 652.9 ng/liter (El-Gendy *et al.*, 1991). Sediments in the Nile delta area had concentrations of PCBs measuring up to 5153 ng/g (El-Gendy *et al.*, 1991). No reports were identified showing measurable concentrations of PCBs in drinking water. PCBs were reported to be undetectable, with a detection limit of 20 ng/liter, at the Grimsby, Ontario water treatment plant (MOE, 1988).

Urban discharges of PCBs contribute substantially to concentrations in sediment, and concentrations as great as 660 ng/g have been reported in sediments of water systems near urban areas (Oliver and Bourbonniere, 1985; MOE, 1986; Kaiser *et al.*, 1990).

3.1.4. Sites of Localized Elevated Concentrations

Sites of localized accumulations of PCBs generally occur as a result of industrial or municipal discharges (Munro *et al.,* 1985; Kirby, 1986) or accidental spills. Waste water discharges from a pulp mill in Nipigon Bay, Lake Superior contained concentrations of PCBs up to 65 ng/liter, believed to be related to PCBs used in various electrical equipment within the mill or contained in materials used in the mill. The mill discharges were considered to contribute up to 950 ng/liter of PCBs to unfiltered water concentrations in the bay (Kirby, 1986). PCBs in industrial discharges in New England have been measured at concentrations as great as 400 μg/liter. Weaver (1984) reported concentrations of PCBs in the New England industrial area ranging from 4400 to 990,000 ppm in soil and from 0.17 to 1.26 mg/m^3 in air. Certain localized regions of the Great Lakes historically have reported elevated PCB concentrations, such as Green Bay, Lake Michigan and Saginaw Bay, Lake Huron. Elevated tissue concentrations of PCBs have been reported for aquatic and fish-eating wildlife from these localized regions (Section 3.3).

3.1.5. Concentrations of PCBs in Food

Temporal trends of concentrations of PCBs in food are documented in data from the Total Diet Study (Market Basket Survey) conducted by the (U.S.) Food and Drug Administration (FDA) (Regulatory Network, Inc., 1992). The purpose of this survey was to provide data for the estimation of dietary intakes of pesticides, industrial chemicals, toxic elements, and essential minerals, and to compare these intakes with recommended or established dietary levels. A total of 234 food items, which represent 100% of the American diet, were collected in retail outlets simultaneously in three cities in each of the four regions of the United States, then analyzed for content of PCBs. Examination of the available information from this survey for the years 1971 to 1989 shows that residues of PCBs in the diet today are less than 1/1000th the concentrations measured in the mid-1970s, and the intake of PCBs has decreased from 6.9 μg/day in 1971 to 0.05 μg/day in the period 1987 to 1990 (Fig. 5-1). A slight increase in the intake of PCBs was evident between 1977 and 1980 (the greatest value during this period was 1.9 μg/day in 1978). However, since then, exposure to concentrations of PCBs through food has been decreasing steadily (Regulatory Network, Inc., 1992).

3.2. Human Health Hazard Assessment

3.2.1. Bioavailability, Metabolic Conversion, Pharmacokinetics, Tissue Deposition, and Excretion

3.2.1.1. Bioavailability

Oral

Studies of the balance between intake and excretion of PCBs showed that 88% of the PCBs ingested in foods were not excreted in the urine or feces, indicating high

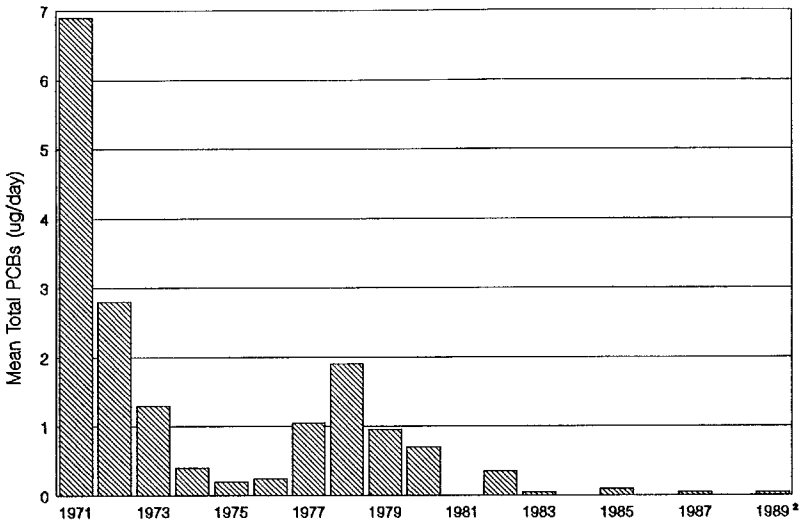

FIG. 5-1. Data from FDA Total Diet Study of 234 food items in the United States. "Adult" intakes 1971 to 1990. 1989 Data represent an average of the years 1988, 1989, and 1990. Reproduced with permission from Regulatory Network, Inc. (1992).

absorption (Price *et al.*, 1972). Other studies concluded that approximately 50% of dietary PCBs are absorbed into the body (Watanabe *et al.*, 1977, 1979). The greater chlorinated PCBs, especially those with chlorine in the 4,4′ ring positions, appear to be selectively absorbed and more slowly excreted (Kuwabara *et al.*, 1979).

Inhalation

Vapors of PCBs that are retained in the lungs are believed to be completely absorbed (Drill *et al.*, 1982); however, since about 50% of inhaled vapors are exhaled, the overall bioavailability of airborne PCBs would be about 50%. The bioavailability of airborne PCBs bound to particles would depend on the particle sizes and the dynamics of particle retention in the respiratory system. Based on airborne particle dynamics in the respiratory system and assuming usual particle size distributions typical of the ambient environment, approximately 13% of airborne PCBs on airborne particles would be retained in the lung, of which 100% would presumably be bioavailable (Brain and Mosier, 1980).

Dermal

PCBs are absorbed through the skin, with reported estimates of approximately 50% in humans (Drill *et al.*, 1982), 17 to 26% in monkeys (Wester *et al.*, 1983), and 33 to 56% in guinea pigs (Wester *et al.*, 1983). The most quantitative data on dermal absorption is based on data of measured PCBs absorbed through the skin using uniformly labeled [^{14}C]PCBs. Using this method, the quantity absorbed was approximately 6% of the amount of the same dose absorbed following oral administration. Since bio-

availability of PCBs following ingestion is about 50% (see ingestion bioavailability section above), the dermal bioavailability indicated by this method would therefore be about 12% (Schmid *et al.*, 1992).

None of the above data provide an estimate of the dermal bioavailability of PCBs bound to particles (e.g., soils). Based on similar physical/chemical properties, PCBs bound to particulates would be expected to behave in a manner similar to 2,3,7,8-tetrachlorodibenzo-*p*-dioxins with respect to dermal absorption, for which 1 to 10% of a dose absorbed to soil is estimated to be absorbed dermally, based on animal studies (Poiger and Schlatter, 1980; Kimbrough *et al.*, 1984; MOE, 1985). Evidence that particulate materials would interfere with the dermal absorption of PCBs is provided through studies that show lower dermal bioavailability of PCBs when applied by cotton gauze to the skin, compared to the application of PCBs in liquid form (Schmid *et al.*, 1992).

Once PCBs are on the skin, it does not appear to be possible to completely remove them. Based on data from guinea pigs, washing the skin immediately after application of PCBs in solution removes about 60% of the applied dose (Wester *et al.*, 1983).

3.2.1.2. Pharmacokinetics

PCBs that are absorbed into the body are relatively quickly cleared from the blood into body tissues. Two phases for clearance of PCBs from the blood have been reported, the first with a half-life of 0.4 days and the second with a half-life of 2 days (Schmid *et al.*, 1992).

PCBs are more slowly eliminated from the body (i.e., from storage in adipose tissue and from lipids in organs such as the liver) by excretion through the kidneys into the urine, and through the liver into the bile, with subsequent elimination in fecal material. In humans, the half-life for such clearance of PCBs from the body has been reported to range from 100 to 300 days (Buhler *et al.*, 1988).

Studies in monkeys and guinea pigs have indicated that total body elimination half-lives for PCBs range from about 4 to 7 days and from 2 to 3 days, respectively (Wester *et al.*, 1983). In guinea pigs, the whole body elimination of PCBs tends to be biphasic, with an initial rapid phase with a half-life of about 2 days, followed by a final slower phase with a half-life of about 12 days (Wester *et al.*, 1983).

3.2.1.3. Tissue Disposition

The ubiquitous nature of PCBs in the environment has resulted in a certain background concentration of PCBs in humans not known to have had any specific exposure to PCBs (i.e., no evidence of occupational exposure or high fish consumption). The concentrations of PCBs in human adipose tissues generally ranged from <0.01 to 0.7 ppm, with a mean value near 0.2 ppm (Niessen *et al.*, 1984; Schnare *et al.*, 1984). Concentrations in mammary gland adipose tissues were substantially higher, ranging from 1.25 to 6.47 ppm (Unger *et al.*, 1984). Milk fat concentrations of PCBs averaged 0.81, 1.44, and 0.5 ppm in samples collected from nursing mothers in Denmark, Sweden, and the United Kingdom, respectively. Human whole milk concentrations of PCBs ranged from 0.022 to 0.068 ppm (mean 0.012 ppm) in Canadian samples

(Mes *et al.*, 1984; CanViro, 1985), to 0.001 to 0.24 ppm in Japanese samples (Ando *et al.*, 1985).

Concentrations of PCBs in blood from populations not exposed occupationally have ranged from 0.001 to 0.004 ppm (Mes *et al.*, 1984; Yakushiji *et al.*, 1984; Ando *et al.*, 1985), whereas concentrations of PCBs in blood from occupationally exposed populations have been reported to be 0.03 ppm or higher (Yakushiji *et al.*, 1984). However, other studies have found that concentrations of PCBs in serum in the range of 10 ppb are common in individuals without any specific occupational or environmental sources of exposure (Fischbein and Rizzo, 1987). Stehr-Green *et al.* (1986) considered serum concentrations of PCBs less than 20 ppb to be in the normal range.

The initial tissue disposition of PCBs in exposed laboratory animals results in greater concentrations in liver and muscle. Since PCBs are hydrophobic and lipophilic, following initial disposition, the slower process of redistribution is reported to take place and, with time, the PCBs concentrate in adipose tissue and skin (Matthews and Dedrick, 1984).

3.2.1.4. Metabolic Conversion

There is an inverse relationship between degree of chlorination and the rate of metabolism (Safe, 1984, 1989). PCBs have been shown to be selectively metabolized by different isoforms of the cytochrome P450-dependent polysubstrate monooxygenase system (P450). Non-*ortho*-substituted PCBs (e.g., 3,3′,4,4′,5,5′-hexachlorobiphenyl) were preferentially metabolized by "3-methylcholanthrene (3-MC)-inducible" forms of P450 (i.e., P450IA1), while poly-*ortho*-substituted PCBs (i.e., 2,2′,4,4′,5,5′-hexachlorobiphenyl) were preferentially metabolized by "phenobarbital-inducible" forms of P450 (i.e., P450B1) (Borlakoglu and Haegele, 1991). In the process of hydroxylation of PCBs, a reactive arene oxide intermediate has been postulated to be generated that potentially could bind covalently to macromolecules such as protein and DNA (Safe, 1989; Borlakoglu and Haegele, 1991). PCBs are also capable of inducing particular forms of P450. Some PCBs behave as 3-MC-type inducers, as phenobarbital-type inducers, or as inducers of both activities. Thus, PCBs can influence their own metabolism.

It is this ability to influence their own metabolism that can be useful in interpreting the significance of tissue concentrations of particular classes of PCBs that are more readily metabolized, compared with others that are more slowly metabolized and excreted, and that tend to accumulate in tissues (Borlakoglu and Haegele, 1991). Very little passive elimination of PCBs has been reported to occur, with excretion usually requiring hydroxylation (mediated by P450) followed by subsequent conjugation of the normally lipophilic PCBs to more water-soluble compounds (sulfates or glucuronides) (Matthews and Dedrick, 1984). As such, isomers not metabolized tend to accumulate in the tissues.

3.2.2. Mammalian Toxicology (Laboratory Animal and Biochemical Studies)

3.2.2.1. Lethal Effects

PCBs have relatively little potential for acute toxicity. For example, the LD_{50} for male rats has been estimated at between 1300 and 11,300 mg/kg body wt, depending

on the Aroclor series (Borlakoglu and Haegele, 1991). Extreme exposures have been associated with diarrhea, chromodacryorrhea, body weight loss, unusual stance and gait, decreased response to pain, and terminal ataxia. Species differences in toxicity are evident; the guinea pig being most sensitive, followed by the rabbit and the rat (EPA, 1979; Drill *et al.*, 1982). The relative sensitivity of humans compared to that of other animals is not well understood. In addition, the degree of chlorination and position of chlorines on the biphenyl ring structure profoundly affect toxicity, with congeners of PCBs containing five or six chlorine groups per biphenyl demonstrating the highest degree of toxicity (Fischbein and Rizzo, 1987; Safe, 1989).

3.2.2.2. Nonlethal Effects

Teratogenicity

In most species of mammals studied, no teratogenic effects have been related to exposure to PCBs; however, abnormalities in the thyroid and increased incidence of cleft palates have been observed in certain strains of mice genetically sensitive to the development of terata (Tilson *et al.*, 1979; Marks *et al.*, 1981). No increase in cleft palates was observed in mice treated with up to 1000 mg 2,2′,4,4′,5,5′-hexachlorobiphenyl/kg body wt on Gestation Day 9; however, doses of 500 and 1000 mg/kg body wt of this isomer did result in an increased incidence of hydronephrosis and hydroureter in C57BL/6N mice (Morrissey *et al.*, 1992).

PCBs have also been shown to protect against the teratogenic effects of chemicals such as 2,3,7,8-T_4CDD. Coadministration of 2,3,7,8-T_4CDD and sufficient doses of PCBs (750 μmol/kg body wt of Aroclor 1254, Beigel *et al.*, 1989; or 1000 mg 2,2′,4,4′,5,5′-hexachlorobiphenyl/kg body wt, Morrissey *et al.*, 1992) provided complete protection against cleft palate formation in C57BL/6 mice (Biegel *et al.*, 1989; Morrissey *et al.*, 1992). Further studies showed that the protective effects of PCBs in this regard were related to those PCBs that exhibit Ah receptor binding properties, while those that do not bind to the Ah receptor were ineffective (Biegel *et al.*, 1989; Morrissey *et al.*, 1992). Although PCBs without chlorine in the *ortho* positions of the phenyl carbon rings have greater Ah receptor binding properties, those with chlorine in the *ortho* positions also have some Ah receptor binding properties. For example, 3,3′,5,5′-tetrachlorobiphenyl and 3,3′,4,4′-tetrachlorobiphenyl, both non-*ortho*-substituted congeners of PCBs, have EC_{50} values for aryl hydrocarbon hydroxylase enzyme induction of 2.8×10^{-5} and 4.3×10^{-7}, respectively, compared to an EC_{50} value of 7.9×10^{-5} for 2,2′,4,4′,5,5′-hexachlorobiphenyl, an *ortho*-substituted PCB congener (Safe, 1990). These data indicate that any teratogenic effects of PCBs would likely occur through similar mechanisms to those of 2,3,7,8-T_4CDD. Since some coplanar PCBs have many similar biochemical/biological properties to 2,3,7,8-T_4CDD, one possible explanation is that the coplanar PCBs are responsible for teratogenic effects of PCBs.

Reproductive Effects

Exposure to PCBs has caused adverse effects on reproduction in a wide range of laboratory animals (Drill *et al.*, 1982). In rodents, these effects have included evidence of embryo- and fetotoxicity, decreased fertility indices in both males and females, and

decreased survival of offspring (EPA, 1979; Drill *et al.,* 1982; Sager, 1983; Sager *et al.,* 1987; Golub *et al.,* 1991). Exposure of monkeys to mixtures of PCBs (approximately 1250 μg/kg body wt/day) has been associated with abnormalities of the estrus cycle and of the blood sex hormone levels (Barsotti and Allen, 1975; Barsotti *et al.,* 1976; Allen *et al.,* 1980) and with behavioral abnormalities in the offspring (Bowman *et al.,* 1978). Based on a study conducted with rhesus monkeys exposed to Aroclor 1016 in the diet (Barsotti and Van Miller, 1983), the EPA (1988) estimated a no-observable-adverse-effect-level (NOAEL) of 10.5 μg/kg body wt/day for adverse reproductive effects (decreased birth weights of offspring).

Developmental Effects

Laboratory experiments in rhesus monkeys and rodents, designed to assess neural or developmental effects of PCBs, have shown altered activity levels, impaired learning, and delayed ontogeny of reflexes. In these experiments, Aroclor 1248 was administered at a dose of 0.084 mg/kg body wt/day to the rhesus monkeys, while 20–100 mg/kg body wt/day of Kanechlor 500 was administered to Sprague–Dawley rats (Allen and Barsotti, 1976; Shiota, 1976). In each case, the dosages used were extreme (near lethal), and were reported to also cause fetotoxic or reproductive effects.

Immune System Effects

Exposures to extreme quantities of mixtures of PCBs cause atrophy of the thymus and thus diminish immune responses in laboratory animals (Kimbrough, 1987; Borlakoglu and Haegele, 1991). Other reported effects of extreme exposures to commercial mixtures of PCBs on the immune system include lymphopenia, lymphoid cell hyperplasia, bone marrow hypocellularity, and impaired regulation between populations of T-lymphocytes (Borlakoglu and Haegele, 1991).

Neurotoxicity

Recent evidence suggests that relatively large exposures to PCBs may result in effects on neurotransmitter substances in the brain and possible neurological effects. Aroclor 1016 (0.8, 1.0, or 3.2 mg/kg body wt/day for 20 weeks) has been shown to reduce dopamine (a neurotransmitter substance) in specific regions (i.e., caudate nucleus, putamen, substantia nigra, and hypothalamus) of the brains of nonhuman primates. No effects were noted in other brain regions or on other biogenic amines (e.g., norepinephrine, serotonin, or their metabolites). A linear relationship between the effects on dopamine and the concentrations of three PCBs (2,4,4′-trichlorobiphenyl, 2,2′,4,4′-tetrachlorobiphenyl, and 2,2′,5,5′-tetrachlorobiphenyl) in the brain was observed (Segal *et al.,* 1990). *In vitro* studies using isolated pheochromocytoma cells also showed decreases in dopamine concentrations proportional to exposures to PCBs. Using this *in vitro* test system, Segal *et al.* (1990) concluded that the effects on dopamine concentrations were due to specific PCBs, with greater activities observed in the *ortho*-substituted nonplanar PCBs. However, the dopamine reductions in pheochromocytoma cells did not appear correlated with the concentrations of PCBs in the cells. In addition,

no behavioral consequences were observed in animals in which dopamine concentrations were affected by exposures to PCBs.

3.2.2.3. Genotoxicity

PCBs are not mutagenic to a variety of strains of *Salmonella typhimurium* (EPA, 1979; Schoeny *et al.,* 1982). Early reports of weak mutagenic activity in *S. typhimurium* tester strains (Wyndham *et al.,* 1976) could not be replicated in the same laboratory (Safe, 1980, 1989) or in other laboratories (Heddle and Bruce, 1977; McMahon *et al.,* 1979). Unscheduled DNA synthesis was elevated in Chinese hamster ovary cell cultures exposed to Aroclor 1254 (EPA, 1979), but no chromosomal aberrations were observed in cultured human lymphocytes exposed to PCBs *in vitro* (Hoopingarner *et al.,* 1972).

The 3,3′,4,4′-tetrachlorobiphenyl (a coplanar PCB) was reported to cause dose-related increases in chromosome breakage in human lymphocytes exposed *in vitro* (Sargent *et al.,* 1989), while the 2,2′,5,5′-isomer of PCBs did not cause chromosome breakage, even at greater concentrations. However, a mixture of the 2,2′,5,5′- and the 3,3′,4,4′-isomers produced clastogenicity at concentrations below those required for chromosome breakage by 3,3′,4,4′-tetrachlorobiphenyl alone. Treatment with PCBs did not result in the formation of micronuclei and was negative in the sperm abnormality test in mice (Heddle and Bruce, 1977). No adverse effects were observed in dominant lethal studies with Aroclor 1242, 1254, and 1260 in rodents (Green *et al.,* 1975; EPA, 1979; Drill *et al.,* 1982).

It has been proposed that PCBs may be metabolized to arene oxide intermediates, and this possibility has raised concerns over their genotoxicity (EPA, 1979; Preston *et al.,* 1981; Drill *et al.,* 1982; Safe, 1989). However, information from various *in vitro* and *in vivo* test systems demonstrates that PCBs are not DNA-reactive.

3.2.2.4. Carcinogenicity

Bioassays in laboratory animals provide one method for the assessment of the potential carcinogenicity of chemicals. The results of animal bioassays are useful as tools to assist in the interpretation of data from studies of accidental or other exposures on human populations. The interpretation of the results from cancer bioassays must be consistent with current understanding of the mechanisms of carcinogenesis. The two-stage theory of carcinogenesis is generally accepted as providing a useful working model of carcinogenesis. In the first stage, the normal cell is converted to a neoplastic cell which may not revert to normal (neoplastic conversion or initiation), and in the second stage the neoplastic cell divides, resulting in the development of an overt neoplasm (neoplastic development) (Williams and Weisburger, 1991). The factors governing neoplastic development, including promotion and progression stages, are dependent on numerous endogenous and exogenous factors which have yet to be fully elucidated (Stott and Watanabe, 1982; Pitot *et al.,* 1991). In contrast, neoplastic conversion or initiation has received a great deal of attention in view of the general consensus, based on correlative experimental observations, that conversion may occur as the result of mutations caused by DNA-reactive (genotoxic) agents at certain critical genomic sites. Alterations in DNA have long been implicated in the carcinogenic process based on several traditional lines of evidence (OSTP, 1985):

(i) many biological carcinogens (e.g., oncoviruses) have been shown to interact with the DNA of host cells;

(ii) various types of radiation and many chemical carcinogens have been shown to be mutagens or to interact with DNA; and

(iii) individuals with genetic diseases resulting in defective DNA repair (e.g., xeroderma pigmentosum) are prone to develop certain cancers, and their cells have increased sensitivity to certain radiations and chemical mutagens.

In addition to the above, the existence of other genetically inherited traits that increase the propensity to develop certain cancers (e.g., retinoblastoma) and experimental evidence of abnormal oncogene function or expression caused by genetic alterations (Bishop, 1983; Guerrero and Pellicer, 1987) provide further evidence for genetic involvement in carcinogenesis.

Early genetic alterations can be assessed by different techniques, including quantitation of DNA adducts resulting from the covalent addition of electrophilic species with nucleophilic sites present on DNA (Asamoto *et al.,* 1991; Hall *et al.,* 1991), or quantitation of specific biological and genetic responses as determined with various *in vitro* and *in vivo* short-term tests (OECD, 1987; Benigni, 1992). The availability of such methods has allowed numerous environmental and industrial contaminants to be classified according to their potential to interact with DNA and to provide preliminary information on their carcinogenic potential.

The information briefly outlined above is important to the interpretation of the mixed conclusions from cancer bioassays of PCBs in laboratory animals. Differences in responses are observed among PCBs with different percentages of chlorine (by weight) and possibly between species and strains of test animals. In experiments in which tumor incidence is increased by treatment with PCBs, there is a large percentage of benign tumors. All studies reported overt signs of liver toxicity and hepatocellular hyperproliferative responses, indicating increased cell replication associated with treatment with PCBs (Table 5-3).

The Institute for Evaluating Health Risks (IEHR, 1991) conducted a detailed review of the histopathology of tissues collected from rats treated with PCBs by Kimbrough *et al.* (1975), NCI (1978), Schaeffer *et al.* (1984), and Norback and Weltman (1985). This detailed review, rather than the original scientific publications, forms the basis for the following assessment of the carcinogenicity of PCBs, because the procedures followed for the review were those developed by the National Toxicology Program using a Pathology Working Group of certified Veterinary Pathologists experienced in the microscopic evaluation and interpretation of hepatic changes in rodents. The incidence of tumors and other hepatic lesions reported for the identified animal cancer bioassays of PCBs have been summarized by the IEHR (Table 5-3). The overall conclusions that can be drawn from the IEHR (1991) review and other information available on PCBs and related chemicals are:

(i) Statistically significant increases in liver tumors are observed in Sherman, Sprague–Dawley, and Wistar strain rats treated with PCBs containing 60% chlorine by weight (i.e., Aroclor 1260 and Clophen A60). In two of the studies, the greater percentage of liver tumors were benign, while in one study there were more malignant liver tumors (IEHR, 1991, Table 5-3).

(ii) Rats treated with PCBs containing lesser percentages of chlorine by weight (e.g., Clophen A30, Aroclor 1254) did not show significant increases in liver tumors, and those tumors observed were primarily benign hepatocellular adenomas (Table 5-3).

TABLE 5-3

LIVER LESIONS IN RATS TREATED WITH PCBS

		No. Examined		Hepatocellular Adenoma		Hepatocellular Carcinoma		Animals with Hepatocellular Adenoma and/or Carcinoma		Centrilobular Hepatocytomegaly		Animals with Focus/Foci of Any Type	
		Ctrl	Test	Ctrl	Test	Ctrl	Test	Ctrl	Test	Ctrl	Test	Ctrl	Test
Aroclor 1260 Sherman 100 ppm Kimbrough *et al.* (1975)	Female	187	189	0	135(71)	1(0.5)	21(11)	1(0.5)	138(73)	1(0.5)	108(57)	25(13)	177(94)
Aroclor 1260 Sprague-Dawley 100 ppm Norback and Weltman (1985)	Male	31	40	0	4(10)	0	1(2.5)	0	5(12.5)	0	15(37.5)	5(16)	16(40)
	Female	45	46	1(2)	29(63)	0	19(41)	1(2)	41(89)	0	5(11)	7(16)	36(78)
Clophen A-30 Wistar 100 ppm Schaeffer *et al.* (1984)	Male	120	128	6(5)	14(11)	2(2)	2(2)	8(7)	16(12.5)	1(1)	2(2)	55(46)	106(83)
Clophen A-60 Wistar 100 ppm Schaeffer *et al.* (1984)	Male	120	125	6(5)	85(68)	2(2)	67(54)	8(7)	114(91)	1(1)	2(2)	55(46)	108(86)
Aroclor 1254 Fischer 344 100 ppm NCI (1978)	Male	24	23	0	1(4)	0	2(9)	0	3(13)	0	3(13)	0	16(70)
	Female	23	24	0	1(4)	0	0	0	1(4)	0	3(12.5)	2(9)	15(62.5)

Source: (IEHR, 1991).

(iii) In all cases in which histopathological diagnoses were not hampered by limitations in tumor-free tissue for assessment, rats treated with PCBs showed a high incidence of hepatocytomegaly, indicative of induction of enzymes and proliferation of endoplasmic reticulum within the hepatocytes (Table 5-3).

(iv) All rats treated with PCBs, regardless of the percentage of chlorine content, showed significant increases in various types of hepatocellular foci. These foci are believed to indicate hyperproliferative responses, in which cell division and replication are increased (Table 5-3).

A number of less comprehensive studies assessing the potential carcinogenicity of PCBs are in the published literature. An increased incidence of liver tumors was observed in female rats, but not male rats, exposed to large doses of Kanechlor-400, the commercial PCBs involved in the Yusho cases in Japan (Kimura and Baba, 1973; Kimura *et al.,* 1976); however, large doses were used in these studies, eliciting severe signs of toxicity in the animals. Studies of several Kanechlor preparations with different percentages by weight of chlorine demonstrated increased liver tumors in mice (Ito *et al.,* 1973) and rats (Ito *et al.,* 1974) at dietary concentrations of 500 ppm, considerably greater than those in the studies reassessed by IEHR (1991) and discussed above.

