



# **UNSEEN POISONS**

Levels of  
Organochlorine Chemicals  
in Human Tissues

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in Human Tissues

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Global Review of Data on  
12 Priority Persistent Organochlorine Pollutants  
and  
Some Other Organochlorines in Human Tissues

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## SUMMARY

Persistent organic pollutants (POPs) are a group of mainly synthetic chemicals which have the property of being persistent in the environment. As a consequence of anthropogenic activities, many POPs have become widespread pollutants throughout the world in recent decades. Some POPs are known to bioaccumulate in the tissue of animals and humans and are toxic to health.

There are numerous POPs which pollute the environment. Some of those which have given rise for particular concern are persistent organochlorines. A previous meeting of the UNEP's governing Council in 1995, identified a list of 12 POPs as substances of clear concern in accordance with the precautionary principle. These chemicals are all organochlorines. They include dioxins and furans, which are produced as unwanted by-products of several industrial processes, PCBs and HCB, which have several uses and are also formed as unwanted by-products, and DDT, chlordane, heptachlor, aldrin, dieldrin, eldrin, toxaphene and mirex which are pesticides.

The 12 POPs prioritised by UNEP have properties of being toxic to health. It is of concern that all these chemicals have been detected in the tissues of humans from the general population of various countries and in the tissues of many wildlife species. It is also of note that even though there are many POPs, most of these chemicals have not been assessed in human tissues.

Greenpeace has issued this report to highlight the levels of persistent organochlorines found in human tissues throughout the world. Countries and populations in which levels are particularly high are identified. Since these substances are toxic, the relevance of current levels to human health is also briefly considered. One of the greatest concerns with respect to health is the potential adverse effects that these chemicals may have on the most vulnerable stages of life - the developing foetus in the womb, and the nursing infant, since they are known to cross the placenta and are present in breast milk.

### Levels of POPs in Human Tissues

Most of the 12 POPs listed by the UNEP are widespread pollutants and they have been found to commonly occur in human tissues world-wide. Levels in tissues are most routinely determined in blood, breast milk or adipose tissue. This report focuses mainly on levels of POPs in breast milk which have been documented in the scientific literature over the past ten years.

The greatest number of studies on human tissue levels of organochlorines were located for dioxins, furans and PCBs. Studies from many countries were found on levels of DDT and HCB, but less research was available on other organochlorine pesticides. Given the persistent and widespread nature of the 12 UNEP listed chemicals, it is considered that there is a lack of data concerning their human tissue levels for many countries, in particular for developing regions of the world. In addition, studies regarding tissue levels of occupationally exposed individuals are also limited.

A general observation from studies presented in this report is that levels of organochlorine pesticides in human milk were highest in countries where these chemicals are still in use, notably in developing countries. Another generalisation which can be made is that levels of dioxins and furans were highest in industrialised countries. This is synonymous with the fact that these compounds are produced as by-products of many industrial processes, in particular processes involving chlorine. There are however exceptions to these generalisations regarding levels of organochlorine pesticides and dioxins/furans in human milk. Many POPs, including PCBs and some organochlorine pesticides, appear to be transported long distances on air currents from warm regions of the globe and subsequently deposited in colder regions. This global fractionation process has resulted in particularly high levels of POPs in Arctic areas. As a consequence, some indigenous people of Arctic regions who rely on a traditional seafood diet have high tissue levels of PCBs and some organochlorine pesticides.

#### ***Dioxins and PCBs***

Dioxins, furans and PCBs are ubiquitous in the global environment. Research has shown that levels of dioxins and furans in human tissues are greater in industrialised countries than in less industrialised countries. In the 1980s, studies showed that levels of dioxins and furans in blood, adipose tissue and breast milk were considerably lower in less industrialised countries, including Thailand, China, northern Vietnam, Pakistan, Africa and Russia, compared to levels in some industrialised European countries and the USA.

Research in the late 1980s and early 1990s showed that breast milk levels in many industrialised countries were in the range of 10-20 ppt TEQ fat. The highest levels, above 20 ppt TEQ, were found in some western European countries and one region in Canada. The lowest levels were found in less industrialised regions, including Pakistan, Russia, Albania, Hungary, Croatia and Norway. Comparatively low levels, recorded in blood, were also evident in China, some other Asian countries and Gaza in the Middle East. Most information on tissue levels of dioxins and furans is available for European countries, USA and Canada. Fewer studies have been conducted in Asia, and data in the scientific literature is very limited for Africa and South America.

Studies show that individuals who were employed in the production of chlorophenols and phenoxyherbicides in the 1960s to 80s were highly exposed to dioxins. TCDD levels in workers from trichlorophenol plants are still elevated by around 10-fold, two decades after production ceased. Children born to workers at a plant in Russia, who are now adults, have levels 150-2000 times higher than the general population due to placental/lactational transfer from their mothers. More recently, high exposures were recorded at a pentachlorophenol plant in China, where blood levels of dioxins/furans (total TEQ) are 50 to 400 times higher than the general population. There are several other occupations where individuals may be exposed to higher than average levels of dioxins/furans in many countries. Elevated tissue levels have been documented in workers at municipal waste incinerators and in certain sectors of the metal industry.

Research on PCBs has revealed that similar levels in human milk are evident in many European countries and Canada. Higher levels have been found in eastern Europe and the former Soviet Union. Very high human tissue levels of PCBs are apparent in

populations in Arctic regions who consume a diet rich in seafood. For instance, blood levels of Inuit in Arctic Quebec who rely on a traditional seafood diet were 15-fold greater than residents of Southern Quebec.

Studies indicate that levels of dioxins and furans in human tissues in Western countries have not increased in recent years. Levels in several European countries appear to have declined somewhat in the past few years. There are difficulties in comparing data for PCBs between studies, but relevant data shows that levels of PCBs in human tissues have remained stable in recent years.

#### ***DDT and DDE***

A summary of data compiled in this report on the levels of several organochlorine pesticides in human milk from different countries is given in table 10.

DDT and its metabolite DDE are widespread contaminants in human tissues. DDE has been detected in virtually all samples of breast milk taken from numerous countries. By far the highest levels in human milk are evident in Asian, African and South American countries where DDT is still used in agriculture or in sanitation campaigns against malaria or tse-tse fly. Despite the undesirable properties of DDT, it is used in developing countries primarily due to cost-benefit efficacy and broad spectrum toxicity. However, given the continued usage of DDT, it can be considered that there is a paucity of data on levels of DDT/DDE in human tissues from these countries in the scientific literature.

Exceptionally high levels in human milk are reported for India (DDT and DDE > 10 ppm). Levels of DDE, (1 to 2 ppm), are found in eastern and some western European countries, Russia and Australia. The lowest levels are found in some western and northern European countries and the US. Levels of DDT in human tissues have declined in recent years in countries where its use is banned, but no decline has been recorded in other countries such as Mexico. Occupational exposure to DDT has been studied in DDT sprayers in Mexico. Adipose tissue levels in the workers were 6-times greater than the general population.

