Level 2 - Details on PCBs

1. **What are PCBs?**
   1.1 How have PCBs been used and how do they enter the environment?
   1.2 What are properties of PCBs?

2. **What happens to PCBs in the environment?**
   2.1 How are PCBs transported in the environment?
   2.2 How do PCBs build up in living organisms?
   2.3 To what extent do PCBs break down or persist in the environment?
   2.4 How much PCBs are found in the environment?

3. **To what extent are humans exposed to PCBs?**
   3.1 To what extent are humans exposed to PCBs through food?
   3.2 To what extent are infants exposed to PCBs through breast milk?
   3.3 To what extent are humans exposed to PCBs through air?
   3.4 To what extent are humans exposed to PCBs through drinking water?

4. **What happens to PCBs when they enter the body?**

5. **What are the effects of PCBs on laboratory animals?**
   5.1 At what exposure levels do PCBs cause harmful effects?
   5.2 What are the effects of PCBs on reproduction?
   5.3 What other biological effects can PCBs have?
   5.4 Through what mechanisms do PCBs act?

6. **How has PCB exposure affected human health?**
   6.1 Has exposure to PCBs lead to more cancer cases?
   6.2 Has exposure to PCBs affected human reproduction and development?
   6.3 Have PCBs caused other health effects?

7. **What are the risks posed by PCB exposure?**
   7.1 What health effects occur at what levels of exposure?
   7.2 What tolerable daily intakes have been established for PCBs?
   7.3 What are estimated daily intakes of PCBs?
   7.4 What are the uncertainties in assessing PCB health risks?

8. **Conclusions**
1. What are PCBs?

PCBs, or polychlorinated biphenyls, are a class of man-made chemicals.

1.1 How have PCBs been used and how do they enter the environment?

The commercial production of PCBs started in 1929 but their use has been banned or severely restricted in many countries since the 1970s and 80s because of the possible risks to human health and the environment.

As PCBs are resistant to acids and bases as well as to heat, they have been used as an insulating material in electric equipment, such as transformers and capacitors, and also in heat transfer fluids and in lubricants. PCBs have also been used in wide range of products such as plasticizers, surface coatings, inks, adhesives, flame-retardants, paints, and carbonless duplicating paper.

Since 1929 around 2 million tonnes of PCBs have been produced, about 10% of which still remain in the environment today.

Sources of PCB pollution:

- Landfills containing transformers, capacitors, and other PCB waste can release PCBs into the air. This environmental contamination may continue to occur due to the disposal of old electrical equipment containing PCBs.
- The incineration of municipal waste may lead to PCB pollution and produce dangerous by-products, such as hydrogen chloride (HCl) and dioxins (PCDDs and PCDFs).
- PCBs can also evaporate from contaminated water bodies, such as the North American Great Lakes.

1.2 What are properties of PCBs?

PCBs, or polychlorinated biphenyls, are a class of man-made organic chemicals. Each PCB molecule contains two phenyl rings. A phenyl ring is a ring of 6 carbon atoms to which hydrogen atoms are attached. In PCBs, chlorine atoms replace some of these hydrogen atoms.

Chlorine atoms may be present at some or all of the 10 possible positions which are numbered 2–6 on one ring, and 2’–6’ on the other ring (see figures below). In total, 209 different PCBs can be formed. These different combinations are called congeners, each having a specific number of chlorine atoms located at specific positions.

One example below shows a PCB with five chlorine atoms, two chlorine atoms at the 3 and 5 positions on one ring and three chlorine atoms at the 2’, 4’ and 6’ positions on the other ring. The other example shows a PCB with chlorine atoms at the 2 position on one ring, and the 2’ position on the other.
Two different systems are used for naming PCBs. In the IUPAC system used in the examples above, the numbers at the beginning of the name specify the sites where chlorines are attached to the phenyl rings. Another system assigns a separate number, from 1 to 209, to each of the 209 specific PCB congeners. (see figures to the right) (see conversion table [see Annex 2, p. 20]

PCBs which have the same number of chlorine atoms attached but at different positions, are referred to as isomers.

The two rings in a PCB molecule can rotate around the bond connecting them. The shape of the molecule is further influenced by the repulsion between nearby chlorine atoms so that the rings of a specific PCB will either lie approximately in the same plane (called coplanar) or in different, more perpendicular planes (termed non-planar). Those PCBs which have both rings lying in the same plane are considered to be most toxic, based on combined health effects considerations. They are also referred to as "dioxin-like". (see question 3)

PCBs were manufactured and sold as mixtures of several congeners, with a variety of trade names, including Aroclor, Pyranol, Pyroclor (USA), Phenochlor, Pyralene (France), Clophen, Elaol (Germany), Kanechlor, Santotherm (Japan), Fenchlor, Apirolio (Italy), and Sovol (USSR).

Physical properties of PCBs:
- PCBs persist in the environment because they are highly unreactive and are largely resistant to breakdown by acids, bases and heat.
- Generally, PCBs are not very soluble in water, but readily soluble in fats. This solubility in fat explains why PCBs can build up in animal fat and along the food chain (see question 2.2) The degree of solubility is largely dependent on the number and position of chlorine atoms in the PCB molecule.

Although in general PCBs do not easily evaporate, especially those with more chlorine atoms, PCB evaporation does occur, and can account for significant amounts of PCB transport (see question 2.1 [see https://www.greenfacts.org/en/pcbs/l-2/2-biomagnification.htm#1])

PCBs can be measured in:
- biological samples, such as human blood, milk, and fatty tissue, as well as in some foods such as animal tissues, fish and dairy products
- environmental samples, such as in air, drinking water, soil, sediment, and solid waste.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55
Section 2, Identity and physical/chemical properties [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#2.0] and Section 3, Analytical methods [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#3.0]
2. What happens to PCBs in the environment?

