Persistent Organic Pollutants Impact on Child Health

World Health Organization

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Abbreviations

AAP	American Academy of Pediatrics
AMAP	Arctic Monitoring and Assessment Programme
ATSDR	Agency for Toxic Substances and Disease Registry
BMI	body mass index
BSE	bovine spongiform encephalopathy
COP	conference of the parties
DDD	dichlorodiphenyldichloroethane
DDE	dichloro-diphenyl-dichloroethylene
DDT	dichloro-diphenyl-trichloroethane
EPA	Environment Protection Agency
EU	European Union
GEMS	Global Environment Monitoring System
IARC	International Agency for Research on Cancer
IFCS	Intergovernmental Forum on Chemical Safety
IgG	immunoglobulin G
ILO	International Labour Organization
IOM	Institute of Medicine
IPCS	International Programme on Chemical Safety
IPM	integrated pest management
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LRTAP	Long-Range Transboundary Air Pollution Convention (Aarhus Protocol on Persistent Organic Pollutants to the Convention)
MDI	mental development index
MRL	maximum residue level

NHANES	National Health and Nutrition Examination Survey
NOS	Neurologic Optimality Score
NTP	National Toxicology Programme
OECD	Organisation for Economic Co-operation and Development
OSPAR	Oslo-Paris Convention for the Protection of the Marine Environment of the North East
PAH	polycyclic aromatic hydrocarbon
PBDE	polybrominated diphenyl ether
PBT	persistent, bioaccumulative, toxic substance
PCB	polychlorinated biphenyl
PCDD	polychlorinated dibenzo-p-dioxin
PCDF	polychlorinated dibenzofuran
PCN	polychlorinated naphthalene
PFOA	pentadecafluorooctanoic acid
PIC	prior informed consent
POP	persistent organic pollutant
POPRC	Persistent Organic Pollutants Review Committee
PTFE	polytetrafluoroethylene
PTS	persistent toxic substance
SAICM	Strategic Approach to International Chemicals Management
TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
UNCED	United Nations Conference on Environment and Development
UNECE	United Nations Economic Commission for Europe
UNEP	United Nations Environment Programme

Foreword

Dear Colleagues,

I am pleased to present to you this booklet titled "Persistent Organic Pollutants – Impact on Child Health". Persistent organic pollutants (POPs) include pesticides and industrial chemicals that were manufactured in great quantities during the 20th century. Their use resulted in beneficial outcomes such as increased crop yields and killing of unwanted pests. Many POPs were considered to be wonder chemicals until scientific information began to emerge about devastating effects in wildlife resulting from contamination of the environment. In humans, mass poisonings resulting from unintentional contamination of food with certain POPs illustrated the devastating health effects of high levels of exposure. Scientific experiments in laboratory animals have revealed the effects of lower levels of POPs on numerous organ systems. Accumulating scientific information in humans has led to concerns about the effects of chronic low-level POPs exposure in humans. There is particular concern that fetuses, infants and children may be at especially high risk. Humans at these early life stages generally have increased exposures compared to exposures of adults. There is rapid growth and differentiation of organ systems during these early periods, resulting in heightened vulnerability to harm. Effects on health are often subtle. Effects of these chemical exposures during "critical windows of vulnerability" of children's development may not manifest until later in their lives.

POPs are dispersed globally and exposure is ubiquitous. Therefore, worldwide efforts have been undertaken by UNEP, governments, WHO and other stakeholders in order to eliminate and reduce the production, use and emission of these chemicals through the Stockholm Convention on Persistent Organic Pollutants. Because other chemicals with characteristics similar to POPs remain in worldwide use today, these efforts to reduce exposure must be ongoing.

Healthcare providers who care for men and women of childbearing age, pregnant women and children may not be fully aware of POPs and their potential impacts on children's health and development. This booklet offers evidence-based information about POPs and their health effects. I commend this booklet to you.

Maria Neira, Director
Public Health and Environment
World Health Organization

I. Summary

Persistent organic pollutants (POPs) are organic (carbon-based) chemicals that remain in the environment for long periods of time. They bioaccumulate and biomagnify as they move through the food chain. POPs are found in certain pesticides and industrial chemicals, and as byproducts of manufacturing processes and waste incineration. POPs were produced in vast amounts during the 20th century and were used for beneficial purposes such as increasing crop yields and killing unwanted pests and other vectors. POPs have low water solubility and high fat solubility and thus accumulate in fatty tissues of living organisms. POPs are transported in the environment in low concentrations by movement of fresh and marine waters. They are semi-volatile, enabling them to move long distances in the atmosphere, resulting in widespread distribution across the earth, including regions where they have never been used. Thus, humans and animals around the world are exposed to POPs at low levels for extended periods of time.

In humans and animals, there are known adverse health effects of exposure to high levels of POPs; the effects may include cancer, damage to the nervous system, reproductive disorders, or disruption of the immune system. Children have suffered adverse effects from high-level exposure. There is also increasing concern that chronic exposure to low levels of POPs may contribute to the burden of disease including increased incidence of breast and other cancers, learning and behavior disabilities and other neurodevelopmental problems, and reproductive problems such as decreased sperm quality and counts.

For most people, exposure to POPs comes from the ingestion of food such as fish, meat, and dairy products although exposure can also occur through inhalation and dermal absorption. Because POPs are ubiquitous, human exposure to POPs starts before conception. Concerns for children's health include the possibility of effects on sperm and ova before children are conceived, and effects resulting from pregnancy when maternal fat stores are mobilized, leading to exposure of the embryo and then to the fetus through the placenta. Postnatal exposure occurs via breast milk.

Compared to adults, children are usually more vulnerable to the effects of environmental pollutants. Exposure to POPs during early life stages

may result in effects not only *in utero* and childhood but also at later stages. Some effects may manifest only after a latency period, during adolescence or adulthood. These later effects may be difficult to attribute to POPs exposure because of the long period of time that has passed. The timing of exposure, and whether it occurs during a developmental "critical window of vulnerability", is considered to be a crucial factor in determining the nature of the health effect.

Mass poisoning incidents have shed light on the effects of exposure to high concentrations of POPs. Other than mass poisonings, however, the effects generally are subtle. Some adverse effects have been shown to occur in experimental animals exposed to concentrations close to those that are commonly found in humans. Experiments in laboratory animals allow researchers to identify the effects of the exposure to a single persistent chemical. Such experiments, however, do not completely reflect real life exposures that consist of multiple exposures to POPs and other chemicals beginning before birth. Although clinical effects may be different in humans when compared to animals, results of animal experiments are the best way to understand the toxic effects of POPs and other chemicals under controlled conditions.

POPs are globally dispersed and therefore, their resulting health risks cannot be managed only by individual countries' regulations. Therefore, the United Nations Environment Programme's (UNEP) governing council set up an international negotiating committee that led to an international agreement to phase out production, use, and release of POPs. The Stockholm Convention on Persistent Organic Pollutants was adopted in 2001 and came into force in May 2004; as of 2 November 2010, there were 172 Parties and 151 signatories to the Convention (Stockholm Convention website). The Convention aims to protect human health and the environment from POPs by eliminating and reducing the worldwide production, use and emission of POPs. The Convention began by targeting an initial list of 12 "Dirty Dozen" pesticides, industrial chemicals and by-products(see Table 1). Although banned in many developed countries, some of these POPs are still present in polluted sites or illegally placed into commerce and used in certain developing countries. In May 2009, 9 additional chemicals were added to the list of POPs. The entry into force of amendments adding these 9 chemicals to the Stockholm Convention took place on 26 August 2010. Many of these so-called "living chemicals" are still produced and in use. Their elimination is made difficult because

there may not be complete information about where these chemicals are present, how to replace them, and how stakeholders may implement successful actions to reduce exposure.

Several other classes of chemicals with characteristics similar to POPs – called persistent toxic substances (PTS) or persistent, bioaccumulative, and toxic (PBT) substances – remain in frequent worldwide use.

Healthcare providers who care for men and women of childbearing age, pregnant women and children may not be fully aware of POPs and their potential effects on children's health, growth and development. There is a need to raise awareness in the health sector about the scientific knowledge and concerns raised by widespread exposure to low levels of these chemicals and their important effects on health. This document will review the range of chemicals classified as POPs with an emphasis on children's health. It will discuss exposure beginning at conception, sources of exposure, effects of high-dose exposures, and concerns about effects of chronic low-dose exposures. Our goals include increasing the medical community's awareness about preventive actions and advocacy aimed at reducing the exposure of young men and women of childbearing age, pregnant women, and children to POPs.

II. Background

1. What are Persistent Organic Pollutants?

Persistent organic pollutants (POPs) are manmade organic chemicals that are among the most hazardous compounds ever synthesized. Many

Table 1
Initial POPs Listed Under the Stockholm Convention

Pesticides	Aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, toxaphene
Industrial chemical	PCB
Unintended by-products	Dioxins, furans

http://www.pops.int/documents/pops/default.htm

POPs are polyhalogenated hydrocarbons that contain chlorine, bromine, or fluorine. POPs include pesticides, industrial chemicals, chemicals used in consumer products, and by-products of certain manufacturing and combustion processes. The characteristics of POPs result in concern for human and other species' health and the global environment because

POPs:

- have long half-lives and so persist in the environment for years or decades;
- bioaccumulate and biomagnify, penetrating the food chain – that is, they concentrate at higher levels as they make their way up the food chain, thus polluting and exposing all living things, including humans;
- are dispersed globally, travelling in air and water currents and in living organisms;
- are linked with serious health effects in humans and other living organisms (UNEP, 2005).

Most POPs are lipophilic – that is, they have a tendency to remain in adipose (fat) tissue. POPs have been measured in a range of living organisms (UNEP, 2005). POPs have been measured in human blood, body fat and breast milk in studies around the world. Because these chemicals are not well metabolized or excreted, even small doses ingested daily accumulate to measurable amounts over time.