Relative to human health, the interpretation of the incidence of tumors observed in rodents exposed to large doses of PCBs that are usually associated with overt signs of toxicity to the liver and other body organs is controversial. There is substantial evidence demonstrating that the livers of aging rats and mice have greater incidences of preinitiated liver cells than do human livers (Popper *et al.,* 1960; Hollander and Burek, 1978; Ogawa *et al.,* 1981; Schulte-Hermann and Parzefall, 1981) and are predisposed to develop liver cancers (Drill *et al.,* 1982; Nutrition Foundation, 1983; Schulte-Hermann *et al.,* 1983). The initiation of hepatocytes in rodent livers is believed to result from "natural" causes, such as carcinogens normally present in the diet and general environment (Schulte-Hermann *et al.,* 1983; Bannasch *et al.,* 1988). In response to the hepatotoxicity and resulting hyperproliferative responses from large doses of PCBs, liver cells would begin to replicate in an attempt to repair damage to the liver. Such hyperplastic/hyperproliferative effects are well documented in the cancer bioassays of PCBs (discussed earlier in this section). The resulting increased populations of preinitiated liver cells and predisposition for liver cancer, combined with hyperplastic/hyperproliferative responses of the liver to overt liver toxicity from exposures of PCBs, would provide an environment for increasing the occurrence of liver tumors. Through such a mechanism, the greater incidence of liver tumors associated with exposures to PCBs would be secondary to the development of liver toxicity; therefore, at doses not causing toxic effects on the liver, no increase in tumors would be expected.

PCBs have been shown to act as promoters, but not initiators, of cancers. Treatment with PCBs alone did not increase the incidence of putative precancerous lesions (gamma-glutamyl transpeptidase-positive liver foci); however, PCBs (Aroclor 1254) did promote the development of such lesions following preinitiation of the rats by treatment with diethylnitrosamine (DENA) (Pereira *et al.,* 1982). PCBs (notably Aroclor 1254) have also been shown to promote, but not initiate, liver tumors in Swiss mice preinitiated with *N*-dimethylnitrosamine (NDMA) (Anderson *et al.,* 1986), and in strain "dd" mice treated with benzene hexachloride (Ito *et al.,* 1973). The cancer-promoting potential of PCBs has also been demonstrated in organs other than the liver. Beebe *et al.* (1991) demonstrated that PCBs will promote the development of

lung cancer in Swiss mice pretreated with NDMA. The 2,2′,3,4,4′,5′-hexachlorobiphenyl congener was shown to be a promoter of lung tumors in NDMA-initiated mice; however, the 2,2′,4,4′,5,5′-hexachlorobiphenyl congener was not a promoter and if administered simultaneously inhibited the promoting activity of 2,2′3,4,4′,5′-hexachlorobiphenyl.

The mechanisms for the cancer-promoting effects of PCBs are not known in detail; however, a number of hypotheses for such actions have been proposed based on the known biochemical effects of PCBs. Mixtures of PCBs are well-known inducers of several phase I and phase II xenobiotic metabolizing enzymes (e.g., several cytochrome P450-dependent monooxygenases, epoxide hydrolase, glutathione *S*-transferase, and glucuronyl transferases) (Safe, 1984). These enzyme systems are involved in the oxidative metabolism of a large number of chemicals, including a number of known carcinogens such as benzo[*a*]pyrene and related polycyclic aromatic hydrocarbons, aflatoxin B_1, and acetylaminofluorene (Safe, 1989). Consequently, exposures to sufficient quantities of PCBs to change the activity of enzyme systems responsible for the metabolism of many naturally occurring chemicals (e.g., sex steroids) and various xenobiotics would be expected to affect the responses of organisms to these chemicals. Depending on the particular metabolites produced by these enzymes, their effects could be enhanced (e.g., as indicated by cancer promotion) or inhibited. PCBs have been shown to decrease the development of liver tumors by various hepatocarcinogens, such as 3′-methyl-4-dimethylaminoazobenzene, 2-acetylaminofluorene, and DENA (Kimura *et al.*, 1976; Safe, 1989). PCBs inhibit the carcinogenicity of aflatoxin B_1 in rainbow trout and the development of skin cancers by various polycyclic aromatic hydrocarbons (Safe, 1989). One mechanism proposed for such cancer-inhibiting effects is through the induction by PCBs of enzyme systems that are involved in the inactivation metabolism of the various carcinogens (Safe, 1989).

The effects of PCBs on enzyme induction may also play a role in their cancer promoting activity. Another possibility is the disruption of cell–cell communication (Swierenga *et al.*, 1990), which is a property of many tumor promoters (Budunora and Williams, 1994). Examples of cancer promotion by PCBs have already been discussed. However, the potential for enhancement of the progression of cancer through increasing rates of cell proliferation, in which the cancer process has already been initiated through events independent of PCBs, may also play an important role in cancer promotion. The consideration of cancer promotion through such mechanisms is important for the interpretation of cancer studies in laboratory animals in which exposures are great enough to result in overt toxicity of organs such as the liver; however, such mechanisms may not be relevant in situations in which exposures are not great enough to produce such toxicity (i.e., exposures more typical of the usual human situation).

There are inconsistencies in how scientific and regulatory agencies judge the potential carcinogenicity of PCBs: The International Agency for Research on Cancer (IARC, 1978, 1987) considers PCBs to be probable human carcinogens, whereas the EPA (1988) and Environment Canada (1988) consider PCBs to be unlikely human carcinogens, but potential reproductive toxicants. The weight of available scientific evidence supports the concept that PCBs are not initiators of cancer and thus, are not direct carcinogenic agents. Any association they may have with cancer in laboratory animals from exaggerated exposures appears to be related to secondary toxic effects on target organs (e.g., liver), to cellular hyperproliferation, and to the promotion of preinitiated

cells that lead to the formation of tumors. Such overt toxic effects of PCBs on target organs appear to occur at exposures substantially greater than those likely to occur from the general environment.

3.2.3. Mechanisms of Toxicity

Many of the toxic and pathological effects attributable to mixtures of PCBs, such as tumor promotion, developmental toxicity, immunotoxicity, and teratogenicity, appear to be secondary to biochemical effects or tissue toxicity of PCBs. As already discussed with respect to the observation of tumors in animals exposed to large doses of PCBs, these effects may be secondary to overt toxic effects on specific organs. Although these gross toxic effects of PCBs associated with large exposures may be in part secondary to their effects on biochemical systems, other direct actions of PCBs on cell membranes and other cellular systems may be important at such extreme rates of exposure. The effects at lesser rates of exposure, however, may be more directly related to the effects of PCBs on biochemical systems.

Over 50 of the 209 PCB isomers are known or suspected inducers of mixed-function oxygenase (MFO) enzyme systems in animal cells. This type of activity is similar, except with respect to potency, to a number of other chemicals, including polychlorinated dibenzo-*p*-dioxins, dibenzofurans, and biphenylethers (Safe, 1989, 1990; Borlakoglu and Haegele, 1991). These enzyme systems involve the hemoproteins known as cytochrome P450IA1, cytochrome P450IA2, cytochrome P450IIA1, cytochrome P450IIA2, cytochrome P450IIB1 (P450b), and cytochrome P450IIB2 (P450c), and their associated microsomal monooxygenase enzyme systems. The most commonly evaluated of these enzyme systems are aryl hydrocarbon hydroxylase (AHH) and ethoxyresorufin *O*-deethylase (EROD). The phase II enzyme systems that metabolize xenobiotics (e.g., glutathione *S*-transferases and glucuronyl transferases) are also induced by PCBs and related chemicals.

The biological effects associated with the induction of various enzyme systems by PCBs and related compounds arise because these enzymes are critical to the homeostasis of steroid hormones (e.g., gonadal hormones, pituitary hormones, thyroid hormones, adrenocortical hormones), vitamins (e.g., particularly fat-soluble vitamins such as vitamin A), various neurotransmitters, and possibly energy metabolizing systems (e.g., various gluconeogenic enzymes). In addition, cellular systems involved in the modulation of hormonal responses through binding to cellular receptor systems may be affected by PCBs and related chemicals. Consequently, a myriad of effects may occur from PCBs and related chemicals, depending on the dose received, the relative sensitivity of the biological system involved, and the potency of the specific isomer. Other chemicals from natural or anthropogenic sources can also induce many of these enzyme systems. For example, many of the polycyclic aromatic hydrocarbons (benzo[*a*]pyrene, methylcholanthrene and related chemicals) were used for a number of years as the standard chemical for studying enzyme induction. The polychlorinated dibenzo-*p*-dioxin, 2,3,7,8-T_4CDD, is the most potent inducer of the aryl hydrocarbon hydroxylase/ethoxyresorufin dehydrogenase (AHH/EROD) enzyme system known to date; consequently, it has been used as an investigative tool to study many of the associated mechanisms involved in AHH and EROD induction (Safe, 1990; Borlakoglu and Haegele, 1991).

Through a variety of studies (Thomas *et al.,* 1972; Poland and Glover, 1974, 1975; Poland *et al.,* 1974, 1976) using genetically inbred strains of mice that were either responsive or nonresponsive to the induction of AHH enzyme systems by 2,3,7,8-T_4CDD, the differences in binding of 2,3,7,8-T_4CDD to cell membranes was identified as the major factor in the degree of response of the mice, and the binding site involved was called the Ah receptor. Subsequently, the Ah receptor was found to be a saturable binding site with high affinity for 2,3,7,8-T_4CDD and was identified in a variety of animal tissues. The currently proposed mechanism of action for polychlorinated dibenzo-*p*-dioxin and polychlorinated dibenzofurans is binding to the Ah receptor system, then an activation step occurs, followed by the formation of nuclear receptor complexes and interactions with nuclear binding sites, which subsequently trigger various biological responses within the cell and thus within the organism (Safe, 1990; Borlakoglu and Haegele, 1991).

A weight-of-evidence evaluation has now been published (Safe, 1990; Borlakoglu and Haegele, 1991) that supports the Ah receptor-mediated response mechanism for polychlorinated dibenzo-*p*-dioxins, dibenzofurans, various polycyclic aromatic hydrocarbons, and certain PCBs. The major difference between the various chemicals involved is their Ah receptor binding potency. The differences in Ah receptor binding potency among these chemicals, and even among different congeners of the same family of chemicals, may be several orders of magnitude. The overall assumption to this "unified" mechanism of action of these chemicals through the Ah receptor system is that their effects on enzyme induction may be additive. In other words, since chlorinated dioxins, furans, biphenyls, and polycyclic aromatic hydrocarbons all affect the same enzyme system(s), their potential to affect organisms in the environment should be considered as additive. This hypothesis forms the basis for expanding the TEFs developed for chlorinated dioxins and furans to include PCBs and perhaps other chemicals that affect the Ah receptor system (Safe 1990; Walker and Peterson, 1991).

Neubert *et al.* (1992) outlined the underlying assumptions of using TEFs for "dioxin-like" chemicals. The authors suggested that these assumptions reflect limitations to the use of TEFs since much of the information needed to evaluate whether or not these assumptions have been met is not available. The assumptions include:

(i) the actions of the isomers must be strictly additive in the dose range to be evaluated;

(ii) the target organ in different species must be identical, over the relevant dose ranges;

(iii) dose–response curves for various toxicological endpoints for a given isomer must run parallel;

(iv) the dose–response curves for a given toxicological endpoint must run parallel for the various isomers;

(v) for extrapolations between species, the kinetics must be identical, or differences have to be taken into consideration;

(vi) with respect to a risk assessment relevant to man, toxic or biological manifestations in the lower dose ranges are of special interest, and LD_{50} or ED_{50} values or effects induced by highly toxic doses are of minor importance; and

(vii) effects to be expected at low exposures must be identical to those observed at the high doses studied.

In December 1990, the EPA conducted a workshop to examine the use of a TEF scheme to be applied to the assessment of PCB exposures. Based on the discussions

at the workshop, the EPA (Barnes *et al.,* 1991) developed a set of criteria to be used as a guideline to determine whether TEF values could be applied for the calculation of a 2,3,7,8-T_4CDD-TEQ exposure rate. These guidelines were:

(i) a need (e.g., an interim regulatory need) for such an approach should be demonstrated;

(ii) the set of chemicals to which the scheme will be applied should be well defined;

(iii) a broad base of toxicity data should be available, covering many endpoints for many isomers;

(iv) a relative toxicity among the different isomers should be generally consistent across many different endpoints (*in vivo* and *in vitro*);

(v) a common mechanism should rationalize the observed structure–activity analysis results; and

(vi) a mechanism should be available for gaining widespread consensus on the TEF values.

Participants of the workshop concluded after examination of the current data available that the use of TEFs for PCBs is not as "straightforward" as for chlorinated dioxins and furans (Barnes *et al.,* 1991). The TEF values described by Safe and coworkers (Safe, 1992, 1990; Harris *et al.,* 1993) account only for endpoints considered to be associated with Ah receptor activity (e.g., weight loss, thymic atrophy, *in vitro* enzyme induction, immunotoxicity, teratogenicity, and dermatological effects) and these TEF values may not be relevant for other endpoints (e.g., neurotoxicity, behavioral abnormalities). In addition, the use of TEFs does not consider the potential activity of metabolic products formed during the metabolism and breakdown of chlorinated polycyclic hydrocarbons in the body.

Actions through the Ah receptor system may not be the sole mechanism of effects induced by PCBs. The possibility that the metabolic activation of PCBs to reactive intermediates may also be involved in the etiology of the toxicity of PCBs cannot be completely discounted (Borlakoglu and Haegele, 1991). A number of studies (Borlakoglu and Haegele, 1991) have demonstrated that various PCBs can reduce the DNA content of liver cells. Studies of mammalian L-929 cells in culture indicate that some PCBs and their possible metabolites can directly interact with DNA, producing strand breaks. The possible arene oxide metabolites were the most potent (Stradnicki *et al.,* 1979). However, these observations are not consistent with the lack of genotoxicity of PCBs (see Section 3.2.2.3) and the relevance to whole animal systems, in which reactive intermediates are either not produced or are readily removed by various detoxification systems, is unknown. In addition, Jehnke *et al.* (1991) have demonstrated that the expression of five oncogenes (namely C-Havas, C-raf, C-yes, C-erbA, and C-erbB) occurs in response to feeding PCBs to rats. These authors have suggested that these oncogene expressions induced by PCBs are regulated at the DNA transcriptional level. Currently, these data are fragmentary and their significance and relevance to concentrations of PCBs typical of those associated with environmental exposures need to be addressed; however, these oncogene expressions do raise questions regarding the completeness of the Ah receptor hypothesis as a mechanism of action of PCBs on biological systems.

3.2.4. Epidemiology Studies

In assessing the potential effects of exposures to chemicals such as PCBs, variables that confound the establishment of causality between adverse effects and PCBs and

the quantitative exposure–response or dose–response relationships of these effects must be addressed through appropriate study design and statistical analyses. A major confounding variable is the extent of simultaneous exposure to other chemicals that may mask or have effects similar to PCBs. In this regard, it is important that the sources of the PCBs to which the study population are exposed are unpyrolyzed, since pyrolysis of PCBs results in many different degradation products, including chlorinated dibenzo-*p*-dioxins and chlorinated dibenzofurans, both of which produce similar adverse effects and are considerably more potent toxicants than PCBs (Kuratsune *et al.*, 1969; Fischbein *et al.*, 1979; Chang *et al.*, 1980a,b; Reggiani and Bruppacher, 1985). The effects of simultaneous exposures to other chemicals are considered to confound the interpretation of most of the studies attempting to establish causal relationships between PCBs and health effects in human populations (James *et al.*, 1993). Various factors affecting responses to chemicals must also be appropriately considered in the study design (e.g., age, sex, socioeconomic status, tobacco usage, prescription/nonprescription drug use).

A number of studies rely on the concentrations of PCBs in blood as an indicator of exposure for the purposes of developing dose–response relationships for adverse health effects. However, the half-life for clearance of PCBs from blood into other tissues of the body is only a few hours (Wester *et al.*, 1983; Buhler *et al.*, 1988; Schmid *et al.*, 1992); therefore, concentrations of PCBs in blood only reflect relatively recent exposures (i.e., exposures over the past few days). Since the clearance half-life of PCBs from various tissues of the body is much slower than from the blood (i.e., several months versus a few days), the effects produced by the action(s) of PCBs on body tissues would be expected to persist even though blood PCB concentrations had decreased substantially from the period when exposures actually occurred (Lawton *et al.*, 1985; Buhler *et al.*, 1988; Schmid *et al.*, 1992). These factors mean that the interpretation of dose–response relationships and that the judgement of causality between various health effects and exposures to PCBs must adequately consider the temporal relationships between effects and the exposures to PCBs.

3.2.4.1. Populations Occupationally Exposed to PCBs

Since the potential for exposures to PCBs may have been greater, and the magnitude of such exposures would be greater, in specific work environments where they were used directly in manufacturing processes than through the general environment, the likelihood of observing adverse effects in such occupationally exposed populations should be greater than that in populations exposed to lesser amounts of PCBs through the general environment. However, the possibility that the most sensitive populations may not be found in such work environments must also be considered. The adverse effects most clearly associated with exposures of PCBs in occupational settings are those on the skin, including rashes, burning sensations, and acne (chloracne) (Ouw *et al.*, 1976; Fischbein *et al.*, 1979; Baker *et al.*, 1980; Maroni *et al.*, 1981a; Lawton *et al.*, 1985; Nethercott and Holness, 1986; IDSP, 1987; James *et al.*, 1993). Other skin abnormalities that are less frequently associated with exposures to PCBs include erythema, swelling, dryness and thickening, pigmentation, and discoloration of fingernails (Ouw *et al.*, 1976; Fischbein *et al.*, 1979; Baker *et al.*, 1980; Maroni *et al.*, 1981b; IDSP, 1987). The severity and frequency of observations of dermatological effects,

however, do not correlate significantly to the duration of exposure (Ouw *et al.*, 1976; Fischbein *et al.*, 1979; Maroni *et al.*, 1981b) or to degree of exposure (Fischbein *et al.*, 1979; Maroni *et al.*, 1981b; Nethercott and Holness, 1986) to PCBs. In addition, the dermal effects of PCBs appear to be reversible once exposure is stopped or when the level of exposure is reduced (Fischbein *et al.*, 1979; Maroni *et al.*, 1981b; Lawton *et al.*, 1985).

Studies of populations working with PCBs and associated chemicals show changes in liver function and increases in serum lipids that appear proportional to the degree of exposure to PCBs (Fischbein *et al.*, 1979; Kreiss *et al.*, 1981; Chase *et al.*, 1982; Smith *et al.*, 1982; Emmett, 1985; Reggiani and Bruppacher, 1985; Acquavella *et al.*, 1986; Nethercott and Holness, 1986; Stark *et al.*, 1986; Stehr-Green *et al.*, 1986; Emmett *et al.*, 1988). Increased xenobiotic metabolism and excretory activities of the liver, as measured by a decrease in antipyrene clearance half-life, have been reported in workers exposed to PCBs in the workplace (Alvares *et al.*, 1977; Fischbein *et al.*, 1979). However, Emmett *et al.* (1988) did not observe a statistically significant difference in antipyrine clearance half-life between exposed and unexposed workers, nor did these authors observe a significant correlation between antipyrine clearance half-life and either serum or adipose concentrations of PCBs. Potential differences in simultaneous exposures to other chemicals may be contributing factors to the contradictory results observed by Alvares *et al.* (1977) and Fischbein *et al.* (1979) compared to those by Emmett *et al.* (1988).

The degree of change in serum enzyme activity indicative of abnormal liver function appears to be related to the dose of PCBs received by electrical workers, as indicated by blood concentrations of lower chlorinated PCBs typically used in manufacturing electrical equipment (Ouw *et al.*, 1976; Maroni *et al.*, 1981a,b); again, the possibility of simultaneous exposures to other chemicals was not addressed. As discussed above, caution must be exercised in the extrapolation of such data to other situations since blood PCBs may be only indicative of relatively recent exposures. The frequency of changes in serum enzymes, indicative of abnormal liver function, was >60% in those electrical workers from work areas resulting in blood concentrations of lower chlorinated PCBs >600 μg/kg, and was approximately 20% in those from work areas resulting in blood concentrations of PCBs between 150 and 600 μg/kg (Maroni *et al.*, 1981b). Other studies indicate that work environments resulting in average blood concentrations of lower chlorinated PCBs in workers in the range of 400 μg/kg (Ouw *et al.*, 1976), 266 ± 328 μg/kg (Fischbein *et al.*, 1979), and 1470 μg/kg (geometric mean of Aroclor 1242 concentrations) (Lawton *et al.*, 1985) were associated with alterations in certain serum enzymes indicative of abnormal liver function. Again, the potential involvement of simultaneous exposures to other chemicals was not addressed in any of these studies. For example, Fischbein *et al.* (1979), Chase *et al.* (1982), and Acquavella *et al.* (1986) concluded that the liver effects observed in workers may be related to recreational alcohol intake.

It has been suggested by Ouw *et al.* (1976) that concentrations of PCBs in blood in the range of 200 μg/kg, assuming relatively constant exposure, represent a reasonable recommended value below which abnormalities in liver function would not occur in humans exposed to PCBs in work environments typical of the electrical industry. The suggested blood threshold value for PCBs of 200 μg/kg is supported by the reassessment of electrical workers studied by Lawton *et al.* (1985) in which blood concentrations of PCBs following improvements in the working conditions (e.g., increased ventilation,

changes in products used, etc.) decreased from 1470 μg/kg in 1976 to 277 μg/kg in 1979. In the 1979 assessment, serum enzymes indicative of abnormal liver functions were not significantly different from workers from control areas where chemical exposures, including PCBs, were much less (Lawton *et al.*, 1985). In addition, Fischbein *et al.* (1979) did not observe a significant correlation between changes in biochemical test results (including SGPT, γGTP, bilirubin and LDH, and excepting SGOT) and average blood concentrations of PCBs of 266 μg/kg in electrical workers from work areas associated with greatest potential for chemical exposures; however, the interpretation of these results is confounded since exposures to lower chlorinated PCBs ceased 2 years prior to the evaluation of the workers. Further evidence of a no-effect blood concentration of PCBs is provided in studies of sewage plant workers in which those from work areas with the greatest opportunity for chemical exposures, including PCBs, had average blood concentrations of PCBs of 75.1 μg/kg, with no changes in serum enzymes (Baker *et al.*, 1980).

Several studies have noted increased serum triglycerides and total cholesterol, and decreased high density lipoprotein concentrations in workers with increased blood concentrations of PCBs (Baker *et al.*, 1980; Maroni *et al.*, 1981b; Smith *et al.*, 1982; Lawton *et al.*, 1985). However, as pointed out by Lawton *et al.* (1985), PCBs in the body partition in proportion to tissue lipid concentration: As serum lipid parameters increase, the concentrations of PCBs would also increase because of their association with lipid materials. Therefore, serum PCBs and serum lipid concentrations appear to represent covariant parameters.

A direct effect of PCBs on the liver has been suggested by results of a study in which 14 of 80 individuals with qualitative evidence of exposures to PCBs had hepatomegaly (Maroni *et al.*, 1981a). While these individuals had no reported history of high alcohol or drug intake, other investigators have reported no such effects due to PCBs, or if they have, the effects were minor or confounded by high alcohol intake (Fischbein *et al.*, 1979; Chase *et al.*, 1982; Acquavella *et al.*, 1986; Nethercott and Holness, 1986). Inconclusive relationships between exposure to PCBs and elevated blood pressure have also been reported (Kreiss *et al.*, 1981; Smith *et al.*, 1982; Stehr-Green *et al.*, 1986).

Recently, the cancer mortality rates were examined in workers from electrical capacitor manufacturing plants in order to assess possible associations between cancer and exposure to PCBs (IDSP, 1987). Four major research groups have published studies in this area, including Brown and Jones (1981), Bertazzi *et al.* (1982), Brown (1986), Bertazzi *et al.* (1987), Gustavsson *et al.* (1987), and Nicholson *et al.* (1987). A recent mortality study of capacitor manufacture workers exposed to PCBs reported a small excess in malignant melanoma and cancer of the brain (Sinks *et al.*, 1992). The excess in malignant melanoma incidence was not related to cumulative exposures to PCBs; however, a relationship, albeit weak, between exposures to PCBs and brain cancer was evident. The authors cautioned that the interpretation of the significance of these observations was limited by the small numbers of deaths in the study population, potential population selection bias, and confounding effects of concurrent exposures to other chemicals used in capacitor manufacture. As a general overview, so few deaths from cancer occurred in all these studies that no one study had sufficient statistical power to support firm conclusions regarding the potential associations between PCBs and humans cancers (IDSP, 1987; EPA, 1988).

In an attempt to overcome this problem, IDSP (1987) combined the data from four study populations with the cooperation of the original researchers, who supplied additional data and analysis. One limitation, however, is that this approach is not capable of accounting for different definitions in study cohorts or that individuals were exposed in different locations with possibly different confounding concomitant exposures to other chemicals. Consequently, it is difficult to assess precise exposure levels and durations for the individuals in the various studies. It was concluded from this analysis that a statistically significant increase in the incidences of cancer of the liver, biliary tract, and gall bladder (combined) was evident in the exposed versus the nonexposed groups. These seven cases of cancer all occurred after 10 years from onset of employment, and six of the cases were classified as primary malignancies. Incidences of lymphomas and leukemias combined were also in excess, but were not statistically significant. Of the 19 cases, 3 occurred within 2 years of employment and 1 case within 5 years. Therefore, it is unlikely that these cases were associated with plant employment. Other excess incidences were noted for rectal cancer and combined kidney and urinary bladder cancer. However, they were not statistically significant, and cancer of these sites have not been shown in controlled animal studies of the effects of PCBs (IDSP, 1987).

The most limiting factor in the interpretation of all the studies on workers exposed to PCBs is the lack of consideration of potential confounding effects of simultaneous exposures to other chemicals (James *et al.*, 1993). Since workers from all the occupational studies were also exposed to other chemicals (e.g., the oils of PCBs used in electrical transformers contain 40 to 60% trichlorobenzenes as diluents of the PCBs), the association of changes in serum enzyme activities, serum lipids, and cancers could be due to the other chemicals without involving PCBs, or due to a combined effect of PCBs and other chemicals. The concerns regarding simultaneous exposures to other chemicals and cancer incidence rates are particularly relevant, considering the evidence that PCBs have substantial cancer promoting activity (see Section 3.2.2.4).

3.2.4.2. Nonoccupationally Exposed Populations

A number of studies are available on human populations exposed to PCBs outside the work environment. The magnitudes of exposures to PCBs in these populations were substantially less than those observed in workers, as discussed above; consequently, the expected magnitudes of the responses would be less. In addition, the potential for simultaneous exposures to other chemicals also exists in nonoccupationally exposed populations and may be more difficult to address than in workers in which the number of other chemicals that may be involved are more likely to be known. The studies of female populations exposed to PCBs through the general environment evaluated reproductive effects, ranging from abortions, premature deliveries, reduced birth weights, decreased head circumference, and possible neurological effects; however, none of the studies adequately addresses the confounding effects of simultaneous exposures to other chemicals or various social/lifestyle factors, such as alcohol consumption, tobacco smoking, caffeine consumption, prescription and nonprescription drug use, or socioeconomic status. Consequently, conclusions of causal relationships between these effects and exposures to PCBs per se are tenuous at present.

Some studies suggest that an increase in the number of spontaneous abortions and premature deliveries occurs with elevated concentrations of PCBs in blood. However,

definitive correlations between PCBs and these effects cannot be established because of the small sample size in these studies and the presence of elevated serum concentrations of other organochlorines in some of the women examined. Wassermann *et al.* (1982) and Bercovici *et al.* (1983) reported that elevated concentrations of PCBs in serum were associated with increased spontaneous abortions and premature deliveries. Concentrations of PCBs in serum of 103.04, 82.00, and 20.69 ppb were measured in women who had recent spontaneous abortions, former spontaneous abortions, or were part of a control group, respectively (Bercovici *et al.*, 1983). Wassermann *et al.* (1982) reported concentrations of PCBs in serum of 128 ppb in women in a premature delivery group compared to those of 26.5 ppb in a control group. It was not clear from the published information on these studies whether the potential confounding effects of various lifestyle factors known to affect parturition (e.g., caffeine consumption, tobacco smoking, nonprescription drug consumption, alcohol consumption) were adequately controlled in the analyses of the data.