2.1 How are PCBs transported in the environment?

In surface waters, PCBs are present in substantial quantities in sediments. Indeed, PCBs tend to attach to the surface of organic matter, clay, and micro-particles that are still suspended in the water or have already settled down. They can remain buried in sediments for a long time and be slowly released into the water and evaporate into air. Releases through water into air occur especially when it is warm and when PCB concentrations in sediments are high as this keeps the PCB levels in water elevated.

PCBs present in air can deposit on land when it rains or snows (wet deposition), or when they attach to particulate matter, such as dust or soot, that settles on the ground (dry deposition). It is also possible that PCBs could be transported by insects which have come into contact with them (see section 2.2 [see https://www.greenfacts.org/en/pcbs/l-2/2-biomagnification.htm#2]).

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55
Section 5.1, Transport and partitioning [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#5.1]

2.2 How do PCBs build up in living organisms?

PCBs tend to build up in living organisms both by uptake from the environment over time (bioaccumulation) and along the food chain (biomagnification). PCBs remain stored in fatty tissues much more than in muscles or other body parts.

The degree of PCB bioaccumulation over time depends on how quickly they are taken up and eliminated by the organism, and on the ability of the organism to break down PCBs. Various animal species can transform some PCB congeners, such as insects, crabs and vertebrates, including some birds, fish, and mammals. The rate and physiological mechanism of PCB metabolism depend both on the animal species and on the specific PCB congener.

In aquatic organisms bioaccumulation of PCBs depends on the species, its habitat, and on the specific type of PCB. As the concentration of PCBs in sediments is several times higher than in water, levels are often high in bottom-feeding species.

PCBs generally biomagnify along the food chain, which leads to greater PCB concentrations in organisms that are higher up in the food chain.

- **In the aquatic environment**, concentrations will thus be greater in shellfish than in the plankton on which they feed, and even greater in animals at the top of the food chain such as large predatory fish or mammals (seals, dolphins, and whales).
- **On land**, the biomagnification occurs, for instance, through the accumulation of PCBs from soil or plant leaves to worms or insects and finally to birds and mammals. PCBs can also be found in the eggs of contaminated birds.
Humans can also accumulate PCBs from food. On average, in humans, the concentration of PCBs in fatty tissues is over a hundred times greater than in the food they eat.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55 Section 5.1, Transport and partitioning [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#5.1]

2.3 To what extent do PCBs break down or persist in the environment?

Some PCBs tend to be more persistent in the environment than others. The extent to which a PCB molecule can be broken down or transformed depends on the number of chlorine atoms it contains and where they are located. PCBs are mainly broken down either by the effect (direct or indirect) of sunlight or by microorganisms. In general, the persistence of PCB congeners increases with the number of chlorine atoms.

Sunlight can play a role in the breakdown of PCBs present in air, water and surface soil.

In the atmosphere, PCBs that are present in the atmosphere tend to react with ozone and water under the effect of sunlight. The reactions result amongst other things in chlorine atoms being removed. The more chlorine atoms there are the longer this reaction takes. The time it takes for half of the amount of PCBs (initially) present to be broken down ranges from 3.5 to 83 days for molecules with 1 to 5 chlorine atoms.

In water, PCBs are essentially broken down by the effect of sunlight (photolysis). In shallow water, in summer sunlight, it takes 17 to 210 days for half of the amount (initially) present to be broken down for molecules with 1 to 4 chlorine atoms. Breakdown by sunlight is slower during winter. PCB congeners with a greater number of chlorine atoms (seven or more) absorb more sunlight and are thus broken down more easily.

In soil and sediment, PCBs are mostly broken down by microorganisms. How quickly PCBs are broken down depends on several factors, including the number and location of chlorine atoms, PCB concentration, the type of microorganisms present, available nutrients, and temperature. Breakdown of PCBs by microorganisms, though slow, can occur whether or not oxygen is present in soil and sediments, and can also occur to some extent in water.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55 Section 5.2, Transformation and degradation [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#5.2]

2.4 How much PCBs are found in the environment?

In outdoor air, average PCB concentration varies between urban and rural locations, and other locations distant from PCB sources. For example, the average PCB concentration measured in a series of North-American cities (5 ng/m$^3$) was 5 to 20 times higher than at two rural locations. In the Arctic and the Antarctic, which are relatively far from any PCB source, the average PCB concentration was 0.2 ng/m$^3$. Since the early 1980s, there has been a slight but continuous decrease in the levels of PCBs in air observed in urban, rural, and coastal areas. By the early 90s, PCB concentrations in rainwater from continental areas had dropped to one quarter or less of their levels in the late 70s, with values decreasing from 20 to 5 ng/litre [0.02-0.005 ng/m$^3$] in rural areas and from 50 to 10 ng/litre [0.05-0.01 ng/m$^3$] in cities.
In indoor air, PCB concentrations in the early 1980s were typically at least ten times higher than in the surrounding outdoor air. This may be due to the fact that PCBs are emitted by certain electrical appliances and devices (such as fluorescent lighting ballasts) and building materials (such as elastic sealants).

In seawater, in industrial areas, PCB levels were observed to be at least 100 times higher than further off-shore, based on samples of water taken from the upper few millimeters of the surface. Particularly high concentrations were reported in the North Sea (0.3–3 ng/litre) and in Galveston Bay, a highly industrialized area in Texas, USA (3.1 ng/litre between 1978 and 1979).

In river sediments, PCB levels have been measured at different depths. Sediment samples showed the highest PCB concentrations in sediment layers buried during the time of maximum PCB manufacture. PCB concentrations are much lower in sediment layers that have formed following the ban on production and use of PCBs.