2. The "Dirty Dozen" and other persistent chemicals

In 1995, recognizing the great concern about these chemicals because of mounting evidence of toxicity, governments began discussion of an international agreement on POPs. The Stockholm Convention on Persistent Organic Pollutants was adopted in May 2001 with the aim of protecting human health and the environment from POPs, targeting an initial 12 POPs (known as the "Dirty Dozen"). Most of these were pesticides; the others were industrial chemicals or unintended by-products of industrial and combustion processes (WHO, 1995). The Convention came into force in May 2004. **Table 1** lists the initial 12 POPs. In May

1 The Stockholm Convention established a subsidiary body of government-designated experts to evaluate candidate POPs as outlined in Article 8 and Annexes D, E, and F of the Convention. The process applies the precautionary principle by recognizing that lack of full scientific certainty should not prevent a candidate substance from proceeding through the process. In October 2009, 3 chemicals – endosulfan, hexabromocyclododecane, and short-chained chlorinated paraffins – were under review.

2009, governments agreed to list 9 additional substances as POPs under the Convention.

Several other regional and global conventions have put forward the goals of identifying hazardous substances and taking global action to protect human health and environment. These include the Aarhus Protocol on Persistent Organic Pollutants to the Long-Range Transboundary Air Pollution Convention (LRTAP), the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal, and the OSPAR (Oslo-Paris Convention for the Protection of the Marine Environment of the North-East Atlantic).

Criteria for evaluating persistence, bioaccumulation, toxicity, and long-range transport characteristics of substances are not harmonized. International conventions, however, share large similarities in defining POPs. Numerous expert groups are working to establish criteria for adding new chemicals with characteristics similar to POPs. These chemicals are referred to as Persistent Bioaccumulative and Toxic (PBT) substances or Persistent Toxic Substances (PTS). While not included as part of the initial "Dirty Dozen" list, PTS are also of concern because of their high toxicity to health and the environment. Some of these chemicals are under review of the Persistent Organic Pollutants Review Committee (POPRC)[1].

3. How POPs enter the environment

POPs originate mainly from uses in industrial processes, waste incineration and agriculture. POPs are released into air, water and land and then enter the food chain. They are globally distributed through the air, and ocean currents, travelling long distances via air–water exchange and cycles involving rain, snow and dry particles. They are transported in food and other products containing POPs. They are also transported by polluted living organisms. They are thus found in places far away from industrial sites or from agricultural areas where they were released, migrating north and south to areas such as both Poles, exposing remote populations of humans and animals, especially those that depend on aquatic foods (Arctic Monitoring and Assessment Programme, 1998).

III. Impacts of POPs on wildlife and humans

1. Persistence in the environment, effects on birds and other species

Dichloro-diphenyl-trichloroethane (DDT), one of the original "Dirty Dozen" POPs, is an organochlorine pesticide that was used in agriculture and public health. DDT is often used to refer to related compounds DDE dichloro-diphenyl-dichloroethylene and DDD dichlorodiphenyldichloroethane**.** These are present in technical grade DDT and are also breakdown products of DDT.

DDT, first synthesized in 1874, was widely used for many years. It was used as an insecticide during World War II to protect soldiers and civilians from malaria, typhus, and other vector-borne diseases. DDT was at first considered to be a wonder chemical until evidence began to emerge about unintended adverse effects on non-target flora and fauna. The earliest data on unexpected reproductive risks came in the early 1950's. Endocrine disruption was widely publicized by Rachel Carson in "Silent Spring" (Carson, 1962). In 1962, Carson wrote about pesticides – especially DDT – as the main cause of a decline of birds singing in the eastern US, and also as the cause of mass songbird mortalities. Heavy and repetitive use of the pesticide is highly toxic to birds. DDT was aggressively used to kill the beetles that spread Dutch Elm disease; this resulted in the bioaccumulation of DDE in earthworms. The levels were high enough that robins and other songbirds ingesting the earthworms received lethal doses, resulting in large losses of birds (Fry, 1995). Even after DDT was banned in 1972 in the USA, DDT-thinned eggshells continued to put many bird species – including bald eagles – at risk of extinction (Raloff, 1994) as eggshells cracked under the weight of mother birds. Reproductive abnormalities in seagulls exposed to large amounts of DDT included feminization of their reproductive tracts.

Abnormalities in other species exposed to other POPs began to be observed. Laboratory studies on white suckers (bottom-breeding fish that inhabit North America) showed that fish exposed to paper mill effluent

Table 2
POPs Listed by the Stockholm Convention

	Uses	Studies in Animals	Acute Human Toxicity	Chronic Human Toxicity	IARC Cancer Classification*	Comments	References
Chemicals listed under Annex A (Elimination) in the Stockholm Convention							
Aldrin	Control of soil pests	Acute toxicity in fish and mammals. Effects on CNS, liver, endocrine and immune systems. Some studies showed reproductive effects, estrogenic properties, and immune system effects in laboratory animals or wildlife.	CNS effects e.g. headache, irritability dizziness, nausea, vomiting, tremors, excitation, convulsions, loss of consciousness, respiratory and CNS depression, possible death.		3		ATSDR 2002a WHO 1989a WHO 1992 IARC 1987a WFPHA 2000 WHO 1989b
Chlordane	Termite control; insecticide for crops			Possible endocrine disrupter	2B	Concern about transfer to fetus and to infant via breast milk	ATSDR 2002b WHO 1984a IARC 1991 IARC 2001
Chlordecone	Agricultural insecticide, miticide, fungicide				2B	neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity, and liver cancer.	UNEP 2007a
Dieldrin	Control of soil pests; tropical disease vector control (tse-tse flies)	Similar to Aldrin	Similar to Aldrin		3		ATSDR 2002a WFPHA 2000

	Uses	Studies in Animals	Acute Human Toxicity	Chronic Human Toxicity	IARC Cancer Classification*	Comments	References
Endrin	Insect and rodent control	Similar to Aldrin	Similar to Aldrin		3		ATSDR 1996 WHO, 1989 WHO, 1992 IARC 1987b WFPHA 200
Heptachlor	Kills insects, termites				2B	Heptachlor metabolized in soils, plants and animals to heptachlor epoxide, which is more stable	ATSDR 2007 WHO 1984b IARC 1991 IARC 2001 WHO 2006c
Hexabromobiphenyl (HBB)	Brominated compound part of a wider group of polybrominated biphenyls (PBBs) used as flame retardants in synthetic fibres, plastics.	Acute and chronic effects and cancer produced in animals		May disrupt endocrine system	Possible human carcinogen		UNEP 2006a Stockholm Convention 2006
Hexabromodiphenyl ether and heptabromodiphenyl ether (commercial octabromodiphenyl ether)	Mixture of several polybrominated diphenyl ethers and congeners (PBDEs) used as flame retardants. Components typically consist of Penta, Hexa, Hepta, Octa, Nona & Deca bromodiphenyl ether isomers	Wild populations are co-exposed to a mixture of PBDEs and other related brominated and chlorinated POPs. Therefore studies can demonstrate associations but not cause-effect relationships between the exposure/ accumulation of components of commercial OctaBDE mixtures and potential adverse effects observed in wildlife.		Because people are exposed to mixtures of PBDEs, human health studies cannot provide conclusive evidence of the hazards of Hexa- to Nona-BDE at environmentally relevant exposure levels.		Within the EU, classified as "Toxic", due to effects on human health, with the risk phrases "may cause harm to unborn child", and "possible risk of impaired fertility". The possible formation of PBDD & PBDF during combustion or other high temperature processes involving c-OctaBDE is a cause of concern	UNEP 2007b WHO 2006a

	Uses	Studies in Animals	Acute Human Toxicity	Chronic Human Toxicity	IARC Cancer Classification*	Comments	References
Hexachlorobenzene (HCB)	Wood preservative, fungicide. Used as an intermediate in manufacturing of synthetic rubber, dyes, pesticides. Produced unintentionally as a byproduct during manufacture of i chemicals and pesticides or resulting from incineration of chlorinated compounds,	Adverse effects on the liver (porphyria cutanea tarda), kidneys, skin, immune system, and blood.	After contamination of seed wheat in Turkey (1956-61), porphyria developed in adults, "pink sore" and death in nursing infants,		2B		ATSDR 2002c WHO 1997
Alpha-Hexachlorocyclohexane (alpha-HCH)	By-product of lindane production	Fatty degeneration and liver necrosis; effects on kidney & immune system	CNS toxicity reported in exposed workers. Inhalation may lead to nose, throat irritation	Exposure increases breast cancer risk; hormonal disorders	2B	Concern that workers might develop liver & kidney toxicity after prolonged occupational exposure.	UNEP 2007c
Beta-Hexachlorocyclohexane (beta-HCH)	Formerly used in agriculture	Effects on liver, kidney	CNS toxicity, GI disturbances		Listed as possible human carcinogen by US EPA 2B	Placental transfer in humans is documented; Breast milk is exposure source	UNEP 2007d
Lindane (gamma-hexachlorocyclohexane, γHCH)	Broad-spectrum insecticide in agriculture; used against ticks and fleas; head lice	Reproductive effects (e.g. reduction in egg production in birds). May disrupt endocrine system.	Ingestion by children has led to neurological effects (vomiting, tremors, seizures) and deaths. Convulsions in adults and children reported after excessive topical application.		2B	Used in small amounts (1%) for human head lice, scabies. Approved for 2nd-line treatment when 1st-line therapies fail, not tolerated	ATSDR 2005 WHO 1991 JMPR 2002 UNEP 2006b