Lower birth weights and smaller head circumference have been reported for infants born to mothers who consumed greater amounts of fish from the Great Lakes than did control (i.e., low fish consuming) populations (Fein *et al.*, 1984). The strength of the proposed association between exposures to PCBs and the reported effects on developing infants is seriously weakened by several factors:

(i) There are a number of inconsistencies in the proposed dose–response relationship between exposures to PCBs and the effects reported. The authors suggested that PCBs in the fish were the cause of the reported effects although no correlation was observed between fish consumption and concentrations of PCBs in umbilical cord blood serum (IDSP, 1987; Paneth, 1991). Follow-up studies of the children in the Fein *et al.* (1984) study were reported by Jacobson *et al.* (1990a,b). The concentrations of PCBs in cord serum at birth, as reported by Fein *et al.* (1984), were correlated with decreased cognitive performance in the children at 4 years of age; however, there was no correlation between concentrations of PCBs in cord serum and maternal fish consumption (the proposed source of the PCBs). In addition, the possible confounding effects of socioeconomic factors, smoking tobacco, alcohol consumption, and other lifestyle factors known to affect cognitive performance were not adequately addressed (this point is discussed further below).

Exposure to PCBs during lactation, however, did not correlate with cognitive performance at age 4 (Jacobson *et al.*, 1990a), but such exposures did correlate with reduced overall activity in the children at age 4 (Jacobson *et al.*, 1990b). The concentrations of PCBs in serum of children at 4 years of age were: 9.1 ± 3.9 ng/ml for those breast fed for at least 6 months; 1.2 ± 1.6 ng/ml for those children breast fed for less than 6 months; and 0.3 ± 0.7 ng/ml for those children not breast fed (Jacobson *et al.*, 1990a). All of these concentrations of PCBs are within the ranges observed in North American populations without occupational exposures to PCBs.

Also, the number of inconsistencies in the reported analyses for PCBs in maternal and cord blood sera, and in breast milk, affect the confidence of the overall evaluation of possible dose–response relationships. It appears that analyses for PCBs were not conducted on serum samples with lipid concentrations less than 200 mg/dl. This decision could bias the interpretation of subsequent correlations with adverse effects in an undetermined manner since the PCBs in blood are associated with blood lipids (i.e., serum samples with lesser quantities of lipid would be expected to contain lesser quantities of PCBs).

The above factors all detract from the verification of a dose–response relationship between PCBs and the effects observed. The deficiency in the criteria for a dose–response relationship, a basic requirement for establishing causality (Hill, 1965; Fox, 1991), and the lack of substantial differences between the concentrations of PCBs in the study and in the general population, indicate that the effects reported on human development in the populations studied were not causally related to exposures to PCBs.

(ii) The second factor affecting the strength of the proposed association is that the women from the elevated fish consumption group also reported significantly greater consumptions of alcohol, caffeine, tobacco, and cold remedy prescription use during pregnancy than those consuming less fish. In addition, the statistical evaluation of these confounding factors was not appropriate (Government of Canada, 1991; Paneth, 1991). Many of these factors are known to result in lower birth weights and lower developmental scores in infants. Furthermore, the studies of different fish consuming populations did not consider the confounding effects of simultaneous exposure through the consumption of fish to other chemicals, including chlorinated organics such as mirex, and hexachlorobenzene, and various metals such as mercury or lead.

The effect of reduced infant head circumference and reduced body weight at birth was not correlated with the concentrations of PCBs in cord serum when the statistical analysis was adjusted for the potential confounding effects of alcohol, caffeine, and drug use during pregnancy. In addition, there were differences in maternal body weights (the high-fish consumers weighed 4.1 kg less) prior to pregnancy. This observation is important because prepregnancy body weight is one of the factors influencing infant birth weights. Further, of the population consuming greater quantities of fish, the proportion with nonspontaneous deliveries was almost 50% higher than the proportion in the group consuming lesser quantities of fish. This observation is important because infants from nonspontaneous deliveries are more prone to apparent developmental deficits as newborns (Paneth, 1991). All these confounding factors seriously detract from the biological plausibility of an association between the amount of exposure to PCBs, as indicated by the concentrations of PCBs in blood, and effects on infant development.

(iii) A third factor affecting the strength of the proposed association is the lack of plausibility and consistency of association that are required (Hill, 1965; Fox, 1991) to establish a causal relationship. Greater umbilical cord serum concentrations of PCBs were marginally associated with cognitive performance parameters (e.g., poorer verbal and memory scores on the McCarthy Scales performance tests and lower scores in the verbal and numerical memory subtests) in the same children 4 years later (Jacobson *et al.*, 1990a). Scores on such tests are affected by socioeconomic status of the subjects and the age at which the tests were conducted. Scores for other components of the McCarthy Scales performance tests (perceptual performance, quantitative, motor, and general cognitive index) were unrelated to *in utero* exposure to PCBs. Also, no correlation was observed between fish consumption and concentrations of PCBs in umbilical cord serum. As a result, no correlation can be made between contaminated fish and scores on the McCarthy Scales performance tests. These factors seriously weaken the plausibility of associations between the effects reported by Fein *et al.* (1984) and exposures to PCBs.

The arguments for plausibility of association are also weakened by observations that, even though postnatal lactational exposures to PCBs are far greater than those

experienced *in utero* (Jacobson *et al.*, 1989), the children exposed to PCBs via lactation for longer periods had significantly greater scores on both the Memory and Verbal Scales tests (Jacobson *et al.*, 1990a). Poorer scores were significantly associated only with infants who consumed the greatest concentrations of PCBs through breast milk (1250 to 2600 ng PCBs/ml milk). Further, the results of the Jacobson *et al.* (1990a) study also indicated that in the 4-year-old children, greater concentrations of PCBs in serum were not associated with cognitive deficits. This result was attributed by Jacobson *et al.* (1990a) to greater intellectual stimulation during infancy in these children, since the children with the greater concentrations of PCBs in serum were breast fed for longer periods than those children with lesser concentrations of PCBs in serum.

The plausibility of the results of the Jacobson *et al.* (1990a) study is further eroded by the report that certain marginal deficits observed in some clusters of the McCarthy tests were associated with greater concentrations of PCBs in the serum of the mother, but not with greater exposures to PCBs through lactation. Furthermore, it was not apparent that the scores obtained in the tests of any of the children were outside the ranges of normal since no such ranges were given. Also, a total of approximately 38 behavioral and neurological tests were conducted on the children, even though the results of only 2 tests were reported to be affected. Some association based on chance alone would be expected from this large number of tests. In addition, the assessment of the test results was based on a "clustering" approach, which is not a standard procedure in evaluating neurological test results from children. No information was available on the effect of the clustering on the interpretation of the results that would be expected from the general population. Therefore, it is not possible to evaluate the importance of this approach in the interpretation of the results of the studies.

The plausibility of the proposed association is further degraded by inconsistencies in the information reported in different publications of the same studies. Jacobson *et al.* (1990b) reported, based on Fein *et al.* (1984), that prenatal exposure to PCBs through mothers consuming fish was associated with decreased birth weights. The same children, assessed 4 years later, had greater serum concentrations of PCBs (attributed mainly to exposures during lactation) than those from mothers consuming lesser quantities of fish, and were also reported by Jacobson *et al.* (1990b) to have reduced activity levels. This result, however, is not in accordance with findings of Jacobson *et al.* (1990a) that the children who had longer lactational exposure had no cognitive deficits when compared to children with shorter lactational exposure. In fact, prior to the controling of confounding variables, the children with longer lactational exposure tended to have greater scores on the McCarthy Scales performance tests (Jacobson *et al.*, 1990a). To explain this finding in the first follow-up study, Jacobson *et al.* (1990a) suggested that the children who were breast fed longer had the greater intellectual stimulation from their mothers. If this argument is accepted, it is difficult to explain "reduced activity levels" in those 4-year-old children having relatively greater concentrations of PCBs in serum, since most of these children were part of the group of infants breast fed for longer periods of time. In addition, no ranges of normal were included for any of the data sets from either the first or the second follow-up study.

(iv) The fourth factor affecting the strength of the proposed associations is that the criteria of consistency of observation that is an essential component in the establishment of causality of association based on epidemiological data (Hill, 1965; Fox, 1991) is not met by the studies reported by Fein *et al.* (1984) and Jacobson *et al.* (1990a,b).

No relationships were observed between blood concentrations of PCBs and reproductive outcomes in a random sample of 100 participants of a study of 1112 women in the Green Bay area of Wisconsin (Dar *et al.*, 1992) (near the same area where numerous effects were observed in wildlife). Although the concentrations of PCBs in the serum were lower than those observed by Fein *et al.* (1984), the analyses were congener specific rather than for total concentrations of PCBs, and therefore are difficult to compare between the two studies. The birth weights of infants in the Dar *et al.* (1992) studies were greater for women with greater fish consumption and greater concentrations of PCBs in maternal serum; these results directly contradict those reported by Fein *et al.* (1984) and Jacobson *et al.* (1990a,b). Greater birth weights have also been reported in other populations in which the mothers consumed greater quantities of fish (Olson *et al.*, 1990). Similarly, Fitzgerald *et al.* (1992) observed that the concentrations of PCBs in breast milk were the same (although the congener profiles were different) between 53 Mohawk women consuming fish from the St. Lawrence River and a population of 109 women from Warren Schoharie County in New York. All these additional studies demonstrate a lack of consistency between fish consumption, concentrations of PCBs in breast milk, and serum and reproductive outcomes as reported by Fein *et al.* (1984) and Jacobson *et al.* (1990a,b).

Other studies designed to evaluate possible causal associations between human development and exposures to PCBs, DDT, and DDE using a cohort of children from North Carolina were conducted by Rogan *et al.* (1986a,b). Prenatal exposures of infants to PCBs, DDT, and DDE were predicted from extrapolations across the nursing period based on breast milk analysis of one sample at one stage of nursing. The daily chemical exposures of the infants were then calculated based on these predicted concentrations of the chemicals in breast milk. No validation of these predictions was reported. The neurological development of the infants was then correlated with the calculated concentrations of PCBs in breast milk fat to estimate a NOAEL of 3.4 ppm and 1.0 ppm, respectively, for Brazelton and Baileys infant development scores. The Brazelton scores are based on 27 behavioral tests and 20 reflex tests that were summarized into clusters (Rogan *et al.*, 1986b) following the procedures outlined by Jacobson *et al.* (1984). Only the values of the cluster scores for tonicity and reflexes were correlated with exposures to PCBs or DDE. Although the effects on the various behavioral parameters were correlated with estimated exposures to PCBs, the plausibility of the results, and therefore the strength of the association, is considered weak due to the fact that the women with higher concentrations of PCBs in milk were also older, had a greater rate of alcohol consumption, and greater tobacco smoking incidence. All these factors are known to affect scores on a wide range of neurological testing regimes for newborn infants. These confounding factors, plus the observation of effects on a small number of infants (i.e., only 49 infants of a total of 856 were exposed to milk concentrations of PCBs above 3.5 ppm, which is reported as the NOAEL, and only 42% of these showed positive tests) indicates that it is unlikely that there was a causal association between the observed effects and exposures to PCBs.

Based on the above analysis, and considering the marginal significance of the observations, the information reported by Fein *et al.* (1984), Rogan *et al.* (1986a,b), and Jacobson *et al.* (1990a,b) do not meet the criteria for the establishment of a causal association for an effect of PCBs on growth and behavior in human populations. If such possible relationships are to be investigated further, it is important that the sci-

entific principles critical to the establishment of a reasonable causal association between events, as outlined by Hill (1965) and Fox (1991), are followed, and that the results of the investigations are reported in a comprehensive manner.

The Yusho incident in Japan in 1968 and the Yu-Cheng incident in Taiwan in 1979 provide additional information on the possible effects in human populations (approximately 1800 and 1900 people, respectively) accidentally exposed to large quantities of PCBs. In both incidents, acute toxicosis resulted from consuming rice bran oil contaminated with an industrial oil that contained PCBs, polychlorinated dibenzofurans, and polychlorinated quinones. In the Yusho incident, the average oil consumption was about 2 g (Kuratsune *et al.,* 1972) and it was estimated to contain 5 ppm PCDFs (Nagayama *et al.,* 1976). In the Yu-Cheng incident, the ranges of PCBs and polychlorinated dibenzofurans in the oil were 53 to 405 ppm and 0.180 to 1.68 ppm, respectively (Chen *et al.,* 1981). Various health effects were observed in both populations, the most common being acneform eruptions and pigmentation of the skin (Kuratsune *et al.,* 1969; Chang *et al.,* 1980a,b). Other symptoms reported were numbness and swelling of limbs, changes in blood cell counts, dysfunction of the liver including increased serum triglycerides, and effects on the immune system (Shigematsu *et al.,* 1978; Chang *et al.,* 1980a,b). Infants born of mothers who consumed the contaminated oil were small for gestational age, displayed skin and nail pigmentation, and had swollen gums and teeth deformities (Taki *et al.,* 1969; Yamaguchi *et al.,* 1971; Yamashita, 1977; Lucier *et al.,* 1987; Sunahara *et al.,* 1987; Rogan *et al.,* 1988; Gladen *et al.,* 1990). Amano *et al.* (1984) examined cancer mortality rates of Yusho victims. Persons greater than 40 years of age had higher mortality rates than expected in males, and incidences of liver cancer were consistently high in both males and females. In a follow-up study in which the subjects averaged about 11 years postexposure, apparent excesses in mortality due to liver cancer and other liver diseases was reported in males; however, the authors noted geographic inconsistencies in their data and did not examine the potential quantitative relationships between rice oil consumption and mortality (Kuratsune *et al.,* 1987). The EPA (1988) reported many shortcomings to the cancer incidence study, including lack of verification of cancer diagnoses originally made by family members, calculation discrepancies on expected figures, and no information about job history, alcohol consumption, or smoking history.

The health effects observed in the Yusho and Yu-Cheng populations have been attributed to exposures to polychlorinated dibenzofurans, as opposed to PCBs, in the contaminated rice oil (EPA, 1988). This conclusion was based on evidence of tissue/blood concentrations of PCBs and PCDFs seen in Yusho and Yu-Cheng patients and concentrations observed in electrical industry workers from the Yusho area of Japan who were exposed to PCBs that did not contain measurable concentrations of polychlorinated dibenzofurans (Takamotsu *et al.,* 1984). The concentrations of PCBs in the blood in the workers were as great or greater than those of the Yusho or Yu-Cheng patients, whereas concentrations of polychlorinated dibenzofurans were high in Yusho and Yu-Cheng patients in contrast to below analytical detection limits in the workers. No adverse health effects were observed in the workers (Masuda and Kuroki, 1982; Takamotsu *et al.,* 1984; Kashimoto *et al.,* 1985). Based on the differences in adverse effects associated with elevated exposures to PCBs in contrast to polychlorinated dibenzofurans in human and animal studies it was concluded that the adverse health effects observed in the Yusho and Yu-Cheng patients exposed to contaminated rice oil were related to exposures to polychlorinated dibenzofurans.

In summary, the available studies of human populations exposed to PCBs indicate that the only documented adverse effects occur on the skin. Changes noted in various serum lipid parameters may be due to lipid partitioning rather than an adverse affect of PCBs. Changes in liver enzymes have been found in a few studies under extreme exposure conditions, but their clinical significance is not known. However, the basis for establishment of evidence of causality between these effects and exposure to PCBs varies among studies (IDSP, 1987; James *et al.,* 1993). A major problem in the interpretation of the available information on possible adverse effects in humans from exposure to PCBs is the confounding effects of simultaneous exposures to other chemicals. James *et al.* (1993) concluded that the available evidence showing a causal association between exposures to PCBs and adverse effects on humans is consistent only for effects on the skin.

PCB Exposure and Concentrations in Blood

Following continuous long-term exposures, the steady-state transfer of PCBs between tissue lipids and blood lipids is the major determinant of blood concentrations of PCBs. Therefore, providing that the body tissue storage capabilities for PCBs were not saturated, the concentrations of PCBs in blood would be determined by:

(i) the dose of PCBs entering the body;
(ii) the steady-state equilibrium of PCBs between blood lipids and fatty tissues;
(iii) the total mass of fatty tissue in the body; and
(iv) the rate of excretion of PCBs from the body.

Due to the large mass of lipid tissues in the body, it is unlikely that the body storage capabilities for PCBs would be saturated at usual exposure rates for PCBs from environmental sources. Therefore, the above assumptions should be valid under usual environmental exposure scenarios.

Application of the first order decay equation shown below was used to estimate the steady-state level of PCBs that would be in the body for a continuous daily exposure of a given amount of PCBs.

$$C_f = \sum C_i e^{-kt},$$

where C_f is the steady state amount of PCBs in the body (μg/person), C_i is the daily input of PCBs into the body (μg/person), k is the elimination rate constant of PCBs from the body ($0.693/t\frac{1}{2}$) ($days^{-1}$), $t\frac{1}{2}$ is the elimination half-life of PCBs from the body (days), and t is the elapsed time (days).

The steady-state concentrations of PCBs in the body, defined as the point in time following a constant degree of exposure when the predicted incremental change in blood concentrations with each dose would be less than 0.01% of the total concentration, were calculated in a study of one individual by the summation of the constant daily uptake rate assuming a half-life of 100 to 300 days for clearance of PCBs from the body (Buhler *et al.,* 1988). Applying this exponential model for the clearance of PCBs by mobilization from adipose tissues, and assuming an oral bioavailability of approximately 50%, a daily dose of 1 μg PCBs/person/day would result in a steady-state body concentration ranging from 71.4 to 208 μg/person.

If it is assumed that a 70-kg person has 7 kg of adipose tissue (i.e., 10% body fat), then the steady-state concentration of PCBs in adipose tissue resulting from an exposure

rate of 1 μg/person/day (or 0.0143 μg/kg body wt/day) would be 10.2 to 29.7 μg PCBs/kg adipose tissue. To estimate the concentrations of PCBs in blood, it was assumed that the concentrations of PCBs in blood lipids were the same as those in adipose tissue. This assumption is based on the observations of Papke *et al.* (1989, 1992) that the concentrations of chlorinated dioxins and furans in adipose tissue and blood lipids were approximately the same in a variety of different human exposure scenarios, and that PCBs and chlorinated dioxins/furans behave in a similar manner in the body.

Since the concentrations of lipids in blood are usually in the range of 0.5% (w/w) of the blood, the steady-state blood concentrations of PCBs, assuming an absorbed dose of 1 μg/person/day (or 0.0143 μg/kg body wt/day), would be 0.051 to 0.15 μg/kg or ppb (i.e., 10.2 to 29.7 μg PCBs/kg adipose tissue × 0.005 fraction lipid in blood = 0.051 to 0.15 μg PCB/kg blood). The exposure duration necessary to achieve these steady-state blood concentrations would range from approximately 500 to 1500 days (i.e., five times the half-lives of 100 to 300 days). If an exposure of 1 μg PCBs/day results in estimated blood concentrations of 0.051 to 0.15 ppb, the dose of PCBs that would result in a given steady-state blood level of PCBs can then be estimated. The estimated daily doses of PCBs calculated to be associated with some steady-state blood levels associated with the presence or absence of PCB-induced effects in humans are discussed below.

Concentrations of PCBs in Blood Associated with Adverse Effects

No adverse effects were observed based upon liver function parameters in workers with concentrations <200 μg PCBs/kg blood (ppb) in occupational settings (Ouw *et al.*, 1976; Maroni *et al.*, 1981b; Lawton *et al.*, 1985). In addition, Baker *et al.* (1980) did not observe any significant adverse effects in workers with concentrations of PCBs in blood of approximately 75 μg/kg. Populations consuming Lake Michigan sport fish known to contain PCBs, plus a variety of other chemicals, had average blood concentrations of PCBs slightly greater than 20 μg/kg in both 1982 and 1989, compared to blood concentrations of PCBs of 7.2 and 6.6 μg/kg in 1982 and 1989, respectively, in populations that did not consume sport fish from the Great Lakes. The doses of PCBs associated with each of these different blood concentrations of PCBs, calculated based on the information outlined above indicating that a dose of 1 μg of PCBs each day would result in a blood concentration of PCBs of approximately 0.051 to 0.15 μg/kg or ppb for a 70-kg individual, are summarized in Table 5-4.

These estimated doses of PCBs, even for human populations exposed to the ambient concentrations of PCBs (e.g., blood concentrations averaging 7 μg/kg) (Hovinga *et al.*, 1992) are 7- to 20-fold greater than the exposure limit for PCBs of 0.1 μg/kg body wt/day recommended by the EPA (1988), and 0.7- to 2.0-fold greater than the exposure limit of 1.0 μg PCBs/kg body wt/day recommended by Health and Welfare Canada (Grant, 1983) or the Food and Drug Administration (Boyer *et al.*, 1991). These exposure limits recommended by the regulatory agencies indicated were developed by the application of uncertainty factors to data from toxicity studies of PCBs in pregnant monkeys (see Section 3.2.2).

No adverse effects were evident in workers with blood concentrations of PCBs in the range of 75 ppb (Baker *et al.*, 1980) to as great as 200 ppb (Ouw *et al.*, 1976; Maroni *et al.*, 1981b; Lawton *et al.*, 1985). According to the blood concentrations of

TABLE 5-4

ESTIMATED DOSES OF PCBs BASED ON BLOOD CONCENTRATIONS OF PCBs[a]

Blood Concentrations of PCBs (μg/kg blood or ppb)	Estimated Oral Dose of PCBs (μg/kg body weight/d)[b]
200[c]	19 to 56
75[d]	7.1 to 21
20[e]	1.9 to 5.6
7[f]	0.7 to 2.0

[a] Concentrations of blood PCBs of occupationally exposed populations (200 and 75 μg/kg), sport fish consumers (20 μg/kg) and non-fish consumers (7 μg/kg) and corresponding estimated doses of PCBs were based on information discussed in the text.

[b] Assuming a body weight of 70 kg; total fat = 10% of body weight; total blood lipid = 0.5%; blood distribution half-lives of 0.4 and two days, and a whole body clearance half-life for PCBs of 100 to 300 days.

[c] Concentrations of PCBs in blood serum in the range of 200 μg/kg were proposed as the concentration that would not be associated with changes in blood enzymes indicative of abnormal liver function (Ouw *et al.*, 1976). In other studies, non-significant but suggestive changes in these enzymes were observed at blood serum concentrations of PCBs of 200 μg/kg, and no suggestive changes were evident at 100 μg/kg (Maroni *et al.*, 1981b).

[d] No changes in blood serum enzymes indicative of abnormal liver function were reported in electrical workers with blood concentrations of PCBs of 75 μg/kg (Fischbein *et al.*, 1979).

[e] Concentrations of PCBs in blood serum of pregnant women from elevated sport fish consuming populations.

[f] Concentrations of PCBs in blood serum of pregnant women who did not consume sport fish.

PCBs predicted from specific exposure rates as outlined in Table 5-4, concentrations of PCBs in blood of 75 ppb would result from exposures 6.9- to 21-fold greater than the Health and Welfare Canada and FDA exposure limits, and 69- to 210-fold greater than the EPA (1988) exposure limit for PCBs. The differences between the currently recommended exposure limits for PCBs and those based on observed blood concentrations of PCBs in various populations where no adverse effects were observed reflect an apparent degree of conservatism in exposure limits developed from the application of arbitrary uncertainty or safety factors to data from controlled laboratory studies in animals.

3.2.5. Conclusions

The approach to the evaluation of the potential risks associated with chemical exposures has been outlined in detail in Chapter 1 of this document. Briefly, the assessment of the potential risks or consequences arising from exposures of humans to PCBs is based on comparisons between the magnitude of exposures to PCBs under various scenarios of concern and the exposure limit for PCBs that is considered not to result in the occurrence of potential adverse effects to human health. Information on the changes in magnitude of the estimated risks over time provides a critical perspective to the overall significance of the exposures and to the impact of various past efforts to control or limit PCBs exposures. This would enable informed decisions on the necessity for and the focus of additional measures that may possibly be needed to limit the releases of PCBs to the environment.

3.2.5.1. Exposure Limits

Ideally, exposure limits for chemicals such as PCBs provide an estimate of the magnitude of exposure to that chemical that could occur over a lifetime to the human population (including sensitive subgroups) without the occurrence of adverse effects. If the chemical has a threshold-type dose–response relationship, the exposure limit would be expressed as a reference dose (RfD), indicating an exposure level below which no responses would be expected. If the chemical has a nonthreshold dose–response relationship, the exposure limit would be expressed as a risk specific dose (RSD), specifying an exposure level associated with a specific degree of risk of occurrence of adverse effects. The scientific basis for these concepts in the establishment of exposure limits is discussed in more detail in Chapter 1 of this document.

For PCBs, the exposure limits used by various agencies are expressed as RfDs, with values ranging from 0.1 to 1.0 μg/kg body wt/day (Table 5-5), based on a weight of evidence that PCBs have a threshold-type dose–response relationship. An exposure limit of 0.1 μg/kg body wt/day has been recommended by the EPA (1988) based upon the application of a 100-fold uncertainty factor to the NOAEL of 0.25 ppm Aroclor 1016 in the diet (equivalent to a dose of 10.5 μg PCBs/kg body wt/day) that was associated with adverse reproductive effects in monkeys (Barsotti and Van Miller, 1983). Based on the reproductive toxicity of Aroclor 1248 in monkeys, Health and Welfare Canada recommended a tolerable daily intake (TDI) (equivalent to an RfD) of 1 μg/kg body wt/day (Grant, 1983). The (U.S.) FDA has set a TDI of 1 μg PCBs/kg body wt/day based upon animal data as well as epidemiological information from exposed human populations (FDA, 1973; Boyer *et al.*, 1991).

In an effort to reduce total human exposures to PCBs, the FDA has set the following tolerance concentrations as unavoidable contaminants in foods and food products (Boyer *et al.*, 1991): Milk (fat basis), 1.5 ppm; manufactured dairy products (fat basis), 3 ppm; eggs, 0.3 ppm; finished feed for food producing animals, 0.2 ppm; animal feed components of animal origin, animal feed concentrates, supplements, pumices, 2 ppm; infant and junior foods, 0.2 ppm; paper food-packaging material, 10 ppm; and fish and shellfish (edible portion), 2 ppm. Tolerance levels for fish and shellfish were reduced from original concentrations of 5 ppm based on new toxicological information.

An alternative method for the evaluation of potential adverse effects from exposure to PCBs would be to compare the concentrations of PCBs detected in blood to the concentrations in the blood reported in the scientific literature for human populations exposed to PCBs in which various adverse effects either were or were not observed. Exposure limits for PCBs that would not produce adverse effects could be estimated,

TABLE 5-5

RECOMMENDED REFERENCE DOSES (RFDS) FOR PCBS

Source	Reference Dose (μg PCBs/kg body weight/d)	Types of PCBs
EPA (1988)	0.1	Aroclor 1016
FDA (1973)	1.0	not specified
Health and Welfare Canada (Grant, 1983)	1.0	Aroclor 1248

providing the exposures associated with the no-adverse-effect blood concentrations of PCBs were known. Although this approach has not been applied previously to PCBs, the establishment of exposure limits based on concentrations of chemicals in blood has been used for lead (EPA, 1989a). An advantage of estimating exposure limits for chemicals based on concentrations of chemicals in human blood is the avoidance of the uncertainties associated with extrapolating toxicological information from laboratory studies using animals to humans.

As with all methods of estimating exposure limits, the validity of using the "blood concentration estimation" approach is dependent on the quality of the information used for estimating blood concentrations of PCBs from specific rates of exposure and for determining the blood concentrations that either would or would not be associated with adverse effects. The basic principles of such an approach are outlined in the following paragraphs, using the information available for the estimation of the concentrations of PCBs in blood from specific rates of exposure and for the blood concentrations of PCBs in humans not associated with adverse health effects.