#### ***Hexachlorobenzene (HCB)***

HCB is a widespread contaminant of human milk, being present in over 90% of milk samples from most countries. Levels in the majority of countries were in the region of 0.05 to 0.2 ppm. Very high levels (>0.6 ppm) were evident in the Czech Republic and Slovakia, possibly due to its formation during the manufacture of chlorinated solvents and former agricultural use. Data from a few European countries show a decreasing trend in levels in recent years. Occupational exposure has been reported to result in elevated HCB levels in workers employed in hazardous waste incineration and from processes formerly used for degassing aluminium.

#### ***Hexachlorocyclohexanes (HCH)***

Gamma-HCH (lindane) and technical grade HCH, which consists of a number of isomeric forms, are persistent pesticides which are not listed by the UNEP. However, gamma and beta-HCH are both commonly detected in human tissues and studies have listed levels in breast milk in several countries. Beta-HCH is the most persistent isomer and it is widespread in breast milk throughout the world. The highest levels (4-

8 ppm) have been recorded in human milk from India and China. High levels (1.5-2.5 ppm) are also evident in Russia and Kazakstan.

#### ***Dieldrin, Aldrin and Endrin***

Dieldrin is found in human milk of many countries, although the percentage of samples in which it can be detected is variable. Levels for several countries are in the range of 0.01 to 0.1 ppm. Very few studies have reported on the levels of aldrin and endrin in human tissues.

#### ***Heptachlor and Heptachlor Epoxide***

Data on levels of heptachlor and its breakdown product, heptachlor epoxide, in human tissues are limited. The chemicals were reported in breast milk from several countries, although the percentage of samples in which they are detected is variable. A previous review noted the highest levels were evident in several western European countries, Israel and Guatemala. In this review, the highest level (0.7 ppm) was recorded for Jordan. Other countries had levels below 0.05 ppm, with the exception of Australia and France.

#### ***Chlordane***

Comparisons between studies of chlordane levels in human tissues are difficult, because there is variation in the different isomeric forms and metabolites of chlordane which are reported. It has been noted that the highest levels are present in the US, reflecting its previous widespread use to control termites. There does not appear to be a decreasing trend in the level of chlordane in human tissue.

#### ***Toxaphene***

Few studies have monitored human tissue levels of toxaphene. It has been detected in human milk from a few countries. Comparatively high levels were apparent in Nicaragua.

#### ***Mirex and Other Organochlorine Pesticides***

Very few studies have monitored levels of mirex in human tissues. In addition, there are other persistent organochlorine pesticides which are still used, such as endosulfan, which are present in human tissues, but are not often measured.

#### **Acceptable Daily Intakes**

Regulatory authorities use the process of risk assessment to estimate permissible levels of contaminants in food which are deemed to be "safe". These levels are known as Acceptable Daily Intakes (ADI) or Tolerable Daily Intakes (TDI).

Human milk contains various POPs which pass to a nursing infant, but unlike foodstuffs, the levels it contains cannot be regulated. The applicability of ADIs to the breast fed infant is questionable because ADIs are designed to prevent adverse health effects over a whole lifetime exposure in a 70 kg adult. Nevertheless, given that an infant is likely to be a more vulnerable lifestage than an adult to toxic insult from chemicals, it has been proposed that ADIs should be lower for infants, and therefore, current ADIs should not be exceeded by breast-fed infants.

It has previously been calculated that ADIs set by US EPA and WHO for dioxins/furans are exceeded by breast-fed infants. In this report, estimates of whether the current ADIs for organochlorine pesticides are exceeded are performed, based on mean levels in breast milk recorded for different countries. Results show that estimated infant intakes which exceed the ADIs are: DDT, in some African, Asian and Latin American countries, and by over 6-fold in India and Zimbabwe; HCB, in several countries, and by 6-8 fold in Czech and Slovak Republic; lindane, in two countries, and in India by up to 12-fold; dieldrin, heptachlor and heptachlor epoxide in several countries.

It is not favourable that current ADIs are exceeded by breast-fed infants, even though the relevance of this to health is unknown. Indeed, it is questionable whether ADIs are protective of human health in general. The process of risk assessment used in their derivation involves many uncertainties. Furthermore, most of the 12 UNEP listed chemicals have been identified as endocrine disrupters, and current endpoints in toxicity tests may not be sensitive enough to detect adverse effects of such chemicals. Research shows that these chemicals can have greater effects at lower rather than higher doses. There is consequently a scientific opinion that *there are no safe doses of endocrine disrupters, just as there are no safe doses of carcinogens.*

#### **Relevance of Current Tissue Levels to Human Health**

Persistent organochlorines have been reported to cause a wide range of adverse health effects in experimental animals, and in humans as a result of occupational or accidental exposure. Effects include toxicity to the liver, reproductive and nervous systems, immune system abnormalities and cancer. There is evidence that some of these chemicals, particularly dioxins and PCBs, have now reached levels in human tissues which are near to, or within an order of magnitude of, levels that are known to cause adverse effects in experimental animals. Highly exposed populations such as Arctic Inuit who consume a seafood rich diet, occupationally exposed individuals, and populations inhabiting contaminated environments could be more at risk. Studies on infants from the general population of industrialised countries have suggested that subtle effects on the nervous and immune system may already be occurring as a result of placental and/or lactational exposure.

#### **The Way Forward**

POPs are a global problem. Some are detectable in human tissues world-wide and the levels of many have not even been assessed. Many POPs, including those listed by the UNEP, are potentially detrimental to the environment and human health.

To wait for scientific proof about the effects and risks posed by individual POPs would take decades. There is only one clear way forward to overcome uncertainties and safeguard the environment and human health – the adoption of the precautionary principle and the implementation of zero discharge strategies. This requires prevention of pollution at source, and implementation of clean production in industry and agriculture. Such action needs to be enforced by legally binding international agreements.

## 1. INTRODUCTION

There are numerous chemicals that come under the category of persistent organic pollutants (POPs). These chemicals resist breakdown by natural processes for long periods of time, and are thus persistent in the environment. The UNEP's Governing Council have listed 12 POPs of clear concern, in accordance with the precautionary principle. They include dioxins and furans, PCBs, HCB, DDT, aldrin, endrin and dieldrin, heptachlor, chlordane, toxaphene and mirex. These chemicals are all organohalogens, specifically, organochlorines.

Many POPs, including some organochlorines, are not only persistent in the environment, but are also soluble in fats (lipophilic). Consequently, they become stored in the fatty tissues of animals and build up (bioaccumulate) as more of the chemical is taken in. The levels of some of these chemicals increase (biomagnify) as one animal eats another, so that the highest levels are found in animals at the top of food chains, including humans. Many persistent organochlorines are also toxic to wildlife and humans.