In fish, reported PCB levels have dropped significantly. For example, PCB concentrations in trout from Lake Ontario decreased by 80% between 1976 and 1994. For several fish species from the Great Lakes, the PCB concentrations in samples collected in the 1990s were generally below 1 µg/kg wet weight.

3. To what extent are humans exposed to PCBs?

Humans are mainly exposed to PCBs via food, air and drinking water.

Overview: Levels of human exposure to PCBs and Tolerable Daily Intake (TDI)  
[see Annex 1, p. 19]

3.1 To what extent are humans exposed to PCBs through food?

Consumption of contaminated foods, particularly meat, fish, and poultry, appears to remain the main source of exposure to PCBs although levels in food have decreased since the late 70s.

In the USA, the dietary intake of PCBs by adults continually decreased after the late 70s and reached a low in the late eighties (see table 7 [see Annex 2, p. 20] ). Between 1991 and 1997 a somewhat higher dietary exposure of about 3–5 ng/kg body weight per day for adults and 2–12 ng/kg body weight per day for children was observed. The consumption of PCB-contaminated fish has been shown to increase PCB levels in the body. Levels of PCBs in human blood serum have been linked to the amount of contaminated fish eaten, with average levels in the USA generally between 4000 and 8000 ng/litre of blood serum.

Table 7: Estimated daily dietary intake of PCBs in the USA from 1976 to 1991  
[see Annex 3, p. 21]

In Japan, a study carried out in the late 90s estimated the intake of three dioxin-like (coplanar) PCBs from 120 food items. Highest concentrations were found in fish and shellfish
(8.39–25.7 ng/kg wet weight basis). The overall PCB intake from all foods was estimated to be 0.00145 ng/kg body weight per day for an adult weighing 50 kg, which represented a relatively high level of PCB contamination in Japan.

Overview: Levels of human exposure to PCBs and Tolerable Daily Intake (TDI) [see Annex 1, p. 19]

This text is a summary of: IPCS - WHO Polychlorinated biphenyls: Human health aspects. Concise international chemical assessment document 55
Section 6.2, Human exposure [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#6.2] and
Section 6.3, Tissue concentrations [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#6.3]

3.2 To what extent are infants exposed to PCBs through breast milk?

The amount of PCBs found in human breast milk has followed a downward trend consistent with the decline in the PCB levels both in the environment and in human tissues. Measurements either consider PCB concentrations in breast milk as a whole or in breast milk fat only. In Canada, the average concentration of PCBs in whole breast milk steadily increased between 1970 and 1982, and then returned to its 1970-value by 1986 (6 000 ng/kg whole breast milk).

In Japan, PCB concentrations found in human milk fat were highest in 1974 and had decreased to about 13% of that level by 1998 (0.2 mg/kg milk fat). Total PCB levels in the breast milk fat of Swedish women also showed a steady decrease (from 0.910 to 0.324 mg/kg milk fat) for the period 1967–1997.

Since the late 80s the average PCB concentrations seen in human milk fat were within a range of 0.2 to 4 mg/kg milk fat.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls: Human health aspects. Concise international chemical assessment document 55
Section 6.2, Human exposure [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#6.2]

3.3 To what extent are humans exposed to PCBs through air?

In cities, the average PCB concentration in outdoor air is typically 5 ng/m$^3$, but concentrations in indoor air tend to be at least 10 times higher. An average adult male would thus take in about 100 ng of PCBs per day if he breathed in urban outdoor air alone and much more if he spent time indoors. Some workers can be exposed to much higher concentrations, for instance in PCB disposal facilities where levels of PCBs in the air can range between 850 and 40 000 ng/m$^3$.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls: Human health aspects. Concise international chemical assessment document 55
Section 6.2, Human exposure [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#6.2]

3.4 To what extent are humans exposed to PCBs through drinking water?

In the USA, PCB levels in drinking water were observed to be lower than 100 ng/litre and sometimes undetectable. The expected exposure of the general US population through drinking water is thus less than 200 ng PCB per day.
In Canada, PCBs have been detected in only 1 out of the 280 municipal drinking-water samples tested, at a concentration of 6 ng/litre (See question 7.3 for effects [see https://www.greenfacts.org/en/pcbs/l-2/7-risks-exposure.htm#3]).

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55 Section 6.2, Human exposure [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#6.2]

4. What happens to PCBs when they enter the body?

PCBs can enter human cells and tissues when contaminated air is breathed in, when contaminated food enters the digestive system, or through contact with the skin. Tests on laboratory animals show that PCBs are readily absorbed through the digestive tract when swallowed, and to a lesser extent through the skin. The main PCB elimination routes are through the faeces, urine, and breast milk.

Once in the gastrointestinal tract, ingested PCBs diffuse across cell membranes and enter blood vessels and the lymphatic system. PCBs, especially those that contain a greater number of chlorine atoms, are readily soluble in fats and thus tend to accumulate in fat-rich tissues such as the liver, brain and skin.

In mothers, PCBs have also been found to pass into the placenta, umbilical cord blood, and breast milk.

PCBs can undergo different transformations in the body and then either be stored in certain tissues or excreted.

Transformations that lead to accumulation: PCBs can easily be transformed into persistent metabolites that are not readily excreted and that can accumulate in specific tissues and body fluids. The biological half-life of these persistent metabolites depends on the structure of the original PCB.

Transformations that lead to excretion: PCBs can leave the blood and enter tissues very rapidly and be transformed into water-soluble substances. These can combine with glutathione and glucuronic acid, that are naturally present in the body, forming a substance that is then excreted in urine and feces. The speed of this process depends on the number and position of chlorine atoms of the original PCB. It is, for instance, slower when there are more chlorine atoms on both phenyl rings and faster if there are two carbon atoms without any attached chlorine atoms next to each other.

