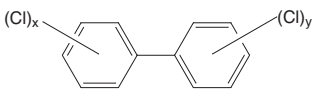
Polychlorinated Biphenyls

CAS No. 1336-36-3

Reasonably anticipated to be human carcinogens

First listed in the *Second Annual Report on Carcinogens* (1981)

Also known as PCBs or chlorodiphenyls



Polychlorinated biphenyls (number of chlorine atoms [x + y] = 1–10)

Carcinogenicity

Polychlorinated biphenyls (PCBs) are *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in experimental animals. Not all PCB mixtures caused tumors in experimental animals.

Cancer Studies in Experimental Animals

Oral exposure to PCBs caused liver tumors in mice and rats. In male mice, dietary administration of mixtures of PCBs with similar average chlorine content — Aroclor 1254 (approximately 54% chlorine by weight) and Kanechlor 500 (52% to 54% chlorine by weight) — caused benign and/or malignant liver tumors (hepatocellular adenoma or carcinoma). In female rats, dietary administration of Aroclor 1260 (approximately 60% chlorine by weight) caused benign and malignant liver tumors (hepatocellular adenoma and carcinoma) (IARC 1978).

Since PCBs were listed in the *Second Annual Report on Carcinogens,* additional studies of dietary exposure in rats have been identified, which found that (1) additional PCB mixtures or individual congeners caused tumors, (2) specific PCB mixtures or congeners caused liver tumors in male rats, and (3) PCB mixtures or congeners caused tumors at additional tissue sites. Dietary exposure to Aroclor 1016, 1242, 1254, or 1260 caused benign or malignant liver tumors (hepatocellular adenoma or carcinoma) in female rats; liver tumors were observed in male rats after exposure to Aroclor 1260 but not the other mixtures. An additional type of liver tumor (hepatocholangioma) was observed in female rats exposed to Aroclor 1254 (Norback and Weltman 1985, Mayes *et al.* 1998). Another PCB mixture, Clophen A, caused liver cancer (hepatocellular carcinoma) in weanling male rats (Schaeffer *et al.* 1984). PCB mixtures also caused tumors at tissue sites other than the liver: Aroclor 1254 caused gastrointestinal-tract cancer (adenocarcinoma) in rats of both sexes (Morgan *et al.* 1981, Ward *et al.* 1985), Aroclor 1260 caused tumors of the thymus and spleen in male rats (Rao and Banerji 1990), and Aroclor 1242, 1254, or 1260 caused benign thyroid-gland tumors (follicular-cell adenoma) in male rats (Mayes *et al.* 1998).

The National Toxicology Program (NTP 2006a,b,c,d) conducted several studies of exposure to individual PCBs or mixtures of two PCBs by stomach tube in female rats. Incidences of benign and malignant tumors of the bile duct and liver (cholangioma, hepatocholangioma, cholangiocarcinoma, and hepatocellular adenoma) and lung (squamous-cell carcinoma or cystic keratinizing epithelioma) were increased by exposure to PCB 126 or 118 alone or to mixtures of PCB 126/153 or PCB 126/118. Exposure to the PCB 126/118 mixture also caused cancer of the oral mucosa (gingival squamous-cell carcinoma), and exposure to the PCB 126/153 mixture and to PCB 118 alone also caused uterine cancer (squamous-cell carcinoma) and tumors of the pancreas (acinar tumors).

The International Agency for Research on Cancer concluded that PCB 126 (3,3′,4,4′,5-pentachlorobiphenyl) was a complete carcinogen in experimental animals. Based on extensive evidence that it acted through the same aryl-hydrocarbon-receptor-mediated mechanism as 2,3,7,8-tetra-chlorodibenzo-*p*-dioxin (TCDD, or dioxin), IARC classified it as carcinogenic in humans (Baan *et al.* 2009).