3.2.5.2. Estimation of Human Exposure to PCBs

The rate of exposure of humans to PCBs can be assessed through uptake of PCBs based on their concentrations in various environmental media to which humans may be exposed (e.g., food, water, air, soils/dusts) or through the measurement of concentrations of PCBs in body tissues and fluids that occur as a consequence of exposures through environmental media under different circumstances. In general, data on the prevalence of PCBs (Section 3.1) indicate that their concentrations in most environmental media were greatest in the early 1970s, and since then have shown a relatively steady decrease with time. These temporal declines in concentrations of PCBs in environmental media coincide with the reductions in the quantities of PCBs entering the environment, largely as a consequence of changes in use patterns of PCBs (Regulatory Network, Inc., 1992). Quantities of PCBs entering the environment since the early 1980s are largely due to accidental and fugitive releases from storage facilities, and continued leaching from disposal sites. The quantities of PCBs currently in environmental media are distributed through various interrelationships among different media, governed largely by the physical/chemical properties of PCBs. For example, long-range atmospheric transport (Hansen, 1987; Lockhart and Muir, 1988; Norstrom and Muir, 1991), mobilization from aquatic sediments (Hansen, 1987; Safe, 1989), and food chain movement from lower to higher trophic levels (Hansen, 1987; Muir *et al.*, 1988; Norheim *et al.*, 1992).

Sediment core samples provide an integrated history of changes in environmental loadings at specific locations with time (see Table 5-2). Sediments are one of the major starting points for movements of PCBs through food chains from lower to higher trophic levels of organisms. Sediment cores from the Great Lakes show increasing concentrations in sediments, from low concentrations in the early 1900s (possibly related to natural sources of PCBs; Gribble, 1992), to greater concentrations in the mid-1970s reflecting anthropogenic sources. Thereafter, sediment concentrations of PCBs show a consistent decreasing temporal trend for sediments deposited between the mid-1970s and the late 1980s (Eisenreich *et al.*, 1983b; Swackhamer and Armstrong, 1986).

The information available on the concentrations of PCBs in air is not adequate for the assessment of temporal changes; however, it does indicate that concentrations of PCBs in air near sites with known contamination can be 10- to 100-fold higher than typical urban areas (Table 5-2). The concentrations of PCBs in ambient air from locations without known point sources do not appear to differ markedly between urban, suburban, and rural areas. PCBs are present in air in remote areas, although the concentrations are 10- to 100-fold less than those near populated areas (Table 5-2).

MacLeod (1981) concluded that the concentrations of PCBs in indoor air in public buildings and residences are approximately 10-fold greater than those measured in outdoor air. Therefore, exposures through indoor air could be greater than from outdoor air, depending on the proportions of time spent indoors versus outdoors.

From the environmental concentrations summarized in Section 3.1, typical daily exposures of humans to PCBs in an urban center have been calculated and are summarized in Table 5-6, assuming approximately 56% of the person's time is spent outdoors and 44% indoors.

Assuming exposures through all these routes occurred simultaneously, the resulting exposure would be less than 0.48 μg PCBs/day (0.007 μg PCBs/kg body wt/day for a 70-kg person), or approximately 15- to 150-fold less than the exposure limits for PCBs recommended by the North American regulatory agencies. However, diet, which is not considered in the above exposure estimates, is the major source of human exposure to PCBs, primarily due to the tendency for PCBs to bioaccumulate in organisms at upper trophic levels that are major components of the human diet (e.g., fish, dairy products, various red meats, possibly high-fat plant products). Human exposures to PCBs through diet decreased by approximately 10-fold over the 1970s (from approximately 6.9 μg PCBs/day in 1971 to approximately 0.7 μg PCBs/day in 1980), then continued to slowly decline to 0.05 μg PCBs/day by 1989, a 138-fold decrease from 1971 (graphically presented in Fig. 5-1, see also Section 3.1.5). These data reflect coincident changes in concentrations of PCBs in various environmental media, as discussed in the previous paragraph, and demonstrate that human exposures to PCBs

TABLE 5-6

ESTIMATED HUMAN EXPOSURES TO PCBs THROUGH VARIOUS MEDIA

Environmental Media	Concentrations[a] of PCBs	Exposure to Media	Bioavailability[c] (%)	Exposures to PCBs (μg/d)
Soil	0.015 μg/g	0.05 g/d[b]	50	0.000375
Air				
- outdoor	9.63 ng/m^3	13 m^3/d[d]	43[e]	0.054
- indoor	100 ng/m^3	10 m^3/d[d]		0.41
Drinking Water	< 20 ng/L	2 L/d[b]	50	< 0.02
Total				0.48

[a] Values from Table 5-2.
[b] Values from EPA, 1989b.
[c] Values from Section 3.2.1.
[d] Assuming 23 m^3 per 24 hours (ICRP, 1976), with 13 m^3 while outdoors and 10 m^3 while indoors.
[e] Includes particles retained in lung (13%) and particles swallowed following clearance from the lung (30%).

through diet have declined substantially between the early 1970s and the late 1980s. Therefore, estimated total exposures to PCBs would range from 7.38 μg/day (6.9 μg/day from diet plus 0.48 μg/day from other sources), based on the 1971 dietary exposure data, to approximately 0.53 μg/day (0.05 μg/day from diet plus 0.48 μg/day from other sources), based on 1989 dietary exposure. On a body weight basis, these exposures are equivalent to approximately 0.11 to 0.008 μg PCBs/kg body wt/day for 1971 and 1989, respectively.

Concentrations of PCBs in tissues and in various body fluids provide a direct indication of temporal trends in magnitudes of exposure. The significance of overall exposures to PCBs can also be evaluated based on the comparison of concentrations of PCBs in body tissues and fluids between the general population and population associated with excessive exposures to PCBs in occupational settings or through accidental releases of various types. The data summarized in Section 3.2.4 on the potential adverse effects of PCBs on humans indicate that blood concentrations were significantly elevated in workers using PCBs, and that the improvement in work environments resulted in substantial decreases in the blood concentrations of PCBs of workers. These data provide evidence that conclusions, made in some publications, that PCBs persist in humans and that the concentrations of PCBs in human tissues do not decrease significantly with decreases in exposure (Swain, 1988, Greenpeace, 1992) are inaccurate (Regulatory Network, Inc., 1992).

Since PCBs accumulate in fatty tissues, useful information on temporal trends regarding exposure to PCBs can be obtained from data on concentrations of PCBs in human adipose tissue. Such information is provided from the National Human Adipose Tissue Survey conducted in the United States, in which adipose tissue specimens from statistically selected samples of surgical patients and autopsied cadavers were analyzed for a series of toxic chemicals. The results were grouped as not detected; detected but less than 1 ppm; between 1 and 3 ppm; or greater than 3 ppm (Regulatory Network, Inc., 1992). An upward trend, at least until 1984, was observed in the percentage of the population having detectable concentrations of PCBs. There were slight differences in the trends determined by the two analytical methods used. For example, in 1984, 98% of samples had detectable concentrations of PCBs as measured by high-resolution gas chromatography/mass spectrometry (HRGC/MS, detection limits 0.01 to 0.03 μg/g lipid), compared to 100% as measured by gas chromatography/electron capture detector (GC/ECD, detection limit 0.33 μg/g wet wt). In addition, the actual concentrations of PCBs reported by the GC/ECD method appeared to be greater than the level determined using the more sensitive HRGC/MS method. For example, analysis of the 1984 samples by the GC/ECD method found all samples at 0.33 μg/g or greater, compared to the HRGC/MS method which found 30 out of 45 samples as not detected or less than 0.33 μg/g. These results underline the importance of considering differences in analytical methods in the interpretation of data on concentrations of PCBs, and indicate that older data not collected using HRGC/MS methods must be regarded with some skepticism, since the concentrations of PCBs may not be as great as indicated.

A preliminary review of the 1986 data indicated that about 93.5% of the population had detectable concentrations of PCBs in adipose tissue, and that there was a downward temporal trend in the percentage of the population with levels of PCBs greater than 1 ppm and greater than 3 ppm. In 1972, 62% of the population had concentrations of PCBs of greater than 1 ppm compared to 2% in 1984 (Fig. 5-2). In 1972, 4% of the population had concentrations of PCBs greater than 3 ppm, and the proportion in-

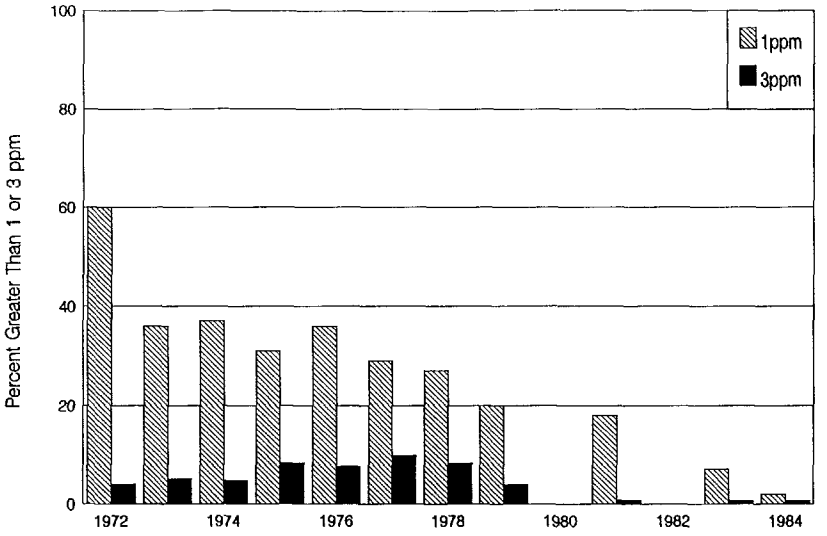

FIG. 5-2. National Human Adipose Tissue Survey results; 1972 to 1984 PCBs concentrations greater than 1 or 3 ppm. Reproduced with permission from Regulatory Network, Inc. (1992).

creased to slightly less than 10% by 1977; however, by 1983 and 1984, <1% of the samples had greater than 3 ppm of PCBs (Fig. 5-2). Robinson *et al.* (1990) reported similar trends in their review of organochlorine residue concentrations in adipose tissue.

Temporal trends in blood serum concentrations of PCBs are not as extensively documented; however, a general downward trend is evident from the early 1970s through the 1980s in populations with or without known occupational exposures to PCBs (Agency for Toxic Substances and Disease Registry, 1991). Serum concentrations of PCBs in Michigan residents declined from 56 μg/kg in 1974 to 21 μg/kg in 1980; this decrease was coincident with a decrease in fish consumption. For residents not consuming fish, median serum concentrations of PCBs declined from 15 μg/kg in 1973 to 6.6 μg/kg in 1983 (Humphrey, 1983). Changes in serum concentrations of PCBs in these populations have been less pronounced since the early 1980s. Concentrations of PCBs in serum from persons consuming sport fish from Lake Michigan averaged 21.1 μg/kg in 1982 and 20.5 μg/kg in 1989; the annual number of fish meals reported by this population were 55.7 in 1982 and 53.5 in 1989 (Hovinga *et al.*, 1992). The concentrations of PCBs in serum of Michigan populations that did not consume sport fish averaged 6.8 μg/kg in 1982 and 6.6 μg/kg in 1989.

Similar trends were also observed in Japanese populations exposed either accidentally or occupationally (Regulatory Network, Inc., 1992). Accidentally exposed individuals had similar blood concentrations of PCBs within 5 years after exposures stopped, as unexposed individuals and concentrations of PCBs in serum from workers exposed decreased at a rate of about 10% per year after exposure stopped.

3.2.5.3. Health Significance of Environmental Concentrations

To evaluate the potential risks to humans from PCBs in the environment, the exposure limits from above were compared with the magnitude of exposures to PCBs

expected from environmental sources (Section 3.1). The exposure limits for PCBs ranged from 0.1 to 1.0 μg/kg body wt/day (Table 5-5). These exposure limits indicate that a 70-kg human may consume 7 to 70 μg of PCBs per day without adverse effects. The above exposure limits are considered conservative, since the conclusions from Section 3.2.4 indicate that no adverse effects are observed in adults with concentrations of PCBs in blood serum in the range of 75 to 200 μg/kg, based on Aroclor 1248 and 1254 gas-chromatographic patterns. In addition, blood serum concentrations of PCBs of approximately 20 μg/kg in pregnant women from elevated sport fish-consuming populations do not appear to be associated with adverse effects in the mothers or their infants. As concluded in Section 3.2.4, the decreased birth weights and head circumference in newborns and cognitive learning abilities in children at the age of 4 years do not meet even minimal criteria required to establish causal associations between the effects observed and exposures to PCBs. The application of pharmacokinetic information to predict exposure rates that would be associated with specific concentrations of PCBs in blood, as discussed in Section 3.2.4, indicates that the exposure limits of 0.1 to 1.0 μg PCBs/kg body wt/day are conservative and that adverse human health effects would not occur at such exposure rates maintained over a person's lifetime.

Based on the exposures calculated in Section 3.2.5, the average dietary exposures to PCBs of a 70-kg person in 1971 were approximately equivalent to the recommended EPA (1988) exposure limit of 0.1 μg/kg body wt/day, and were about 10-fold less than the exposure limit of 1 μg PCBs/kg body wt/day recommended by Health and Welfare Canada and the Food and Drug Administration (Table 5-5). By 1989, the predicted exposures were more than 12.5- to 125-fold less, respectively, than the two different exposure limits. Information based on total diets of infants (up to 6 months old) and toddlers (2 years old), collected as part of the FDA total diet study (Regulatory Network, Inc., 1992), showed that both age groups were exposed to an average of 0.001 μg PCBs/kg body wt/day (Gunderson, 1988), or approximately 100- to 1000-fold less, respectively, than the two exposure limits.

Since fish is a major source of dietary exposure of humans to PCBs (Regulatory Network, Inc., 1992), there have been concerns about potential excessive exposures to PCBs of populations consuming great quantities of fish, particularly those consuming sport fish from water systems known to contain elevated concentrations of PCBs (Hansen, 1987; Hovinga *et al.*, 1992). The concentrations of PCBs in serum from Michigan residents that consumed >10 kg of sport fish per year were approximately 3.7-fold greater than nonfish eaters (i.e., 56 μg PCBs/kg blood sera in fish eaters in 1974 compared to 15 μg/kg in nonfish eaters in 1973; Humphery, 1983). Further studies of these populations showed that the concentrations in the fish-eating population had decreased to 21 and 19 μg PCBs/kg blood serum, compared to 7.1 and 6.6 μg PCBs/kg blood serum (ppb) in nonfish eaters in 1982 and 1989, respectively (Hovinga *et al.*, 1992). Based on studies in occupationally exposed populations, no adverse effects (as indicated by changes in blood enzymes indicative of abnormal liver function) were observed at concentrations of 75 to 200 μg PCBs/kg blood serum, indicating that no adverse health effects would be expected in the Michigan populations.

A number of studies have demonstrated that workers exposed simultaneously to PCBs and other chemicals showed exposure-related adverse effects, ranging from skin abnormalities to signs of abnormal liver functions. When exposure of the workers was reduced by improvements in the work environment, concentrations

of PCBs in the blood and the observed adverse effects disappeared. The decreases in the concentrations of PCBs in various environmental media, in human diets, and human body tissues and fluids all demonstrate that decreases in environmental loading rates of PCBs result in decreases in exposures and subsequent declines in body tissue/fluid concentrations. Since concentrations of PCBs in various environmental media are expected to continue to decline from those currently reported, albeit at a slower rate than in the 1970s, future exposures to PCBs are expected to decline.

Overall, a weight-of-available-evidence evaluation indicates that no adverse health effects would have been expected based on average dietary exposures to PCBs that occurred between 1971 and 1989 and on available data of blood concentrations of PCBs in occupationally exposed and nonoccupationally exposed populations in the 1980s. These conclusions are further supported by the degree of conservatism in the exposure limits for PCBs as indicated by the estimated exposure levels required to yield various blood concentrations of PCBs based on the application of pharmacokinetic data from humans.

3.3. Aquatic Wildlife Hazard Assessment

3.3.1. Bioavailability, Pharmacokinetics, and Bioaccumulation

3.3.1.1. Bioavailability

PCBs are persistent in the aquatic environment and are biomagnified through aquatic food chains (Evans *et al.,* 1991). There are over 200 PCBs and, as with their environmental fate, not all PCBs display the same degree of biomagnification and toxicity in aquatic organisms. The biomagnification and toxicity of PCBs in fish and other aquatic organisms are dependent on a variety of factors, including:

(i) degree of chlorine substitution;
(ii) chlorine substitution pattern;
(iii) exposure period;
(iv) concentrations of PCBs in environmental media; and
(v) various physical/chemical characteristics of the aquatic media (e.g., dissolved organic carbon, suspended sediment concentrations, sediment organic carbon concentrations).

PCBs with five to seven chlorines biomagnify to a greater extent than those with greater chlorine substitutions, since those with greater than seven chlorines are molecularly too large to pass through biological membranes (Shaw and Connell, 1984; Gobas *et al.,* 1986). PCBs with less than five chlorine substitutions, are more easily metabolized and eliminated from the body (Niimi and Oliver, 1983). PCBs without substitutions in the *ortho* molecular positions and with chlorine atoms in both *para* positions and at least one *meta* position form coplanar structures in which the benzene rings lie in flat planes. Such non-*ortho*-substituted (also called coplanar) PCBs are believed to have greater toxic potency to aquatic organisms than are *ortho*-substituted or noncoplanar PCBs (Tanabe *et al.,* 1987; Brunström and Andersson, 1988; Smith *et al.,* 1990; Brunström, 1991).

PCBs tend to be relatively insoluble in water and lipophilic, with fairly large binding coefficients, or K_{oc} values, with organic carbon. The values of these physical/chemical properties vary among various isomers (see Section 2). These properties result in preferential partitioning of some PCBs to particulate materials and sediments in the aquatic environment in which the PCBs have the potential to bioaccumulate through aquatic food chains. The K_{oc} and K_{ow} values of different PCBs are the major factors that determine their bioavailability and uptake by aquatic invertebrates. The characteristics of the aquatic environment also affect the degree of bioaccumulation. Several studies have reported that the bioaccumulation of PCBs in invertebrates is inversely related to the sediment organic carbon content in their environment (Rubinstein *et al.*, 1983; McElroy and Means, 1988), since PCBs bound to organic carbon in sediment are less available for uptake by invertebrates.

In experiments with polychaetes (*Capitella capitata*), Shaw and Connell (1984) found that the adsorption of molecules of PCBs onto a surface was influenced mainly by their stereochemistry. Non-*ortho*-substituted PCBs were the most efficiently adsorbed and the optimum uptake and bioaccumulation of PCBs in the polychaete were observed for PCBs having from five to seven chlorine atoms. Those with less chlorines had less favorable K_{ow} values, while those with more chlorines had less favorable stereochemistry. Similar observations have been reported in other aquatic species. For example, PCBs with greater K_{ow} values bioaccumulated to a greater extent in the mayfly (*Hexagenia limbata*) (Gobas *et al.*, 1989) and in the oyster (*Crassostrea virginica*) (Ernst, 1984).

The bioavailability of PCBs for fish is also influenced by a variety of factors. Fathead minnows, allowed direct contact with hydrosoils contaminated with PCBs in both static and flowthrough tests, accumulated tissue concentrations of PCBs at rates six times faster than those of minnows screened from direct exposure to sediments. Fish selectively bioaccumulated the greater chlorinated PCBs of Aroclor 1254 (Halter and Johnson, 1977).

3.3.1.2. Pharmacokinetics

The uptake and elimination kinetics of PCBs vary with the physical/chemical properties and among different aquatic species. Uptake rates for PCBs were similar for the amphipod, *Pontoporeia hoyi*, and the mysid, *Mysis relicta* (Evans and Landrum, 1989). Elimination constants were relatively small in both species, although *P. hoyi* was approximately six times more efficient at eliminating PCBs than *M. relicta*. Since the tissue concentrations of PCBs depend on the balance between the rates of uptake and elimination, the bioconcentration factor (BCF) of *M. relicta* was about four times greater than that of *P. hoyi* (Table 5-7).

The absorption efficiencies and elimination half-lives ($t_{\frac{1}{2}}$) of PCBs in aquatic organisms vary with the PCBs and the species. Absorption efficiencies of 31 PCBs ranged from 62 to 85% (average 75 ± 6%), but did not appear to be directly related to the degree of chlorination (Table 5-8). The elimination $t_{\frac{1}{2}}$ in whole fish ranged from 5 days to greater than 105 days and generally increased with lipophilicity. The elimination $t_{\frac{1}{2}}$ in muscle tissue ranged from <5 to 127 days. Structure–activity analyses of PCBs with different $t_{\frac{1}{2}}$ values in whole fish indicated that elimination was more rapid for lighter PCBs, those having no chlorine substitution in the *ortho* positions, and those having two adjacent unsubstituted carbons.

TABLE 5-7

TOXICOKINETIC PARAMETERS FOR 2,2',4,4',5,5'-HEXACHLOROBIPHENYL IN *Pontoporeia hoyi* AND *Mysis relicta*

Species	K_u (Uptake Constant)	K_d (Elimination Constant)	BCF	Half-life
P. hoyi	53.5 mL/g/h	-0.00078/h	101,663	45.6 d
M. relicta	57.5 mL/g/h	-0.00013/h	442,231	222 d

Source: Evans and Landrum, 1989.

The overall conclusion from the available information is that kinetics of PCBs in rainbow trout were influenced by a nonselective uptake process and a selective elimination process based on the chlorine content and chlorine substitution pattern of the PCBs (Niimi and Oliver, 1983). In addition, the elimination rates of PCBs appear to be slower at lower temperatures (Zhang *et al.*, 1983).

Studies of the uptake and elimination kinetics of tri-, tetra-, and pentachlorobiphenyls present in a technical mixture of PCBs (Clophen A40) by juvenile sole (*Solea solea*) showed that total concentrations of PCBs, on a lipid basis, were greatest in the muscle and least in the brain. In general, the total concentration of PCBs in the various organs was dependent on the lipid content of the organs. The uptake of PCBs appeared to be proportional to their relative concentrations in the commercial mixture of PCBs (Clophen A40) (Boon, 1985). Thus, the uptake of PCBs by the organism did not depend on molecular structure of the compound, an observation in agreement with the results reported by Niimi and Oliver (1983).

Since the rates of uptake of most PCBs are relatively greater than their rates of elimination, most PCBs exhibit the potential for bioaccumulation. The PCBs with the more rapid rates of elimination bioaccumulate to a lesser degree, reach maximum concentrations in organs sooner, and are, therefore, less persistent than those with

TABLE 5-8

ABSORPTION EFFICIENCIES AND BIOLOGICAL HALF-LIVES OF HOMOLOG GROUPS OF PCBS IN RAINBOW TROUT ADMINISTERED A SINGLE ORAL DOSE

		Half-Life, Days	
Homolog Group of PCBs	Percent Absorbed	Whole fish	Muscle
Dichlorobiphenyls	62-80	5-85	< 5-56
Trichlorobiphenyls	77-78	190-196	81-86
Tetrachlorobiphenyls	68-83	44-890	29-127
Pentachlorobiphenyls	75-85	155 to > 1,000	62-101
Hexachlorobiphenyls	64-84	850 to > 1,000	77-91
Octachlorobiphenyl	78	> 1,000	78
Nonachlorobiphenyl	80	> 1,000	84
Decachlorobiphenyl	63	> 1,000	122

Source: Niimi and Oliver, 1983.

slower rates of elimination. Biological elimination half-lives of PCBs have been determined for a large number of organs (Table 5-9). In general, trichlorobiphenyls were eliminated more rapidly than most tetrachlorobiphenyls. For pentachlorobiphenyls, two displayed rapid elimination rates (short elimination half-lives) (PCBs 82 and 84), while three others (PCBs 99, 105, and 118) had slower elimination rates (greater $t\frac{1}{2}$ values) and would therefore tend to be more persistent. The more persistent PCBs have a 4,4′-chlorine substitution pattern. Two of these PCBs (105 and 118) are considered among the most potent PCBs. The biological $t\frac{1}{2}$ values were similar for muscle, dark skin, liver, gills, and gut, but were relatively less for the brain (Boon, 1985).

The whole-body elimination of a tetrachlorobiphenyl (52) was much faster in the sole than was reported for the rainbow trout by Guiney *et al.* (1977). Bruggeman *et al.* (1981) reported similar half-lives for two PCBs in the goldfish (*Carassius auratus*) as those reported by Boon (1985) in the sole.

Fish poorly metabolize PCBs, compared to that of other animal groups such as terrestrial mammals (Creavan *et al.*, 1965; Hutzinger *et al.*, 1972), which could be due to a relatively lower activity of mixed-function oxygenase enzyme systems which metabolize xenobiotics. Only trace amounts of metabolic products from 2,2′- and 2,4-dichlorobiphenyl, 2,2′,4- and 2,5,4′-trichlorbiphenyl, 2,2′,5,5′-tetrachlorobiphenyl, and 2,2′,4,5,5′-pentachlorobiphenyl were reported in several fish species (Metcalf *et al.*, 1975; Sanborn *et al.*, 1975; Melancon and Lech, 1976). Other studies reported no detectable metabolic products in fish exposed to monochloro- to pentachlorobiphenyls

TABLE 5-9

ELIMINATION KINETICS OF PCBS IN VARIOUS ORGANS OF THE SOLE, FOLLOWING A SINGLE ORAL INJECTION

	Homolog Group of PCBs		
Tissue	Trichlorobiphenyls	Tetrachlorobiphenyls	Pentachlorobiphenyls
Gut			
t½	12-13	9-34	6-53
Day 200 Residue (%)	0	0-0.4	0-6.6
Dark Skin			
t½	7-11	7-29	< 2-41
Day 200 Residue (%)	0-7.8	0-4.4	0-23.2
Brain			
t½	5-8	7-12	< 2-36
Day 200 Residue (%)	0	0-1.2	0-11.2
Gills			
t½	7-10	8-37	4-73
Day 200 Residue (%)	0	0-0.8	0-12.9
Liver			
t½	11-17	8-61	4-107
Day 200 Residue (%)	0-4.9	0.3-5.9	0-29.4
Muscle			
t½	11-20	24-40	6-70
Day 200 Residue (%)	0	0-10.1	0-37

Source: Boon, 1985.

TABLE 5-10

COMPARISON OF CONCENTRATIONS OF PCBs IN WHOLE ADULT FISH WITH THOSE IN WHOLE FISH EGGS

Species	Eggs		Adults	
	Parameter Measured	Concentration of PCBs	Parameter Measured	Concentration of PCBs
Striped bass	Sum of TCB, P_5CB, and H_6CB	0.32 ng/g	Sum of TCB, P_5CB, and H_6CB	1.3 ng/g
Lake trout	AHH-active PCBs	1.9-3.5 μg/g	Total PCBs	12.2 μg/g

Source: Smith *et al.*, 1990.
TCB = Trichlorobiphenyl.
P_5CB = Pentachlorobiphenyl.
H_6CB = Hexachlorobiphenyl.
AHH-active PCBs = those polychlorinated biphenyls with activity in the induction of arylhydrocarbon hydroxylase activity in fish.

(Hutzinger *et al.*, 1972). Norstrom (1987) concluded that most fish have very little activity of the enzyme systems necessary to metabolize PCBs with four or more chlorine atoms per molecule into water-soluble metabolites that would be more readily excreted, although this conclusion is not supported in more recent studies in which significant metabolism of PCBs was observed in fish (Janz and Metcalfe, 1991).

PCBs are believed to be metabolized in birds and mammals mainly by the insertion of oxygen between two adjacent carbon atoms on the benzene rings. The hepatic microsomal oxygenases form a transient and unstable arene oxide intermediate. The unstable arene oxide is metabolized to hydroxylated PCBs that are subsequently conjugated with sulfates and glucuronides and excreted in urine or bile, respectively (Sundstrom *et al.*, 1976). For rapid metabolism of PCBs in most animals, at least one adjacent pair of *meta,para* carbons must be unsubstituted, probably because the large chlorine atoms on adjacent carbon atoms block the action of metabolizing enzymes on the PCBs.

A secondary metabolic mechanism is the insertion of oxygen between the *ortho* and *meta* positions on the benzene rings (Norstrom, 1987). The polar bear readily metabolizes PCBs with (4-), (3,4-), (2,3,5-) and (2,3,5,6-) chlorine substituents on one ring and those with unsubstituted *meta,para* positions. However, the polar bear does not appear to metabolize PCBs with unsubstituted *meta* positions (Norstrom, 1987).