	Uses	Studies in Animals	Acute Human Toxicity	Chronic Human Toxicity	IARC Cancer Classification*	Comments	References
Mirex	Control of fire ants and other ants. Fire retardant	Moderate acute toxicity in mammals and is toxic to fish. There is evidence of potential endocrine disruption mediated effect			2B		ATSDR 1995b WHO 1984c
Penta chlorobenzene (PeCB)	Past use as pesticide, flame retardant, and combinated with PCBs in dielectric fluids. Not clear whether still used as a pesticide or flame retardant on its own; however, PeCB can be found as an impurity of pentachloronitrobenzene (quintozene) and other pesticides	Acute and subchronic toxicity to the liver and kidney. PeCB has teratogenic effects in mammals at high doses. Suckling pups developed tremors, and in pregnant female rats the mean foetal weight decreased in the highest dose group. Acute and chronic adverse effects seen in exposed marine and freshwater organisms at low concentrations.				Classified within EU as "Harmful if swallowed" and "Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment".	UNEP 2007e
Polychlorinated biphenyls (PCBs)	Primarily used in electrical industry, also as additives in paint, carbonless copy paper, sealants and plastics. Still exist in transformers, capacitors	Rats that ate food containing high PCB levels for two years developed liver cancer.	Skin conditions are the most commonly observed effects in those exposed to large amounts of PCBs.	Children prenatally exposed may have developmental and endocrine effects, or may weigh less at birth.	2B	Completely destroyed only under extremely high temperatures (over 1100 °C) or in presence of certain combinations of chemicals and heat. When PCBs in transformers are involved in fires, combustion can result in production of highly toxic PCDD, PCDF.	ATSDR 2000 WHO 1993 UNEP 2006c

	Uses	Studies in Animals	Acute Human Toxicity	Chronic Human Toxicity	IARC Cancer Classification*	Comments	References
Tetrabromodiphenyl ether andpentabromodiphenyl ether (commercial pentabromodiphenyl ether)	Mixture of bromodiphenyl ether congeners, mainly BDE-99 and BDE-47. PBDE is used for the generic term polybromodiphenyl ether, covering all congeners of the family of brominated diphenyl ethers (BDEs). The most common use has been as fire retardant in polyurethane foam.			Some studies have demonstrated reproductive toxicity, neurodevelopmental toxicity and effects on thyroid hormones (Lilienthal, McDonald). The neurotoxic effects of PBDEs are similar to those observed for PCBs and so children exposed to PBDEs are likely to be prone to subtle but measurable developmental problems.		Pregnant women, embryos and infants, may be more vulnerable because of effects on thyroid hormone balance, and central nervous system development.	UNEP 2006d
Toxaphene (camphechlor)	Agricultural insecticide, tick & mite control in livestock	Highly toxic in fish; strong evidence for endocrine disruption. Animal carcinogen			2B		ATSDR 2010 WHO 1984d WHO 1990
Chemicals listed under Annex B (Restriction) in the Stockholm Convention**							
DDT	Control of insects causing malaria, typhus, and other vector-borne diseases. Agricultural use.	Harmful effects in wildlife include thinning of eggshells in birds, feminization and altered sex ratios, impacts on the nervous system and behaviour. Oral exposure in laboratory animals may -> liver cancer		A range of effects reported in laboratory animals have not been confirmed in human studies.	2B	May be used for malaria control (against anopheles mosquito) as recommended by the WHO.	ATSDR 2002d IPCS 1995 WHO 2007 JMPR 2000

	Uses	Studies in Animals	Acute Human Toxicity	Chronic Human Toxicity	IARC Cancer Classification*	Comments	References
Perfluorooctane sulfonate (PFOS)	PFOS-related chemicals used in products such as surface treatments of fabric for soil/stain resistance, coating of paper, and in specialised applications such as fire fighting foams.	Appears to be of low toxicity to fish but more toxic to other aquatic organisms. Evidence of high acute toxicity to honey bees. Studies in experimental animals show that exposure results in liver and thyroid tumours.		Studies of workers have shown an association between exposure and the incidence of bladder cancer			UNEP 2006e OECD 2002
Chemicals listed under Annex C of the Stockholm Convention-POPs (unintentionally produced chemicals)**							
Polychlorinated dibenzo-p-dioxins (PCDDs) and Polychlorinated dibenzofurans (PCDFs)	Often referred to as dioxins and furans, PCDDs and PCDFs have never been intentionally used or manufactured for reasons other than laboratory purposes. Unintentionally formed during manufacture of certain pesticides and other chemicals and as product of incineration and open burning of chlorinated substances and plastics. Have been found in automobile exhaust, tobacco smoke, wood and coal smoke and waste burning. Formed at very low yield, during paper bleaching and waste incineration. Open burning of waste is the main source in many regions.	Much information on the toxicity of these chemicals is based on extensive studies in experimental animals of the most toxic member of the family – 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Animal studies have shown reproductive and developmental effects, including reduced viability, structural alterations, growth retardation and functional alterations. There is evidence of neurobehavioural effects and effects on immune and endocrine functions, including thyroid function.	Contamination of rice oil in Japan in 1968 led to "oil disease" in adults; exposed fetuses developed physical and neurological abnormalities. Similar effects occurred in Taiwan in 1979.	TCDD and related compounds can produce a wide variety of effects in animals and might produce many of the same effects in humans	2,3,7,8-TCDD is the most toxic of all dioxin compounds, and is carcinogenic to humans based mainly on studies of cases involving accidental or occupational heavy exposure.	Because of this evidence in animals, particularly at high doses but in some cases at doses close to those with relevance for human beings, there is concern about the potential for these same effects to occur in humans, especially the effects of prenatal exposure	UNEP 2006

	Uses	Studies in Animals	Acute Human Toxicity	Chronic Human Toxicity	IARC Cancer Classification*	Comments	References
Hexachlorobenzene (HCB)	Wood preservative, fungicide. Used as an intermediate in manufacturing of synthetic rubber, dyes, pesticides. Produced unintentionally as a byproduct during manufacture of i chemicals and pesticides or resulting from incineration of chlorinated compounds,	Adverse effects on the liver (porphyria cutanea tarda), kidneys, skin, immune system, and blood.			2B		ATSDR 2002c WHO 1997
Pentachlorobenzene (PeCB)	Past use as pesticide, flame retardant, and combinated with PCBs in dielectric fluids. Not clear whether still used as a pesticide or flame retardant on its own; however, PeCB can be found as an impurity of pentachloronitrobenzene (quintozene) and other pesticides.	Acute and subchronic toxicity to the liver and kidney. PeCB has teratogenic effects in mammals at high doses. Suckling pups developed tremors, and in pregnant female rats the mean foetal weight decreased in the highest dose group. Acute and chronic adverse effects seen in exposed marine and freshwater organisms at low concentrations.				Classified within EU as "Harmful if swallowed" and "Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment".	UNEP 2007e
Polychlorinated biphenyls (PCBs)	Primarily used in electrical industry, also as additives in paint, carbonless copy paper, sealants and plastics. Still exist in transformers, capacitors	Rats that ate food containing high PCB levels for two years developed liver cancer.*	Skin conditions are the most commonly observed effects in those exposed to large amounts of PCBs.	Children prenatally exposed may have developmental and endocrine effects, or may weigh less at birth.	Probably carcinogenic to humans	Completely destroyed only under extremely high temperatures (over 1100 °C) or in presence of certain combinations of chemicals and heat. When PCBs in transformers are involved in fires, combustion can result in production of highly toxic PCDD, PCDF.	ATSDR 2000 WHO 1993 UNEP 2006c

¥ - Annexes to the Stockholm Convention require Parties to take certain measures with regard to POPs

- Annex A (Elimination) – Parties must take measures to eliminate the production and use of the chemicals listed under Annex A. Specific exemptions for use or production are listed in the Annex and apply only to Parties that register for them.
- Annex B (Restriction) – Parties must take measures to restrict the production and use of the chemicals listed under Annex B in light of any applicable acceptable purposes and/or specific exemptions listed in the Annex.
- Annex C (Unintentional Production) – Parties must take measures to reduce the unintentional releases of chemicals listed under Annex C with the goal of continuing minimization and, where feasible, ultimate elimination.

At its fourth meeting held in May 2009, the Conference of the Parties (COP) adopted amendments to Annexes A, B and C to list 9 additional chemicals as persistent organic pollutants under the Stockholm Convention (http://chm.pops.int/Convention/The%20POPs/tabid/673/language/en-US/Default.aspx)

* IARC Cancer Classifications

Group 1: Carcinogenic to humans
Group 2A: Probably carcinogenic to humans
Group 2B: Possibly carcinogenic to humans
Group 3: Not classifiable as to its carcinogenicity to humans) due to inadequate evidence of carcinogenicity in humans and limited evidence of carcinogenicity in experimental animals
Group 4: Not classifiable as to its carcinogenicity to humans

(often rich in dioxin and related compounds) took longer to mature, experienced reduced fertility and had lower than normal blood steroid concentrations. Alligators in Lake Apopka in Florida were feminized after exposure to large amounts of the pesticide difocol (whose chemical structure resembles that of DDT) spilled into the lake by the Tower Chemical Company. Reproductive activity in these alligators plummeted. Prenatal exposure to low levels of dioxins feminized the behavior of male rats during adulthood. Environmental estrogens were thought to contribute to reproductive problems plaguing Florida panthers (Raloff, 1994). Reproductive and immune effects were seen in Baltic seals exposed to polychlorinated biphenyls (PCBs)(Vos, 2000).

Many authorities state that it is important to accept that evidence of damage in wildlife is relevant to human health (Colborn, 1995). Adverse health effects associated with POPs exposure have been observed in high trophic level wildlife. The "wildlife-human connection" draws on the evidence of health effects in wildlife to predict the risk of adverse health effects in humans exposed to POPs. Although it is difficult to establish with complete certainty that POPs adversely affect humans, the accumulating "weight of evidence" strongly implicates that exposure to these chemicals results in endocrine and immune dysfunction, reproductive impairment, developmental abnormalities, and neurological function in many vertebrate species (Ross, 2001).