Cancer Studies in Humans

At the time PCBs were listed in the *Second Annual Report on Carcinogens,* very few epidemiological studies had evaluated the relationship between human cancer and exposure specifically to PCBs. An excess incidence of melanoma was reported in a small group of workers exposed to the PCB mixture Aroclor 1254, but the workers were probably also exposed to other agents (IARC 1978). Since PCBs were listed in the *Second Annual Report on Carcinogens*, numerous epidemiological studies of PCBs and cancer have been identified. In 1987, IARC classified the evidence of carcinogenicity in humans as limited, based primarily on studies reporting excesses of liver and/or bile-duct cancer. Excess liver and bile-duct cancer was reported among women occupationally exposed to PCBs in capacitor manufacturing and individuals exposed to PCBs from contaminated cooking oil. A cohort study of Italian capacitor-manufacturing workers found an excess of gastrointestinal-tract tumors (including liver and bile-duct tumors) among men and lymphohematopoietic cancer among women. However, IARC noted that these studies had a number of limitations, including small numbers of cases, inability to evaluate exposure-response relationships, and possible confounding from exposure to other chemicals (IARC 1987).

Since the 1987 IARC review, additional occupational cohort studies or follow-up studies have been conducted, as well as numerous population-based case-control studies of PCB residues in fat or blood, with exposure primarily from dietary sources. As in the studies reviewed by IARC, increased risks of liver or bile-duct cancer were reported in several cohort and follow-up studies of capacitor workers (Gustavsson and Hogstedt 1997, Mallin *et al.* 2004, Prince *et al.* 2006b); risks increased with increasing cumulative exposure (Prince *et al*. 2006a). One case-control study also reported increased risk of bile-duct cancer (Ahrens *et al.* 2007). However, not all studies found increased risks. Some of the occupational studies and case-control studies found excesses of cancer at other tissue sites, such as the gastrointestinal tract, brain, testes, or skin (malignant melanoma), but the findings were not always consistent across studies. The occupational cohort studies were limited by small numbers and limited exposure assessment; most of the studies did not report PCB levels (Carpenter 2006, Knerr and Schrenk 2006, Golden and Kimbrough 2009). In addition, workers were exposed to mixtures of congeners, and the proportion of each congener could have varied from batch to batch and from study to study (Hopf *et al.* 2009).

Measurement of specific PCBs (or groups of congeners) in the peripheral blood, adipose tissue, or carpet dust was associated with increased risk of non-Hodgkin lymphoma (NHL) in most of the population-based nested case-control studies (Hardell *et al.* 1996, Rothman *et al.* 1997, Colt *et al.* 2005, De Roos *et al.* 2005, Engel *et al.* 2007a,b, Spinelli *et al.* 2007), and some of the studies reported exposure-response relationships. Two studies found no evidence of an association between NHL and exposure to PCBs (Fritsche *et al.* 2005, Cocco *et al.* 2008). A retrospective cohort mortality study that followed 1,940 individuals who had been poisoned by ingesting PCB-contaminated oil in Taiwan reported increased mortality from Hodgkin disease (Hsieh *et al.* 1996). The findings for NHL or lymphohematopoietic cancer in occupational retrospective cohort studies were inconsistent (Engel *et al.* 2007b).

Many population-based case-control studies and cohort studies of breast cancer in relation to PCBs in serum, plasma, or adipose tissue have been conducted. In general, cohort studies usually used samples stored prior to cancer diagnosis for measurement of PCB levels. Some studies found positive associations between breast cancer and specific PCB congeners or groups of congeners; however, findings from studies of breast cancer were conflicting (Salehi *et al.* 2008).