The rates of uptake and clearance of PCBs also appear to depend on life stage, reproductive stage, and diet of aquatic organisms (Eisler, 1986). No elimination of PCBs was measurable over a 12-day period in larvae of codfish (Zhang *et al.*, 1983), indicating slower elimination rates than in adults. Recently fed copepods (*Acartia tonsa*) cleared PCBs more rapidly than unfed copepods. Females cleared PCBs twice as quickly as males, and concentrations of PCBs in eggs were up to four times those in females, suggesting that egg production may account for the more rapid clearance of PCBs in females (McManus *et al.*, 1983). Egg maturation and spawning in fish and lactation in mink resulted in a significant reduction in the body burden of persistent PCBs (e.g., 2,2′,5,5′-tetrachlorobiphenyl) (Vodicnik and Peterson, 1985; Wren *et al.*, 1987; Wren, 1991). Others have also shown that the accumulation of PCBs in fish eggs by transfer from maternal tissues to the eggs during oocyte maturation accounts

for the elimination of substantial quantities of PCBs from the adult (Guiney *et al.,* 1979; Niimi, 1983; Vodicnik and Peterson, 1985; Cook *et al.,* 1991; Walker and Peterson, 1991). Table 5-10 summarizes the concentrations of PCBs in eggs versus those in adult fish (Smith *et al.,* 1990). Generally, the concentrations of PCBs in adult fish appeared to be approximately four to six times higher than those in eggs.

In aquatic mammals, substantial quantities of PCBs appear to be transferred through milk during lactation. For example, Bleavins *et al.* (1981) reported that concentrations of PCBs in 2-week-old mink were 16 times greater than those at birth, and it has been suggested that the increased mortality observed in nursing kits during the 1960s was a result of transfer of PCBs during lactation (Eisler, 1986).

3.3.1.3. Bioaccumulation

PCBs in the water column (either in solution or bound to colloidal or suspended organic carbon) (Baker *et al.,* 1986; Oliver and Niimi, 1988) or found in food items are absorbed into aquatic organisms (Oliver and Niimi, 1988). Once absorbed, PCBs preferentially distribute to tissues in proportion to the tissue–lipid or fat concentrations (Oliver and Niimi, 1988; Southworth, 1990; Norheim *et al.,* 1992). Those isomers of PCBs with a rate of uptake that is more rapid than their rate of clearance from body tissues accumulate to greater tissue concentrations over the lifetime of the organism. Consequently, there is a tendency for tissue concentrations of some PCBs to increase with the age of the organism (Oliver and Niimi, 1988; Allan *et al.,* 1991; Norheim *et al.,* 1992). In addition, organisms higher on food chains tend to have greater tissue concentrations of PCBs. Therefore, predator–prey relationships influence the accumulation of PCBs by organisms.

The bioaccumulation potential of PCBs is species dependent. Bioconcentration factors (BCFs) for PCBs were 10,000 to 100,000 for algae (Ernst, 1984; Eisler, 1986) and about 10,000 for freshwater plankton (Oliver and Niimi, 1988). The measured BCFs of Aroclor 1254 from the water by selected freshwater and marine invertebrates varied from 60 to 340,000 (Table 5-11). The protozoan *Tetrahymena* and the crayfish had relatively low bioaccumulation values, while that for *Daphnia magna*, by comparison, was quite high. The accumulation of PCBs by the sandshrimp was inversely related to animal size (McLeese *et al.,* 1980). Bioaccumulation factors for 32 days of exposure ranged from 3.5 for 0.1 g shrimp to 1.9 for 2.9 g shrimp. The bioconcentration factors between water and body tissues for most freshwater invertebrates were of similar magnitude and tended to increase with increasing exposure duration. Since PCBs are only slightly soluble in water, and most PCBs in the water column would be associated with dissolved or particulate organic carbon (Baker *et al.,* 1986), the significance of bioconcentration factors from water to various organisms is difficult to interpret. The less the organic carbon concentration in the water, the greater the apparent bioconcentration factors, particularly for organisms at lower trophic levels where uptake of PCBs directly from water may be a more important exposure route compared to uptake through food chains.

PCBs are also found in invertebrates that feed on detritus in the sediments. In a study using three invertebrate species, Rubinstein *et al.* (1983) found that the sandworm (*Nereis virens*) accumulated more PCBs from the same exposure conditions than either the clam (*Mercenaria mercenaria*) or the shrimp (*Palaemonetes pugio*). The sandworm

TABLE 5-11

BIOCONCENTRATION FACTORS (BCFs) FOR AROCLOR 1254 IN AQUATIC ORGANISMS

Ecosystem	Organism	Exposure Duration (d)	Tissue	Aroclor 1254 concentration in medium (μg/L)	BCF	Reference
Freshwater	Cladoceran (*Daphnia magna*)	4	whole	1.1	47,000	NAS, 1979
	Phantom midge (*Chaoborus punctipennis*)	4-14	whole	1.3	23,000-25,000	NAS, 1979
	Amphipod (*Gammarus pseudolimnaeus*)	4-21	whole	1.6	24,000-27,000	NAS, 1979
	Mosquito larvae (*Cules tarsalis*)	4	whole	1.5	18,000	NAS, 1979
	Crayfish (*Orconectes nais*)	4	whole	1.2	1,700	NAS, 1979
		21	whole	1.2	5,100	NAS, 1979
	Grass shrimp (*Palaemonetes kodiakensis*)	4	whole	1.3	12,000	NAS, 1979
		21	whole	1.3	17,000	NAS, 1979
	Protozoan (*Tetrahymena pyriformis*)	4	whole	1.0	60	EPA, 1980
Marine	American oyster (*Crassostrea virginica*)	168	soft parts	5.0	85,000	Ernst, 1984
	Rotifer (*Brachionus plicatilis*)	45	lipid	---	340,000	EPA, 1980
		45	dry tissue	---	51,000	EPA, 1980

Source: Eisler, 1986.

lives on the sediment surface feeding on detritus and organically rich sediments and consequently is exposed to PCBs by sediment ingestion, by food, and by absorption from organic carbon in the water column. In contrast, the clam relies on the overlying water column for feeding and respiration, and the grass shrimp lives in close association with aquatic plants. Thus, these species are primarily subject to exposure to PCBs in the water column, which would account for the smaller bioaccumulation observed in the clam and the grass shrimp.

The bioaccumulation of PCBs is demonstrated by data available from the Lake Ontario ecosystem. The concentrations of PCBs increased with movement upward in the ecosystem, from water (0.001 ng/g) to alewives and sculpins (approximately 1500 to 1600 ng/g wet wt) to salmonids (approximately 4200 ng/g wet wt, respectively). The concentrations of PCBs in suspended solids and bottom sediments were approximately 400 to 500 ng/g dry wt, respectively. In organisms, the increases in concentrations of PCBs appear to parallel the lipid content of tissues (e.g., 0.5% lipid in plankton compared to 11% lipid in salmonids).

There were also changes in the characteristics of PCBs at different levels of the ecosystem. Generally, the percentage chlorine in the PCBs was greater at higher trophic levels of the ecosystem. The percentage chlorine in the PCBs, by weight, was about 52% in lake water, 56.3% in salmonids, and 57% in bottom feeding sculpins (Oliver and Niimi, 1988). The tri- and tetrachlorobiphenyls were found in greater percentages in water and lower trophic levels (plankton, mysids, and amphipods) than small fish and salmonids. The penta- and octachlorobiphenyls were fairly uniformly distributed through trophic levels, and the hexa- and heptachlorobiphenyls were in greater percentages in small fish and salmonids. The greatest part of the partitioning of uptake for different PCBs occurred lower on the food chain (plankton and mysids) (Oliver and Niimi, 1988), indicating that the uptake of materials from water, or desorption from sediments, to lower organisms varied substantially for different congeners. However, once in the food chain, bioaccumulation was relatively uniform for different congeners. Bioconcentration factors from water to plankton for the pentachlorobiphenyl congeners were in the 10,000-fold range. Bioaccumulation factors from plankton to mysids (4- to 10-fold) to smelts (4- to 8-fold) to salmonids (approximately 4-fold) ranged from approximately 64- to 320-fold (Oliver and Niimi, 1988).

Concentrations of PCBs expressed on a wet weight basis in eggs of several piscivorous bird species were of similar magnitude to the tissue concentrations in adult birds (Table 5-12). A dosage of 5 mg/kg Aroclor 1254 in kestrels resulted in concentrations of 40 mg/kg in the egg (Lincer, 1972); however, the concentrations of PCBs in female tissues were not reported.

PCBs have been estimated to biomagnify as much as 25 million times, from concentrations in lake water to those in food chain predators such as the bald eagle, which is considered a top predator (Norstrom *et al.*, 1978). However, biomagnification factors from concentrations in water to those in such organisms are relatively meaningless, since organisms at high trophic levels are exposed to PCBs primarily through their food, not from water, and PCBs do not remain dissolved in water due to their lipophilicity and hydrophobicity.

There are significant differences observed in the biomagnification of the various PCBs. PCB 153 (2,2′,4,4′,5,5′-hexachlorobiphenyl) was almost always the component

TABLE 5-12

COMPARISON OF CONCENTRATIONS OF PCBs IN ADULT PISCIVOROUS BIRDS WITH THOSE IN EGGS

	Eggs				Adult			
Species	Parameter Measured	Location	Concentration of PCBs (μg/g ww)	Reference	Parameter Measured	Location	Concentration of PCBs (μg/g ww)	Reference
Herring gull	Total PCBs	Great Lakes, Detroit River	3.1-28	Allan *et al.*, 1991	Total PCBs	Wisconsin (SW shore of Lake Superior)	7.4-34	Kozie and Anderson, 1991
BCNH[a]	Total PCBs	(U.S.) (Various)	0.6-19	Custer *et al.*, 1983a,b	Total PCBs	(U.S.) (Various)	6.3-110	Ohlendorf and Miller, 1984
BCNH	Total PCBs	Lake Michigan, Green Bay	15-921	Heinz *et al.*, 1985	Total PCBs	Lake Michigan	23-127	Heinz *et al.*, 1985
Bald Eagle	Total PCBs	Lake Superior	13-14	Allan *et al.*, 1991	Total PCBs (in brain, breast)	Michigan Island, Lake Superior	14-40	Kozie and Anderson, 1991

[a] Black Crowned Night Heron.

of PCBs found in greatest concentrations in fish, piscivorous birds, and mammals (Norstrom, 1987; Muir *et al.*, 1988; Oliver and Niimi, 1988; Norheim *et al.*, 1992). The PCBs showing the greatest bioaccumulation in the alewife–herring gull food chain of Lake Ontario included 2′,3,4,4′,5′-pentachlorobiphenyl, 2,2′,3,4,4′,5′-hexachlorobiphenyl, 2,2′,3′,4,5,5′,6′-heptachlorobiphenyl, and 2,2′,3,3′,4,4′,5,5′-octachlorobiphenyl. The great blue heron and gannet had PCB accumulation patterns as follows, with 2′,4,4′,5′-tetrachlorbiphenyl, 2,3′,4,4′-tetrachlorbiphenyl, 2,2′,4,4′,5′-pentachlorobiphenyl, and 2′,3,4,4′,5′-pentachlorobiphenyl being the dominant isomers (Norstrom, 1987; Muir *et al.*, 1988; Oliver and Niimi, 1988; Norheim *et al.*, 1992). Bioconcentration factors for PCBs transferred from the spottail shiner to Forster's tern eggs for 3,3′,4,4′-tetrachlorobiphenyl, 3,3′,4,4′,5-pentachlorobiphenyl, and 3,3′,4,4′,5,5′-hexachlorobiphenyl were 0.17, 64, and 176, respectively (Kubiak *et al.*, 1989).

The concentrations of several PCB isomers in components of a pelagic Lake Ontario food chain were assessed in an effort to determine if coplanar PCBs can be "enriched" in concentration (Metcalfe and Metcalfe, 1993). Di-*ortho*-, mono-*ortho*-, and non-*ortho*-substituted PCBs were measured in water, sediment, and three invertebrate and five vertebrate species. Calculated biomagnification factors indicated that no "enrichment" of coplanar PCBs in relation to other PCBs occurred in this north central Lake Ontario food chain.

In the Canadian Arctic, arctic cod muscle had an isomer pattern of PCBs of an Aroclor 1242:1254:1260 mixture of 0.6:3:1, including the PCBs-8/5 to PCBs-70/76 of the dichloro- to tetrachlorocongeners (Muir *et al.*, 1988). In contrast, relatively greater quantities of PCBs with greater chlorine substitution are seen in other large marine fish, and lesser chlorinated PCBs predominate in smaller marine fish. In the herring–ringed seal–polar bear food chain, the pattern of accumulation of PCBs in the seal was similar to the patterns observed in birds, with relatively greater amounts of (2,5)-substituted components (Norstrom, 1987). However, the pentachloro- and hexachlorocongeners of PCBs predominated in seals in contrast to the hexachloro- and heptachlorocongeners that predominated in polar bears in the Canadian Arctic, with the absence of or much reduced quantities of the 2,5-, 3,4-, and 2,3,5-chlorine-substituted isomers (Muir *et al.*, 1988). The PCBs which accumulated in polar bears all had chlorine atoms in a minimum of the 2,4,2′,4′ ring positions (Norstrom, 1987; Muir *et al.*, 1988; Norheim *et al.*, 1992). No quantitative measures of bioaccumulation were given. Six PCBs (IUPAC Nos. PCBs-99, PCBs-153, PCBs-138, PCBs-180, PCBs-170, and PCBs-194) comprised approximately 99 and 86% of the total PCBs in liver and adipose tissue, respectively, of polar bears (Norheim *et al.*, 1992).

Based on field studies of the biomagnification of PCBs in the invertebrate species, *M. relicta* and *P. hoyi*, and a major fish predator, the deepwater sculpin (*Myoxocephalus thompsoni*), researchers found that organisms having the greatest concentrations of PCBs (sculpins and *P. hoyi*) also contained greater proportions of the penta- and hexachlorinated PCBs (Evans *et al.*, 1991). PCBs were not greatly biomagnified between some trophic levels, such as mysids to plankton or amphipods to plankton; however, biomagnification was considerably greater from macrobenthos (amphipods and mysids) to sculpins and from sediments to amphipods (Table 5-13). Other researchers also observed a much greater differential partitioning of PCBs at the lower end of the food chain (from dissolved organic carbon in water to plankton to mysids) than at the higher end (mysids to smelt to salmonids) (Oliver and Niimi, 1988). Offshore in the Great Lakes, *P. hoyi* was estimated to contain about 12 times more PCBs than offshore

TABLE 5-13

BIOMAGNIFICATION FACTORS FOR PCBs BETWEEN SUCCESSIVE TROPHIC LEVELS IN LAKES MICHIGAN AND ONTARIO FOOD WEBS[a]

Trophic Level	Lake Michigan	Lake Ontario Western	Lake Ontario Eastern	Mean
Mysids: Plankton	1.3	1.3	1.5	1.4
Amphipods: Plankton	3.2	5.4	8.5	5.7
Fish: Plankton	12.9	21.8	19.1	17.9
Amphipods: Mysids	2.4	4.3	5.9	4.2
Fish: Mysids	9.2	17.3	13.2	13.2
Fish: Amphipods	4.0	4.0	2.3	3.4
Amphipods: Sediment	12.2	4.0	2.3	3.4

Source: Evans *et al.*, 1991.

[a] Data for Lake Ontario were calculated from Borgmann and Whittle (1991).

M. relicta, and to recycle 22–61 times more PCBs than *M. relicta*, suggesting that *P. hoyi* would be an important macroinvertebrate species in the storage and recycling of total PCBs in the offshore environment.

3.3.2. Laboratory Studies

3.3.2.1. Lethal Effects

The acute lethal effects of PCBs to aquatic life vary with the specific PCBs, the duration of the observation period following exposure, and the species and developmental stage of the organism. In general, the acute lethality of Aroclor PCBs in several species of freshwater and marine organisms increases with increasing time of observation following initial exposure (Tables 5-14 and 5-15). Crustaceans and younger developmental stages were the most sensitive groups tested, and the acute lethality of commercial mixtures of PCBs appeared to increase as the percentage chlorine by weight increased (e.g., Aroclor 1242 had a lower LC_{50} values than Aroclors 1248 or 1254) (Johnson and Finley, 1980).

Invertebrates

The hydra and members of the insect family, such as the damselfly, dragonfly, and stonefly, appeared to be relatively more resistant to PCBs than other invertebrates (Table 5-14). Some invertebrates can accumulate PCBs from the aquatic environment without any overt signs of toxic effects. *Daphnia* exposed to selected PCBs (tetra, penta, hexa) accumulated 1.81 to 132 mg/kg PCBs, but showed no signs of toxic effects (Dillon *et al.*, 1990).

Fish and Shellfish

Delayed lethality is observed in fish exposed to PCBs. LC_{50}'s for several species of fish to various Aroclor PCBs are summarized in Table 5-15. In a 6-month study on

TABLE 5-14

ACUTE TOXICITIES OF AROCLOR PCBs TO SELECTED AQUATIC INVERTEBRATE SPECIES

Ecosystem	Organism	Compound (Aroclor) Tested	Exposure Period (d)	LC_{50} (μg/L)	Reference
Freshwater	Crayfish (*Orconectes nais*)	1242	7	30	NAS, 1979
		1254	7	80-100	NAS, 1979
	Amphipod (*Gammarus pseudolimnaeus*)	1242	4	10	NAS, 1979
		1242	10	5	NAS, 1979
		1248	4	52	NAS, 1979
		1254	4	2,400	NAS, 1979
	Grass shrimp (*Palaemonetes kadiakensis*)	1254	7	3	NAS, 1979
	Damselfly (*Ischnura verticalis*)	1242	4	400	Johnson and Finley, 1980
		1254	4	200	Johnson and Finley, 1980
	Dragonfly (*Macromia* sp.)	1242	4	800	Johnson and Finley, 1980
		1254	5	800	Johnson and Finley, 1980
	Cladoceran (*Daphnia magna*)	1254	14	1.8-24	EPA, 1980
		1254	21	1.3	EPA, 1980
	Stonefly (*Pteronarcella badia*)	1016	4	424-878	Johnson and Finley, 1980
	Hydra (*Hydra oligactis*)	1016	3	5,000	Adams and Haileselassie, 1984
		1254	3	10,000	Adams and Haileselassie, 1984
Marine	Grass shrimp (*Palaemonetes pugio*)	1254	4	6.1-7.8	Ernst, 1984
		1016	4	12.5	EPA, 1980
	Brown shrimp (*Penaeus aztecus*)	1016	4	10.5	EPA, 1980
	Pink shrimp (*Penaeus duorarum*)	1254	12	1.0	EPA, 1980

Source: Eisler, 1986.

the effects of individual and combined exposure to PCBs and DDE on growth and mortality of Lake Michigan lake trout fry (Berlin *et al.*, 1981), mortality of fry exposed to PCBs was less than control fry before Day 56. However, between Days 57 and 136, mortality rates increased dramatically and were significantly higher than those of the controls at the end of the study. By the end of 176 days, the total cumulative mortality ranged from 30.5 to 64.9% in the groups exposed to PCBs, while the controls ranged from 19.3 to 26.3%. Growth was not significantly affected by exposure to PCBs.

TABLE 5-15

ACUTE TOXICITIES OF AROCLOR PCBS TO SELECTED FISH SPECIES

Ecosystem	Organism	Compound (Aroclor) tested	Exposure Period (d)	LC_{50} (μg/L)	Reference
Freshwater	Rainbow trout (*Oncorhynchus mykiss*)	1016	4	114-159	Johnson and Finley, 1980
		1242	5	67	Johnson and Finley, 1980
		1248	5	54	Johnson and Finley, 1980
		1254	5	142	Johnson and Finley, 1980
		1254	10	8	NAS, 1979
		1260	20	21	NAS, 1979
	Bluegill (*Lepomis macrochirus*)	1016	4	390-540	Johnson and Finley, 1980
		1242	5	125	Johnson and Finley, 1980
		1242	15	54	NAS, 1979
		1248	20	10	NAS, 1979
		1254	25	54	NAS, 1979
		1260	30	150	NAS, 1979
	Channel catfish (*Ictalurus punctatus*)	1016	4	340-560	Johnson and Finley, 1980
		1242	15	110	NAS, 1979
		1248	15	130	NAS, 1979
		1254	15	740	NAS, 1979
		1260	30	140	NAS, 1979
	Salmonids (4 spp.)	1016	4	134-1,154	Johnson and Finley, 1980
	Yellow Perch (*Perca flavescens*)	1016	4	240	Johnson and Finley, 1980
		1242	4	> 150	Johnson and Finley, 1980
		1248	4	> 100	Johnson and Finley, 1980
		1254	4	> 150	Johnson and Finley, 1980
		1260	4	> 200	Johnson and Finley, 1980
Marine	Sheepshead minnow-fry (*Cyprinodon variegatus*)	1254	21	0.1-0.32	Ernst, 1984
	Sheepshead minnow-adult	1254	21	0.9	EPA, 1980

Source: Eisler, 1986.

Sheepshead minnow appeared to be the most sensitive species to acute lethal effects of PCBs (Table 5-15), and the adult stage appears to be more tolerant than the fry. The channel catfish appeared to be the most tolerant species; however, some tests may not have been conducted for a long enough time period to observe the delayed lethality that is associated with this group of chemicals. Several studies reported that the toxic potency of several Aroclor mixtures (e.g., Aroclor 1242, 1248, and 1254) were more toxic than single Aroclors. The range in LC_{50} values for fish was not as large as that for invertebrates and was approximately in the mid-range for invertebrates.

In general, early life stages of fish are more sensitive than adults to PCBs (Table 5-16). However, no signs of toxic effects were noted in rainbow trout eggs exposed to

TABLE 5-16

LD_{50} VALUES OF CONGENERS OF PCBs FOR EARLY LIFE STAGES OF THE RAINBOW TROUT

Congener of PCBs	LD_{50} (ng/g egg)
3,3',4,4',5-Pentachlorobiphenyl (126)	74.0 (44-83)
3,3',4,4'-Tetrachlorobiphenyl (77)	1,348 (1,064-1,621)
2,3,3',4,4'-Pentachlorobiphenyl (105)	> 6,970
2,3',4,4',5-Pentachlorobiphenyl (118)	> 6,970
2,2',4,4',5,5'-Hexachlorobiphenyl (153)	> 6,970

Source: Walker and Peterson, 1991.

PCBs until the onset of hatching (Hansen, 1987; Walker and Peterson, 1991), and mortality occurred only from hatch to the swim-up stage. The signs of toxicity included a low incidence of half-hatching mortality and sac fry mortality associated with subcutaneous yolk sac edema. The LD_{50} values for the five PCBs tested for early life stage mortality in rainbow trout are summarized in Table 5-16. Three PCBs, 105, 118 (both coplanar PCBs), and 153 (noncoplanar), did not cause egg, sac fry, or fry mortality at egg doses as high as 6200 to 6970 μg/kg.

In laboratory studies, fish exposed to concentrations of PCBs similar to those observed in Great Lakes fish showed reduced survival, reproduction, and growth (Mayer *et al.,* 1985). However, correlations with total organochlorine concentrations do not adequately explain the poor reproductive performance observed in salmon in the Great Lakes, since mortality of fry increased from 22 to 92% between 1975/1976 (Berlin *et al.,* 1981) and 1980/1981 (Mac *et al.,* 1985), while the total concentrations in the fish of PCBs and other organochlorines decreased. Williams and Giesy (1992) hypothesized that these poor correlations may be due to reproductive/growth effects from specific PCBs with coplanar structures (non-*ortho*-chlorine substituted PCBs) that are believed to act through the Ah receptor system, similar to 2,3,7,8-tetrachlorobibenzo-*p*-dioxin (Kubiak *et al.,* 1989; Safe, 1990). To evaluate this hypothesis, studies were conducted on chinook salmon collected from Lake Michigan. Salmon, collected in 1986 with mean total concentrations of PCBs in eggs of 7.02 mg/kg, on a wet weight basis [83.9 mg/kg lipid, or 0.2 to 12 μg/kg wet wt of non-*ortho*-substituted PCBs congeners; or 29 to 514 T_4CDD-TEQ as calculated by three different methods (Safe, 1990; Newsted, 1991; Tillitt *et al.,* 1991b)], showed significant differences in mortality of eggs (mean 11%) and fry (mean 4%) among clutches of eggs from different females; however, egg and fry mortality did not correlate with the concentrations of total PCBs or concentrations expressed as T_4CDD-TEQ or individual PCBs (IUPAC PCBs 77, 126, 105, and 118). The authors concluded that the lack of correlation between various PCB exposure parameters and survival of eggs and fry may indicate that other factors are responsible for the rearing mortality observed, including egg ripeness, genetics, spawning condition of the female fish, and possibly toxicity equivalency values related directly to reproductive parameters in fish rather than mammalian toxicity parameters (Williams and Giesy, 1992).

The degree and pattern of chlorine substitution influence the toxic potency of the various PCBs. Coplanar PCBs that are without chlorine atoms in the *ortho* position appear more toxic than the more angular PCBs. The acute exposure, lethality assess-

ment of 10 PCBs toward the fathead minnow (*Pimephales promelas*) indicated that the only PCB that significantly affected fish survival was PCB 18, 2,2',5-trichlorobiphenyl (Dillon and Burton, 1991); however, Walker and Peterson (1991) found greater toxic potency for coplanar PCBs.

Piscivorous Birds and Mammals

Mink appear to be more sensitive to the adverse effects of PCBs than other wildlife under field conditions (Wren, 1991), while the guinea pig appears to be the most sensitive to PCBs based on laboratory studies (EPA, 1979; Drill *et al.*, 1982). Exposure of mink to 0.5 μg 3,3',4,4',5,5'-hexachlorobiphenyl/g of fish diet caused 100% mortality (Aulerich *et al.*, 1985), whereas exposures of mice to 30 μg/g diet resulted in 20% mortality (Bioacca *et al.*, 1981). Mink that died following consumption of Great Lakes fish spiked with PCBs had total concentrations of PCBs in liver and fat of 4.2 and 11.0 μg/g, respectively (Aulerich *et al.*, 1973); however, the potential confounding effects of other chemicals in the fish (e.g., chlorinated dioxins/furans, mirex, and other chlorinated pesticides) were not considered in these studies. A tolerable daily limit for mink has been estimated at less than 1.5 μg total PCBs/kg body wt. Oral and intraperitoneal acute LD_{50} values for PCBs in the mink are presented in Table 5-17.

3.3.2.2. Nonlethal Effects

Growth Effects

Exposures to sufficient quantities of PCBs have been shown to affect normal growth and development in a variety of aquatic wildlife. The literature identified responses of specific aquatic wildlife species summarized below.

Phytoplankton. Concentrations of Aroclor 1254 as low as 0.1 μg/liter resulted in growth reductions in marine diatoms and the alga *Scenedesmus quadricauda*, and affected the population structure of phytoplankton communities (EPA, 1980). *Asterionella japonica* was found to be more resistant to the effects of PCBs on growth than

TABLE 5-17

TOXICITIES OF AROCLOR PCBS TO THE MINK FOLLOWING SINGLE-DOSE EXPOSURE

Route of Administration	Aroclor	LD_{50} (g/kg body weight)	Reference
Oral	1221	0.75-1.0	Aulerich and Ringer, 1977; Ringer, 1983
	1242	3.0	Aulerich and Ringer, 1977; Ringer, 1983
	1254	4.0	Aulerich and Ringer, 1977; Ringer, 1983
Intraperitoneal	1221	0.5-0.75	Aulerich and Ringer, 1977
	1242	1.0	Aulerich and Ringer, 1977
	1254	1.25-2.25	Aulerich and Ringer, 1977

Ditylum brightwellii. All clones of *D. brightwellii* showed growth inhibition at concentrations of PCBs of 25 μg/liter (Cosper *et al.,* 1984). Growth under high light intensity increased the sensitivity to PCBs in most clones.