2. Studies in experimental animals

Experiments in laboratory animals often are used to study the effects of chemical exposure in controlled research situations. These experiments generally enable researchers to identify the effects of the exposure to a single persistent chemical. Although effects on health and behavior may be different in humans when compared to animals, results of animal experiments are often the best way to understand the toxic effects of POPs and other chemicals under controlled conditions. Some adverse effects have been shown to occur in experimental animals exposed to concentrations close to those that are commonly found in humans. These experiments, however, are not able to entirely reflect real life exposures that consist of multiple exposures to POPs and other chemicals beginning even before birth. Some of the research findings seen in animals exposed to POPs are listed in **Table 2.**

3. Human health effects

3.1 Effects of exposures to high levels of POPs

Exposure to high levels of POPs has resulted in serious adverse health effects. Porphyria affecting more than 4,000 people occurred in Eastern Turkey from 1956 through 1961 due to the ingestion of hexachlorobenzene added to wheat seedlings (Cripps, 1980). An estimated 3,000–4,000 people ingested bread prepared from grain treated with fungicides composed of 10% hexachlorobenzene at approximately 2 kg/1,000 kg wheat. While affected adults developed porphyria, nursing babies developed *pembe yara* (pink sore), a condition characterized by weakness, seizures and an annular rash. There was an extremely high rate of mortality in breastfed children (under 2 years of age) of mothers who ingested the bread. (Cam, 1960; Peters, 1976)

Mass poisonings also occurred in Asia when cooking oil was inadvertently mixed with heat- degraded PCBs, resulting in heavy contamination with polychlorinated dibenzofurans (PCDFs – partially oxidized PCBs). In 1968, about 1200 people in the Kyushu province of Japan ingested contaminated oil over 20 to 90 days. These people eventually developed "Yusho" (oil disease). Exposed people had reproductive dysfunction, severe chloracne, hyperpigmentation, eye discharge, headache, vomiting, fever, visual disturbances and respiratory problems. Thirteen women were pregnant at the time of exposure; one of their children was stillborn and pigmented ("cola-colored"). Some live-born children were small, hyperbilirubinemic, pigmented, had conjunctival swelling, and dilatation of the sebaceous glands of the eyelid. Up to 9 years later, the children showed apathy, lethargy, and soft neurologic signs. (AAP, 2003)

A similar outbreak of disease resulting from contaminated rice oil occurred in Taiwan in 1979. One hundred seventeen children born during or after this contamination were exposed to PCBs and PCDFs through their mothers' body burdens. They were examined in 1985 (and subsequently) and found to have ectodermal defects such as excess pigmentation, dental caries, poor nail formation, and short stature. They continued to have persistent behavioral abnormalities (Chen, 1994) and cognitive impairment. The delays were as severe in children born up to 6 years after exposure as in those born within a year or 2 of exposure in 1979. Older children (who were not exposed) resembled control children (Chen, 1992).

A chemical plant explosion in Seveso, Italy in 1976 resulted in the release

of large quantities of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), a congener of dioxin. The highest recorded serum levels of TCDD in humans occurred in children in the most heavily exposed areas. Children living in the area near the explosion had chloracne, most prominent on areas that were not protected by clothing; some had abnormal liver function tests (Mocarelli, 1986).

Approximately 20 million gallons of herbicides, including Agent Orange (equal mixture of 2,4,5T and 2,4 D), were used in Vietnam for defoliation and crop destruction between 1962 and 1971. (The term Agent Orange, came from the orange stripe on the 55-gallon drums in which it was stored. Other herbicides including Agent White and Agent Blue were used to a lesser extent). The health impacts observed in relation to Agent Orange exposure are thought to have been mostly due to TCDD contamination. Most studies of the health effects of Agent Orange focus on US veterans. Shortly following their military service in Vietnam, some veterans reported health problems attributed to exposure to Agent Orange or other herbicides (US Department of Veterans Affairs website). The Institute of Medicine (IOM) stated that there is sufficient evidence of a positive association between Agent Orange exposure and the development soft-tissue sarcoma, non-Hodgkin's lymphoma, Hodgkin's disease, chloracne and chronic lymphocytic leukemia (US Department of Veterans Affairs website). Other health effects in US Army Chemical Corps veterans include diabetes, hypertension, heart disease and chronic respiratory conditions (Kang, 2006). Many Vietnamese had greater exposure to Agent Orange; spraying with Agent Orange resulted in TCDD contamination detectable in adipose tissue and breast milk many years later (Schecter, 1995).

In 1999 in Belgium, 500 tons of animal feed were contaminated with PCBs and dioxins and distributed to animal farms in Belgium, France, Germany and the Netherlands. In Belgium, 2 million chickens had to be destroyed; neurobehavioral and cancer effects are expected in humans (van Larebeke, 2002).

3.2 Concern about human health effects of chronic exposure to low levels of POPs

POPs are toxic at high levels as illustrated by mass poisoning incidents. Exposure to high levels of POPS may cause adverse health effects including death, disease, and birth defects among humans and animals. Specific effects can include cancer, allergies and hypersensitivity, damage

to the central and peripheral nervous systems, reproductive disorders and disruption of the immune system. What remains less clear is whether significant adverse health effects can occur from background levels (Damstra, 2002a). Of most concern are possible effects of low levels on the developing fetus, infants and children. Low levels of other toxicants such as lead and mercury can have effects on children's development. For lead and mercury, lower levels of exposure, previously thought not to be harmful, are now understood to have lasting adverse effects (AAP, 2003). Low levels of POPs may similarly have effects in developing humans.

There is also increasing concern that chronic exposure to low levels of POPs may contribute to public health trends including increased cancer incidence (breast cancer and others), learning disabilities and other neurodevelopmental problems, and reproductive problems such as decreased sperm counts and quality, male genital anomalies, endocrine and immune diseases. (Aneck-Hahn N, 2007; Bhatia, 2005)

Epidemiological findings and experimental evidence available thus far suggest an association between low level chronic exposures to certain POPs and disease outcomes, and could also be relevant to other POPs. The effects of POPs and PTS are usually studied for one chemical, or a group of chemicals, at a time. However, exposure to multiple contaminants found in the environment could produce increased adverse effects by synergistic toxicity mechanisms (McLachlan, 1995).

3.3 Health effects in children

Several scientists state that data are not yet conclusive about the health effects of background levels of POPs in children: "Data exist that support harmful effects of POPs. Examples include associations with altered neurodevelopment, thyroid economy, and estrogen and immune function. Yet for all such associations, human evidence regarding causality at low doses remains equivocal at best, owing to inconsistent results, inadequate replication, and other questions. In the laboratory, the neurotoxic, immunotoxic, and hormonal activity of many of these compounds has been established, and the issue has been whether effects occur at background exposure levels, not whether the compounds are toxic" (Longnecker, 2001a). Other scientists concur that more research is needed before definitive conclusions can be reached (Damstra, 2002a, Kimbrough, 2001). An approach consistent with the precautionary principle, however, acknowledges that exhaustive proof of a substance's

toxicity should not be required due to the gravity of the short- and long-term toxic effects of low dose exposure. Lack of scientific certainty does not exclude a precautionary approach to managing chemicals in order to protect health and the environment "…when there are threats of serious or irreversible damage". (UNCED Rio Declaration, 1992).

3.4 . Neurodevelopmental effects

The information below highlights the potential vulnerability of the embryo, fetus and young child to POPs and emphasizes the possibility of prolonged neurotoxicity because of direct exposure of children or exposure of their parents.

The evidence for PCB effects on neurodevelopment is growing (Schantz, 2003). "Extensive evidence from animal studies shows that PCBs are neurotoxins, even at low doses" (Longnecker, 2003). Lower exposures to POPs have been evaluated in prospective cohort studies of fish-eating populations. These demonstrated adverse developmental and neurodevelopmental findings at significantly lower exposures than were experienced from mass poisonings.

In North Carolina in the US, a prospective cohort study found that infants exposed to higher *in utero* PCB concentrations were significantly more likely to be hyporeflexive (Rogan, 1986) and had seven-point lower scores, on average, on the psychomotor section of the Bayley Scales of Infant Development up to 24 months. The children had no detectable cognitive deficits at 5 years of age (Gladen, 1991).

In Michigan in the US, investigators examined the relationship between low-level PCB exposure from Lake Michigan fish and developmental outcomes in children. Women who consumed 12 or more kilograms (26 pounds) of Lake Michigan fish during the previous 6 years were interviewed, as were women who ate no fish. Children of women with higher PCB exposures showed negative effects of PCBs on memory in 7-month-olds (Jacobson, 1985) and 4-year-olds (Jacobson, 1990), and lowered IQs in 42-month-olds (Patandin, 1999a; Walkowiak, 2001) and 11-year-olds (Jacobson, 1996). Prenatal exposure to PCBs rather than exposure through human milk seemed to account for most of the findings (Walkowiak, 2001). There may be subclinical effects on newborn thyroid function (Brouwer, 1999).

A study in New York State in the US examined offspring of eaters and non-eaters of Lake Ontario fish. Negative effects of prenatal PCB exposure on visual recognition memory were described at 6 and 12 months of age (Darvill, 2000).