In a case where both children and their mothers were exposed to PCBs through their diet, levels of PCBs in blood dropped more rapidly in the children. This may be partly explained by the children’s growth, as their increasing tissue mass may lower the PCB concentration in blood due to dilution, rather than elimination.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55 Section 7, Comparative kinetics and metabolism in laboratory animals and humans [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#7.0]
5. What are the effects of PCBs on laboratory animals?

5.1 At what exposure levels do PCBs cause harmful effects?

**Single exposure:** In laboratory tests, animals were fed a single dose of one of several different PCB mixtures available on the market. Those tests determined doses at which different mixtures would cause the death of half of the animals (LC50). This occurred in rats with a single dose between 1 010 and 4 250 mg PCBs per kg body weight and in minks with a single dose between 750 and 4 000 mg PCBs [7 500 000 - 4 000 000 000 ng] per kg body weight depending on the specific PCB mixture. Results may have been affected by factors such as animal breed, age, and sex, as well as by the purity of the PCB formulation.

For example, there is evidence that young rats (3–4 weeks old) are more vulnerable to PCB mixtures than adults. Effects of PCBs on rats include diarrhea, breathing difficulties, dehydration, decreased response to pain, and coma. PCBs were found to mainly damage the lungs, the stomach, and the pancreas.

**Short-term exposure:** Over a 7 day period, a small number of rats were given different daily doses of a commercial PCB mixture (Aroclor 1254). The lowest tested dose that has been reported to harm them was 2.5 mg/kg body weight per day (LOAEL), which caused a significant increase in relative liver weight and a decrease in the level of a thyroid hormone in the blood.

**Cancer:** Over a period of approximately 2 years, in twelve different experiments, male and female rats were given various concentrations of several commercial PCB mixtures in their food. The results showed that, in nine out of twelve studies, the number of rats that developed tumors of the liver increased significantly with the dose of PCB mixture ingested. The lowest PCB doses associated with the development of these tumors ranged from 1.4 to 5.4 mg/kg body weight/day depending on the type of PCB mixture tested, and on the strain and sex of the rats. It is possible that impurities in some of the PCB mixtures may have affected the findings. Other significant observed effects of exposure to PCB mixtures were a greater number of thyroid tumors in male rats, and fewer cases of mammary gland tumors in female rats.

In more limited studies, PCB mixtures have also been shown to induce liver tumors in different strains of mice.

In addition, studies have established that PCBs with relatively high chlorine content can ‘promote’ the formation of liver tumors in rats and mice and lung tumors in mice, if such tumors were previously ‘initiated’ by exposure of the animals to genotoxic carcinogens. Whether or not less highly chlorinated PCBs also promote the formation of tumors has not been evaluated.

Several studies on mice in which low doses (0.1 mg/mouse) of a relatively highly chlorinated PCB mixture (Aroclor 1254) were applied to the skin showed little or no effect on cancer formation.

In summary, PCBs, particularly the highly chlorinated mixtures, are associated with cancer of the liver in animals.
5.2 What are the effects of PCBs on reproduction?

Harmful effects on fertility and reproductive organs have been seen in rats, mice, and monkeys exposed to PCBs through their food.

Rats that were fed relatively high doses of PCBs showed:

- an increase in testes weight (at 3.5 mg/kg body weight per day),
- a decreased fecundity (at 12.5 mg/kg body weight per day),
- a reduced sperm count (at 25 mg/kg body weight per day), and
- a decreased number of young per litter (at 35.4 mg/kg body weight per day).

Adverse reproductive effects have been observed in offspring of female rats exposed to a mixture of relatively highly chlorinated PCBs (Aroclor 1254) during lactation. This suggests that PCBs transferred during breast-feeding can have a long-lasting effect.

Exposure to a moderately chlorinated PCB mixture did not increase testicular weight in newborn male rats, when 0.4 mg/day was injected under their skin for 25 days (NOAEL).

Monkeys that were fed PCBs showed:

- a prolonged menstruation (at 0.1 mg/kg body weight per day), and
- a decreased fecundity (0.2 mg/kg body weight per day).

No adverse effects on fecundity were observed below 0.005 mg/kg body weight per day [i.e. a NOAEL for monkeys of 5 000 ng / kg body weight /day].

Effects on female hormonal activity, have been widely investigated in vivo and in vitro with rats and mice. The studies indicate that PCBs may increase or mimic estrogen activity or, alternatively in the case of dioxin-like PCBs, prevent estrogens from acting. Differences in the composition of the PCB mixtures tested probably account for the different results seen. Effects on estrogen activity stem from the fact that certain forms of PCBs are structurally similar to estrogen and can therefore bind to the same cellular receptors. Effects on female hormonal activity, have been widely investigated in vivo and in vitro with rats and mice. The studies indicate that PCBs may increase or mimic estrogen activity or, alternatively in the case of dioxin-like PCBs, prevent estrogens from acting. Differences in the composition of the PCB mixtures tested probably account for the different results seen. Effects on estrogen activity stem from the fact that certain forms of PCBs are structurally similar to estrogen and can therefore bind to the same cellular receptors.

Developmental effects of ingested PCBs have been tested on several animal species. Exposure to PCBs of females during pregnancy and lactation may interfere with the development of the fetus or offspring.

In monkeys, several behavior tests on the offspring of exposed females showed deficits such as a reduced ability to respond to changes in the rules which they needed to follow to obtain a reward (with a LOAEL of 0.03 mg/kg body weight per day). Newly born monkeys exposed to a mixture constructed to resemble the PCB composition in human milk showed behavioral impairment (with a LOAEL of 0.0075 mg [7 500 ng] /kg body weight per day ). In one study, deficits in the development of nervous system were observed after exposure to high levels of non-planar PCBs, but not after exposure to coplanar (dioxin-like) PCBs.