The 12 prioritised POPs listed by the UNEP have been produced or used in bulk quantities in many countries. Dioxins, PCBs and HCB are still produced as unwanted by-products in combustion and other industrial processes. The other chemicals are pesticides. Most of these have been banned or have restricted use in many developed countries. However, their use continues in some developing countries.

Once released into the environment, many POPs, including some persistent organochlorines, become airborne and may be transported for thousands of kilometres in the atmosphere before condensing and falling back to the earth's surface. As a result of long-distance transport and their immense production and usage, many POPs have become widespread global contaminants. There is evidence that some are carried on air currents from warmer regions to polar regions. This process, known as "global fractionation" is believed to be the reason why high concentrations of these chemicals are now found in Arctic and Antarctic regions, where they have never even been used (Wania and Mckay 1996).

Human exposure to many persistent organochlorines is unavoidable since these chemicals are present in food. Due to their lipophilicity and bioaccumulative properties, the highest levels are present in meat, fish and dairy products (Hall 1992). Pesticide residues may also remain in some foods and low levels may occur in drinking water (Culliney *et al.* 1992, HMSO 1995). Although food is the major pathway of exposure to many persistent organochlorines for the general population, exposure by inhalation or dermal contact is also possible.

### 1.1 POPs in Human Tissues

As a consequence of the persistent, lipophilic, bioaccumulative properties of many POPs, and tendency of some to biomagnify within food chains, long-term exposure to relatively small concentrations of these compounds leads to the accumulation of considerable deposits in animal and human tissues. Studies which have monitored levels of organochlorine POPs in human tissues provide scientific evidence that humans are exposed to these chemicals. Indeed research from numerous countries has

demonstrated that measurable quantities of organochlorine pesticides, PCBs and PCDD/Fs are present in human adipose tissue, blood and breast milk (Jensen and Slorach 1991). Measuring levels of POPs in tissues is one of the most accurate and precise ways of assessing human exposure to these environmental pollutants. This information is also extremely useful for studying the relationship between human exposure to POPs and health effects (Schechter 1998).

Levels of POPs in human tissue are most commonly assessed in blood, adipose tissue or breast milk. Studies have shown that levels are generally similar in these three media (Thomas and Colborn 1992). In the present report, emphasis is placed on levels of organochlorines on the UN POPs list in human milk. Monitoring of human milk concentrations may be used to assess both temporal and geographical variations in human exposure to persistent, lipophilic contaminants (Dewailly *et al.* 1996). In this report, studies from many different countries are considered, in order to provide an indication of differences in world-wide levels of these compounds in humans. The majority of these studies have reported on human tissue levels within a region of a country rather than nation-wide levels, although tissue levels throughout countries are often similar. Trends in the levels of organochlorines in human tissue with time over the past few years are also discussed. However, information on trends has only been published for a few countries where studies have monitored levels on a regular basis, or where national programmes have been carried out and made available by government health agencies (Mes 1994).

Information for the present report was located by performing searches of the scientific literature over the past 10 years using BIDS ISI Science Citation Index data base service. A greater number of studies on concentrations of organochlorines in human milk were located in the literature compared to levels in blood and adipose tissue.

### 1.2 Problems Comparing Human Tissue Levels of Organochlorines in Different Countries

There are several problems which can hinder comparisons between studies which document the levels of organochlorines in human tissues. These problems arise from differences in the scientific methods which are used to measure the concentrations of contaminants. For example, differences between studies may occur in sample collection, storage, preparation, the method used for chemical analysis, mathematical analyses and data interpretation (Thomas and Colborn 1992). A difference in the sensitivity of an analytical method for instance could affect whether or not a compound is detected. Fortunately, analytical methods used in many recent studies are similar, making comparisons between studies possible.

In the present report, comparisons of organochlorine pesticide concentrations in human milk from different countries are made. There are however some discrepancies in the sample collection methods used between these studies, which may cause differences in the recorded levels of organochlorines in the milk. For instance, a factor which is known to affect the contamination levels in breast milk is parity. Primiparous women (first time pregnancy) can have higher levels of organochlorine chemicals in breast milk than multiparous (second, third pregnancy etc.), because lactation reduces the maternal body burden of organochlorines. Some studies have accounted for the influence that parity can have on breast milk concentrations of



organochlorines by only selecting primiparous women (eg. Dewailly *et al.* 1996). However, many studies have not controlled for this factor and have analysed samples from both primiparous and multiparous women.

Since a number of differences in the methodologies occur in studies from various countries, results of these studies are not directly comparable. However, in the present report, a comparison of such studies is made because this can at least give an approximate indication of the variation in levels of organochlorine contaminants between different countries.

Concentrations of environmental contaminants in human tissues are reported either on a whole weight basis of the tissue concerned, or more often on the basis of concentration in extractable fat (lipid) of the tissue. With regard to breast milk, the fat content is highly variable between individuals, and the fat content influences the concentration of fat soluble chemicals, such as organochlorines, in the milk. It is therefore more favourable for organochlorine concentrations in breast milk to be expressed on a milk fat basis since these chemicals are clearly associated with the lipid fraction in milk (Quinsey *et al.* 1996).

In this report, organochlorine concentrations in human milk which have been reported in the literature are given on a milk fat basis wherever possible. Unfortunately, data on breast milk in studies from some countries is only reported on a whole weight basis. These data are presented here in separate tables, because results on wholeweight and lipid basis are not directly comparable.

### **1.3 Relevance of Current Human Tissue Levels of Organochlorines to Human Health**

Dioxins, PCBs and several organochlorine pesticides have been associated with adverse health effects in humans and animals (eg. Allsopp *et al.* 1995, Allsopp *et al.* 1997). A wide array of effects have been documented including endocrine disruption, neurotoxicity, immunotoxicity, reproductive disorders and cancer. In humans, such effects have been reported following relatively high exposure to these chemicals as a result of accidental or occupational exposure. However, studies also indicate that some effects may occur at tissue levels which are at, or near to, those of the currently found in general population as a consequence of unavoidable everyday human exposure to these compounds.

Scientists have hypothesised that endocrine disruption - the disruption of hormone systems in wildlife and humans - could be the mechanism by which some chemicals cause many adverse effects on health. This has potentially implicated endocrine-disrupting chemicals in possible health effects on the general population such as decreasing sperm counts, increases in reproductive problems, reduced intellectual capacity and behavioural problems.

Chemicals which are known or suspected to disrupt the endocrine system based on experimental evidence, include most of those POPs listed by the UNEP. These are dioxins, PCBs, and the organochlorine pesticides DDT, DDE, chlordane, dieldrin, hexachlorobenzene, mirex and toxaphene (Allsopp *et al.* 1997). The organochlorine chemicals listed by the UNEP as priority POPs may also cause toxic effects through mechanisms other than endocrine-disruption. For example, dioxins and certain PCBs

appear to cause a broad range of health effects through their actions on a receptor in the body, known as the Ah receptor.