Properties

PCBs are a class of biphenyl compounds with one to ten hydrogen atoms replaced by chlorine. At room temperature, they range in physical state from light- to dark-yellow oily liquids to white crystalline solids and hard noncrystalline resins (IPCS 1992, HSDB 2009). PCBs are produced commercially by chlorination of biphenyl, resulting in 209 possible PCB congeners (Silberhorn *et al.* 1990). However, McFarland and Clarke (1989) reported that about half of these molecules accounted for nearly all environmental contamination by PCBs, and they considered only 36 to be environmentally relevant, because of their potential toxicity, environmental prevalence, and relative abundance in animal tissues. Commercial PCB formulations are complex mixtures of chlorinated biphenyls that vary in the degree of chlorination, and similar mixtures can show significant lot-to-lot variation in composition (ATSDR 2000). Of the 209 possible PCB congeners, about 100 are present in commercial PCB mixtures, and about 70 have been detected in human adipose tissue (Mühlebach *et al.* 1991). At least 20 of the 209 possible congeners have not been identified in commercial mixtures of PCBs (Kimbrough 1987).

Physical and chemical properties of PCBs are affected by the numbers and positions of chlorine atoms (Carpenter 2006). PCBs with fewer chlorine atoms tend to be more soluble in water, more volatile, and more easily metabolized. Larger numbers of chlorine atoms are associated with increased resistance to biodegradation, which can increase bioaccumulation in the environment. PCBs are practically insoluble in water, but soluble in organic solvents and fats (IPCS 1992). They are very stable and persistent in the environment. Physical and chemical properties representative of PCBs are listed in the following table.

Property	Information
Molecular weight	292.0 to 360.9[a]
Specific gravity	1.44 at 30°C[a]
Melting point	340°C to 375°C[a]
Log K_{ow}	7.1[b]
Water solubility	0.0007 g/L at 25°C[b]
Vapor pressure	0.000494 mm Hg at 25°C[c]

Sources: [a]HSDB 2009, [b]ChemIDplus 2009, [c]SRC 2009.

PCBs have been categorized as "dioxinlike" or "non-dioxinlike," based on their ability to exert biochemical and toxic effects similar to those of TCDD through activation of the aryl hydrocarbon receptor (Carpenter 2006, Knerr and Schrenk 2006). Dioxin-like activity is seen for PCB congeners with chlorine atoms occupying meta (carbon atoms 3, 3′, 5, or 5′) and para (carbon atoms 4 or 4′) positions, with no more than one ortho (carbon atoms 2, 2′, 6, or 6′) chlorine; these molecules are likely to exist with a planar conformation. Twelve tetra-, penta-, hexa-, or hepta-chlorobiphenyls meet these criteria and have been assigned toxic equivalency factors (TEQs) of 0.0001 to 0.1 by the World Health Organization based on their toxicity relative to that of TCDD, which has the highest toxic potency for activation of the aryl hydrocarbon receptor (TEQ = 1.0). PCB 126 has a TEQ of 0.1, which is the highest value for this class of molecules.

The relative concentrations of PCB congeners change as a result of physical and chemical processes and selective bioaccumulation and biotransformation as they move through the environment, including living organisms (Beyer and Biziuk 2009). The mixtures resulting from these processes differ substantially from the original material. PCBs in the biosphere are mainly penta-, hexa-, and heptachlorinated congeners, with an average chlorine content of over 50%. In contrast, the average chlorine content of commercially used mixtures was less than 42% (Mühlebach *et al.* 1991). Dehalogenation can occur in freshwater and estuarine sediments. PCBs can also be biodegraded aerobically or anaerobically by bacteria or other microorganisms (Beyer and Biziuk 2009). Metabolism of PCBs requires at least one pair of adjacent unchlorinated carbon atoms that can result in initial formation of an arene oxide (Mühlebach *et al.* 1991).

Use

Before 1974, PCBs were used in the United States for both enclosed applications, such as transformers, capacitors, and heat transfer and hydraulic fluids, and open applications, such as inks, flame retardants, adhesives, carbonless duplicating paper, paints, plasticizers, wire insulators, metal coatings, and pesticide extenders (IARC 1978, ATSDR 2000). After 1974, all uses of PCBs were limited to enclosed applications (transformers and capacitors), and after January 1979, no PCBs were used in the manufacturing of transformers or capacitors. The only remaining permitted uses of PCBs are as a mounting medium in microscopy, as an immersion oil in low-fluorescence microscopy, as an optical liquid, and for other research and development purposes (ATSDR 2000).