The effect of PCBs on the developing immune system of young rats was evaluated. Fifteen weeks after birth, the rats treated with high doses of PCBs had a smaller thymus gland and a reduced number of immune cells suggesting that PCBs had impaired the development of the immune system. The lowest dose at which no adverse effects on the development of the immune system of rats were observed (NOAEL) was 1 mg/kg body weight per day
[1 000 000 ng/kg body weight/day]. It was noted that highly chlorinated PCBs were more immuno-suppressive to mice than those with low chlorine content. Effects on the development of the liver, thyroid, and kidney have also been found.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55
Section 8.5.1, Effects on fertility, [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#8.5.1]
Section 8.5.2, Estrogen-related effects [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#8.5.2] and
Section 8.5.3, Developmental effects [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#8.5.3]

5.3 What other biological effects can PCBs have?

It appears that PCB mixtures do not directly damage genes, according to tests carried out in-vitro and in-vivo on many species, as well as on human white blood cells.

Two main effects have been observed; the reduced production of antibodies in response to an immunological challenge and changes in some of the organs of the lymphatic system such as the spleen and the thymus, of the. Observed effects of PCBs on the immune system included a reduction in the production of antibodies, an increased susceptibility to disease, and a decreased thymus weight.

Adult animals appear to be less sensitive than the fetus to the effects of PCBs. The effects of PCB exposure on the immune system of adult animals depend on the amount and specific type of PCB. These effects occur in all animal species examined at high doses, and only in some, such as the rhesus monkey, at low doses. For example, monkeys exposed for 55 months to a PCB mixture with relatively high chlorine content (Aroclor 1254) produced a weaker immune response than monkeys that had not been exposed (control group). The observed effect was even more pronounced at higher doses.

Certain PCB mixtures have been shown to affect the transmission of nerve impulses in different areas of the brain and the spinal cord in rats and monkeys.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55
Section 8.4, Genotoxicity and related end-points, [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#8.4]
Section 8.6, Immunotoxicity [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#8.6] and
Section 8.7, Neurochemical effects [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#8.7]
5.4 Through what mechanisms do PCBs act?

The shape of a particular PCB depends on the position of the chlorine atoms (see question 1.2 [see https://www.greenfacts.org/en/pcbs/l-2/1-polychlorinated-biphenyls.htm#2]) and determines the way it acts in an organism. The two phenyl rings that make up a PCB molecule can either lie approximately in the same plane (coplanar PCBs) or in different, more perpendicular planes (non-planar PCBs).

**Planar PCBs** are also called “dioxin-like”, because they can cause similar harmful effects in the body. They can bind strongly to a cellular receptor, the Ah receptor, and thereby affect the hormonal system and the way cells grow and develop. Those PCBs that bind strongly to the Ah receptor induce certain types of enzymes involved in energy production in the cell. A different set of enzymes of this family are induced by PCBs that have a less planar structure and therefore bind less strongly to the Ah receptor.

**Non-planar PCBs** do not act like dioxins, because they do not bind to the Ah receptor. However, at high doses, they do have effects on the development of the nervous system and on dopamine levels, and can contribute to tumor formation.

**Estrogen-like PCBs** can bind to cellular receptors for the estrogen hormone, and cause subtle hormonal disturbances and adverse effects on reproduction. Any hormonal effect is likely to depend on the species, tissue, and developmental stage.

In addition to the effects of the PCBs themselves, some of their break-down products may also be endocrine disruptors. They may for instance have a negative effect on thyroid hormone levels, inhibit enzyme activity in the adrenal glands, interact with estrogen receptors, alter cellular processes in the lung and affect the reproductive system.

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**6. How has PCB exposure affected human health?**

PCB exposure varies greatly from person to person in terms of amount and type of PCB mixture. In addition, humans can be exposed to different contaminants in PCB mixtures, as well as PCB combustion by-products. Differences in exposure make it difficult to establish a clear relationship between PCB exposure and any observed effects on human health.

Nonetheless, the evidence suggests that exposure to PCBs is associated with an increased risk of certain cancers of the digestive tract, liver and skin. PCB exposure is also associated with reproductive deficiencies, such as reduced growth rates, retarded development, and certain neurological effects which may or may not persist beyond infancy. The immune system can also be affected, leading to increased infection rates, and changes in the skin such as chloracne and pigmentation disturbances.

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This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55
Section 8.8, Mode of action [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#8.8]

This text is a summary of: IPCS - WHO Polychlorinated biphenyls : Human health aspects. Concise international chemical assessment document 55
Section 9.0, Effects on humans [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#9.0]
6.1 Has exposure to PCBs lead to more cancer cases?

Fifty studies conducted since 1976, mainly on people exposed to PCBs at work, indicated increases in mortality from cancers of the gastrointestinal tract, the liver, the organs and tissues involved in the production of blood, including bone marrow, the spleen, tonsils, and lymph nodes, and from malignant melanoma.

Exposure at workplaces was studied at several plants manufacturing PCB-impregnated capacitors, where exposure occurred through the air. Other studies involved exposure through foods, such as fish and rice oil or rice bran-oil, which had been contaminated with PCBs, but also with other toxic chemicals. The variation between these studies and the mixed results means that no consistent picture emerges for PCB-induced cancer of any particular organ/tissue. However, one study found a strong dose-response relationship between serum PCB levels and non-Hodgkin lymphoma, a cancer of the lymphatic system.