It is difficult to predict the possible effects of current body burdens of organochlorines on health in the general population. In a review of scientific data on dioxins, the US EPA suggested that the potential for adverse impacts on human metabolism, reproductive biology, and immune competence are at, or within one order of magnitude of average background body burden levels in the general population. They also noted that individuals at the high end of the general population range may be experiencing some of these effects (US EPA 1994). Of perhaps the greatest concern is the possible impact that organochlorines may have on the developing young. The transplacental passage of organochlorines to the developing foetus has been well documented and these chemicals may also pass to the infant via mother's milk. There is evidence which suggests that endocrine-disrupting chemicals, including some organochlorines, may have reached levels in the environment where they could cause adverse effects on development in humans and animals. Such effects are subtle rather than gross, representing a diminished potential, such as reduced fertility, reduced intellectual capacity and weakened immune system (eg. Colborn *et al.* 1993, Colborn 1996). Recently, there has been concern among some scientific experts that impacts of endocrine-disrupting chemicals on health could pose a long-term threat to world biodiversity and to human society (Alleva *et al.* 1995).

#### **1.3.1 Highly Exposed Members of the Population**

The present report discusses human tissue concentrations of organochlorines found in various countries. Individuals who are subjected to higher exposures than the population at large are also identified. For most of the organochlorines, these individuals include nursing infants, occupationally exposed individuals, and people who have a high fish or sea mammal consumption such as Inuit and other Arctic indigenous people.

#### **Occupational Exposure**

Tissue levels of organochlorines in occupationally exposed individuals are briefly discussed in this report. In comparison with studies on tissue levels in the general population, research on tissue levels in occupationally exposed individuals is limited. It is also of concern is that adverse health effects have been associated with occupational exposures to some organochlorines, and these chemicals are still produced or used in many areas of the world.

#### **Nursing Infants**

With regard to nursing infants, persistent chemicals which have accumulated in a woman's body during her lifetime pass into her breast milk and hence to her infant. Indeed, lactation is one way that a mother can significantly reduce her own body burden of organochlorines, but this is at the expense of her nursing infant (Schecter 1996c). The fully breast-fed infant is nourished solely by human milk usually for a period of up to 6 months. Such exclusive consumption, which differs markedly from that of the general population as a whole, potentially exposes the infant to contaminants in breast milk at a time when intake of contaminants per body mass is at its highest. As breast milk is at the top of the food chain, it contains higher

concentrations of organochlorines than most other diets, thus placing breast-fed infants at special risk for potential toxic effects (see Quinsey *et al.* 1996).

Despite potential disadvantages of breast feeding to infants, because of chemical contaminants in milk, it is important to recognise that breast feeding conveys many advantages. Breast feeding has both nutritional and immunological benefits and promotes good health generally. In many countries, breast feeding confers measurable benefits such as decreased rates of infectious disease and increased rates of growth and development (Sonawane 1995). The advantages of breast feeding have therefore led to its encouragement and recommendation by health experts, even though there is concern over chemical contaminants in human milk (eg. WHO 1996, MAFF 1997).

Exposure of the foetus in the womb to organochlorines via placental transfer, and exposure of the infant via breast milk are of great concern to health, because these chemicals may interfere with processes of growth and development. Immature physiological functions of the foetus and infant theoretically make these age groups more vulnerable to chemical exposure (Ostergaard and Knudsen 1998). The World Health Organisation (WHO 1986) concluded that infants may be more vulnerable than older children to chemicals for several reasons, including their larger body surface area compared to weight, higher metabolic rate and oxygen consumption, and different body composition. In addition, infants may be more susceptible to organochlorines because of their immature liver and kidneys, and the central nervous system is not fully protected in infancy. Also, several components of the immune system are not fully developed at birth and it is possible for chemicals to interfere with the development of this system (Ostergaard and Knudsen 1998). In sum, both the foetus and infant are potentially the most vulnerable lifestages to toxic insult from chemical exposure. It is important to note that effects caused during development may not just affect the health of the foetus or infant, but may cause permanent irreversible damage. Some effects may not even become apparent until later in life (Colborn *et al.* 1993).

For persistent organochlorines listed by UNEP, there is experimental evidence that some adversely affect developmental processes (eg. ASTDR 1997). In addition, those which are endocrine-disrupters could potentially be detrimental to development. Subtle effects on development have been associated with exposure to PCBs and /or dioxins in more highly exposed members of the general population (Allsopp *et al.* 1995, Allsopp *et al.* 1997). In the Netherlands, studies on healthy women and their children from the general population revealed that subtle effects on the nervous system were associated with *in utero* and lactational exposure to PCBs and dioxins (Koopman-Esseboom *et al.* 1995, Ilsen *et al.* 1996).

### 1.3.2 Acceptable Daily Intakes of Organochlorines

In an attempt to protect public health, regulatory agencies perform risk assessments to set levels of chemical contaminants in the food supply which deemed to be 'safe' and therefore permissible. Depending on the regulatory body concerned, permissible levels set for consumption of chemical contaminants in food are known by as Acceptable or Admissible Daily Intakes (ADIs), and Tolerable Daily Intakes (TDIs).

The ADI of a chemical has been defined as the daily intake of a chemical that, during a lifetime, appears to be without appreciable risk on the basis of all the facts known at

that time (see Stevens *et al.* 1993). The concept of the ADI is based on the assumption that a threshold exists below which a chemical does not cause toxicity. They are usually based on experiments on the toxicity of the chemical concerned in laboratory animals, from which a lowest observable effect level (LOAEL) or no observed adverse effect level are obtained. In general, the lowest dose value is used to determine a 'safe' level in humans. This result is then divided by a safety factor, usually the arbitrary number of 100, to account for differences in response of laboratory animals and humans, and differences in sensitivity among humans (Ostergaard and Knudsen 1996).

ADIs have been set by the World Health Organisation (WHO) for a number of organochlorine pesticides including total DDT compounds, HCB, (aldrin + dieldrin), heptachlor, heptachlor epoxide, total chlordane and lindane (WHO 1997), see table 11. ADIs have not been established for oxychlordane, aldrin, *trans*-nonochlor, p,p'-DDE, p,p'-DDT, isomers of PCBs, and a and B-HCH (Quinsey *et al.* 1996). ADIs for dioxins have been set by a number different regulatory bodies such as US EPA and WHO (US EPA 1994b, WHO 1992). WHO have very recently reassessed the TDI they previously set for dioxins. ADIs/TDIs for dioxins are further discussed in section 2.5.1).