Because of great public concern about PCB contamination, the Dutch government initiated a prospective longitudinal study on possible adverse effects starting in the neonatal period. A cohort of 418 healthy pregnant women was recruited between 1990 and 1992. Half intended to breast feed for at least 6 weeks and half intended to formula feed. Milk lipids in infant formula are of vegetable origin with a negligible content of PCBs and dioxins. Exposure measures were maternal and cord blood, and breast milk. A "neurologic optimality score" (NOS) was developed based on neonatal reflexes and postural tone. Neuropsychological development was evaluated shortly after birth and at 3, 7, 18, 42 and 84 months of age. After adjusting for covariates, prenatal PCB exposure was *not* associated with poorer NOS in the immediate newborn period. Breast milk exposure to total PCBs and total dioxins was associated with poorer NOS; breast fed infants had more hypotonia (Huisman, 1995a). Breast milk may have a role in poorer outcome or may be a more reliable marker for prenatal exposure. The authors stressed that the abnormalities were "very minor" and that there are numerous advantages of breast feeding. When children were examined at 18 months (Huisman, 1995b) and 42 months (Lanting, 1998), transplacental exposure to PCBs was associated with small neurological deficits; neither PCB nor dioxin exposure via breast milk was associated with a poorer outcome. Lower scores on the Dutch version of the Bayley Scales of Infant Development (a frequently used standardized test of infant cognitive development) were seen in 3 month-old infants exposed to higher PCB levels *in utero* (Koopman-Esseboom, 1996). There were no effects of prenatal exposure to PCBs or dioxin seen at 7 months or at 18 months. There were no adverse effects seen of prenatal or lactational PCB exposure on neurological function at 42 months of age (Lanting, 1998) although cognitive function was impaired (Patandin, 1999a). In school-aged children, negative effects of prenatal PCB and dioxin exposure on cognitive and motor abilities were seen when parental and home characteristics were less optimal but these effects were not measurable in children raised in more optimal environments.

In California, a prospective cohort of 360 pregnant Mexican immigrants exposed to DDT and DDE showed lower MDI (mental development

Table 3

Some Endocrine Disrupting Effects of POPs and Selected Other Chemicals* (www.who.int/ceh/capacity/POPs.pdf)

Effect	
Estrogenic	**DDT, dieldrin,** endosulfan, methoxychlor, **PCBs,** alkylphenols, phthalates, mycotoxins, phytoestrogens
Anti-estrogenic	**Dioxins, PCBs,** phytoestrogens
Anti-androgenic	**DDT,** vinclozolin
Anti-thyroid	**PCBs, dioxins**
Anti-progestins	**PCBs, DDT**

This table illustrates the complexity of effects that may be caused by different chemicals, and the fact that the same chemical may have different effects. For example, DDT may have estrogenic, anti-estrogenic or anti-progestin effects. Phytoestrogens (estrogens contained in plants) may be estrogenic and anti-estrogenic.
*Chemicals listed in BOLD are POPs

index) on Bayley scores at 6 and 12 months but not 2 years of age. The author concluded that prenatal exposure to DDT, and to a lesser extent DDE, was associated with neurodevelopmental delays during early childhood although breastfeeding was found to be beneficial even among women with high levels of exposure (Eskenazi et al, 2006).

Polybrominated diphenyl ethers (PBDEs) are persistent bioaccumulative compounds widely used as flame retardants. Prenatal PBDE exposures were examined in relation to children's subsequent neurodevelopment in a longitudinal cohort study of pregnant women initiated after 11 September 2001. After adjusting for possible confounding factors, researchers demonstrated that children had statistically significant adverse effects in their mental and physical development in relation to cord blood PBDE concentrations (Herbstman, 2010).

3.5 Endocrine effects

"Endocrine disruptors" are exogenous synthetic or natural chemicals that when absorbed into the body can mimic, modify or block the action of naturally occurring hormones. Endocrine disruptors bind to cellular hormone receptor sites such as estrogen, androgen and thyroid receptors. The binding chemicals vary in strength and effect. "Endocrine disruption" also concerns complex processes involving multiple hormones, such as pubertal growth and development. In 1999, the United States National

Academy of Sciences issued "Hormonally Active Agents in the Environment" listing chemicals that have been tested for estrogenicity. These included many common pesticides, plastics and industrial compounds (National Research Council, 1999). Estrogenicity is the most well- known endocrine disruption effect of chemicals but DDE is an anti-androgen (Kelce, 1995), and some pesticides and PCB congeners can occupy the thyroid receptor (Rickenbacker, 1986). Some of the endocrine effects of POPs and other chemicals are listed in **Table 3**. In 2002 the International Programme on Chemical Safety (IPCS) of the WHO/UNEP/ILO published a global assessment of the state of scientific knowledge relative to environmental endocrine disruption (IPCS, 2002). This publication is in process of being updated.

Several studies of the effects of POPs on endocrine function in children have been summarized (Rogan, 2003). In a US study of background exposure to PCBs and DDE, adolescent boys who had higher prenatal background exposure were taller (difference in adjusted mean height = 6.3 cm) and heavier (difference in adjusted mean weight = 6.9 kg) than boys with lower exposure; there was no effect on the age that puberty was attained. Lactational exposure to DDE had no effect; there was also no effect of prenatal or lactational exposure to PCBs. In white girls, the highest prenatal PCB exposures were associated with higher weights (an average of 5.4 kg). There was some suggestion that girls with the highest prenatal exposures reached puberty sooner.

A change in sex ratio of newborns was observed after the 1976 factory explosion in Seveso, Italy, that released 1 kg of the extremely toxic dioxin congener TCDD. In 1996, it was observed that 48 girls but only 26 boys were born to most exposed families between 1977 and 1984. Subsequent data showed that the decrease in male births occurred only in families in which the men had been exposed before the age of 19, suggesting a preconception effect on sperm (Mocarelli, 2000).

Two studies of child development related to background exposure to PCBs showed a relationship of higher prenatal exposure and hypotonia at birth (Jacobson, 1984). This is thought to be due to the effects of PCB on the thyroid gland (Collins, 1980).

In the Taiwan rice oil poisoning, adolescent males exposed prenatally to PCBs and PCDFs had normal progression through puberty but had smaller penises when compared to a non-exposed group (Rogan, 1988).

Adolescent girls were unaffected (AAP, 2003). Another study showed decreased sperm motility in the exposed group (Guo, 2000).

Evidence linking duration of lactation with DDT and DDT is inconsistent (Cupul-Uicab, 2008; Rogan, 200). In Limpopo, researchers found that significantly higher levels of DDT in some men living in houses sprayed with DDT (compared to men living in houses that were not sprayed) were associated with adverse effects on male reproductive health, ie while the average sperm parameters were in the "normal" WHO range for infertility, many individual values were lower than the average considered by Andersson et al 2008 to indicate impaired fertility. A recent study by Bornman et al on urogenital malformations in newborn boys suggests increased rates of malformations among those women who lived in DDT treated areas, however no dose response information was available (Bornman et al, 2010).

Obesity has recently been proposed as another adverse health effect of exposure to endocrine disrupting chemicals, including some POPs, during critical stages of development. Data suggest that fat cells and mechanisms involved in weight homeostasis may be affected by endocrine disruptors early in life and lend support to the concept that diseases manifesting in adulthood may have their origins in early life (Newbold, 2008)

3.6 Diabetes

Low-level exposure to some POPs has been linked with an increased risk of diabetes. Associations of serum concentrations of POPs with diabetes prevalence were investigated in 2,016 adult participants in the National Health and Nutrition Examination Survey (NHANES) between 1999–2002. Six POPs (2,2,4,4,5,5-hexachlorobiphenyl, 1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin, 1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin, oxychlordane, p,p_dichlorodiphenyltrichloroethane, and trans-nonachlor) were selected because they were detectable in at least 80% of participants. Compared with subjects with serum concentrations below the limit of detection, after adjustment for age, sex, race and ethnicity, poverty-income ratio, BMI, and waist circumference, diabetes prevalence was strongly positively associated with lipid-adjusted serum concentrations of all six POPs (Lee, 2006). This association warrants further investigation.

3.7 Immunologic effects

Research in animals has shown that dioxin exposure is associated with thymic

Table 4
Possible Routes of Exposures at Each Life Stage

	Pre-conception	Trans-placental	Breast Milk	Ingestion: Food	Ingestion: – Soil, dust, mouthing of objects	Inhalation	Dermal	Intravenous: Leaching from medical products
Ovum/sperm	X							X
Fetus		X						X
Infant			X	X	X	X	X	X
Toddler			X	X	X	X	X	X
Child				X	X	X	X	X
Adolescent				X		X	X	X
Adult				X		X	X	X

Table 5
Major Sources of Human Exposure

Source	How POPs enter body
Food	Deposited in waterways, taken up by invertebrates, accumulate in fish and animals eaten by people; pesticide residues in foods.
Soil	Transported by air currents and storm systems. Deposited through contact with solid surfaces or through precipitation then ingested or absorbed through skin.
	Persistent soil residues of banned pesticides such as DDT, dieldrin are ingested or absorbed through skin
Indoor environment	Building materials, furniture, textiles carpets and curtains, packing materials, electric and electronic appliances containing PBDEs.
Toys, other objects	Chemical released when object is mouthed
Air	Inhalation of fumes from burning of items containing PCBs, PBDEs. Heating of transformers, waste burning in the open.
Leaching from medical products	Phthalates are examples of chemicals (not considered POPs) that may leach from intravenous tubing attached to patients.

atrophy, down-regulation of cytotoxic T- or B-lymphocytic differentiation, poorer antibody response and reduced lymphocytic activation (Thundiyil, 2007). A study of Inuit children revealed a significant association between elevated prenatal pesticide exposures to hexachlorobenzene and a higher incidence of otitis media in the 1st year of life (~50% increase) (Dewailly, 2000). A significant negative association between serum dioxin levels and plasma immunoglobulin G (IgG) was still evident 20 years after exposure during the Seveso accident, with a nearly 25% difference in IgG levels between the highest and lowest exposed quartiles (Baccarelli, 2002).