6.2 Has exposure to PCBs affected human reproduction and development?

Various studies examined effects on fertility due to PCB exposure through fish consumption and at the work place. In a study of New York women, a decrease in the ability to conceive was observed amongst those who regularly ate locally-caught fish that were contaminated with PCBs. In men, a study of 55 transformer repair workers found no association between exposure to PCBs and sperm counts. However, in another study, for men with a low sperm count the ability of sperm to move decreased as the concentration of three coplanar PCBs in their blood serum increased. Another study reported higher levels of certain PCBs in infertile men compared with the control population.

Since the 1980s numerous studies have investigated the effects of PCB exposure both during and after pregnancy on child growth and development. Researchers can estimate the degree of PCB exposure in the womb by measuring the level of PCBs in the umbilical cord blood serum. By analyzing breast milk samples, the extent of PCB transmission from mother to child can be deduced.

Effects of exposure to PCBs on the developing fetus have been investigated in women who consumed PCB-contaminated fish from Lake Michigan over a 6-year period. Overall fish consumption and levels of PCBs in cord blood serum were associated with lower birth weight, smaller head circumference, and shorter pregnancies.

Fish consumption during pregnancy was related to lesser neuromuscular maturity of the newborn. PCB-contaminated fish consumption has also been linked to impaired involuntary muscle actions and abnormally weak reflexes.

High levels of PCBs in umbilical cord blood serum have repeatedly been linked with poor performance in standard tests carried out to assess the mental and motor abilities of the newborn. Follow-up studies on children aged 4 and 11 indicated that PCB exposure in the womb was linked to impaired memory and attention, specifically short term memory and performance in IQ tests. Contrastingly, other follow up studies have shown that psychomotor deficits do not persist beyond childhood. Although one study indicated exposure to PCBs...
through breast-milk did not affect memory performance, another study showed lower mental development in 7-month old infants fed with breast milk containing high levels of three common non-planar PCBs.

6.3 Have PCBs caused other health effects?

The effects of PCBs exposure on the immune system of adults and children have been examined in two different studies.

An analysis of blood samples showed that Swedish males who consumed a large amount of fish from the Baltic Sea had higher PCB levels and lower numbers of natural killer cells in their blood than a group of males who did not consume any fish. It should be noted, however, that the presence of DDT may have influenced the results.

Another study on infants exposed to PCBs and dioxins both before and after birth found no relationship between exposure and respiratory abnormalities. When these children were three and a half years old, a follow-up assessment showed that higher PCB levels in the blood plasma were associated with a higher frequency of recurrent middle-ear infections and chicken pox.

Information on neurological effects of PCB exposure in adults is limited. People (accidentally) exposed to PCBs in the workplace reported headaches, dizziness, depression, fatigue, and a tingling sensation in the hands. People regularly consuming fish from PCB-contaminated waters performed poorly on tests requiring reasoning, word naming, auditory recall, and complex motor tasks. However, heavy metals and pesticides may also have been present in these contaminated fish. Significantly higher concentrations of PCBs, especially two highly chlorinated PCBs, were found in the brains of Parkinson’s disease patients than in control groups. Adults that ingested rice oil contaminated with PCBs and dioxins showed various neurological symptoms such as numbness, weakness, and limb pain, partial loss of sensation, and headaches. Exposure also caused a reduction in the speed of nerve impulse transmission.

Skin problems, particularly rashes and chloracne, have been observed in workers exposed to PCB mixtures used in commercial processes, as well as among people who ingested rice oil contaminated by PCBs and dioxins.

Characteristic skin changes included blocked pores, acne, hyper-pigmentation, skin thickening, and deformed nails. Such skin problems affected many parts of the body and improved over time.

In infants born to exposed mothers, similar skin problems were commonly observed but generally diminished as the infants grew older.
7. What are the risks posed by PCB exposure?

The risks posed by PCB exposure have been evaluated by analysing data from studies using PCB mixtures most commonly used in industry, to which workers may have been directly exposed.

This approach has been preferred to other scientific approaches in this case, because of the availability of appropriate data. In other cases, assessment methods may focus on "dioxin-like" health effects of different PCBs (through the use of toxic equivalent factors) or on actual measures of total PCB body burden in humans.

As PCBs persist in the environment, the general population is still potentially exposed to a variety of PCBs via food, air, and water. Although mixtures used in industry are not identical to the combinations of PCBs present in the environment (or in breast milk), these mixtures have been found to have similar harmful effects.

The studies on humans showed several types of health effects linked to PCB exposure. Findings from animal studies have been used to quantify the human health risks posed by exposure to different amounts and mixtures of PCBs. This is largely because in studies on humans that had been exposed there is insufficient information about the degree and type of PCB-exposure or about simultaneous exposure to other potentially harmful substances.

7.1 What health effects occur at what levels of exposure?

A series of long-term studies carried out on large numbers of rhesus monkeys showed that exposure to a mixture of highly chlorinated PCBs (Aroclor 1254) caused adverse effects on their immune system at intake levels as low as 5 000 ng/kg body weight per day (LOAEL).

Exposure to PCBs over a longer period of time was shown to negatively affect the development of the nervous system leading to behavioral and learning problems in monkeys. Comparable results have been found in human population groups with similar exposure histories. In monkeys, the lowest dose at which such behavioral changes were observed was 7 500 ng/kg body weight per day (LOAEL).

Only at much higher levels have PCBs been shown to induce tumors in the liver of rodents.

Overview: Levels of human exposure to PCBs and Tolerable Daily Intake (TDI)
[see Annex 1, p. 19]

7.2 What tolerable daily intakes have been established for PCBs?

Tolerable Daily Intake (TDI) is an estimate of the amount of a substance that can be taken in by humans on a daily basis over a lifetime without appreciable human health risk.
For a typical PCB mixture (Aroclor 1254), a Tolerable Daily Intake for humans of 20 ng/kg body weight per day was determined based on the lowest level of PCBs that gave rise to adverse effects (LOAEL) in a particular animal species (rhesus monkeys).