The food consumption patterns of infants and children are different from those of adults, but no separate ADIs have been yet been established for infants or children. In the present system, ADIs set for dioxins and organochlorine pesticides are designed to prevent adverse health effects over a whole lifetime exposure in a 70kg adult, where a mixed diet has a dilution effect on the consumption of contaminants (Quinsey *et al.* 1996). The application of ADIs to intake of organochlorines over the short-time period of breastfeeding is unclear (Sonaware 1995). Nevertheless, it is of great concern that current levels of some organochlorines in human milk mean that the ADI is exceeded when applied to infant intake. Since infants may be more susceptible to the toxic effects of chemicals than adults, because for example, they are undergoing rapid tissue growth and development, then it is most likely that current ADIs are higher than appropriate for infants (Quinsey *et al.* 1996). It is noted by these authors that infancy is a critical period in development and guidelines for the intake of organochlorines should not be exceeded.

In this report, an attempt is made to estimate whether ADIs would be exceeded for a breast-fed infant, based on levels of organochlorines in breast milk reported for different countries. This is possible by calculating the "Estimated Dietary Intake" (EDI), which is the amount of a contaminant taken in through diet. For a breast-fed infant, the EDI for a particular organochlorine is the intake of that chemical it would have through breast milk. The EDI can be compared to the ADI to find out whether it is exceeded (Dogheim *et al.* 1991).

Several studies on levels of organochlorines in breast milk have calculated EDIs to determine whether an infant's intake of various organochlorines exceeds the ADI. To calculate the EDI, estimations of the volume of milk consumed by the infant and the fat content of the milk are made. Typically, values used are 0.75 litres of milk per day for a baby weighing 5 kg in the first 2 to 3 months of life, and a milk fat content of 3.5% (WHO personal communication, Quinsey *et al.* 1996). However, in reality the actual volume of milk intake varies widely from one individual to another, and the fat content of breast milk is also variable. The use of estimated values to calculate the

EDI therefore only gives an approximation of the actual intake of contaminants in the milk. A more accurate way to calculate intake of organochlorines by an infant is to measure the concentration of an organochlorine in breast milk from each mother, and the volume of milk her baby consumes each day. Whether an individual baby's intake of an organochlorine exceeds the ADI is then known. However, very few studies have measured the daily volume of milk taken in by each individual baby. One recent study did measure actual intakes of milk by individual babies and subsequently calculated whether or not the ADI was exceeded for various organochlorines. It reported that actual intakes of organochlorines by infants determined in this way was different to results calculated using estimated milk intakes. The study therefore concluded that using inferred estimated milk intakes were not reliable indicators of actual intakes. Despite this finding, it is nevertheless deemed scientifically acceptable to estimate milk intakes (Quinsey *et al.* 1996).

In this report, the concept of the EDI is used to provide an approximate guide to the extent to which ADIs are exceeded in different countries, based on average levels in breast milk. Figures for volume of milk intake and milk fat content used in calculations are as those given above.

## 2. POLYCHLORINATED DIBENZO-p-DIOXINS (PCDDs), POLYCHLORINATED DIBENZOFURANS (PCDFs) and POLYCHLORINATED BIPHENYLS (PCBs)

### 2.1 Introduction

The term "dioxins" is a common term, but not proper chemical nomenclature, for a class of chemicals known as polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). The number of chlorine atoms in these compounds varies between 1 and 8, resulting in a possible 75 different PCDDs and 135 PCDFs. The most toxic congener (member of the group) of these chemicals is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Another group of chemicals, the PCBs, constitute a group of 209 congeners. Certain PCBs have been found to exert similar toxicity to TCDD, and are known as dioxin-like PCBs. Other related groups of chemicals which have dioxin-like toxicity include the brominated and chloro/brominated dioxins (see section 2.7). A recent analytical study reported the presence of more than 100 phenolic organohalogenated substances in human blood, that is chlorinated, brominated and mixed chloro-brominated phenols, hydroxylated and dihydroxylated PCB metabolites (Wehler *et al.* 1997). There is evidence that chemicals which cause dioxin-like toxicity exert their toxic effects by binding to a receptor in cells known as the Aryl Hydrocarbon (Ah) receptor.

Analytical techniques developed during the past few decades have made it possible to measure PCDD/Fs and PCBs down to parts per trillion, and on occasion, parts per quadrillion levels in human tissues (Schechter *et al.* 1994). Studies have focused on the levels of 17 PCDD/F congeners in adult human tissues. These 17 toxic congeners are the 2,3,7,8-substituted PCDD/Fs (Schechter 1994). The techniques for measuring PCDD/Fs and PCBs improved greatly in accuracy in the early 1990s (WHO 1996).

PCBs have been measured by a variety of methods. Levels have been reported as an approximation of total PCB content expressed in terms of a commercial PCB mixture

such as Aroclor 1242 or 1260, or as individual PCB congeners. It is only in the past few years that techniques have been developed to measure levels of the dioxin-like congeners. These include non-ortho, mono-ortho and di-ortho PCB congeners. These PCBs are especially toxic, since they act like dioxins in the body. They have recently been found to be present in significant concentrations in human tissues.

The concentration of PCDD/Fs and dioxin-like PCBs in environmental or biological samples, are often converted and expressed in terms of toxic equivalents (TEQ). This system is a means of expressing the combined toxicity of mixtures of PCDD/Fs and PCBs, rather than indicating just the concentration. The system most commonly adopted is the International TEQ (Schechter 1994).

In the International TEQ system, the most toxic congener, TCDD, is assigned a dioxin toxic equivalency factor (TEF) of 1.0. Other congeners are given a TEF value ranked in relation to this. For example, one of the least toxic congeners included in the TEQ system is OCDD which is designated the lowest TEF value of 0.001. To determine the TEQ value of a congener, the concentration of the congener is multiplied by its TEF value. The total toxicity (total TEQ) for a mixture of PCDD/Fs and PCB, can then be established by summing values for the individual congeners together (NATO/CCMS 1988, Ahlborg *et al.* 1994). Note that throughout this section and in the corresponding tables, the levels of PCDD/Fs and PCBs are expressed as International TEQ, specifically parts per trillion TEQ, calculated on an extractable fat basis, unless other units are specified. There are other TEQ systems in use, for example Nordic TEQs, in which the TEF values vary slightly from the International TEQ system, so that they are not directly comparable. In this report, there are a few figures that are presented as Nordic rather than International TEQs, and this is clearly denoted in the text.

With regard to PCBs, the TEQ system only considers those congeners which are thought to exert their effects through the Ah receptor, that is, dioxin-like PCBs. However, there are PCBs which act via mechanisms other than the Ah receptor. These PCBs are not considered by the TEQ system but they are not necessarily harmless (see Fisher *et al.* 1998).

### 2.2 Studies on Tissue Levels of PCDD/Fs in the General Population of Different Countries

Many studies published in the 1980s and 90s have reported on the levels of PCDD/Fs in human milk, blood and adipose tissue. In this review of the data, emphasis is placed on breast milk levels for which most literature was found to be available.