3.8 Cancer

Dioxin has been classified as a known human carcinogen (NTP, 2005). Within the listing of substances classified as "reasonably anticipated to be a human carcinogen" are DDT, hexachlorobenzene, furan, mirex, PBBs and PCBs. The International Agency for Research on Cancer (IARC) classified these substances (except PBBs) as 2 B – possibly carcinogenic to humans. Studies of the Taiwanese cohort exposed to PCB-contaminated rice oil documented excess mortality from many cancers, especially of the liver and lung (Thunyidil, 2007). There are no studies of the relationship of cancer to prenatal, infant or childhood exposures to POPs. Because children have a long life span, however, there is concern that health effects might manifest later in life, after long latency periods.

IV. Routes and sources of exposure to POPs

1. Ingestion, inhalation, dermal exposure

People may be exposed to POPs through the routes of ingestion, inhalation, and dermal contact. Children are additionally exposed prenatally beginning at conception, then through the placenta because of the mother's previous or current exposures. Infants are exposed through breastfeeding. Preconception exposures also are a concern. Routes of exposure at different life stages are listed in **Table 4**; sources of exposure are listed in **Table 5**.

The main route of exposure for most people in the general population is through ingestion of food. Fruits, vegetables, and grains contain small amounts of POPs; the highest exposure source is from animal fats.

POPs often enter the food supply through waterways, via air transport, and through persistent residues in soil. When released into rivers, lakes and oceans, POPs collect in sediments and are then ingested by small invertebrates at the bottom of the food chain. Once inside these organisms, POPs accumulate in fatty tissues. Fish that eat pesticide-contaminated invertebrates accumulate greater amounts of chemicals. A large, mature fish is likely to contain higher residues. Because of this biomagnification, the highest concentrations are found in animals at the top of the food chain: humans, predatory birds, seals and other predatory animals. POPs are also transported long distances in the bodies of migratory species (birds, fish and mammals).

POPs enter soil through a process of transport by air currents and storm systems – sometimes over great distances – and deposition through contact with solid surfaces or through precipitation. Persistent soil residues of pesticides such as DDT and dieldrin, banned for decades in most countries, are another source of POPs. Due to their persistent and long range transport characteristics POPs pesticide residues can be found in foods even in countries where their use have been banned a long time ago. For this reason the Joint FAO/WHO Food Standards Programme, Codex Alimentarius Commission Codex Committee on Pesticide Residues (CCPR) sets maximum residue levels (MRLs) for POPs pesticides (FAO/WHO, 1997). Stockpiles of POPs that are not securely disposed of or destroyed are another source of exposure (UNEP, 2002).

Not only is ingestion an important route of exposure for POPs pesticides in the general population, but ingestion is also an important source of exposure for the general population's exposure to PCBs and dioxins. PCBs are still in use in transformers in many countries and awaiting replacement. In many cases, high amount of PCBs are still not being destroyed or safely disposed of. The deadline for implementation of the POPs Treaty for PCBs is in 2025. In many regions, dioxins are often produced from the open burning of waste or from incinerators, resulting in a major source of exposure for many communities. Harrad et al. (2004) found significant levels of PBDEs in the diets of both vegans and omnivores. MacIntosh et al. (2001) analyzed 379 solid food samples for 10 pesticides, and found DDE in 21% of samples. The Institute of Medicine (IOM, 2003) published a report on "Dioxins and Dioxin-like Compounds in the Food Supply", and found significant levels of dioxins and PCBs in almost all foods containing animal fats. Even vegetables and grains were found to

contain measureable levels of these compounds, but at lower levels than in meats, fish and dairy products. One major factor contributing to the relatively high levels of dioxins and PCBs in animal fats is the common practice in some regions of feeding waste animal fats back to the food animals; these fats contain contaminants that have accumulated over time. While cow fat is no longer fed to cows because of mad cow disease (also known as bovine spongiform encephalopathy, BSE), it is fed to pigs and chickens, but this is not a global practice. Pig, chicken and fish fats are often fed to other food animals, carrying with them contaminants that have accumulated in the food supply over many years.

People relying on contaminated species for subsistence foods (e.g. Inuit populations in northern Canada and Greenland, and women from the Faroe Islands) have been shown to have higher levels of exposure to POPs (Ross, 2000; Fangstrom, 2000). Sports fishermen and heavy consumers of fatty fish in contaminated areas have been shown to have high residues of POPs (Jacobson, 1996; Svensson, 1995).

High risk situations from higher level exposures may be experienced by adults when they work with POPs (such as certain pesticides). High risk situations may also be experienced by children whose parents are occupationally exposed, who are involved in unusual chemical accidents or disasters or their abatement, populations that live near heavily polluted sites (POPs stockpiles) or where waste is burned in the open or incinerated, and in populations whose diets rely heavily on foods high on the food chain such as the Arctic Inuits who base their nutrition on the consumption of marine mammals.

In the field of public health only 2 POPs pesticides (DDT, lindane) are used. DDT is used in indoor residual applications for the control of vector-borne diseases control (e,g, malaria, leishmaniasis). In some countries, lindane and DDT were used as wood preservatives, and were detected in hair of pre-school children. (Neuber, 1999) Lindane is still used widely as a pharmaceutical agent primarily for the treatment of head lice. Alternatives for lindane are generally available. It is still used as a human pharmaceutical in second line treatment to control head lice and scabies.

The PBDEs pose potential problems because they are widely used in household products such as rugs, upholstery, curtains, and electronics, and have many other uses. The major route of exposure to humans appears to be through inhalation of indoor air and exposure to household dust.

(Rudel, 2003; Jones-Otazo, 2005) Levels of PBDEs in blood and breast milk the US population appear to be significantly greater than those found in Europe and other developed countries (Schecter, 2005). The health effects of PBDEs are only beginning to be understood, but PBDE's are known to be endocrine disruptors and have neurologic toxicity. (Rudel, 2003) PBDEs and other POPs are also found in many e-waste components. As e-waste is exported and recycled in many developing countries, children, particularly scavengers, are increasingly exposed Alternatives for some uses of PBDEs have not been clearly identified or available. This situation has led some governments and sectors to request that these chemicals be exempt from the POPs treaty. Although they have been widely used for a long time, PBDEs are not well labeled in products, thus posing an important problem for safe disposal. This situation may also complicate the implementation of actions designed to apply the POPs Treaty globally.

2. Breast milk exposure

Nursing infants are exposed to POPs through breast milk. DDT was first reported in breast milk in 1951 (Laug, 1951) and since then, uncontaminated milk has not been found (Longnecker, 2001a). Because DDT is still used to control malaria epidemics in endemic regions that do not have access to other effective alternatives, people living in these areas are still at high risk of direct exposure. Pollutants including hexachlorobenzene, dieldrin, heptachlor, chlordane, and PCBs are commonly found in the breast milk of women who do not have occupational exposures or other unusual exposures (Solomon, 2002).

Lipophilic POPs are transferred into human milk because of its high fat content. Human milk is the major dietary source of POPs for nursing infants. The quantities transferred are up to 20% of the maternal body burden, much larger than are found in infant formula. The nursing infant is left with a detectable body burden of pollutants for years (Niessen, 1984). An infant breastfeeding for 6 months may receive as much as 14% of his or her cumulative lifetime exposure of dioxins and PCBs (Patandin, 1999b). This exposure may contribute significantly to the body burden when the infant attains adulthood and reproductive years.

Fortunately, POPs concentrations have fallen as a result of decreasing use. Swedish investigators reported on trends for organochlorine compounds in breast milk in women living in the Stockholm region (Noren, 2000).

They measured PCBs, polychlorinated naphthalenes (PCNs), PCDDs, PCDFs, PBDEs, pesticides (DDT, DDE, hexachlorobenzene, dieldrin) and methylsulfonyl metabolites of PCBs and DDE in human milk sampled during different periods between 1967 and 1997. Levels of organochlorine compounds in human milk decreased during the study period. An infant's exposure to the sum of organochlorine compounds in 1997 was estimated to be 1/10th of that in 1972. In contrast, concentrations of PBDEs increased during 1972 – 1997 by a factor of 60 reflecting environmental contamination and increasing background levels. Preliminary estimates of the daily PBDE intake by nursing infants via human milk concluded that the daily intake for breastfed infants is between 1 and 2 orders of magnitude higher than adults (WHO, 2006a).

Breast milk monitoring serves an important sentinel function in detecting exposure to toxic contaminants at early stages and provides the opportunity to take measures before adverse health effects appear. Monitoring should be run globally as an indicator of the effectiveness of implementation of the POPs Treaty in different countries and regions The WHO has summarized data on POPs in human milk in several European countries (ENHIS, 2007). There were differences among countries, as much as 3 – 5-fold for dioxin levels. All countries showed decreasing levels of POPs between 1988 – 2002. In contrast, there were increases in PBDEs and perfluorinated compounds. Beginning in 1976, the WHO has collected and evaluated information on levels of POPs in food, including human milk, through its Global Environment Monitoring System (GEMS)/ Food Programme. WHO guidelines describing biomonitoring of human milk are available (Biomonitoring of Human Milk for Persistent Organic Pollutants. http://www.who.int/foodsafety/chem/pops/en/). These recently revised guidelines for developing a national protocol describe the basic study design that can be used to monitor human exposure over time in order to, among other things, see if the Stockholm Convention is effective in reducing the release of these chemicals into the environment. The guidelines continue to support monitoring POPs for human health and food-chain contamination purposes.

Although there has been concern about the potential risks of POPs in human milk, breast milk is considered the optimal food source for newborn babies. The presence of dioxins and PCBs in human milk is not an indication for avoiding breastfeeding (Pronczuk, 2004).