In order to determine this Tolerable Daily intake for humans the lowest level of PCBs that gave rise to adverse effects in animals (LOAEL) was divided by an overall uncertainty factor of 300, which takes into account possible differences in susceptibility between humans and experimental animals and between different individuals.

The available data are not sufficient to determine tolerable PCB concentrations in air or what doses can be ingested over a short period of time without appreciable health risk.

7.3 What are estimated daily intakes of PCBs?

In the USA, estimates of the daily intake of PCBs from the main sources of exposure have been calculated. The total daily intake from drinking water, air, and food (listed from lowest to highest) is believed to range from 1 to 8 ng/kg body weight.

Table: Estimated daily PCB intakes in the USA in adults

<table>
<thead>
<tr>
<th>Source</th>
<th>Estimated daily intake in ng/kg body weight per day</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>drinking-water</td>
<td>Less than 0.2</td>
<td>Based on a 70-kg individual drinking 2 litres of water per day, which contains 6 ng/litre [0.006ng/m$^3$] of PCBs</td>
</tr>
<tr>
<td>air</td>
<td>0.3 to 3</td>
<td>Based on the typical range of urban PCB levels of between 1 and 10 ng/m$^3$</td>
</tr>
<tr>
<td>food</td>
<td>0.5 to 5</td>
<td>Fish, poultry, and meat are the primary contributors to the PCB intake</td>
</tr>
<tr>
<td>Total</td>
<td>1-8</td>
<td></td>
</tr>
</tbody>
</table>

The estimated total daily intake is approximately 1 000 times lower than the lowest PCB intake that caused adverse effects in animals (5 000 ng/kg body weight per day) and 4 times lower than the tolerable daily intake for PCBs (20 ng/kg body weight per day).

Overview: Levels of human exposure to PCBs and Tolerable Daily Intake (TDI) [see Annex 1, p. 19]

7.4 What are the uncertainties in assessing PCB health risks?

This assessment of PCB health risks is limited by several uncertainties:

- Laboratory animals (rhesus monkeys) used in the studies on which the calculation of a Tolerable Daily Intake is based may be more sensitive to PCB exposure than humans.
- Studies were only carried out on a limited set of PCB mixtures, which may not fully represent actual exposures.
Most studies consider only mixtures of PCBs – rather than individual congeners – that might have different mechanisms of action.

The risk assessment reflects the exposure of the general population, but may not adequately cover certain circumstances, such as eating large amounts of PCB-contaminated fish or breathing air containing elevated PCB levels downwind of contaminated sites.

This text is a summary of: IPCS - WHO Polychlorinated biphenyls: Human health aspects. Concise international chemical assessment document 55

Section 10.4, Uncertainties in the health risk assessment [see http://www.inchem.org/documents/cicads/cicads/cicad55.htm#10.4]

8. Conclusions

PCBs, or polychlorinated biphenyls, are a class of 209 man-made organic chemicals containing carbon, hydrogen and differing amounts of chlorine. The commercial production of PCBs started in 1929 but their use has subsequently been banned or severely restricted in many countries since the 1970s and 80s because of the possible risks to human health and the environment.

PCBs have been used in a wide range of products such as plastics, paints, and adhesives. Since PCBs are resistant to acids and bases as well as to heat, they have also been used in electric equipment, heat transfer fluids and lubricants. Disposal of waste that contains PCBs in landfills or incinerators can lead to environmental contamination.

PCBs can persist in the environment and accumulate in animals and along the food-chain. Humans may be exposed to PCBs by ingesting contaminated food and water or inhaling contaminated air. In the human body PCBs can remain in fatty tissues and in the liver and may be transferred from mother to child through the placenta or breast milk. The speed at which PCBs are transformed in the body and the extent to which they are either stored or excreted depend on the type of PCB.

Studies on humans and animals have shown harmful effects on fertility. Furthermore, exposure of the child during pregnancy or through breast-feeding can affect its development. Effects on the immune system have been observed in animals, in children exposed to PCBs during development in the womb, and in adults exposed through PCB-contaminated food. Groups of workers that have been exposed to high levels of PCBs (as well as to other chemicals) have shown an increase in certain cancers.

Based on these findings, a tolerable daily intake for humans of 20 ng/kg body weight per day has been established for a commercial PCB mixture with relatively high chlorine content (Aroclor 1254).
Annex

Annex 1:

Overview: Levels of human exposure to PCBs (from environmental sources)* and Tolerable Daily Intake (TDI)

The table below presents amounts of PCBs found in the environment or in food products in various studies, as well as the Tolerable Daily Intake (TDI) set by the WHO. The figures do not represent average exposure at a global level, but results of specific studies with a limited geographical and time scale. Direct comparisons between figures are thus not possible (even if the units presented are similar). Comparisons are further complicated by the fact that some studies measured the total amount of PCBs found in the environment, while others measured only certain types of PCBs, generally the most toxic ones which account for most though not all of the overall PCB toxicity.