Studies have shown that levels of dioxins differ somewhat between different human tissue types. Blood lipid generally contains the highest dioxin and furan levels, secondly adipose tissue lipid, and finally milk lipid (Schechter 1998).

A general observation of human tissue levels of PCDD/Fs on a world-wide basis is that the highest levels are evident in industrialised countries. This is due to the release of these chemicals as by-products of many industrial processes, notably those involving production, use or disposal of organochlorines. In addition, dietary habits may also play a role in the levels of PCDD/Fs in human tissues. The highest levels of PCDD/Fs are present in meat, fish and dairy products (MAFF 1992). It is therefore



probable that diets in counties involving consumption of high levels these foodstuffs could result in increased levels of PCDD/Fs in human tissue.

Several studies were carried out in the 1980s that investigated levels of PCDD/Fs in human tissues from a number of countries (reviewed by Schecter 1994). These studies showed that levels of PCDD/Fs in human milk, blood and adipose tissue varied widely between different countries (see tables 1a, 1c, 1d). Levels were considerably lower in less industrial countries, such as Thailand, China, Pakistan, Africa, northern Vietnam and Russia. Higher levels were characteristic of more industrial countries, such as the USA and some European countries, reflecting higher chemical use and contamination in these regions. Within each country itself, there was usually little geographic variation in levels of PCDD/Fs. An exception to this is Vietnam, where levels are much higher in South Vietnam than in North Vietnam. This is because of the use of Agent Orange in South Vietnam the war, a herbicide which was contaminated by dioxins, and also as a result of more industrial contamination. When the individual dioxin congeners are considered, characteristic patterns emerge for some countries. For example, European tissue samples have higher levels of a congener (2,3,4,7,8-PnCDF) than US and Canadian samples, which may be due to the use of more leaded petrol in Europe (Schecter 1994).

#### **Blood**

Table 1a shows results of studies on blood levels which spanned 1980 to 1991. In these studies, samples from individuals were taken and then pooled together before analysis. Results showed that similar total TEQ levels were found in Europe and in the US. For example, levels of 41 ppt TEQ were recorded in the US and levels of 42 ppt TEQ in Germany. Studies conducted in the 1990s show that levels in these countries are now lower. For example, a value of 26 ppt TEQ was recently recorded for the US (table 1b). For the most toxic dioxin congener, TCDD, an average of 3 to 6 ppt TEQ is reported for the US (US EPA 1994).

More recently levels of dioxins in humans have been characterised for the first time in three Middle Eastern countries (table 1b), (Schecter *et al.* 1997). Blood samples were collected in 1995 and 1996 from the Palestinian West Bank, Gaza and Israel. Samples taken in the Binghamton, New York, in 1996 are also given. It appears that levels in Israel (26.6 ppt TEQ) are similar to those now present in the US (26.8 ppt TEQ). Levels are somewhat lower in the West Bank (16.9 ppt TEQ) and Gaza (8.4 ppt TEQ), reflecting levels in less industrialised countries (Schecter *et al.* 1997). Recent analysis of blood samples in Germany showed levels (16.5 ppt TEQ) were lower than those recently measured in the US (Papke and Ball 1997). Sources of dioxins in the Middle East are believed to be food imported from Europe and elsewhere, use of herbicides such as 2,4-D phenoxyherbicides, incineration of plastics and toxic chemicals and other incineration. Incineration of waste is common and dioxin standards for emissions have not yet been established. Large municipal waste incinerators are planned in Israel (Schecter *et al.* 1997).

#### **Adipose Tissue**

Table 1c shows adipose tissue levels of PCDD/Fs (TEQ) which were reported for various countries. There was more variation in adipose tissue levels between countries than reported for blood levels. However, research on adipose tissue involved fewer samples compared to work on blood levels, which reduces confidence in the accuracy

of the mean TEQs reported (Ryan *et al.* 1987, Schecter 1994, US EPA 1994). The levels found in Japan, Europe, North America and South Vietnam were similar. In comparison, levels in China and North Vietnam are lower than in the more industrialised countries (Ryan *et al.* 1987).

Recently, a study reported adipose tissue levels of PCDD/Fs in Korea, an industrialised Asian country (Kang *et al.* 1997). The mean level of PCDD/Fs in 32 individuals was 18 ppt TEQ. This value is in the same order of magnitude as levels reported for China and South Vietnam in the 1980s, but lower than levels in other industrialised countries. A recent study in two different regions in Japan, 1992, recorded levels of 50.4 and 43.8 ppt TEQ in adipose tissue. Lower levels were found in the same two regions in 1993 were reported, respectively 17.4 and 25.6 ppt (Sawamoto *et al.* 1994). This study was based on very limited sample numbers although levels are not dissimilar to those reported in the 1980s, 38 ppt TEQ (see table 1c).

#### **Breast Milk**

Table 1d shows levels of PCDD/Fs found in breast milk in the 1980s for various countries reported by Schecter (1994). Again these studies showed that higher levels were evident in industrialised countries while lower levels were found in less industrialised countries. For instance, levels were similar (20-27 ppt TEQ) in USA, Canada, Japan, Germany and highest in South Vietnam. Lower levels (9-13 ppt TEQ) were found in Russia, Pakistan and North Vietnam. The lowest levels (3 ppt TEQ) were found in Thailand and Cambodia.

The most comprehensive set of studies to date on the levels of PCDD/Fs and PCBs in human tissue from many countries was performed by the World Health Organisation (WHO) on breast milk samples in the late 1980s and early 1990s (WHO 1996). This research was undertaken to assess the exposure to PCDD/Fs and PCBs that infants would be subjected to by breast-feeding and the possible health risks of such exposure. Other, more detailed studies on breast milk levels within countries during this period have also been carried out in The Netherlands and in Germany (see Liem and Theelen 1997, Furst *et al.* 1994). In addition, several studies undertaken in recent years have been published on breast milk levels in western countries. These include studies in Sweden (Noren 1993), Norway, Sweden and Denmark (Clechaas *et al.* 1992), Germany (Beck *et al.* 1994), Netherlands (Koopman-Esseboom *et al.* 1994), UK (Wearne *et al.* 1996), France and Spain (Gonzalez *et al.* 1993, Jimenez *et al.* 1996), Japan (Hashimoto *et al.* 1995), New Zealand (Bates *et al.* 1994) and USA (Schecter *et al.* 1996).

The WHO study collected breast milk samples initially in 1987-88 and in a second round of studies in 1992-93. In the second round, samples of breast milk from women in 17 countries were taken from 39 different areas with different pollution levels. With the exception of two countries, The Netherlands and Denmark, samples for each country were pooled, (i.e. mixed together), and subsequently analysed for PCDD/Fs and PCBs.