Invertebrates. Decreased shell growth was reported in oysters exposed to 10.1 μg/liter of Aroclor 1016, 17 μg/liter of Aroclor 1248, 14 μg/liter of Aroclor 1254, and 60 μg/liter of Aroclor 1260 (EPA, 1980). Similar results were reported for shrimp (Ernst, 1984).

The 21-day exposure of *D. magna* to 0.1 and 1.0 μg/liter of seven PCBs (Dillon *et al.,* 1990; details as described in Section 3.3.2.1) resulted in increases in total biomass with some isomers, and decreases with others. These results suggest that certain PCBs may be an energy source, while others have greater toxic potency.

Fish. Conflicting results have been reported for effects of PCBs on growth of fish. Brook trout fry exposed for 48 days to 1.5 μg Aroclor 1254/liter showed decreased growth (Johnson and Finley, 1980) and sole which were orally injected with a 10-mm^3 solution containing 3.7 $\mu g/mm^3$ Clophen A40 experienced considerably reduced growth rates compared to controls (Boon, 1985). However, growth of lake trout fry exposed to waterborne PCBs and DDE for 176 days was apparently unaffected (Berlin *et al.,* 1981).

Piscivorous birds and mammals. The evidence identified for potential effects of exposures of PCBs on growth and development of piscivorous birds and mammals was mainly for mink. Decreased food intake, body weight loss, and decreased kidney and heart weights, plus increased mortality, were observed in mink given oral doses of 7 mg Aroclor 1254/kg body wt for 28 days (Hornshaw *et al.,* 1986).

Other studies observed that the toxic effects of exposures to PCBs from ingestion of Great Lakes fish were greater than direct exposures to PCBs per se (Aulerich *et al.,* 1971, 1973; Aulerich and Ringer, 1977; Hornshaw *et al.,* 1983). These results were interpreted as indicating that the greater toxicity of PCBs in fish was due to toxic metabolites of PCBs formed in the fish; however, this interpretation appears highly speculative since no measurements of metabolites of PCBs in the fish tissues were conducted. It would appear more plausible that the increased toxic response observed when PCBs were administered fish was due to the simultaneous exposures to other chemicals in the fish or potential interactions between PCBs and other chemicals in the fish. Fish from the Great Lakes are known to contain elevated concentrations of a number of chemicals, including chlorinated dioxins/furans, various chlorinated pesticides, and other nonchlorinated chemicals related to natural and anthropogenic sources.

Teratogenicity

Piscivorous birds and mammals. Teratogenicity in piscivorous birds and mammals is discussed in the field study section.

Reproductive Effects

Invertebrates. PCBs produce various effects on reproduction of aquatic invertebrates, with variations depending on the type of PCBs and the invertebrate species tested. No effects on reproduction were observed in *D. magna* exposed to 0.1 and 1.0 μg/liter of

seven PCBs in a static renewal system for 21 days. The number of neonates produced was either not affected or enhanced by the exposures of PCBs (Dillon *et al.,* 1990; details as described in Section 3.3.2.1).

However, eggs of the sea urchin, *Arbacia punctulata,* exposed to 0.5 mg/liter Aroclor 1254 for 1 hr prior to fertilization, showed reduced success of fertilization and decreased survival. Eggs were markedly more tolerant to exposure to PCBs at time of insemination than afterwards (Adams, 1983).

Fish. PCBs can impair reproductive performance of fish. The threshold concentrations of PCBs, above which reduced survival of developing eggs in Baltic flounder (*Platichthys flesus*) and the cyprinid minnow (*Phoxinus phoxinus*), were 0.12 and 24 mg PCBs/kg ovary (fresh weight), respectively (Ernst, 1984). Rainbow trout having whole body concentrations of 0.4 mg Aroclor 1242/kg fresh weight produced eggs with low survival and numerous fry deformities (EPA, 1980). Eggs and fry of Atlantic salmon showed 46 to 100% mortality at tissue concentrations of PCBs of 0.6 to 1.9 mg/kg on a fresh weight basis or 14.4 to 34 mg/kg on a percentage lipid basis (Niimi, 1983). Exposure of adult sheepshead minnow (*Cyprinodon variegatus*) to 0.14 μg Aroclor 1254/liter resulted in decreased embryo survival. The concentration of Aroclor 1254 in the embryos was about 7 mg/kg fresh wt (EPA, 1980). Brook trout exposed to 200 μg/liter Aroclor 1254 for 71 weeks experienced complete reproductive failure; the NOEL was 0.94 μg/liter (EPA, 1980). (The relatively high waterborne exposures used in this study suggest a carrier solvent was used and the results may therefore be of limited use). Freeman and Idler (1975) demonstrated that PCBs interfered with *in vitro* androgen biosynthesis in the brook trout, causing regression of the testes and reduced hatchability of eggs in the females.

Piscivorous birds and mammals. Several laboratory studies have demonstrated that exposures to PCBs and related chemicals can cause adverse reproductive performance in birds and mammals, such as herring gulls, bald eagles, double-crested cormorants, ranch mink, and leghorn chicken (Heaton *et al.,* 1991; Summer *et al.,* 1991; Ludwig *et al.,* 1993). Studies in which these species were fed Great Lakes fish contaminated with a variety of chemicals, including PCBs and PCDDs/PCDFs, demonstrated that the bald eagle appeared to be the most sensitive of these wildlife species, followed by the double-crested cormorant and the herring gull. The leghorn chicken and the ranch mink, two domesticated species, were more tolerant than the bald eagle but more sensitive than the double-crested cormorant. The developing embryos of various chicken breeds were found to be more sensitive to PCBs than the embryos of three species of duck, two species of gull, and a domestic goose (Brunström and Reutergardh, 1986; Brunström, 1988). Thus, domestic avian species appear to be more sensitive to reproductive effects from PCBs than wildfowl species (Custer and Heinz, 1980). In addition, studies have shown that the leghorn chicken is similar in sensitivity to PCBs/PCDDs/PCDFs to the rat (Poland and Glover, 1973; Bradlaw and Casterline, 1979; Brunstrom and Darnerud, 1983; Brunstrom, 1986, 1989, 1990; Brunstrom and Andersson, 1988). These data are important when comparisons of the potential adverse effects to a variety of species from exposures to environmental sources of these chemicals must be evaluated.

Mink exposed to quantities of PCBs that resulted in liver concentrations of 1.23 μg PCBs/g showed impaired reproductive success (Platonow and Karstad, 1973). Mink with concentrations of PCBs in body fat of 13.3 μg/g from the consumption of Great Lakes fish showed decreased reproduction and none of the kits that were born survived

(Hornshaw *et al.,* 1983). No kits were whelped to females with 24.8 μg PCBs/g in fat tissue. Reduced growth and survival of mink kits were observed in females exposed to quantities of PCBs from Great Lakes fish resulting in liver concentrations of 2.0 μg PCBs/g (Wren *et al.,* 1987).

Biochemical Effects

Exposures to sufficient quantities of PCBs, and a number of other chemicals, are known to increase the activity of several MFO enzymes involving the cytochrome P450 system, including AHH, ethoxycoumarin-*O*-deethylase, and EROD (Safe, 1989, 1991; Janz and Metcalfe, 1991; Tyle *et al.,* 1991). However, the relevance of changes in the activity of the MFO enzymes relative to adverse effects is not clear, although negative effects on reproduction could occur if the enzyme changes were of sufficient magnitude to result in imbalances in various reproductive hormones that are substrates for these enzymes. Irrespective of the arguments regarding their potential as indicators of adverse effects, the induction of the hepatic MFO enzyme system has been proposed as a biochemical marker of xenobiotic exposure in aquatic and terrestrial animals. However, since this enzyme system can be induced by a number of chemicals, and substantial variations in inherent activity are reported relative to season of the year and reproductive cycling in animals, it is difficult to identify specific causal relationships between particular chemicals and MFO induction in organisms in the environment because of simultaneous exposures to mixtures of chemicals of natural and anthropogenic origin that have MFO-inducing activity (Hodson *et al.,* 1992; Munkittrick *et al.,* 1992; Van der Kraak *et al.,* 1992). The specific responses of MFO enzyme systems in several aquatic species exposed to PCBs are summarized below.

Fish. PCBs induce the AHH enzyme systems of fish following exposures to sufficient concentrations. Janz and Metcalfe (1991) reported that the potency of PCBs in AHH induction in rainbow trout varied with the PCB isomer and with the time of year. ED_{50} values (the dose that would result in a 50% increase in enzyme activity) for AHH induction following injection of PCBs isomers into the fish ranged from 330 μg/kg for 3,3′,4,4′,5-pentachlorobiphenyl to 665 μg/kg for 3,3′,4,4′-tetrachlorobiphenyl. ED_{50} values were less, indicating greater susceptibility of the organisms to PCBs during the summer months (e.g., 90.7 μg/kg for the tetrachlorobiphenyl congener). The sensitivity of AHH enzyme systems to induction by PCBs in fish appears to be similar to those of laboratory rats, based on similar ED_{50} values in the two species (Janz and Metcalfe, 1991).

Piscivorous birds and mammals. PCBs induce the activity of the MFO enzyme systems in birds and mammals following exposures to sufficient concentrations. Studies with yellow-legged herring gulls and kestrels exposed to PCBs have shown increased activity in a variety of MFO enzymes, including aldrin epoxidase, EROD, and aminopyrine *N*-demethylase (Fossi *et al.,* 1989; Elliott *et al.,* 1991). Whole body concentrations of PCBs in gulls ranged from 12 to 17 ppm (dry weight). However, other xenobiotics, such as HCB, lindane, DDE, and heavy metals, were also detected in the tissue. Orally administered doses of PCBs ranging from 0.05 to 4 mg/kg caused induction of enzyme activity in kestrels. Concentrations of PCBs in adipose tissue which were associated with the administered dose ranged from 3.3 to 182 mg/kg (wet weight). Fossi *et al.* (1989) noted that sensitivity of aldrin epoxidase in the yellow-legged herring

gull to induction by PCBs was markedly increased during the reproductive period. Treatment with PCBs of the grey seal (*Halichoerus grypus*) tissues (*in vitro*) resulted in increased biosynthesis of steroid hormones, including cortisol in adrenal tissue and testosterone in testicular tissue (Freeman and Sangalang, 1977).

Amphibians and reptiles. The limited evidence from turtles indicate that the MFO enzyme activities of reptiles are inherently less than those of mammalian species based on comparison with the guinea pig. In addition, the consequences of induction of the MFO enzymes by PCBs appear to be different between turtles and guinea pigs. These differences could speculatively be related to inherent differences in the homeostasis of hormonal systems between turtle and mammals. Compared to the guinea pig, the microsomal fraction of cells from the marsh turtle (*Mauremys caspica*) had lower protein and cytochrome P450 concentrations, a vital component of the MFO enzyme system (Goldman and Yawetz, 1991). In addition, Goldman and Yawetz (1991) demonstrated significant differences between the guinea pig and the marsh turtle in the profile of metabolites produced by MFO enzymes associated with microsomes isolated from the adrenal gland. While products of both the corticosteroid and androgenic pathways were detected in the guinea pig, only products of the corticosteroid pathway were present in the marsh turtle. The relative abundance of metabolites of the corticosteroid pathway was greater in the marsh turtle than in the guinea pig. The overall effect of Aroclor 1254 treatment in the guinea pig was inhibition of the metabolism of progesterone; while in the marsh turtle, an increase was observed.

3.3.2.3. Genotoxicity/Carcinogenicity

The information identified on the potential genotoxic and carcinogenic properties of PCBs has been discussed in Section 3.2. No specific information was identified on these properties in aquatic wildlife. The potential carcinogenic and genotoxic properties of PCBs in aquatic wildlife would be expected to be qualitatively similar to those observed in mammalian systems; however, quantitative differences in sensitivity may be expected due to differences in metabolic and sensitivity factors between species.

3.3.3. Field Studies

Laboratory studies on aquatic wildlife provide evidence of potential effects of chemicals under controlled conditions; however, the relevance of such data to the overall interpretation of potential environmental effects requires confirmation through studies of organisms in the natural environment. This section summarizes the information from the field studies identified on the assessment of potential effects of PCBs. Unique problems arise in the interpretation of data from field studies due to the difficulties in accounting for the wide range of variables associated with the complexities of the natural environment. One of the major difficulties in the interpretation of causal relationships between specific chemicals and adverse effects on organisms are the confounding effects of simultaneous exposures to a large number of chemicals of natural and anthropogenic origins. Constantly changing environmental conditions (e.g., habitat loss) that affect the types and magnitudes of responses of organisms to chemicals in the environment also confound the establishment of causality.

3.3.3.1. Fish and Shellfish

Adverse reproductive effects, believed by Ankley *et al.* (1991) to be due to planar chlorinated hydrocarbons, including coplanar PCBs, have been documented in chinook salmon and lake trout from Lake Michigan (Mac, 1988). The mean concentration of total PCBs in salmon eggs in which decreased reproduction was observed was 3.80 ± 1.06 μg/g wet wt, while the mean concentration in the muscle samples from adult salmon was 1.50 ± 0.44 μg/g (wet wt) (about 2.5-fold less). These concentrations, expressed as 2,3,7,8-T_4CDD-TEQ, were 91.6 ± 18.4 pg/g in eggs and 18.4 ± 11.2 pg/g in adult muscle tissue. These concentrations of T_4CDD-TEQ in egg and muscle samples from chinook salmon were less than the concentrations, as determined by the enzyme inducing reactions in H4IIE tissue cultures, of 2,3,7,8-T_4CDD-TEQ in eggs of piscivorous birds (i.e., terns, cormorants) from areas in the Great Lakes (Tillitt *et al.,* 1989). This difference suggests that fish may exhibit greater sensitivity to adverse reproductive effects of PCBs than birds; however, caution is required in the interpretation of 2,3,7,8-T_4CDD-TEQ, based on the discussions of the relevance of applying TEF values to the assessment of PCBs (see Section 3.2.3).

There was a statistically significant inverse relationship between the total concentration of PCBs in eggs and hatching success of the fish, with an effective concentration corresponding to about 100 pg 2,3,7,8-T_4CDD-TEQ/g egg. These data suggest that a marked maternal transfer of both 2,3,7,8-T_4CDD-TEQ and PCBs occurs between adult chinook salmon and eggs, and that PCBs, in particular those PCBs which were presumed 2,3,7,8-T_4CDD-related activity, may be implicated in the reproductive impairment observed among Lake Michigan chinook salmon. However, the overall interpretation of these results is confounded by the presence of a number of other chemicals in fish from Lake Michigan; notably, DDT and its various metabolites, mirex, a variety of other organic chemicals, mercury, lead, and a number of other inorganic chemicals. These confounding effects weaken the conclusion that adverse reproductive effects observed in Lake Michigan chinook salmon are causally or solely related to PCBs.

Concentration of PCBs in Fish and Shellfish

The concentrations of PCBs in bivalves, including mussels and oysters, have been measured in various locations in the United States, including California, Chesapeake Bay, North Carolina, and the Atlantic Coast, beginning in the early 1970s through to the mid-1980s. Steady declines in concentrations of PCBs, ranging from a few-fold to about 20-fold, were observed in bivalves from these regions (National Oceanic and Atmospheric Administration, 1988). The nationwide mussel monitoring program conducted by the (U.S.) Environmental Protection Agency reported substantial decreases in concentrations of PCBs in three areas that had been considered "hot spots of PCBs" in the early 1970s. Tissue concentrations of PCBs in these hot spots either continued to decline or remained unchanged through the early 1980s (Regulatory Network, Inc., 1992). Significant decreases have also been found in concentrations of PCBs in molluscs in several states for the years 1986 to 1990 (NOAA, unpublished data). Mean concentrations of PCBs decreased over a 4-year time period from approximately 190 ng/g dry wt in 1986 to 120 ng/g dry wt in 1990.

Significant decreases in whole body concentrations of PCBs in Great Lakes fish were also observed during the 1980s. The concentrations of PCBs have declined in fish (Fig. 5-3) and in several colonial birds around the Great Lakes (Bishop and Weseloh, 1990). This trend is discussed further under Concentrations of PCBs in Piscivorous Birds and Mammals.

Between the early 1970s and the mid-1980s, the concentrations of PCBs in flatfish (bottom feeding species such as flounder, sole, and dabs) in the northeast United States, the Southern California Coast, and Washington decreased by factors ranging from 2- to 10-fold (NOAA, 1988). Concentrations of PCBs in menhaden, an important ecological species which serves as a prey species for larger fish, sea birds, and marine mammals, also declined from 1969 to 1979. However, menhaden in Long Island Sound and the New York Bight still had relatively great concentrations of PCBs in the late 1970s.

Since the late 1970s, the concentrations of PCBs in the striped bass in the Hudson River have decreased from average values of 11.63 ppm in 1978 to 2.18 ppm in 1990 (NYDEC, 1991). Less dramatic decreases in concentrations of PCBs in striped bass have also been reported in Long Island Sound and the New York Harbor (NOAA, 1988). In contrast, concentrations of PCBs in striped bass from waters off Rhode Island increased between 1979 and 1985.

Other species of freshwater fish in the Hudson River area were also monitored for PCBs between 1970 and 1980. Concentrations of PCBs decreased in brown bullhead,

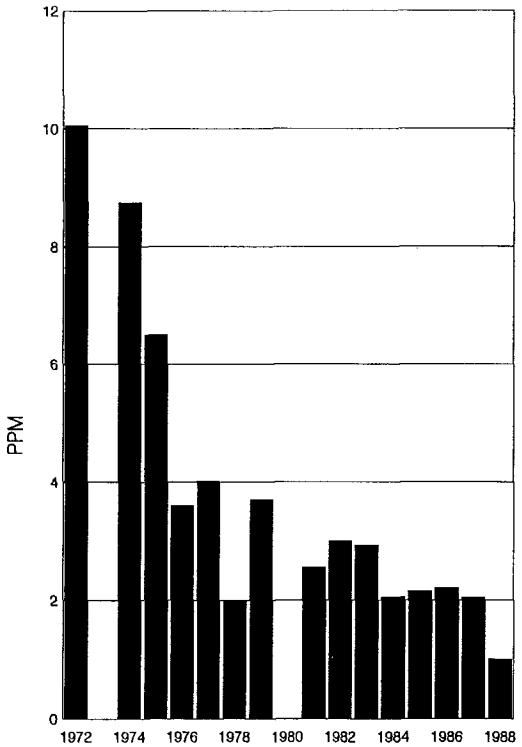

FIG. 5-3. Average concentrations of PCBs in Coho salmon muscle tissue, Credit River, Lake Ontario, 1972 to 1988. Reproduced from Government of Canada (1991). (No data were collected in 1973 and 1980).

white and yellow perch, and Atlantic tomcod in several industrialized rivers (NYDEC, 1991), with an average reduction of about 50% occurring in New York riverine fish between 1975 and 1978 (Armstrong and Sloan, 1980). The concentrations of PCBs also decreased in fish from the New York lakes between the mid-1970s and 1980 (NYDEC, 1991).

3.3.3.2. Amphibians and Reptiles

A variety of developmental effects and decreased reproductive performance has been observed in turtles from locations with elevated concentrations of chlorinated organic chemicals. Snapping turtle (*Chelydra serpentia*) eggs, collected between 1986 and 1989 from two locations on Lake Ontario, had the highest concentrations of chlorinated organic chemicals and had the highest incidence of deformities. Eggs collected from the Algonquin Park area (a wilderness park in central Ontario) had the lowest concentrations of chlorinated organic chemicals and had the fewest abnormalities (Bishop *et al.*, 1991). The abnormalities found in hatching turtles and embryos included deformed tails (most common), deformed hind- and forelimbs, missing claws, enlarged yolk sacs, missing eyes, deformed carapaces, deformed craniums and nostrils, and deformed upper and lower jaws. Logistic regression analysis showed a significant relationship between abnormalities and individual PCBs and abnormalities and the sum of total PCBs. The only compound which significantly coincided with abnormal development in turtles in all years and sample types was 2,3,3′,4,4′-pentachlorobiphenyl. These results suggest that exposures to PCBs are associated with adverse reproductive effects in turtles; however, due to the presence of many other chemicals in the eggs and the lack of information concerning their relative contributions, potencies, and potential interactions, the interpretation of a causal relationship solely to specific PCBs was confounded (Bishop *et al.*, 1991).

3.3.3.3. Piscivorous Birds and Mammals

Field studies of piscivorous birds and mammals have reported a variety of reproductive and teratogenic effects purported to be a result of exposure to PCBs. Decreased reproductive performance and/or population decline at some time since the late 1950s have been reported in at least nine top-predator bird species around the Great Lakes, including the bald eagle (*Haliaeetus albicillus*) (Wiemeyer *et al.*, 1984), herring gull (*Larus argentatus*) (Keith, 1966; Ludwig and Tomoff, 1966; Gilbertson and Hale, 1974; Fox *et al.*, 1988), double-crested cormorant (*Phalacrocorax auritus*) (Tillitt *et al.*, 1989; Fox *et al.*, 1991), black-crowned night heron (*Nycticorax nycticorax*) (Colborn, 1991), Caspian tern (*Sterna caspia*) (Tillitt *et al.*, 1989), Forster's tern (*Sterna forsteri*) (Harris and Trick, 1979; Trick, 1982; Hoffman *et al.*, 1987; Kubiak *et al.*, 1989), osprey (*Pandion haliaetus*) (Steidl *et al.*, 1991), ring-billed gull (*Larus delawarensis*), and common tern (*Sterna hirundo*) (Colborn, 1991). Effects noted include low hatching success, fewer fledglings, poorer nest attentiveness by adults, thinner eggshells, crossed beak, shorter beak, reduced femur length, and ossified foot. The prevalence of bill defects in cormorants in the Green Bay (52.1/10,000) and Beaver-Mackinac (12.3/10,000) areas of Lake Michigan was significantly greater than that in areas of Lakes Superior, Huron, or Ontario, Northern Ontario, or the Canadian Prairies

(Fox *et al.*, 1991). These observations suggest that factors specific to the Green Bay/Beaver-Mackinac areas were responsible for the defects. Where data were reported, the concentrations of PCBs associated with these effects ranged from 6.2 to 456 μg/g in eggs. However, the concentrations of other chemicals commonly found in biota from the Great Lakes (e.g., chlorinated dioxins and furans, DDT and its metabolites, various chlorinated pesticides, and a number of inorganic chemicals) that were likely present in the eggs were generally not reported. Further, few of these studies considered the potential effects of loss of habitat, and its potential interactions with chemical agents, on reproductive performance.

Studies of the lower Fox River and Green Bay on Lake Michigan indicate 2,3,7,8-substituted polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans, and coplanar PCBs (as assessed through AHH induction in the H4IIE rat hepatoma bioassay), were present at elevated concentrations in piscivorous birds [Forster's tern (*S. forsteri*), common tern (*S. hirundu*)] and insectivores [red-winged blackbirds (*Agelaius pheoniceus*) and tree swallow (*Tachycineta bicolor*)] that consume insects with sediment-dwelling life cycle components (Tillitt *et al.*, 1991a,b; Ankley *et al.*, 1992,1993; Jones *et al.*, 1993). Subsequent chemical analyses of tissues (eggs and fledging young) indicated that greater than 90% of the potency of the PCBs/PCDDs/PCDFs in the H4IIE bioassay was due to four coplanar PCBs in the mixture (IUPAC PCBs 169, 126, 77, and 105) (Ankley *et al.*, 1992). Analytical data of sediments from the Fox River and Green Bay indicated total concentrations of PCBs in the range of 31 to 6750 μg/kg, and a total T_4CDD-TEQ of 12.2 to 643 pg/g based on toxicity equivalency values of 0.01 for PCB 77, 0.001 for PCB 105, 0.1 for PCB 126, and 0.05 for PCB 169 (Ankley *et al.*, 1992). From these data Ankley *et al.* (1992) concluded that the effects observed on bird populations in the Fox River/Green Bay area appear to be related to exposures to coplanar PCBs, that specific cause–effect relationships could not be identified, and that further work is required to better define potential risks.

Based on the interpretation of the results from laboratory and field studies, a causal relationship appears to be evident between chemicals, including PCBs, associated with a disease known as chick edema, and the syndrome characterized by embryo mortality, edema, and deformities (referred to as "GLEMEDS" by the authors) in Great Lakes piscivorous birds (Gilbertson *et al.*, 1991). Black-crowned night heron embryos near San Francisco with 4.1 ppm PCBs were 15% smaller at pipping than controls, and there was a significant inverse correlation between PCBs and embryo weight at hatching (Hoffman *et al.*, 1986). An increased incidence of abnormalities, including bill defects and eye and foot deformities, was observed in a colony of common terns and roseate terns at Long Island Sound in 1969 and 1970 (Hays and Risebrough, 1972). Eggs from this colony were found to contain increased concentrations of PCBs. Gilbertson (1983) reported high mortality, edema, porphyria, liver enlargement, fatty infiltration, and necrosis, as well as growth retardation and embryo deformities (symptoms similar to chick edema disease) in Great Lakes herring gulls. Similar signs were found in other species. Retrospective analyses of the eggs of some of these species revealed the presence of the toxic, chick edema active compounds 2,3,7,8-T_4CDD, 3,3′,4,4′,5-pentachlorobiphenyl and 2,3,3′,4,4′-pentachlorobiphenyl (Stalling *et al.*, 1985; Kubiak *et al.*, 1989). Concentrations of PCBs in eggs of Forster's tern associated with adverse reproductive effects (reduced hatchability, delayed hatch, reduced number of fledglings) were: Total non-*ortho* PCBs–1.37 to 41 ng/g (wet wt); total PCBs–6.2 to 25.9 μg/g (wet wt), PCBs in 2,3,7,8-T_4CDD TEQ–21.75 pg/g (Kubiak *et al.*, 1989). It should be noted that the

TEFs used in this Kubiak paper were based on early work by Safe (Sawyer *et al.*, 1984). More recent information published by Walker and Peterson (1991) reports a more minor role for PCBs compared to dioxins with TEFs for PCBs several fold less than suggested by Safe (1990). TEFs were discussed in more detail in Section 3.2.3.

Concentration of PCBs in Piscivorous Birds and Mammals

Teratogenic effects, impaired reproduction, or complete reproductive failure reported in several species of piscivorous birds on the Great Lakes since the 1950s appear causally related to increased environmental concentrations of a number of chlorinated organic chemicals, including PCBs, observed at that time (Mineau *et al.*, 1984; Bishop and Weseloh, 1990; Gilbertson *et al.*, 1991). In the early 1970s, the concentrations of a range of chlorinated organic chemicals in herring gulls and other waterbirds were among the highest reported in the world. Since the changes in use characteristics of PCBs in 1972 and the cessation of production of PCBs in 1978, the concentrations of PCBs have declined in fish (Fig. 5-3) and herring gull eggs (Fig. 5-4) around the Great Lakes (Bishop and Weseloh, 1990). Results from monitoring programs in effect since 1971 indicate that the highest concentrations of PCBs in herring gull eggs occurred in the early and mid-1970s (Bishop and Weseloh, 1990). Concentrations in eggs declined substantially in the late 1970s (Fig. 5-4). However, in the early 1980s, concentrations of PCBs in herring gull eggs showed a slight increase in some regions of the Great Lakes, coincident with an increase in concentrations of PCBs in spottail shiners, their main prey. It has been suggested that PCBs were being recycled through the Great Lakes ecosystem from sources such as leaching from landfill sites, disturbance from lake bottoms, and atmospheric transport (Bishop and Weseloh, 1990).