<table>
<thead>
<tr>
<th>Type of Environment</th>
<th>Environmental Level*</th>
<th>Daily Intake</th>
<th>GreenFacts comments</th>
<th>See question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outdoor Air</td>
<td></td>
<td></td>
<td>Have been measured for an average adult male inhaling 23 m³ of urban outdoor air per day and weighing 70 kg</td>
<td></td>
</tr>
<tr>
<td>-Urban (N. America)</td>
<td>Average 5 ng per m³</td>
<td>On average approximately 1.5 ng per kg body weight per day</td>
<td>This average daily intake is calculated for an average adult male inhaling 23 m³ of Urban outdoor air per day and weighing 70 kg</td>
<td>3.3 [see <a href="https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#3">https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#3</a>]</td>
</tr>
<tr>
<td>-Rural (Arctic &amp; Antarctic)</td>
<td>0.02 to 0.5 ng per m³</td>
<td>-</td>
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</tr>
<tr>
<td>Indoor Air (in PCB disposal facilities, measured for various Aroclors)</td>
<td>850 to 40 000 000 ng per m³</td>
<td>-</td>
<td>Lower PCB levels found in homes and laboratories – e.g. 100-310 ng/m³</td>
<td>3.3 [see <a href="https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#3">https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#3</a>]</td>
</tr>
<tr>
<td>Drinking Water (in the USA)</td>
<td>less than 100 ng per litre</td>
<td>less than 3 ng per kg body weight per day (USA population)</td>
<td>This average daily intake is calculated for an average adult drinking 2 litres per day and weighing 70 kg</td>
<td>3.4 [see <a href="https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#4">https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#4</a>]</td>
</tr>
<tr>
<td>Food (USA)</td>
<td>-</td>
<td>3-5 ng per kg body weight per day (adults) 2-12 ng per kg body weight per day (children)</td>
<td>-</td>
<td>3.1 [see <a href="https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#1">https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#1</a>]</td>
</tr>
<tr>
<td>Breast milk (in a single study on breastfeeding Canadian women)</td>
<td>6 000 ng per kg whole breast milk</td>
<td>less than 1000 ng per kg body weight per day (during the intake from these 3 PCB’s accounts for 60%period of the overall toxicity found in Japanese foodbreast feeding)</td>
<td>This daily intake was calculated by GreenFacts from a single study assuming an infant weighing 6 kg that would drink less than a kg of breast milk.</td>
<td>3.2 [see <a href="https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#2">https://www.greenfacts.org/en/pcbs/l-2/3-human-exposure.htm#2</a>]</td>
</tr>
<tr>
<td>Tolerable Daily Intake (TDI)**</td>
<td>-</td>
<td>20 ng per kg body weight per day (averaged over the whole life)**</td>
<td>Calculated by applying an uncertainty factor of about 300 to the above LOAEL**</td>
<td>7.2 [see <a href="https://www.greenfacts.org/en/pcbs/l-2/7-risks-exposure.htm#2">https://www.greenfacts.org/en/pcbs/l-2/7-risks-exposure.htm#2</a>]</td>
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</tbody>
</table>

* Environmental PCB levels may have decreased since these measurements were made.

** In order to determine whether or not PCBs constitute a significant risk to the average human, the Average Daily Intake (ADI) can be compared with the Tolerable Daily Intake (TDI) which has been established for PCBs.

- The Tolerable Daily Intake (TDI) of PCBs for humans has been set at **20 ng per kg body weight per day** (over the whole life).
- This has been determined from the Lowest Observed Adverse Effect Level (LOAEL) of one specific PCB mixture, Aroclor 1254, on the immune systems of rhesus monkeys.
- The protective uncertainty factor of 300 used in calculating the human Tolerable Daily Intake (TDI) from this lowest observed LOAEL data is thought to protect humans sufficiently because Aroclor 1254 contains several quite toxic individual PCBs. Rhesus monkeys are thought to be more sensitive to PCBs than humans.

Annex 2:

Table 1: PCB nomenclature conversion table.

Two different systems are used for naming PCBs:

In the IUPAC system the numbers at the beginning of the name specify the sites where chlorines are attached to the two phenyl rings. In this table, the top row indicates the position of the chlorine atoms one one phenyl ring and the first column their position on the second phenyl ring.

Another system developed by Ballschmiter & Zell (1980) assigns a separate number, from 1 to 209, to each of the 209 specific PCB congeners. These numbers are indicated inside the table below.

An example how to relate the two systems is provided below the table.

<table>
<thead>
<tr>
<th>Chlorine positions on each ring</th>
<th>None</th>
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</tbody>
</table>

Example (illustrated by shaded area in table): To determine IUPAC and alternative names for PCB 156:

1. Locate PCB 156 within table.
2. Identify the associated column heading (2345) and row heading (34) values.
3. The IUPAC name for PCB 156 is 2,3,4,4',5'-hexachlorobiphenyl.

Various additional names for this congener include 2,2';4,4'-hexachlorobiphenyl, 2345-3'-4'-hexachlorobiphenyl (group starting with lower number appears first), 2345-34-hexachlorobiphenyl, and 233'44'S-hexachlorobiphenyl. Adapted from Frame et al. (1996).

### Annex 3:

**Table 7: Estimated daily dietary intake of PCBs in the USA.**

<table>
<thead>
<tr>
<th>Year</th>
<th>Dietary intake (µg/kg body weight per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>1986–1991</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1982–1984</td>
<td>0.0005</td>
</tr>
<tr>
<td>1981–1982</td>
<td>0.003</td>
</tr>
<tr>
<td>1980</td>
<td>0.008</td>
</tr>
<tr>
<td>1979</td>
<td>0.014</td>
</tr>
<tr>
<td>1978</td>
<td>0.027</td>
</tr>
<tr>
<td>1977</td>
<td>0.016</td>
</tr>
<tr>
<td>1976</td>
<td>Trace</td>
</tr>
</tbody>
</table>

* ATSDR (2000). Estimated intakes are based on an average "total diet" composition (which varies slightly) and not on individual food items. Average body weights are assumed to be 9 kg for infants, 13 kg for toddlers, and 70 kg for adults. Accordingly, the average dietary intake for 1982–1984 would be 0.0108 µg, 0.0104 µg, and 0.035 µg for the infant, toddler, and adult, respectively.

* ND = not detected.