Results of the 1992-3 study are given in table 2a. The highest PCDD/F levels (20 to 30 pg TEQ/g fat or ppt) were found in Belgium, Canada (Gaspé and Hudson Bay regions), Finland (Helsinki), Spain (Gipuzkoa) and The Netherlands. In the majority



of milk samples, levels were in the range of 10 to 20 ppt TEQ. The lowest levels (4-10 ppt TEQ) were measured for Albania, Hungary, Pakistan and the less industrialised regions in Croatia, Norway and the Russian Federation (WHO 1996). The results were thus complementary with research conducted the 1980s by Schecter *et al.* (1994) discussed above on breast milk since they also demonstrated that levels of PCDD/Fs were lower in less industrialised countries.

Several studies have reported on levels of PCDD/Fs in human milk from countries that were not assessed in the WHO study (see table 2b). A study on levels in France (Gonzalez *et al.* 1993) reported a level of 20.1 ppt TEQ. This is similar to levels in some other European countries. This study also recorded a level of 13.3 ppt TEQ for Spain which is somewhat lower than the level of 19.4 ppt TEQ reported by WHO. A study on breast milk samples taken 1986-91 in Estonia, Finland, Norway and Sweden showed that similar levels of PCDD/Fs in breast milk were apparent in these countries (Mussalo-Rauhamaa and Lindstrom 1995). Data for these countries are presented in table 2b since the WHO study (WHO 1996) did not report figures for Estonia or publish figures for Sweden. A study in New Zealand reported a mean TEQ of 16.5 ppt for urban women and 18.1 ppt for rural women (Bates *et al.* 1994). A recent study in Japan reported levels of PCDD/Fs in human milk (Hashimoto *et al.* 1995). Figures for this study were presented on a whole milk basis rather than on a lipid basis and so are not directly comparable with figures from studies presented here. However, the authors documented that levels found in breast milk samples taken from several places in Japan were similar to other industrialised countries in Europe. This concurs with results for Japan in the 1980s (table 1d), which showed that Japanese levels were similar to European, Canadian and North American levels (Schecter *et al.* 1994).

Slight regional differences in levels of PCDD/Fs have been found to occur within some countries. For instance, slightly but not statistically significantly elevated levels were reported for urban or industrial areas compared to rural areas in Austria, Belgium, Canada, Norway and Sweden in 1988 by WHO. A study in the Netherlands found that human milk contained levels of a number of PCDD/Fs and dioxin-like PCBs which were significantly higher in the western industrialised areas of the Netherlands compared to the more rural north (Koopman-Esseboom *et al.* 1994).

To summarise on concentrations of PCDD/Fs in human tissues, it is evident that levels are generally higher in more industrialised countries and lower in less industrialised countries. On the same theme, regional differences within countries have also been found. Importantly, information on tissue levels of dioxins has been generated largely by researchers in the West, and the most wide-reaching study has been co-ordinated by WHO (WHO 1996). Analysis of PCDD/Fs is relatively expensive and WHO has certified fewer than 50 laboratories world-wide for the analysis of PCDD/Fs (Schecter 1998). The majority of studies have been performed in western countries, and most information published for European countries. Data is also documented for several Asian countries in the 1980s, discounting India, and one study in the 1990s investigated levels in three Middle Eastern countries. Only very limited data was available for Africa (1980s) and no studies were found for South American countries.

### 2.3 Studies on Tissue Levels of PCBs in the General Population of Different Countries in the 1980/90s

In addition to PCDD/Fs, some studies have also measured levels of PCBs in human tissues. Recent studies which have monitored PCDD/Fs and dioxin-like PCBs, have found that PCBs contribute substantially to the total dioxin TEQ.

Comparisons of levels of PCBs in human tissues is difficult, because in some studies PCB mixtures have been measured while in others specific PCB congeners have been measured. In addition, the congeners which have been assessed vary from study to study. Finally, the techniques used to measure PCBs have vastly improved in the past few years. Due to such differences in published studies, this report only discusses data from different countries for which comparisons can be made.

#### *Breast milk*

The WHO 1992-3 study measured dioxin-like PCBs (non-ortho and mono-ortho PCBs) and several indicator PCBs. The specific congeners which were measured were: non-ortho PCBs with IUPAC numbers 77, 126 and 169; mono-ortho PCBs nos. 105 and 118; marker PCBs nos. 28, 52, 101, 138, 153, 180. The study showed that levels of these compounds did not correspond to the ranking of high to low levels of PCDD/Fs which had been found for the different countries. Thus, countries which had displayed high levels PCDD/Fs in human breast milk did not necessarily also have comparably high levels of PCBs. In fact, most countries and regions were found to have similar levels of PCBs, and only a few had significantly higher or lower levels. The majority of samples had levels of dioxin-like PCBs below 15 ppt TEQ. High levels of dioxin-like PCBs (20-30 ppt TEQ) were found in Lithuania and in two samples from Canada (in Basse Cote-Nord, Hudson Bay), whilst levels of marker PCBs were higher in the Czech Republic (Uherske Hradiste), Slovak Republic (Michalovce) and Canada (Hudson Bay). Notably lower levels of all PCBs were found in Albania, Pakistan and Hungary. Results of the WHO study and other studies on areas in the former Soviet Union, show that while levels of PCDD/Fs are similar to many European countries, levels of PCBs are notably higher (Traag and Yuft 1997).

In The Netherlands, a recent study on 78 individual breast milk samples also measured dioxin-like PCBs. The specific non-ortho congeners which were measured (nos. 77, 126 and 169) were the same as those in the WHO study, but in addition to the mono-ortho congeners measured by the WHO study (nos 105 and 118), this study also measured other mono and di-ortho congeners (nos. 156, 157, 167, 180 and 189). The study concluded that dioxin-like PCBs contributed to about half the total TEQ and PCDD/Fs the other half. For example, the average total TEQ value in the study was 43 ppt TEQ, for which PCDD/Fs contributed 23.5 ppt and PCBs the remainder. Examining data in table 2a from the WHO study reveals that the contribution that PCBs make to the total dioxin TEQ varies considerably between different countries. For example, in Belgium PCBs are very low in comparison with PCDD/Fs, whereas in Tromso, Norway the TEQ for PCBs is twice that of the PCDD/Fs. The WHO study also reported that the contribution that mono-ortho and non-ortho PCBs made to the PCB TEQ varied from one region or country to another (WHO 1996).