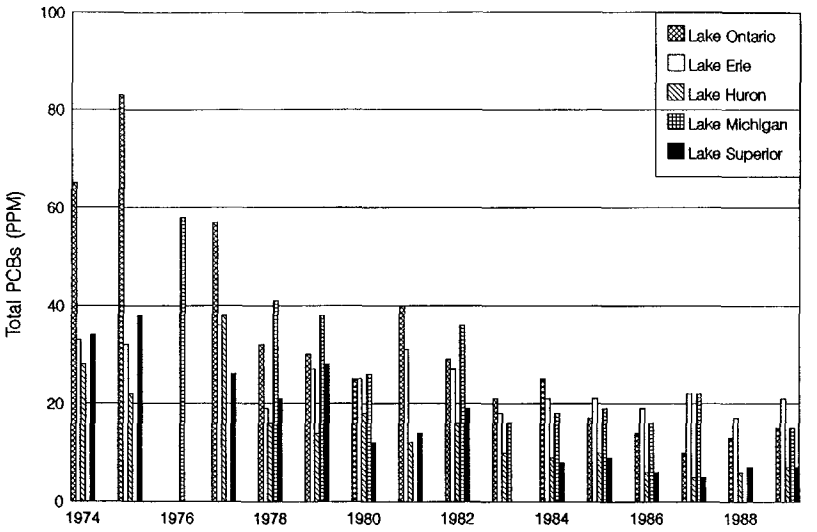

FIG. 5-4. Total concentrations of PCBs in Herring gull eggs collected from the Great Lakes, 1974 to 1989. Islands were Snake Island, Lake Ontario; Middle Island, Lake Erie; Double Island, Lake Huron; Big Sister Island, Lake Michigan; Granite Island, Lake Superior. Reproduced from Allan *et al.* (1991).

A similar situation has been observed in other piscivorous bird populations around the Great Lakes (Struger and Weseloh, 1985; Noble and Elliot, 1986; Gilbertson *et al.,* 1991). By the early 1960s, the double-crested cormorant had essentially ceased breeding in the Lake Michigan area and populations were also declining in the other Great Lakes. Similarly, the bald eagle virtually disappeared from the shores of Lakes Ontario and Michigan, and populations also declined from Lakes Huron and Superior (Gilbertson *et al.,* 1991). Although populations of bald eagles have not yet reestablished on Lakes Huron and Ontario, the Lakes Erie and Superior populations appear to be reproducing normally. Reductions in chemical concentrations in the Great Lakes are thought to have contributed to a 56% annual increase in double-crested cormorant populations between 1974 and 1982 (Price and Weseloh, 1986). Similar trends have been reported on the west coast. Noble and Elliot (1986) reviewed the trends of contaminant concentrations in seabirds and found that most contaminants, especially DDE and PCBs, declined in piscivorous birds between 1970 and the 1980s. Elliot *et al.* (1989) confirmed this trend in a more detailed study.

PCBs have also been measured in polar bears in remote areas of the world. No changes in concentrations of PCBs in polar bears were evident between 1978 and 1989 (Norheim *et al.,* 1992); however, the authors point out that this may be due to heterogeneity of the samples with respect to age, sex, nutritional status, and other factors. The concentrations of PCBs in adipose tissue and liver of polar bears from the Svalbard area of Norway ranged from 32 ± 30 μg/g in adipose tissue to 13 ± 23 μg/g in liver in adult bears, and 15 ± 9.2 μg/g in adipose tissue to 12 ± 16 μg/g in livers of juvenile bears (Norheim *et al.,* 1992). These concentrations were greater than those of 4 to 8 μg PCBs/g adipose tissue and 0.4 to 1.2 μg PCBs/g liver reported for polar bears in the Canadian Arctic (Muir *et al.,* 1988).

Chlorinated organic chemicals, including PCBs, have also been detected in whales. Muir *et al.* (1990) quantified total PCBs and other chlorinated organic chemicals in blubber samples collected from beluga whales, *Delphinapterus leucas,* from four geographic areas in Canada (Hudson Bay, Cumberland Sound, Jones Sound, and Beaufort Sea). Total PCBs, polychlorinated camphenes (PCCs), total DDT-related chemicals, and total chlordane-related chemicals were detected in blubber samples from all locations. PCCs were the major organochlorines detected in blubber of arctic belugas with concentrations approximately 2-fold greater than total chlordane, and 1.5-fold greater than total PCBs and DDTs.

Concentrations of PCBs in whale blubber ranged from 0.96 ± 1.00 μg/g (wet wt) in females from western Hudson Bay to 75.8 ± 15.3 μg/g (wet wt) in males from the St. Lawrence estuary. Blubber concentrations of PCBs and total DDT were significantly greater in samples from the St. Lawrence than those from the arctic populations. The concentrations of total PCBs in blubber from St. Lawrence belugas ranged from 53.9 to 89.2 μg/g for males and 14.5 to 68.7 μg/g for females. The concentrations of total PCBs for all other sites combined ranged from 2.53 to 4.91 μg/g for males and 0.96 to 2.46 μg/g for females. The average concentrations of total PCBs were approximately 25-fold higher for St. Lawrence belugas than those for arctic belugas. Concentrations of total PCBs were generally higher in blubber samples from male beluga compared to those from females. This phenomenon is often observed in pinnipeds and cetaceans and has been attributed to loss of body residues via lactation (Muir *et al.,* 1990).

Differences were noted in the PCB profiles found for St. Lawrence River belugas compared to other sites. The tetra-, penta-, and hexacongeners predominated in arctic

belugas, while the hexa- and heptacongeners were present at greater concentrations in St. Lawrence specimens. The homolog pattern of PCBs in St. Lawrence belugas more closely resembled a 1:1 mixture of Aroclor 1254:1260 than did the pattern in arctic belugas. It was suggested by Muir *et al.* (1990) that this difference in PCBs pattern may be the result of greater enzyme activity in St. Lawrence belugas resulting in excretion of the less recalcitrant PCBs, and/or differing sources of exposure to PCBs between the St. Lawrence and arctic environments. Exposure to PCBs of St. Lawrence belugas was thought to be a more direct route from PCBs discharged directly in the Great Lakes basin, while exposure of arctic belugas to PCBs was suggested to be largely from atmospheric deposition. Direct exposure to local sources of PCBs in the arctic, such as in transformers from DEW line stations, was not considered to be an important source of PCBs to marine mammals by the authors; however, neither the magnitude of these sources nor possible exposures through aquatic food chains were addressed.

Chlorinated organic chemicals have also been detected in the North Atlantic right whale (Woodley *et al.*, 1991). Detectable concentrations of DDE, DDT, dieldrin, chlordane, and PCBs were reported in all or most blubber samples which were collected in 1988 and 1989. Concentrations of PCBs ranged from trace (0.05 to 0.1 μg/g wet wt) to 1.9 μg/g wet wt. Although the concentrations of PCBs were greater than the other chemicals, the concentrations of PCBs were lower than those found for other cetaceans, including arctic belugas (Muir *et al.*, 1990). Woodley *et al.* (1991) also noted that the concentrations of PCBs in North Atlantic right whales are lower than those which may effect reproductive performance in marine and terrestrial mammals, suggesting that other factors may be responsible for the lack of population recovery of this endangered species.

A variety of chlorinated organic chemicals have been measured in juvenile and adult seals from the Wadden Sea (Reijnders, 1980). Of all the chemicals measured, PCBs were present at the greatest concentrations, ranging from 76.4 μg/g (wet wt) to 701 μg/g (wet wt), and it was suggested that PCBs were responsible for the poor reproductive performance observed in this population.

Later studies suggested that PCBs may also inhibit immune function in Baltic seals (Brouwer and Van Den Berg, 1986; Brouwer, 1989; Brouwer *et al.*, 1989), possibly related to deficiencies in vitamin A and thyroid hormones (Brouwer *et al.*, 1989) induced by PCBs causing seals to be relatively susceptible to viral attack. Vitamin A (retinol in its various forms) is a fat-soluble vitamin, important for normal vision, reproduction, and development (Government of Canada, 1991). Thyroxine is a thyroid hormone which is important for normal growth and development. Lesser concentrations of plasma retinol and thyroxine were observed in seals fed fish from the Wadden Sea than seals fed control fish. The concentrations of PCBs and DDE in the Wadden Sea fish were significantly greater than those in control fish; however, the fish were not analyzed for other organic and inorganic chemicals. Since laboratory studies in which animals received large doses of PCBs indicated changes in the concentrations of retinol (vitamin A) and thyroid hormones, Brouwer *et al.* (1989) suggested that the PCBs with non-*ortho* chlorine substitutions or metabolites of PCBs in fish impair normal vitamin A and thyroxine homeostasis. This, in turn, was suggested to cause reduced concentrations of vitamin A and an increased susceptibility to stress. It has been suggested that the reduction of both retinol and thyroxine is caused by the interference of the retinol–thyroxine plasma carrier protein complex by PCBs, metabolites of PCBs, or secondary products related to effects caused by these chemicals (Reijnders,

1986; Brouwer *et al.,* 1989). The results from these studies suggest that the effects observed in Baltic seal may be the result of excessive exposure to PCBs; however, evidence of viral epidemics in seals in relatively pristine environments, and the incomplete consideration of exposures to other chemicals present in the Baltic Sea, confound the establishment of a causal association between high mortality in seals and exposures to PCBs.

The information provided through the field studies summarized in this section indicates that PCBs, and possibly several other chemicals as well as factors impairing habitat requirements, have been associated with adverse effects and population declines in various aquatic species. The information also demonstrates that these populations can recover with reductions in the concentrations of chemicals in their environment. Further reductions in concentrations of PCBs, and other organic chemicals, are anticipated in the 1990s with the decline in the quantities released into the environment through the adoption of improved use technologies and the reduction of existing sources. However, the magnitude of these apparent recoveries in wildlife species and the declines in the concentrations of chemicals in the environment will not likely be as dramatic as those of the 1970s (Bishop and Weseloh, 1990). For example, although most major sources releasing PCBs and other chemicals to the environment have been addressed, a number of sources of direct releases remain (e.g., landfill leaching, emissions from storage facilities, accidental spills), plus indirect sources from the recycling of PCBs through the environment (e.g., long-range atmospheric transport), (see Section 2.3 for discussion) continue to add and distribute PCBs in the environment. Various destruction procedures for PCBs provide a means of eliminating the possible releases of those currently in storage. The destruction of PCBs that are recycling through the environment will be a slow process as natural physical and biological degradation processes remove PCBs from the environment. Recent research on the relative environmental fate and toxicological characteristics of specific PCBs demonstrates that there are substantial differences between isomers (e.g., non-*ortho*-substituted PCBs have potentially greater toxicity than *ortho*-substituted PCBs and the more chlorinated isomers are more resistent to degradation compared to the less chlorinated groups). Such information is consistent with the predictions that the rate of decrease of environmental concentrations of PCBs will be slower in the future than that observed in the 1970s and early 1980s. In addition, this information provides important lessons to society regarding the types of chemicals to be avoided in the future.

3.3.4. Mechanism of Toxicity

Understanding the mechanisms whereby chemicals produce their toxic effects is important to the establishment of exposure limits designed to avoid adverse effects. A great deal of information is known regarding the factors affecting the development of adverse effects from exposures to PCBs (see Sections 3.2.2 and 3.2.3). PCBs which are substituted in both *para* positions and in at least one *meta* position of each ring, but have no *ortho* chlorines, are the most toxic to fish (Tanabe *et al.,* 1987; Brunström and Andersson, 1988; Smith *et al.,* 1990; Brunström, 1991; Walker and Peterson, 1991). It is believed that these non-*ortho*-substituted PCBs attain a planar conformation (i.e., the two benzene–carbon ring structures of PCBs are on the same molecular plane) similar to that of 2,3,7,8-T_4CDD (McKinney and Singh, 1981). The greater the amount

of chlorine in the *ortho* positions of the carbon rings of PCBs, the greater the angle of twist between rings, thus forcing the two carbon ring structures into different molecular planes (Shaw and Connell, 1984). The more "planar" the molecular conformation, the greater the binding affinity of the PCB molecule with the cytosolic Ah receptor. Once the PCB/receptor complex is formed within the cytosol of cells, it is believed to translocate to the cell nucleus, where it interacts at a nuclear receptor site to alter gene expression, resulting in changes in protein synthesis. One of the known effects of these increases in protein synthesis is the production of greater quantities of specific enzymes, such as the MFO enzymes AHH and EROD.

The various toxic, dose-related effects associated with exposures to quantities of PCBs that exceed the dose–response threshold (e.g., embryotoxicity, growth retardation, deformities, edema, immunosuppression, porphyria, and alteration of Vitamin A status) are believed to be due to the changes in enzyme activities induced by PCBs. These changes in enzyme activity are believed to result in a number of species- and tissue-specific changes to normal homeostasis of various biological functions within the body (Safe, 1989, 1991; Gilbertson *et al.*, 1991). Further details on the potential mechanisms of action of PCBs are discussed in Section 3.2.3. From the point of view of estimating an exposure limit for PCBs, the information on the mechanism of action indicates that PCBs alter the action of normal biological processes and do not appear to produce self-propagated lesions indicative of a theoretical nonthreshold exposure–response relationship. Since the activity of the naturally occurring enzyme systems affected by PCBs fluctuate as a normal part of biological functions (e.g., the activities of the MFO enzyme system normally fluctuate during reproductive cycles), some changes in the activities of these enzymes can occur without the production of adverse effects. Such mechanisms are consistent with a threshold-type dose–response relationship. This information forms the basis for the procedures used in the estimation of an exposure limit for PCBs.

3.3.5. Conclusions

3.3.5.1. Exposure Limits

The information summarized in the previous section on mechanisms of toxicity indicate that an exposure threshold should exist, below which no adverse effects from PCBs would occur. Concentrations of PCBs in water less than 0.014 μg/liter (ppb) do not appear to be associated with adverse effects to aquatic life (Eisler, 1986), although concentrations as low as 0.006 μg/liter resulted in measurable accumulation by various species of filter-feeding shellfish. The EPA (1980) has established maximum acceptable toxicant concentration (MATC) values for several aquatic species with respect to selected Aroclor PCBs (Table 5-18). However, the PCBs with greater quantities of chlorine, and with chlorine substitutions associated with greater toxic potential, are relatively insoluble in water and tend to partition to dissolved organic carbon and suspended sediments in the water column and bottom sediments, depending on specific sedimentation characteristics of the water body in question. Consequently, the PCBs of greatest environmental concern tend not to be taken up from the water column by organisms at upper trophic levels; rather, they tend to accumulate through the food chain, beginning with uptake from sediments by benthic invertebrates which are the

TABLE 5-18

MATC VALUES FOR AROCLOR PCBs AND SELECTED SPECIES OF AQUATIC ORGANISMS BASED ON EXPOSURE FOR LIFE CYCLE, PARTIAL LIFE CYCLE, OR EARLY LIFE STAGE

Ecosystem	Organism	Aroclor PCBs	MATC[a] (μg/L)
Freshwater	Cladoceran, *Daphnia magna*	1248	1.2-3.5
		1254	2.5-7.5
	Amphipod, *Gammarus pseudolimnaeus*	1242	2.8-8.7
		1248	2.5-5.1
	Insect (midge), *Tanytarsus dissimilis*	1254	0.5-1.2
	Brook trout, *Salvelinus fontinalis*	1254	0.7-1.5
	Fathead minnow *Pimephales promelas*	1242	5.4-15.0
		1248	0.1-0.4
		1254	1.8-4.6
		1260	1.3-4.0
Marine	Sheepshead minnow, *Cyprinodon variegatus* (early life stage)	1016	3.4-15.0
		1254	0.06-0.16

Source: EPA, 1980.

[a] The lower value in each pair indicates the highest concentration tested which produced no measurable effect on growth, reproduction, survival, and metabolism during chronic exposure; the higher value indicates the lowest concentration which produced a measurable effect.

prey of higher organisms. Fish are potentially exposed to greater concentrations of PCBs in their diet compared to the waterborne route of exposure. This potential for food chain accumulation raises questions regarding the degree of protection to aquatic life that would be achieved through water quality objectives for chemicals with physical/chemical properties comparable to PCBs. These concerns have been reviewed and discussed in detail by Gray *et al.* (1991). The protection of aquatic life would be better achieved using criteria for body tissue concentrations, body tissue:sediment concentration ratios, or dietary concentrations. Among sensitive species of teleosts, total tissue concentrations of PCBs in excess of 500 μg/kg fresh wt in diets, 400 μg/kg in whole body, and 300 μg/kg in eggs have been demonstrated to be harmful. These values provide a general guide for the lower end of the range of concentrations of PCBs that would adversely affect aquatic life. The application of a 10-fold safety factor to these values suggests that tissue concentrations in the range of 30 to 50 μg/kg (ppb) could be used as evaluation tools to assess potential effects from PCBs to aquatic life.

With respect to piscivorous birds and mammals, there is a paucity of specific exposure information from which exposure limits for PCBs could be developed. However, laboratory and field studies provide some information on tissue concentrations associated with adverse effects in piscivorous wildlife. The lower end of the range of concentrations of PCBs associated with decreased reproduction was approximately 6 μg/g in eggs of piscivorous birds near the Great Lakes. Smaller embryo weights at hatching were observed at tissue concentrations of approximately 4 μg/g. Mink exposed to quantities of PCBs that resulted in liver concentrations between 1 and 2 μg PCBs/g showed a minor impairment in reproduction. These values provide a general guide for the lower

end of the range in concentrations of PCBs that would adversely affect piscivorous birds and mammals. The application of a 10-fold safety factor to these values suggests that tissue concentrations in the range of 0.1 to 0.2 μg/g (ppm) could be used as evaluation tools to assess potential effects to piscivorous wildlife from PCBs.

However, the above exposure criteria for PCBs do not consider the potentially greater toxic potency of the coplanar isomers of PCBs. In order to account for such factors, it has been proposed (Safe, 1990; Walker and Peterson, 1991) that toxicity equivalency factors be applied to specific congeners of PCBs to express their concentrations in terms of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin toxicity equivalents. The assessment of acceptable exposures using this approach would require the comparison of the T_4CDD-TEQ concentrations against exposure limits for 2,3,7,8-T_4CDD. If the expression of exposure limits for PCBs based on 2,3,7,8-T_4CDD-TEQs is appropriate, it appears that this approach would increase the apparent toxicity of PCBs by approximately 3.5-fold (Williams *et al.,* 1992), or, in other words, would decrease recommended exposure limits by about 3.5-fold. The significance of using TEFs to evaluate PCBs is discussed further in Section 3.2.3.

Walker and Peterson (1991) reported on the relative potencies of polychlorinated dioxins, furans, and PCBs relative to 2,3,7,8-T_4CDD for producing early life stage mortality in rainbow trout. Newly fertilized eggs were injected with graded doses of dioxins, furans, and PCBs. LD_{50}'s were determined based on mortality from hatching onset to swim up. Toxicity equivalency factors calculated for PCBs, based on the ratio of 2,3,7,8-T_4CDD LD_{50} to congener LD_{50}, were significantly lower (one to two orders of magnitude lower) than TEFs reported based on mammalian data (Safe, 1990) (Table 5-19). Alternatively, TEFs derived for some 2,3,7,8-substituted dioxins and furans were higher than the TEFs reported by Safe (1990). The authors suggested that TEFs derived from mammalian data were poor predictors of relative potency for salmonid species.

3.3.5.2. Health Significance of Environmental Concentrations

Current environmental concentrations of waterborne PCBs summarized in Section 3.1 are generally well below concentrations that would be associated with adverse

TABLE 5-19

TOXICITY EQUIVALENT FACTORS (TEFS) FOR PCBS[a]

PCB Isomer	Safe (1990) TEF	Walker and Peterson TEF
3,3',4,4'-Tetrachlorobiphenyl (77)	0.01	0.00016
3,3',4,4',5-Pentachlorobiphenyl (126)	0.1	0.005
2,3,3',4,4'-Pentachlorobiphenyl (105)	0.001	< 0.00007
2,3',4,4'5-Pentachlorobiphenyl (118)	0.001	< 0.00007
3,3',4,4',5,5'-Hexachlorobiphenyl (169)	0.05	-

Source: Safe (1990) and Walker and Peterson (1991).

[a] Both TEF systems use 2,3,7,8-T_4CDD as 1.0.

\- No TEF reported.

effects in aquatic organisms as outlined in Table 5-18. Reported LC_{50} values for freshwater invertebrates ranged from 1.3 to 10,000 μg/liter with the majority of values in the 80 to 800 μg/liter range. Corresponding values for fish ranged from 8 to 1154 μg/liter. Surface water concentrations of PCBs listed in Table 5-2 ranged from below the detection limit to 0.950 μg/liter, with the majority of the values in the range of 0.0003 to 0.008 μg/liter. Therefore, the difference of 10- to over 1000-fold between the MATC values and reported concentrations of PCBs demonstrates that adverse effects on aquatic organisms from PCBs in water would be highly unlikely. However, the evaluation of the environmental fate of PCBs (see Section 2.3), and information on the bioaccumulation characteristics of PCBs (Oliver and Niimi, 1988), indicated that water was not one of the environmental media in which the PCBs with greater quantities of chlorine would accumulate. Therefore, potential adverse effects on aquatic organisms from PCBs cannot be predicted based solely on their concentrations in water.

The available data demonstrate that the major route of exposure of organisms higher on the food chain is through the diet, rather than direct uptake from water (refer to Section 3.3.1). Clearly, piscivorous birds and mammals at the upper end of the aquatic food chain are exposed to PCBs through the consumption of their prey. Exposures to the historically extreme concentrations of PCBs in the diet of piscivorous birds and mammals, together with several other organic chemicals (e.g., mirex, chlorinated dioxins and furans, DDT and its environmental breakdown products), are believed to be a major factor in the historical decline in numbers of several piscivorous bird species on the Great Lakes. Teratogenic effects, impaired reproduction, or complete reproductive failure were reported in several species of piscivorous birds in various regions of the Great Lakes beginning in the 1950s and continuing through the 1970s. Evidence of increased concentrations of chlorinated organic chemicals, including PCBs, was first observed in the tissues and eggs of piscivorous species since they are top food chain predators and their diets are almost exclusively fish.

In the early 1970s, the concentrations of a range of chlorinated organic chemicals, including PCBs, in herring gulls and other water birds on the Great Lakes were among the highest reported in the world (Bishop and Weseloh, 1990). The concentrations of PCBs in eggs, and residues in the birds, declined dramatically in the late 1970s.

Populations of the double-crested cormorants in specific areas of the Great Lakes also experienced severe declines from the 1950s to 1970s. Similarly, the bald eagle was not found along the shores of Lakes Ontario and Michigan, and populations also declined from Lakes Huron and Superior (Gilbertson *et al.*, 1991). Due to the multiplicity of chemicals in the aquatic environment, the decline and recovery of several piscivorous bird species were influenced by environmental concentrations of a variety of chemicals, including PCBs. It should be noted that loss of habitat also played a role in the decline in numbers of some piscivorous bird species and would continue to be a factor in slow recoveries today.

The available evidence indicated substantial decreases in tissue concentrations of PCBs and recoveries in the numbers of some piscivorous bird populations since the late 1970s. Although populations of bald eagles have not yet reestablished on Lakes Huron and Ontario, the Lakes Erie and Superior populations now appear to be reproducing normally. Struger and Weseloh (1985) reported that residues of DDE in Caspian terns decreased from a mean of 13.8 ppm to 5.2 ppm (wet wt) between 1972 and 1981. Reductions in concentrations of chemicals in the Great Lakes are thought

to have contributed to a 56% annual increase in double-crested cormorant populations between 1974 and 1982 (Price and Weseloh, 1986). In addition, studies of teratogenic effects in cormorants between 1979 and 1987 demonstrate that bill defects are currently largely limited to the Green Bay/Beaver-Mackinac areas of Lake Michigan. No defects were observed in various regions of Lake Huron or around Lake Erie (Fox *et al.*, 1991). These observations indicate that the potential adverse effects of PCBs (possibly together with other chemicals and influenced by factors affecting suitable habitat) currently observed appear to be related to specific areas, possibly associated with point sources, rather than a general problem across a wider area.

Further reductions in concentrations of PCBs will likely occur in the future; however, the magnitude of these declines will probably not be as dramatic as those of the mid-1970s to mid-1980s (Bishop and Weseloh, 1990). It is generally evident that the sources of entry of PCBs to the environment have diminished. However, smaller direct sources from various sites, indirect sources from the recycling of PCBs through the environment, and possible unquantified natural sources (refer to Section 2) continue to contribute to the total quantities of PCBs entering the environment. The quantities of PCBs from indirect sources are expected to slowly decline with time as natural processes remove PCBs from the environment. These removal processes include physical and biological degradation processes and the burial of PCBsthrough natural sedimentation in lake systems. The net effect will be a continuing decrease in the PCBs available to benthic invertebrates, thus diminishing the input of PCBs to the aquatic food chain.

A continuing concern is the occurrence of coplanar PCBs (non-*ortho*-chlorine substituted PCBs). The coplanar PCBs, though generally present at lesser concentrations than nonplanar PCBs in commercial mixtures, have been reported to bioaccumulate to a greater degree in organisms at higher trophic levels of food chains, primarily because the coplanar PCBs are more slowly metabolized (Muir *et al.*, 1988; Oliver and Niimi, 1988; Safe, 1990; Norheim *et al.*, 1992). Since analytical capability for the measurement of the coplanar isomers is a relatively recent development (i.e., approximately the past 5 years), there is little information available on temporal changes in their concentrations in environmental media and biological systems.

However, recent evidence would suggest that coplanar PCBs are not accumulated to a greater extent compared to the nonplanar isomers (Metcalfe and Metcalfe, 1993). The discrepancies between these observations may be related to differences in PCB congener profiles of the site-specific sources and in biodegradative activity of the ecosystem. Nonetheless, the recovery of various wildlife populations, from regions such as the Great Lakes where adverse reproductive effects were believed to be related to PCBs and other chemicals, demonstrates that current concentrations of PCBs are not causing widespread adverse effects. The existence of confounding factors in the Great Lakes area, such as loss of habitat, particularly suitable breeding habitat, high density of human populations with associated domestic, municipal and industrial activities, and simultaneous exposures to a large number of chemicals, limits the establishment of definitive causal relationships between specific factors and the effects observed. Several independent studies have demonstrated that adverse effects on biological systems in the Great Lakes are focused in specific areas (Fox *et al.*, 1991; Ankley *et al.*, 1992, 1993; Jones *et al.*, 1993), suggesting the involvement of point sources associated with specific activities. Additional research is needed to delineate the possible relationships between PCBs, coplanar PCBs, and various potential adverse effects on aquatic wildlife.

3.4. Terrestrial Wildlife Hazard Assessment

The information identified on the potential hazards to terrestrial and nonpiscivorous wildlife from PCBs, as distinct from the information discussed in Section 3.2 on mammals, is summarized in this section.

3.4.1. Bioavailability, Metabolic Conversion, Pharmacokinetics, and Bioaccumulation

3.4.1.1. Bioavailability and Pharmacokinetics

Little information is available specifically on the bioavailability, pharmacokinetics, and bioaccumulation of PCBs in terrestrial wildlife. The available data suggest that the same principles are involved for terrestrial wildlife as for aquatic and laboratory animals.

PCBs with *meta–para* unsubstituted carbon atoms for at least one ring are eliminated more rapidly in the pigeon than PCBs with *ortho–meta* unsubstituted carbon atoms. Tissues having greatest microsomal monooxygenase activity had the most rapid elimination rates. The distribution of total PCBs in the pigeon was 90% in adipose tissue, 2% in kidneys, and 1% each in the brain, muscle, and heart (Borlakoglu *et al.*, 1991).

There are several reports on the tissue concentrations of PCBs in chickens and their transfer to eggs (Platonow and Reinhart, 1973; Tumasonis *et al.*, 1973). A study of the dietary uptake and distribution of PCBs in white leghorn chickens indicated that the PCBs were more potent toxic agents when they were stored for several weeks in the hen, presumably compared to shorter storage periods (Bush *et al.*, 1974). The authors suggested that the increased toxicity could be due to selective uptake and accumulation of the more toxic isomers or toxic metabolites. Similar results on the transfer of PCBs from adult females to eggs were reported for pheasants given 50-mg capsules of PCBs and sacrificed 28 days later. Only about 4 mg was excreted in the feces, about 4.2 mg was excreted into eggs, and 40.5 mg was retained in the adult hen (Dahlgren *et al.*, 1972). In screech owls, a dosage of 3 mg/kg Aroclor 1254 resulted in 7 mg/kg in eggs (McLane and Hughes, 1980). These results were similar to those reported for fish and various species of piscivorous wildlife (See Section 3.3).