Table 6
Working definitions for stages in human development

Developmental stage/ event	Time period
Preconception	Prefertilization
Preimplantation embryo	Conception to implantation
Postimplantation embryo	Implantation to 8 weeks of pregnancy
Fetus	8 weeks of pregnancy to birth
Preterm birth	24–37 weeks of pregnancy
Normal-term birth	40 ± 2 weeks of pregnancy
Perinatal stage	29 weeks of pregnancy to 7 days after birth
Neonate	Birth to 28 days of age
Infant	28 days of age to 1 year
Child	Young child 1–4 years of age Toddler 2–3 years of age Older child 5–12 years of age
Adolescent	Beginning with the appearance of secondary sexual characteristics to achievement of full maturity (usually 12–18 years of age)

(EHC 237. WHO)

V. Special Susceptibility of Children

Compared to adults, children often are more susceptible to the adverse effects of environmental toxicants because of differences in exposures and differences in susceptibility. Susceptibility varies with life stage. Life stages are listed in **Table 6.**

1. Differences in exposure

1.1 General concepts

Infants, children and adolescents consume more food and liquids per kilogram of body weight than do adults. Their dietary patterns are different from those of adults and often less variable during different developmental stages. Young children have higher inhalation rates resulting in higher inhalational exposures and a higher body surface area to body weight ratio resulting in higher dermal exposures. Children's normal behaviors,

such as crawling on the ground and putting their hands and objects in their mouths, can result in exposures not experienced by adults. Children are often unaware of or ignore environmental risks, may be not able to remove themselves from danger and usually do not read labels.

1.2 Early life stage exposures

Adverse effects may result from maternal and/or paternal exposures prior to conception as POPs have toxicity to sperm and oocytes (Campagna, 2001; Long, 2007; Aneck-Hahn, 2007; Hauser, 2003). Exposure can occur in utero during pregnancy when maternal fat stores are mobilized resulting in transfer of toxicants to the embryo and to the fetus through the placenta. Exposure can occur through ingestion of breast milk.

2. Differences in susceptibility

Once exposures occur, children's abilities to absorb, metabolize and detoxify chemicals generally differ from adults' abilities. The fetus, infant and child may be more susceptible to POPs because of the rapid development of their organ systems, reduced levels of certain detoxifying enzymes, and smaller fat deposits for sequestering lipophilic POPs (Damstra, 2002a). Development has been subdivided into stages (**Table 6**) with unique susceptibilities and vulnerabilities to environmental influences at each stage. These distinct life stages are defined by dynamic processes occurring at the molecular, cellular, organ system, and organism level. It is the differences in these life stages along with exposures that will define the nature and severity of environmental impacts (WHO, 2006b). Age-specific periods of susceptibility are termed "critical windows of exposure" or "critical windows of development". These are times when immature humans are highly sensitive to any adverse effects of POPs and other chemicals. Even within a given developmental stage, shorter intervals of exposure may determine susceptibility for particular outcomes.

Different organ systems develop at different rates; for each developmental stage, there are both broad windows of susceptibility and more specific periods of susceptibility e.g. central nervous system development and radiation exposure (Faustman et al., 2000). In most cases, however, the exact time when organ systems are susceptible to the actions of toxic chemicals is unknown. Limited data are available on susceptibility during the adolescent period, but because greater interest is developing about the effects of hormonally active agents, more information is becoming

available (WHO, 2006b).

Depending on timing, a developing human may be "programmed' with long-lasting (perhaps lifelong) adverse consequences to the nervous, endocrine and reproductive systems and to immune function (Damstra, 2002b; WHO, 2004). Children have more years of future life ahead of them compared to adults, They thus have more time to develop chronic diseases that take decades to appear and that may be triggered by early environmental exposures; this "long shelf life" allows for the expression of effects with long latency periods.

Children's social standing places them at increased risk. Children are politically powerless individuals who cannot protect themselves and thus require that adults understand their vulnerabilities and institute protective measures. In more polluted environments, adverse effects are exacerbated or magnified. Poverty may force people to live in polluted sites and to eat contaminated foods.

VI. A Global Approach to POPs

1. Policies

The international community has called for urgent global actions to reduce and eliminate releases of POPs. Agenda 21 ("21" refers to the 21st century), that was adopted at the UN Conference on Environment and Development (also known as the Earth Summit) in Rio de Janeiro in June 1992, is an international commitment for sustainable development. It is a blueprint for action to be taken globally, nationally and locally by organizations of the UN, governments, and major groups in every area in which humans impact the environment. One-hundred seventy-nine governments in attendance at the conference adopted the program. Agenda 21 Chapter 19 is devoted to chemicals: "Environmentally sound management of toxic chemicals including prevention of illegal international traffic in toxic and dangerous products" (UNCED Rio Declaration, 1992).

In pursuing the goals presented in these agreements, the International Programme on Chemical Safety (IPCS) was created in 1980 and has greatly contributed to the global efforts in sustainable management of chemicals. The IPCS is a joint venture of three organizations working in cooperation: the WHO, the International Labour Organization (ILO), and UNEP.

Following the agreement stated in Agenda 21, another international organization, the Intergovernmental Forum on Chemical Safety (IFCS), convened in April 1994 and provided an important framework for international discussion of chemical safety issues. The IFCS has played an instrumental role in global movement on chemical safety, working as an open, transparent, and inclusive forum. Another initiative of the IFCS was the compilation of a series of recommendations for governments and other stakeholders to implement, with the objective of preventing the exposure of children to harmful chemicals. (IFCS, 2005) For example, the IFCS recommended international standardization of toy safety standards. The IFCS also produced several texts; the document titled "Managing Chemicals in a Changing Climate to Protect Health" (IFCS, 2008) raises the issues of how climate change may impact the way chemicals are used, and the way they move and transform in the environment, thereby altering human exposure. After considering the vulnerability of children to toxic chemicals (IFCS, 2006) as well as existing information gaps, the IFCS advocated for increased dialogue among governments, toy manufacturers, retailers, and consumers.

There have been various international initiatives to address hazardous chemicals, including POPs, at the global level. These include the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal (entered into force in 1992), the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (entered into force in 2004), and the Stockholm Convention on Persistent Organic Pollutants (entered into force in 2004). In 2006, the International Conference on Chemicals Management adopted a framework for an integrated approach to the management of chemicals – the Strategic Approach to International Chemicals Management (SAICM).

POPs chemicals were for the most part introduced and initially used by industrialized countries, yet the lasting consequences will be felt everywhere and can be especially damaging to the most vulnerable – poorer and indigenous communities. Wealthier countries were among the first to detect the dangers, to reduce use, and to start cleaning up stockpiles and reducing use and internal commercialization in the country or region. Sadly this was not accompanied by a ban on exports which meant that developing countries continued to receive chemicals that they did not have the infrastructure to manage.

2. Research needs

In large doses, POPs are toxic to wildlife and to humans. There are many examples of adverse effects of lower levels of POPs in wildlife and in humans but many research gaps remain. These include the effects of lower levels of POPs and their impact on the initiation and progression on certain human conditions or diseases. Of particular concern are questions regarding exposure of parents during the preconception period, prenatal exposures, postnatal exposures through breastfeeding, and exposures during childhood and adolescence.

Questions include:

- The relationship of prenatal exposures to endocrine-disrupting POPs to birth defects such as hypospadias
- The relationship of prenatal and childhood exposures to other hormonally-influenced conditions such as early puberty and decreased sperm counts and sperm quality
- The relationship of prenatal and childhood exposures to onset and progression of adult diseases such as breast cancer
- The role of exposure timing - preconception, during pregnancy, and early childhood
- The role of exposure to mixtures of chemicals and multiple exposures
- The impact of climate change on exposure to POPs
- The identification of "hot spots" of POPs contamination
- The development of biomonitoring techniques to determine children's exposure levels
- The risks and benefits of alternatives to currently used chemicals – such as alternatives to PBDE-containing flame retardants in children's clothing and consumer products.

Identifying and evaluating exposed human populations is difficult because of the wide exposure to many chemicals in the environment, health effects due to chronic exposure to low doses of chemicals and long-term effects. Long-term epidemiological studies are required to evaluate and establish

the relevance of these exposures. More studies in humans and animals must be done before any definitive assessment can be made regarding the causative role of POPs and illness including hormonally-dependent cancers. The lack of scientific certainty regarding chemicals toxicity should not, however, prevent decision makers from taking a precautionary approach to managing chemicals. Continuing education must be available so that health professionals and public health agents are able to understand the potential effects of low doses of POPs chemicals and promote actions to prevent potential harmful exposures.

VII. Protection of children and communities from exposure

POPs are pervasive in the environment as a result of manufacturing and widespread dispersal over decades. The main way to reduce exposure is through regulation – banning their manufacture through laws and enforcement. The IOM in the US recommended that the government increase the availability of foods low in animal fats in government-sponsored breakfast and lunch programs and in child- and adult-care food programs (IOM, 2003). In some cases as in the Arctic Inuit community, however, survival depends on the high animal fat component in their food.

Individuals may take certain steps to reduce exposure. Paediatric professionals and public health officials can play a role in educating families with the goal of minimizing exposure and protecting women of childbearing age, pregnant women and children. This will require that clinicians and nurses in paediatrics, family practice, obstetrics, public health agents and also experts in labour (occupational) health become educated about POPs. Ideas can be promoted by opinion leaders, educators, and by professional and academic societies. The private sector also plays an important role

Chronic exposure to low doses of POPs for most people in the general population comes from ingestion of food; exposure generally occurs over time and does not result in overt symptoms. To minimize exposure, clinicians and public health officials can encourage families to limit consumption of certain foods beginning early in life especially if populations reside near polluted sites. This strategy will lessen children's exposures; it will also lessen the body burden of young women entering their reproductive years, reducing the transplacental and lactational exposures of their future

children.

Foods containing the highest concentrations of POPs may vary depending on the community, region and lifestyle. These foods often include fatty cuts of beef, bacon, frankfurters, full-fat cheeses, butter and fatty fish (such as salmon, particularly farmed salmon) (Thundiyl, 2007). Families should be encouraged to eat "low on the food chain", increasing consumption of fruits, vegetables and whole grains when possible. Consumption of meat products low in fat should be encouraged. A diet rich in these foods has additional health benefits such as promoting a healthy weight and blood pressure. Whenever possible, it is prudent to become informed about the origin and production methods used so as to be able to choose the best quality food.