Production

PCBs were first produced commercially in the United States in 1929. They are no longer produced in the United States except for limited uses in research and development (IARC 1978). Four Aroclor mixtures — 1016, 1242, 1254, and 1260 — accounted for 92% of all PCB production between 1958 and 1977 (Mayes *et al.* 1998). The chlorination reaction was stopped when the chlorine content reached 42% for Aroclor 1242, 54% for 1254, and 60% for 1260. Aroclor 1016 was produced with a chlorine content of 41% by fractional distillation of Arochlor 1242, a process that excluded more highly chlorinated congeners, which have higher boiling points. Since 1970, nine PCB mixtures (Aroclor 1016, 1221, 1232, 1242, 1248, 1254, 1260, 1262, and 1268) accounted for 35% of all PCBs commercially produced and 98% of the PCBs sold in the United States. Domestic production peaked at 85 million pounds in 1970, decreasing to about 41 million pounds by 1974, when the Monsanto Chemical Company produced an estimated 40 million pounds of PCBs. Kanechlors were PCB mixtures produced in Japan, and Clophens were PCB mixtures produced in Germany. U.S. import or export of PCBs has not been permitted since 1979 (ATSDR 2000).

Exposure

Evidence that people living in the United States are exposed to PCBs is provided by several National Health and Nutrition Examination Surveys (NHANES) conducted between 1976 and 2008. The clearest pattern of decline was seen in total serum concentrations of eight mono-*ortho*-PCBs in pooled samples from 1973 (210.7 ng/g of lipid) to 2003 (26.4 ng/g) (Schecter *et al.* 2005). The U.S. Environmental Protection Agency (EPA) considered this 87% decline to be evidence of the effectiveness of measures to control the production and release of PCBs in the United States. Moreover, the mean serum PCB concentrations within age groups decreased over time across the three NHANES surveys conducted from 2001 to 2006, and the concentrations were highest in the oldest age group. For example, in 2007–2008, the mean serum concentration of PCB-153 in adults aged 60

or older (60.8 ng/g of lipid) was about 10 times that in 12- to 19-year-old adolescents (4.9 ng/g) (Sjödin *et al.* 2014).

A major source of human exposure to PCBs is dietary (IARC 1978). Because PCBs are soluble in fats and oils, the major U.S. commodities in which PCBs have been found are fish, cheese, eggs, and animal feed. PCB residues have been detected in human milk and fat samples collected from the general U.S. population. The average daily human intake of PCBs via food was estimated at 0.027 µg/kg of body weight in 1978, but declined to less than 0.001 µg/kg in 1991 (ATSDR 2000). PCBs have frequently been identified at relatively high concentrations in the blood, fat, and milk of native Inuit populations living in Arctic regions, whose diet is high in fish and marine animals. For example, the mean concentration of PCBs in fat tissue collected from a native population in Greenland was 5,719 µg/kg of lipid, and the concentrations were highest in older individuals. PCBs also accumulate in the breast milk of women in this population. In a 1989–90 study, the mean PCB concentration in breast milk from native Inuit women who consumed large quantities of marine mammal tissue was 1,052 µg/kg of lipid, resulting in a high daily intake by their infants (10 µg/kg). Serum PCB concentrations were also found to be higher in individuals who regularly ate fish than in those who occasionally or never ate fish (Humphrey *et al.* 2000). In 2000, it was reported that serum PCB concentrations in individuals without unusual exposure had ranged from about 0.9 to 1.5 ppb in recent years (ATSDR 2000). The half-life of PCBs in serum is 3 to 5 years for high serum concentrations and 13 to 17 years for lower serum concentrations (Carpenter 2006). In addition to ingestion, humans can be exposed to PCB by inhalation or dermal contact (ATSDR 2000).