3.4.1.2. Bioaccumulation

According to Travis and Blaylock (1992) plants may accumulate chemicals via three mechanisms: Root uptake, atmospheric deposition of particles, and air-to-plant transfer of vapor phase chemicals. Travis and Blaylock (1992) estimated the bioconcentration of organic chemicals from the soil to vegetation via root uptake. This method is based on measured data which demonstrated that the bioconcentration factor for an organic chemical in vegetation is inversely proportional to the square root of the octanol–water partition coefficient (K_{ow}). Root uptake of organics has been correlated with K_{ow} and has been shown to decrease as K_{ow} increases (Baes, 1982; Briggs *et al.*, 1982; Travis and Blaylock, 1992). Therefore, the lesser chlorinated PCBs would be expected to be accumulated by plants to a greater extent than the more chlorinated congeners.

The limited information available on bioaccumulation of PCBs in terrestrial wildlife also suggests similarities to aquatic wildlife. Hansen and Storr-Hansen (1992) reported that house flies (*Musca domestica*) exposed for 72 hr to PCBs attained maximum body concentrations between 24 and 48 hr, and there was a marked reduction in the tissue concentrations of most PCBs between 48 and 72 hr. The variation observed among concentrations of different PCBs and among different age classes of flies was believed to be partially attributable to different rates of monooxygenase-mediated biotransformation of PCBs. The uptake of PCBs has also been reported in plants (Weber and Mrozek, 1979). Soybeans accumulated 0.016% of the applied concentration after 16 days exposure (from seed) and fescue grass accumulated 0.17% after 50 days.

3.4.2. Laboratory Studies

3.4.2.1. Lethal Effects

Birds (Including Terrestrial Birds and Aquatic, Nonpiscivorous Birds)

Birds appear to be more resistant to the lethal effects of PCBs than mammals (Eisler, 1986). LD_{50}'s for various bird species ranged from 604 to >6000 mg Aroclor/kg diet (Table 5-20). Residues of 310 mg/kg fresh wt or more in the brain were associated with an increased incidence of death for all avian species.

Mammals (Nonpiscivorous)

Acute LD_{50} values of Aroclor PCBs toward selected terrestrial mammals are summarized in Table 5-21.

3.4.2.2. Nonlethal Effects

Teratogenicity

Birds. Comparisons of the teratogenic effects of PCBs in ducks, geese, herring gulls, and several strains of chickens showed considerable variation in sensitivity among bird species, with the chicken being the most sensitive (Brunström and Darnerud, 1983; Brunström, 1988). Embryos of all breeds of chicken tested were extremely sensitive to 3,3′,4,4′-tetrachlorobiphenyl, one of the most toxic isomers of PCBs, with 70 to 100% mortality at a dose of 20 μg/kg egg (Brunström, 1988). Liver lesions, hydropericardium, subcutaneous edema, shortened beak, and microphthalmia were found in both dead and living chick embryos treated with PCBs. Embryos of the other species tested, however, were considerably less sensitive. For example, doses of up to 5000 μg/g egg for ducks and 1000 μg/g egg for geese and herring gulls caused no significant increase in embryo mortality or terata. Turkey embryos were about 50 times less sensitive to TCB than chick embryos (Brunström and Lund, 1988). Embryos of the common eider duck were also considerably less sensitive to 3,3′,4,4′-tetrachlorobiphenyl and to 3,3′,4,4′,5-pentachlorobiphenyl than chick embryos (Brunström *et al.*, 1990). Caution is required, however, in the extrapolation of these data indicating teratogenic

TABLE 5-20

ACUTE TOXICITIES OF AROCLOR PCBS TO SELECTED BIRD SPECIES

Species	Aroclor	Exposure Period	LD_{50} (mg/kg diet)	Reference
Mallard (*Anas platyrhynchos*)	1242	5 d on treated diet plus 3 d untreated	3,182	Heath *et al.*, 1972
	1248		2,798	Heath *et al.*, 1972
	1254		2,699	Heath *et al.*, 1972
	1260		1,975	Heath *et al.*, 1972
Ring-necked pheasant (*Phasianus colchicus*)	1221	5 d on treated diet plus 3 d untreated	> 4,000	Heath *et al.*, 1972
	1242		2,078	Heath *et al.*, 1972
	1248		1,312	Heath *et al.*, 1972
	1254		1,091	Heath *et al.*, 1972
	1260		1,260	Heath *et al.*, 1972
Northern Bobwhite (*Colinus virginianus*)	1221	5 d on treated diet plus 3 d untreated	> 6,000	Heath *et al.*, 1972
	1242		2,098	Heath *et al.*, 1972
	1248		1,175	Heath *et al.*, 1972
	1254		604	Heath *et al.*, 1972
	1260		747	Heath *et al.*, 1972
Red-winged blackbird (*Agelaius phoeniceus*)	1254	6 d	1,500	Stickel *et al.*, 1984
Mallard	1242	Single dose	> 2 g/kg body weight	NAS, 1979
	1254		> 2 g/kg body weight	NAS, 1979
	1260		> 2 g/kg body weight	NAS, 1979

Source: Eisler, 1986.

TABLE 5-21

ACUTE TOXICITIES OF AROCLOR PCBS TO SELECTED TERRESTRIAL MAMMALS

Route	Species	Aroclor	Exposure Period	LD_{50}[a]	Reference
Dietary	Raccoon (*Procyon lotor*)	1254	8 d	> 50 mg/kg diet	Montz *et al.*, 1982
	Cottontail rabbit (*Sylvilagus floridanus*)	1254	12 wk	> 10	Zepp and Kirkpatrick, 1976
Dermal	Rabbit	1221	Single dose	4.0 g/kg body weight	EPA, 1980
		1242		8.7	EPA, 1980
		1248		11.0	EPA, 1980
		1260		10.0	EPA, 1980

Source: Eisler, 1986.

[a] Units for dietary LD_{50}s are mg/kg diet; those for dermal LD_{50}s are g/kg body weight.

effects of PCBs in chickens to predict effects seen in the general environment at lower exposures. Khera (1984) published criteria for the assessment of the teratogenic effects of chemicals which stipulate that teratogenic effects should only be assessed as exposures that are not associated with evidence of maternal toxicity. This stipulation is based on observations in mammalian systems demonstrating that terata can develop as secondary outcomes of overt maternal stresses related to malnutrition, excessive maternal systemic toxicity, etc. Therefore, the observation of terata in chick embryos in which 70 to 100% mortality was observed may have little relevance to predicting teratogenic effects at exposures or tissue concentrations not associated with overt maternal toxicity such as the much smaller rates of exposure that would result from environmental sources of PCBs.

Reproductive Effects

Birds. While there appear to be substantial differences in the susceptibility to reproductive effects from exposures to PCBs among species of birds, total dietary concentrations of PCBs below 5 ppm do not appear to affect reproduction (Peakall, 1986). Dietary concentrations of 10 ppm (Aroclor 1248) caused severe embryonic mortality and concentrations of 5 ppm were associated with decreased egg production in chickens (Peakall 1975, 1986). Hatchability was markedly reduced in ring doves fed 10 ppm Aroclor 1254 (Peakall and Peakall, 1973), and a single intraperitoneal injection of 40 mg PCBs/kg body wt to doves was associated with retarded egg laying, reduced hatchability, and changes in retinoid dynamics during oogenesis and *in ovo* (Spear *et al.*, 1989). Diets containing 3 ppm Aroclor 1248 fed to screech owls 8 weeks before egg laying did not affect reproduction, the number of eggs laid, eggs hatched, young fledged, or eggshell thickness (McLane and Hughes, 1980). However, American kestrels fed diets containing 3 ppm PCBs produced eggs with shells that were 5% thinner than controls. No effects on reproductive performance were reported (Lowe and Stendell, 1991). Peakall *et al.* (1990) cited 40 mg/kg in bird eggs as being the "best estimate" of a critical level for reproductive effects.

Immune System Effects

Birds. Coplanar PCBs can produce adverse effects on the developing immune system, as indicated by studies in the chicken and mouse. Lymphoid cell development was affected in a dose-dependent manner by three coplanar PCBs, including 3,3′,4,4′-tetrachlorobiphenyl, 3,3′,4,4′,5-pentachlorobiphenyl, and 3,3′,4,4′,5,5′-hexachlorobiphenyl, with impairment in the development of the bursa and thymus of the developing chick embryo exposed *in ovo* and of the thymus anlagen in mouse tissue cultures exposed *in vitro* (Andersson *et al.*, 1991). The P_5CB coplanar PCB was the most potent in reducing the numbers of viable lymphocytes. The ED_{50} values for inhibition of lymphoid development in the bursa were estimated as 50, 4, and 300 μg/kg for 3,3′,4,4′-tetrachlorobiphenyl, 3,3′,4,4′,5-pentachlorobiphenyl, and 3,3′,4,4′,5,5′-hexachlorobiphenyl, respectively. A dose-dependent inhibition of lymphoid development also occurred in *in vitro* mouse thymus culture treated with the coplanar PCBs, and the EC_{50} values were 2×10^{-7}, 2×10^{-9}, and 3×10^{-7} for 3,3′,4,4′-tetrachlorobiphenyl, 3,3′,4,4′,5-pentachlorobiphenyl, and 3,3′,4,4′,5,5′-hexachlorobiphenyl, respectively. The mono-

ortho-chlorinated analogues of 3,3′,4,4′-tetrachlorobiphenyl and 3,3′,4,4′,5-pentachlorobiphenyl were also tested and found to be much less potent than the coplanar PCBs.

Chick edema disease. One of the first diseases associated with exposures to mixtures of chlorinated organic chemicals, including PCBs, was chick edema disease, characterized by reduced weight gains, droopiness, labored breathing, unsteady gait, increased morbidity, and sudden death in young chicks (Flick *et al.,* 1965a; Vos *et al.,* 1970). Characteristic lesions of chick edema disease at autopsy include hydropericardium, subcutaneous and peritoneal edema, swollen liver, liver necrosis and hemorrhage, kidney degeneration, and swollen and pale kidneys (Sanger *et al.,* 1958; Schmittle *et al.,* 1958). Other associated lesions include porphyria, embryo deformities, and AHH induction (Flick *et al.,* 1965b; Vos and Koeman, 1970; Poland and Glover, 1973). Many technical mixtures of PCBs contain varied concentrations of known chick edema-active chemicals (Vos *et al.,* 1970; Bowes *et al.,* 1975; Albro and Parker, 1979; Huckins *et al.,* 1980; Albro *et al.,* 1981; Kannan *et al.,* 1987, 1988). PCBs have been reported to cause an increase in plasma triglyceride concentration in birds (Borlakoglu *et al.,* 1990), potentially affecting lipoprotein clearance from circulation. More recent assessments indicate that chlorinated dioxins and furans are major factors in chick edema disease (Gilbertson *et al.,* 1991).

Biochemical Effects

Birds. As with other animal species, PCBs induce MFO enzyme systems in various tissues in birds. The induction of MFO enzymes is believed to occur when PCBs bind with the cytosolic aryl hydrocarbon receptor system. The ligand/receptor complex is then translocated to the cell nucleus, where the complex interacts at a nuclear receptor site to alter gene expression, resulting in protein synthesis and enzyme induction. The various toxic, dose-related effects observed following exposures to elevated concentrations of PCBs are believed to be due to the changes in enzyme activities induced by PCBs and followed by a number of species- and tissue-specific changes in normal homeostasis of various biological functions within the body (Safe, 1989, 1991; Gilbertson *et al.,* 1991).

PCBs have been shown to induce cytochrome P450–methylcholanthrene inducible type enzymes, such as AHH and EROD, and to cause an accumulation of porphyrins in Japanese quail and in chickens (Vos *et al.,* 1971; Goldstein *et al.,* 1976; Miranda *et al.,* 1987). Pigeons given a single intraperitoneal injection of 500 mg/kg body wt of Aroclor 1254 in corn oil showed significant increases in hepatic microsomal proteins (100-fold) and in the activities of the enzymes cytochrome P450 (11-fold), cytochrome b_5 (7-fold), NADPH–cytochrome c-(P450) reductase (7-fold), ethoxycoumarin-*O*-deethylation (9-fold), aldrin epoxidase (22-fold), ethoxyresorufin-*O*-deethylation (48-fold), and *N*-demethylation of dimethylnitrosamine (28-fold) (Borlakoglu *et al.,* 1991). Induction of the hepatic microsomal monooxygenase system has also been reported for the barn owl (*Tyto alba*) (Goldman and Yawetz, 1991) and the American kestrel (Fossi *et al.,* 1989).

Mammals. As with other animals, MFO enzyme induction is also associated with elevated exposures of terrestrial mammals to PCBs. Wild cotton rats (*Sigmodon hispidus*) exposed to PCBs in a contaminated habitat had an increase (144%) in hepatic

cytochrome P450 activity over rats from a controlled environment. Other effects noted were increased liver to body weight ratios, enlarged hepatocytes, increased amount of smooth endoplasmic reticulum, and displaced mitochondria (Elangbam *et al.*, 1991).

Wild-trapped, white-footed mice exposed to 25 ppm PCBs in the diet showed increased liver weights and decreased phenobarbital sleeping times (Sanders and Kirkpatrick, 1977). Reproduction was inhibited at 200 ppm in the diet (decreased mean litter sizes), and decreased weanling survival was noted at dietary concentrations of 10 ppm Aroclor 1254 (Merson and Kirkpatrick, 1976). EROD and pentoxyresorufin (PROD) activities, used to characterize AHH and phenobarbital-type enzyme induction in livers, following 21 day dietary exposure of white-footed mice to 0, 2.5, 25, 50, and 100 ppm Aroclor 1254, were significantly increased in males and females on the 25, 50, and 100 ppm diets. EROD was significantly increased in females on the 2.5 ppm diet, but not PROD. EROD activity reached a plateau in animals on the 25, 50, and 100 ppm diets, whereas PROD activity continued to increase through all dietary concentrations. No effects were observed on food consumption, body weights, kidney weights, spleen weights, paired adrenal weights, or testes weights at any dietary concentration. Increased liver weights were observed in both sexes, with a 100% increase at the 100 ppm diet, and no increase in animals on the 2.5 ppm diet. A significant reduction in phenobarbital sleeping time was observed in animals from the 25 ppm diet group (Simmons and McKee, 1992).

Differences were observed in isomer profiles in mice compared to the Aroclor 1254 used in the diet. Five major peaks were observed in mice [2,2',4,4',5-tetrachloro (99), 2,3',4,4',5-pentachloro (118), 2,2',4,4',5,5'-hexachloro (153), 2,3,3',4,4'-pentachloro (105), and 2,2',3,4,4',5'-hexachloro (138)] compared to >17 peaks in the diet. No peaks were detected in the mice that were not observed in the diet. The PCBs retained by the mice had chlorines at both the *meta* and *para* positions, both of which would interfere with the oxidative hydroxylation of the PCBs, increasing their biological half-lives (Simmons and McKee, 1992).

The concentrations of PCBs observed in the mice are summarized in Table 5-22.

TABLE 5-22

TISSUE CONCENTRATIONS OF PCBS OBSERVED IN WHITE-FOOTED MICE

Diet (ppm)	Sex	Tissue Concentrations (mg/kg tissue) Whole Body Wet Wt	Lipid	Lipid/ Wet Wt
0	M	ND	ND	
25	M	25.1±5.5	312±173	12.4
50	M	45.2±5.2	647±444	14.3
100	M	76.2±8.4	1,053±166	13.8
0	F	ND	ND	
2.5	F	2.0±0.4	34±14	17.0
25	F	18.6±1.6	269±111	14.5
50	F	39.1±8.7	695±65	17.8
100	F	73.2±8.4	297±85	17.7

Source: Simmons and McKee, 1992.
ND not detected.

3.4.2.3. Genotoxicity/Carcinogenicity

The information identified on the potential genotoxic and carcinogenic properties of PCBs has been discussed in Section 3.2. No specific information was identified on these properties in terrestrial wildlife. The potential genotoxicity and carcinogenic properties of PCBs in terrestrial wildlife would be expected to be qualitatively similar to those observed in other mammalian systems; however, quantitative differences in sensitivity may be expected due to differences in metabolic and sensitivity factors among species.

3.4.2. Mechanism of Toxicity

The proposed mechanisms of toxicity of PCBs in terrestrial wildlife are considered to be the same as those for other species, as summarized in Section 3.2.3.

3.4.3. Conclusions

3.4.3.1. Exposure Limits

There were no data available in the literature reviewed.

3.4.3.2. Health Significance of Environmental Concentrations

No data were identified on the occurrence of adverse effects of historical concentrations of PCBs on terrestrial wildlife. Based on potential exposure pathways for terrestrial wildlife to PCBs, the potential risks would be expected to be similar to humans, with consideration of differences in the importance of various exposure pathways. White-footed mice (Simmons and McKee, 1992) appear to show a sensitivity to PCBs (Aroclor 1254) similar to that of laboratory mice. Data from bird species indicate that domestic chickens are at least as sensitive to the toxic effects of PCBs as wild, nonpiscivorous birds. Since the pathways for exposures of terrestrial wildlife to PCBs are similar to those of humans, and terrestrial wildlife appear to show similar sensitivities as other animals to the toxic effects of PCBs, the basic exposure/hazard assessment conducted for humans (see Section 3.2) would appear to be applicable to other terrestrial species.Therefore, no adverse effects would be expected to occur in terrestrial wildlife from exposures to current environmental concentrations of PCBs.

4. SUMMARY AND CONCLUSIONS

This section provides the summary and conclusions of the evaluation of the potential adverse impacts of PCBs on the environment based on the information presented in Section 2 on the sources and environmental fate and in Section 3 on the consequences of exposure to PCBs in human, aquatic, and terrestrial systems.

4.1. Sources, Physical/Chemical Properties, and Environmental Concentrations

In the past, it was believed that there were no natural sources of PCBs; however, PCBs were identified in ash from the 1980 volcanic eruption of Mt. St. Helens (Pereira

et al., 1980) and as subunits of two glycopeptides identified from *Amycolatopsis* sp. (Box *et al.*, 1991). The quantities of PCBs from such sources are not known; therefore, their contribution to the quantities of PCBs in the environment cannot be assessed. It is clear that human activities are responsible for the majority of PCBs historically observed in the environment.

Historically, commercial PCBs were produced mainly for the electrical industry since the PCBs had many desirable characteristics, primarily related to their heat absorbing capacity and electrical insulating properties. PCBs also had a number of other commercial uses, including heat exchange fluids, carbonless copy paper, packaging materials, and paint additives. Commercial PCBs were a mixture of chlorinated biphenyls with varying percentages of chlorine by weight. The term PCBs denotes a family of 209 isomers with varying numbers and ring positions of chlorine atoms substituted for hydrogen on the two benzene rings. The congener groups range from the three monochlorinated isomers to a fully chlorinated decachlorobiphenyl isomer. The different isomers of PCBs show a wide range of physical/chemical properties. For example, water solubilities range over 5.5 million-fold from the monochloro- to the decachlorobiphenyl, vapor pressures over 100,000-fold (both decreasing with degree of chlorine substitution), and lipid solubilities range over 10,000-fold (increasing with degree of chlorine substitution).

These differences in properties of the various isomers of PCBs are reflected in their distribution and environmental fate in the environment. Although generalizations may not be appropriate for a group of chemicals with such widely varying properties, the PCBs with greater quantities of chlorine are generally persistent in the environment, and the rate of degradation of PCBs decreases as their chlorine content increases. The rates of photodegradation of PCBs in the atmosphere and at water surfaces increase as the degree of chlorination increases. Degradation rates by soil microorganisms and animal systems, on the other hand, are generally much more rapid for the lesser chlorinated PCBs.

Between the early 1930s and 1972, there were no restrictions on the myriad commercial uses of PCBs. Such unrestricted use, combined with their physical/chemical properties, has resulted in their widespread transportation and distribution throughout the environment. Thus, when analyses for PCBs in the environment were first conducted on a broad scale in the early 1970s, they were found to be widespread in the ecosystem, with significant concentrations in biological systems in remote areas such as the Arctic and the Antarctic. Since 1972, the use of PCBs has been restricted to controllable closed systems (e.g., electrical transformers and capacitors), and in 1978 their production was discontinued thereby reducing the total quantities of PCBs available to enter the environment. However, even after production stopped, PCBs continued to enter the environment from old equipment still in use or in storage and from points of high local concentrations such as landfills and sites where PCBs are stored.

The initial concentrations of PCBs reported in various environmental media and biological systems have decreased substantially since their use was controlled in 1972 and production terminated in 1978. The rates of decrease of concentrations of PCBs in various environmental media were most rapid in the early 1970s, immediately following restrictions in use. Since the early 1980s, environmental concentrations have continued to decrease, although more slowly than during the 1970s. However, localized areas of higher environmental concentrations remain. Complex mechanisms

of environmental mobilization and long-range transport continue to distribute PCBs throughout the environment from large sites of concentration in aquatic systems such as the Great Lakes, the Northern Atlantic, and the Baltic. Since PCBs are no longer produced, environmental concentrations should continue to decline as the PCBs are mobilized from these depots and degraded by natural environmental systems. Active programs are required for the destruction of point sources of PCBs, such as stored old equipment, to eliminate the dissipation of PCBs from point sources.

4.2. Health Significance of Environmental Concentrations

The determination of cause–effect relationships between the potential adverse effects from exposures to PCBs through the various environmental media is complicated by at least two factors: (i) the simultaneous occurrence of a number of other chemicals (some closely related to PCBs) arising from various human activities and natural sources; and (ii) by a variety of factors affecting the well being of organisms through changes in habitat quality (e.g., elevated ammonia and decreased oxygen in aquatic systems, changes in and loss of habitat associated with increased land use for human activity). Laboratory studies, in which these factors can be controlled, demonstrate that PCBs are not particularly potent toxicants on a short-term exposure basis; rather, they show a delayed type of toxicity primarily associated with chronic, long-term exposure. In addition, a number of toxic effects observed at the upper end of the dose–response curve in laboratory studies may not be relevant at the lower exposures that typically occur in the environment. All of these factors must be considered in the assessment of potential cause–effect relationships between exposures to the historical, current, and predicted future concentrations of PCBs in the environment and potential adverse effects on the ecosystem, including humans.

Based on an evaluation of the available evidence, the toxic effects of PCBs which are of most concern appear to be associated with the alteration in endogenous enzyme systems important for normal homeostasis of biological systems. Changes in the activity of these various enzymes result in many secondary effects, such as changes in hormonal homeostasis with an array of consequences on reproduction, growth and development, and general maintenance of body functions. The coplanar PCBs appear to have greater potency in causing such effects than the nonplanar congeners. In addition, the coplanar PCBs appear to act, particularly on the induction of the mixed-function oxygenase enzyme systems, in a similar manner to other polycyclic chlorinated hydrocarbons such as the 2,3,7,8-substituted polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans, and possibly other chemicals. There are substantial differences in the potency of enzyme induction among these different chemicals and among different isomers of PCBs. To account for these differences in potency when assessing the potential consequences of the concentrations of these chemicals observed in the environment, it has been proposed that TEFs be applied. The use of TEFs would enable the potential adverse effects of these chemicals to be considered as a group assuming they act in an additive manner proportional to their T_4CDD-TEQ concentrations. Although there is considerable evidence supporting this "unified" mechanism of toxic action of these chemicals, the applicability of generalized TEFs with respect to potential toxicity of these chemicals to all species, and the indication that other mechanisms of action of PCBs are independent of enzyme induction effects (Stradnicki *et al.*, 1979;

Borlakoglu and Haegele, 1991; Jehnke *et al.,* 1991; Williams and Giesy, 1992), require additional research.

Based on the information on the degree of exposure to PCBs required before adverse effects occurred in occupationally exposed populations, it is unlikely that significant adverse health effects to humans (Section 3.2.4.1) would be associated with exposures to PCBs from the ambient environmental concentrations observed historically in air, water, soils, or fish in the early 1970s. Substantial decreases in concentrations of PCBs in the typical human diet in the United States, and corresponding decreases in human exposures through diet, were reported between the early 1970s and the early 1980s. Through the 1980s the concentrations of PCBs in the United States diet continued to slowly decline, such that potential exposures in 1990 were over 100-fold less than those in 1970.

Concerns have been raised regarding potential adverse human health effects from exposures to PCBs that are considerably less than those observed in occupationally exposed populations. Human epidemiological studies have been inadequate in identifying clear causal associations between exposures from ambient environmental concentrations of PCBs and alleged effects. Recent studies of people consuming large quantities of sport fish indicated that their blood levels of PCBs were within the range reported for the North American population. No other chemical parameters were measured in these populations, and simultaneous exposures to a variety of other chemicals known to be present in sport fish, together with socioeconomic and lifestyle differences between the sport fish and nonsport fish consumers, confound the interpretation of the causes of the effects reported and prevent the establishment of clear causal relationships to PCB exposures.

Based on laboratory and various field studies, no adverse effects would be expected in aquatic life at higher trophic levels of the food chain (e.g., fish) from exposures to the concentrations of PCBs currently observed in surface waters. However, as with several hydrophobic/lipophilic chemicals, greater exposures of aquatic life to the PCBs with greater chlorine content would occur through diet rather than by direct uptake from water. PCBs have been shown to biomagnify such that greater concentrations occur in aquatic species and fish-eating animals at higher trophic levels. The concentrations of PCBs have declined since the early 1970s by approximately 10-fold in predatory fish (e.g., salmonids) and in the eggs of birds that consume fish. Several studies have attributed decreases in populations of fish-eating birds (e.g., herring gulls, double-crested cormorants, bald eagles) between the 1950s and 1970s and the subsequent population recoveries since the early 1970s to the presence and subsequent decline in the concentrations of PCBs in these organisms. However, the decline of the concentrations of PCBs in aquatic wildlife is also coincident with declines in concentrations of hexachlorobenzene, dieldrin, DDE, alkyl mercury, chlorinated dioxins/furans, alkylated lead and mirex (Allan *et al.,* 1991), and with changes in habitat factors. Few of these studies considered the potential involvement of these other chemicals, either singly or in combination with PCBs.

In addition, habitat factors independent of chlorinated organic chemicals must be considered when comparing temporal changes in wildlife populations. Recent studies have concluded that the correlations between current concentrations of total PCBs, specific coplanar PCBs, and total T_4CDD-TEQ concentrations in predator fish species (e.g., salmonids) were not sufficiently strong to explain decreases observed in egg hatching and fry survival observed in fish from the Green Bay region of Lake Michigan.

In addition, the reproductive effects observed in fish-eating and insect-eating birds on the Great Lakes could not be attributed solely to PCBs. Such results indicate that either the ecosystem is recovering and the magnitude of the responses have decreased to the point where clear causal associations are more difficult to establish or that other factors, either independently or in combination with PCBs, may be involved in producing the adverse environmental effects. If PCBs are causally related to the various effects reported, the rate of occurrence of adverse effects should continue to decline in the future as the environmental concentrations of PCBs continue to decrease through natural physical and biological degradation processes and through continual burial by sedimentation.

The extensive use of PCBs prior to the mid 1970s led to widespread occurrence and accumulation of PCBs in biota. This could have been predicted based on what is now known regarding physical/chemical properties and environmental fate. Reductions in the overall environmental loading rates of PCBs through restricted use in controllable closed systems, banned production, destruction of waste PCBs, and natural burial/degradation processes coincided with substantial decreases in the concentrations of PCBs in environmental media and in various biological systems, including humans and aquatic wildlife. These changes in concentrations of PCBs in environmental media and in biological systems coincided with reduced concentrations of several other chlorinated organic chemicals and with recoveries in fish-eating bird populations. Evidence of adverse effects in wildlife remains in areas of continuing high concentrations of these chemicals. Subtle biochemical effects considered to be associated with chlorinated organic chemicals continue to be observed in piscivorous birds, but these effects do not appear to be limiting populations. The data indicate that ambient concentrations of PCBs would not be expected to produce adverse effects in humans. The fact that adverse effects on reproductive performance observed in wildlife in the past appear to be lessening as the concentrations of PCBs and other persistent chemicals in the environment are decreasing provides evidence that the environment can recover following changes in use of chemicals, even for very persistent substances such as those typified by PCBs. These observations also provide evidence that careful uses of chemicals, which avoid exceeding the assimilative capacity of the environment and thereby keep the exposures below the thresholds for adverse effects, can be maintained without harm to human health or the environment.

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