Organic produce is grown with fewer pesticides but tends to be more expensive and less readily available than non-organic. Locally grown and in-season produce is less likely to contain pesticides. Some POPs in fruits and vegetables appear to be concentrated mainly in the outer skins, washing is recommended to remove residues, as is peeling of root and wax-coated vegetables (IOM, 2003). Some other POPs, however, penetrate deep into seeds and fruits, and cannot be removed. Preventing or limiting exposure to pesticides can be accomplished through the use of integrated pest

management (IPM), a strategy designed to reduce dependency on pesticide use, while maintaining production levels of crops. Agenda 21 states that IPM should be the guiding principle for pest control. "Integrated pest management, which combines biological control, host plant resistance and appropriate farming practices, and minimises the use of pesticides, is the best option for the future, as it guarantees yields, reduces costs, is environmentally friendly and contributes to the sustainability of agriculture." (WHO, 2002)

Fish is a good source of protein and omega-3 fatty acids. It is often inexpensive. Clinicians and public health officials should advise families to choose fish low in PCBs and mercury when possible. Lists of safer fish alternatives are provided by some countries and available for some regions. Fish grown in farms and closed lakes tend to concentrate chemical pollutants at higher levels than fish from open seas. Because organic contaminants concentrate in fat and skin, fish should be trimmed of visible fat, including the skin, before it is consumed. Broiling the fish allows the fat to drip away from food. Families who engage in subsistence fishing or sport fishing may have high exposures; public health fish advisories should be followed in order to avoid fish high in contaminants. Pregnant and nursing women and women of childbearing age should also be advised to avoid eating fat from sheep and other animals likely to have high POPs levels.

The WHO emphasizes the beneficial role of breast milk as the optimal food for infants and young children. The presence of dioxins and PCBs in human milk does not represent an indication to avoid breastfeeding. (Pronczuk, 2004) The WHO, UNICEF and other international organizations (such as the AAP) recommend exclusive breastfeeding for 6 months of age, as a key intervention to ensure optimal growth and development, and survival of children. After 6 months of age, continued breastfeeding up to 2 years or beyond is a critical component of appropriate complementary feeding (WHO/UNICEF Global Strategy for Infant and Young Child Feeding, 2002).

For children who are not breastfed. full-cream milk is an important source of fat and nutrients during the first two years of life. Skimmed (non-fat) milk is not recommended as a major food source for children under two because it does not contain essential fatty acids, it is deficient in fat-soluble vitamins and has a high potential renal solute load in relation to energy (WHO Guiding principles for feeding non-breastfed children 6-24 months of age, 2005).

VIII. Summary information on POPs

More information about selected POPs of most relevance to clinicians is included below:

POPs Pesticides

DDT. Agricultural and commercial use of DDT was once widespread in the US but DDT was banned from manufacture in 1972 after 4 decades of extensive global use. DDT continues to be produced and applied under conditions of Annex B of the Stockholm Convention (this is the only exemption to the ban on use for countries that are Party to the Convention). The Stockholm Convention allows DDT to be used in public health situations for disease vector control as recommended by and under the guidance of the WHO. The WHO recommends the use of DDT for indoor residue spraying only to control the anopheles mosquito that carries the malaria parasite. After special notification of the Secretariat of the Convention and WHO, DDT may be used to control malaria outbreaks. DDT is currently used in some Asian and African countries. A special mechanism for reporting was established by the POPs Convention to strictly control the uses and applications of DDT under this exemption. A recent document highlights the commitment of the WHO to achieving sustainable malaria control in the context of the Stockholm Convention (WHO, 2007).

Organochlorine pesticides developed after DDT and widely used after World War II included **aldrin, dieldrin, endrin, chlordane, heptachlor, lindane and pentachlorophenol**. Their discovery marked a major achievement in agriculture that was beneficial to the world economy (Kuvarega, 2007). Once adverse effects due to their persistence and accumulation in the environment became known, most uses were discontinued.

The POPs pesticides added to the Stockholm Convention list in 2009 are 1) **Alpha-Hexachlorocyclohexane (alpha-HCH),** 2) **beta-Hexachlorocyclohexane (beta-HCH),** a by-product of production of **lindane;** 3) **chlordecone;** and 4) **lindane (gamma-hexachlorocyclohexane, γ-HCH).**

Lindane has been used as a broad-spectrum insecticide and is still used in small amounts (1%) formulated into shampoos and lotions to control head

lice and scabies in humans. It is approved for the second-line treatment of these conditions. Lindane is to be prescribed only when first-line therapies fail or cannot be tolerated; thus children may be exposed. Lindane is used as an insecticide in dog dips and shampoos. Globally, 52 countries have banned the use of lindane and 33 have restricted its use (UNEP, 2007).

POPs industrial chemicals

Products such as **polychlorinated biphenyls (PCBs)** became important in industry because they are very stable chemicals with low volatility at normal temperature, are relatively fire-resistant, and do not conduct electricity. PCBs were manufactured beginning in 1929 in the US and 1930 in Germany. After World War II, their production and use expanded to other countries. PCBs were used primarily in the electrical industry as heat exchange fluids, in electric transformers and capacitors, and also as additives in paint, carbonless copy paper, sealants and plastics. Products that may contain PCBs include old fluorescent lighting fixtures and electrical devices with PCB-capacitors. PCBs can be released as by-products of combustion and industrial processes (Noren, 2000). Production was banned in the US and northern Europe in the late 1970s but most PCBs persist in the environment. Even though PCBs are no longer manufactured, they are still found in many transformers, capacitors and other electrical equipment currently in use.

The POPs industrial chemicals added to the Stockholm Convention in 2009 list are 1) **hexabromobiphenyl (HBB);** 2) **commercial octabromodiphenyl ether (c-OctaBDE);** 3) **commercial pentabromodiphenyl ether (c-PentaBDE**; 4) **pentachlorobenzene (PeCB);** and 5) **perfluorooctane sulfonate (PFOS)**.

POPs unintentionally produced chemicals

Polychlorinated dibenzo-p-dioxins (PCDDs) and **polychlorinated dibenzofurans (PCDFs)**, often referred to as **dioxins** and **furans**, were never used or manufactured for any reason other than laboratory purposes. The IARC identified 2,3,7,8-TCDD as the most toxic of all dioxin compounds, and as carcinogenic to humans, based mainly on studies of cases involving accidental or heavy occupational exposure.

Other Persistent Toxic Substances (PTS)

A growing number of chemicals are recognized as persistent or semi-

persistent in the environment. Persistent toxic substances (PTS) share properties with POPs. Although PTS are not POPs, it is expected that they will be included in future conventions and expanded international agreements. The list of PTS has not been specifically defined. PTS include heavy metals such as mercury, cadmium and lead. The following compounds also are included.

Pentadecafluorooctanoic acid (PFOA) is an industrial surfactant best known for processing polytetrafluoroethylene (PTFE), a chemical manufactured by the Dupont company under the brand name Teflon®. PFOA also is a by-product of a telomerization process producing perfluorinated alcohol commonly used in household surface finishes and indirect contact applications in flexible food packaging, and is a by-product produced during the fabrication of water- and stain-resistant clothes and other products. Fluorotelomer compounds are used in food packaging to make them resistant to grease. The perfluoroakyl acids chemicals have been identified in parts per billion in human serum samples taken from the general population and in certain wildlife samples, and are toxicants in animals (Lau, 2004). The presence of these chemicals in humans and wildlife has drawn attention from regulatory agencies and the public. In the US, EPA launched a global stewardship program inviting companies to reduce PFOA releases and its presence in products by 95 percent by no later than 2010 and to work toward eliminating these sources of exposure five years no later than 2015 (US EPA, 2005).

Polychlorinated naphthalenes (PCNs) are a group of substances based on the naphthalene ring system. PCNs have been used as cable insulation, wood preservatives, engine oil additives, electroplating masking compounds, capacitors, and in dye production.. PCNs started to be produced for high volume use in 1910 but their production decreased in the late 1970s. In experiments done in animals, PCN has been shown to be very toxic to liver. The pattern of toxicity of PCNs resembles that of TCDD. The potency of several PCN congeners is in the same range as some PCB congeners (UNECE, 2002). Because of health concerns to humans, worldwide PCN production had almost halted by 1983, except for small amounts used in testing and research.

Polycyclic aromatic hydrocarbons (PAHs) are a group of chemicals formed during incomplete burning of coal, oil, gas, wood, garbage, or other organic substances such as tobacco and charbroiled meat. Other sources

of PAHs include asphalt and roofing tar. PAHs are found throughout the environment in air, water, and soil. PAHs are linked to cancer in both animals and humans (ATSDR, 1995a). In humans, PAH exposure by inhalation or skin contact has been linked to cancer. Laboratory studies in animals show that PAHs cause tumors when PAHs are inhaled, ingested, or come into contact with skin. PAHs cause birth defects, and are toxic to the skin, blood, reproductive and immune systems in animals. EPA has classified the following 7 PAH chemicals as probable human carcinogens: benz[a]anthracene, benzo[a]pyrene, benzo[b]fluoranthene, benzo[k] fluoranthene, chrysene, dibenz[a,h]anthracene, and indeno[1,2,3-c,d] pyrene. In IARC classification benzo[a]pyrene is classified as Group 1 (carcinogenic to humans), dibenz[a,h]anthracene as Group 2 A (probably carcinogenic to humans), benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, chrysene and indeno[1,2,3-c,d]pyrene as Group 2 B (possibly carcinogenic to humans)(IARC, 2010).

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