The release of PCBs from prior industrial uses and their persistence in the environment have resulted in widespread contamination of water and soil. PCBs were identified at 500 of 1,598 hazardous-waste sites proposed for inclusion on EPA's National Priorities List. For 2007, EPA's Toxics Release Inventory listed 57 facilities that produced, processed, or otherwise used PCBs and released a total of 2,307,203 lb of PCB wastes to land (TRI 2009).

PCBs have been measured in air, water, soil, and human tissues in all parts of the world. PCBs are released to air from contaminated soil, water, and hazardous-waste sites, and atmospheric transport is the most common mechanism for global dispersion. Although the concentration of vapor-phase PCBs can be significantly elevated near PCB-contaminated hazardous waste sites, the more volatile congeners can dissipate relatively rapidly. PCBs in the atmosphere may be deposited to soil, water, and plants at distant sites by settling and by washout from precipitation. Once in water, PCBs may be removed by revolatilization to the atmosphere, uptake by fish or other organisms, or sedimentation and burial. Most of the PCBs lost from the waters of the Great Lakes were revolatilized to the atmosphere. PCBs may also enter organisms, including edible freshwater fish, directly from the water, and biomagnify through the aquatic food web.

EPA estimated that people within 12 miles of commercial incinerators might be exposed to PCBs released to air (ATSDR 2000). Incineration has declined as a method for disposal of PCB-contaminated materials, because incineration can be incomplete if the combustion temperature is not high enough, leading to formation of highly toxic by-products, such as hydrogen chloride, polychlorinated dibenzodioxins, and polychlorinated dibenzofurans (Beyer and Biziuk 2009).

In 1977, the National Institute for Occupational Safety and Health estimated that 12,000 workers potentially were exposed to PCBs (ATSDR 2000).

Regulations

Coast Guard (Dept. of Homeland Security)

Shipboard incineration of PCBs is prohibited.

Department of Transportation (DOT)

PCBs are considered hazardous substances and marine pollutants, and special requirements have been set for marking, labeling, and transporting these materials, including transporting them in tank cars.

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.
Urban Air Toxics Strategy: Identified as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.

Clean Water Act

Designated a hazardous substance.
Effluent Guidelines: Listed as a toxic pollutant.
Water Quality Criteria: Based on fish or shellfish and water consumption = 0.000064 µg/L; based on fish or shellfish consumption only = 0.000064 µg/L.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 1 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed category of substances subject to reporting requirements.

Resource Conservation and Recovery Act

Listed as a hazardous constituent of waste.

Safe Drinking Water Act

Maximum contaminant level (MCL) = 0.0005 mg/L.

Toxic Substances Control Act

Extensive regulations governing the manufacturing, processing, distribution in commerce, use, and disposal of PCBs have been developed.

Food and Drug Administration (FDA, an HHS agency)

Maximum permissible level in bottled water = 0.0005 mg/L (as decachlorobiphenyl).
The action level for PCBs in red meat is 3 ppm (fat basis).
Specific provisions are set to prevent PCBs contamination in establishments manufacturing food-packaging materials.
Specific provisions are set to prevent PCBs contamination in the production, handling, and storage of animal feed.
Temporary tolerances for PCBs in milk, dairy products, poultry, eggs, fish and shellfish, and infant food range from 0.2 to 3 ppm.
Temporary tolerances for PCBs in animal feed range from 0.2 to 10 ppm.

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2018, specific PELs may not reflect the more current studies and may not adequately protect workers.
Permissible exposure limit (PEL) = 0.5 mg/m^3 for chlorodiphenyl 54% chlorine; = 1.0 mg/m^3 for chlorodiphenyl 42% chlorine.

Guidelines

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

Immediately dangerous to life and health (IDLH) limit = 5 mg/m^3.
Recommended exposure limit (REL) = 0.001 mg/m^3.
Listed as a potential occupational carcinogen.

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