## Blood

Studies on blood concur with research on breast milk in that they also show that PCBs may also contribute significantly to the total TEQ. In a recent study, blood samples of 5 individuals of the general population in Kansas City, Missouri were analysed. The study found that the total PCDD/Fs plus dioxin-like PCBs in these US samples averaged 69.2 TEQ. (All measurable non-ortho PCBs, 77, 126 and 169, and mono and di-ortho PCBs were analysed). Of the total TEQ, PCDDs contributed 26%, PCDFs 7% and PCBs 68% (non-ortho 9% mono-ortho 56%, diortho 2%). These results imply that PCBs may contribute substantially to total dioxin TEQ in blood in US adults. Similarly, a study in Wales, UK, found that PCBs made an important contribution to the total dioxin TEQ. This research indicated that PCBs contributed at least twice as much to the total TEQ than PCDD/Fs (Duarte-Davidson 1993).

## 2.4 Time Trends

Methods for analysing PCDD/Fs and PCBs in breast milk have improved remarkably during the 1990s. Results of the second (1992-3) round of the WHO study were consequently more accurate than those of the first round due to this fact, and because of improved study design, for example, less laboratories used to analyse samples. In the first round, when results from different countries were compared, only a tendency could be reported on human milk levels because of inaccuracies in the data which may have arisen from sample analysis. Despite such possible inaccuracies, data on the levels of PCDD/Fs and marker PCBs in the first and second round of studies have been compared in an attempt to identify any trends in the levels of these chemicals that may be occurring with time.

### PCDD/Fs

For the 11 countries studied in the first and second round, which included some Scandinavian and European countries and Canada, it was concluded that levels of PCDD/Fs were not increasing with time. In fact, the levels in some countries in 1992/3 had decreased compared to 1987/8. Some countries showed a dramatic decrease of up to 50%. The overall annual decrease in PCDD/F levels in Europe and Canada was estimated to be 7.2% per year (standard deviation 0.8%). Table 2a shows levels of PCDD/Fs found in the 1987/8 and 1992/3 studies. Trends cannot be established for countries outside of Europe and Canada in the WHO study because data from these countries was not gathered in the first round of studies.

A study in Sweden showed that there was a decrease in the levels of PCDD/Fs in breast milk between 1980 and 1985, but not between 1985 and 1989 (Noren 1993). Detailed studies in the Netherlands (reviewed by Liem and Theelen 1996) and in Germany (Furst *et al.* 1994) have also shown that breast milk levels of PCDD/Fs have declined in recent years. Studies in these countries constitute the most extensive dataset based on individual analysis of breast milk samples, although again some uncertainties in results due to the study designs cannot be ruled out. In the Netherlands, a survey in 1993 found a mean level in breast milk of 23.5 ppt TEQ. This was 32% lower than the mean level of 34.2 ppt TEQ which was found in 1988. Similarly, a recent analysis of data based on individual breast milk samples and pooled breast milk samples in Germany, found that levels had decreased by 30% from 23 ppt TEQ in 1991 to 16 ppt TEQ in 1995. At the same time, blood levels were also

indicator PCB levels in breast milk (Liem and Theelen 1997). However, a diet survey has revealed reductions in the dietary exposure to these PCBs between 1978 and 1993. It has been suggested that this discrepancy between human tissue levels and levels in dietary foodstuffs may occur because PCBs have longer elimination half-lives (take longer to be eliminated from the body) than PCDD/Fs. The WHO study was inconclusive regarding trends in PCBs because different, and sometimes less reliable, analytical methods were used by some laboratories in the first round of the study (WHO 1996).

## 2.5 Highly Exposed Populations

### 2.5.1 Nursing Infants

Nursing infants are exposed to chemical contaminants from their mother's breast milk. Studies that have examined levels of PCDD/Fs and PCBs in breast milk, compared with the amount of these compounds excreted by the infants, have shown that they are highly absorbed by the infants. For instance, it was found for most PCDD/F and PCB congeners that the absorption from mother's milk of the ingested compounds was over 95% (Dahl *et al.* 1995).

The quantities of PCDD/Fs and PCBs that are absorbed by the infant via breast-feeding have prompted concern. Studies have shown that while the mother's body burden of these chemicals decreases during lactation, at the same time the infant's body burden increases. For example, the decreasing maternal body burden was shown in a study of Swedish women. It was found that the level of PCDD/Fs and PCBs in breast milk decreased by at least 12% per month during the first 3 months of breast-feeding (Lindstrom *et al.* 1994, Dahl *et al.* 1995). Another study on a woman who nursed twins for two years reported the levels of PCDD/Fs in breast milk decreased from 16.9 to 3.1 ppt TEQ during this period, and levels in blood fell from 14.9 to 4.9 ppt TEQ (Schechter *et al.* 1996b and 1996c). The decrease in a mother's body burden of PCDD/Fs with a concomitant increase in the body burden of the child was illustrated by a study on a German woman and her first and second child. Both infants were breast fed for 6-7 months. Following breast-feeding, the level of PCDD/Fs in blood from the first child was 37.5 ppt TEQ and in the second child was 16.0 ppt TEQ. These levels significantly exceeded those of the mother. When each child was 1 year old, the level of PCDD/Fs in the first child's blood was 3.6 times higher than the mother and the level in the second child's blood was 2.9 times higher (Abraham *et al.* 1996).

ADIs have been set for PCDD/Fs, but these are highly variable depending on the regulatory body in question. For example, the Tolerable Daily Intake set by WHO is 10 picogram TEQ per kg body weight per day (pg TEQ/kg/d), (WHO 1992). This TDI was updated very recently to 1-4 pg TEQ/kg/d. The ADI set by US EPA in their draft reassessment of dioxins is 0.006 pg TEQ /kg/d (US EPA 1994b). This is 100 to 666 times lower than the TDI set by WHO.

Regulatory agencies can assess foodstuffs to make sure that levels of chemicals in the food do not exceed the established limits that are set for the protection of public health. Unlike commercial foods, breast milk cannot be regulated (Rogan and Ragan 1994). It is however possible to estimate the intake of chemicals by an infant via breast milk and compare the intake with the ADI. For example, the US EPA

reported to decline from a level of 42 ppt TEQ in 1989 to 19 ppt TEQ in 1994 (Furst *et al.* 1994) and to 16.5 ppt TEQ in 1996 (Papke and Ball 1997). In the UK, breast milk levels were reported to fall by 35% between 1987/88 and 1993/94 (Wearne *et al.* 1996).

Taken together, these European studies suggest that measures taken in the past few years to reduce dioxin emissions and subsequent contamination of the environment and food chain, may have already resulted in the reduction of human body burdens in these countries. Results from diet studies in the Netherlands and Germany and the UK also indicate that dietary intake levels have decreased (Liem and Theelen 1997, see Schecter *et al.* 1996, Wearne *et al.* 1996). It has been suggested that declining levels in food and human milk and blood may reflect environmental regulations for incinerators and a decrease in the use of leaded petrol. Nevertheless, it has been noted that it is difficult to explain in biological terms the extent of the decline in human levels of dioxins over a short time period, because the half-lives of elimination of dioxins (7 to 11 years) would predict a slower decrease with time (Schecter *et al.* 1997).

Although the above studies suggest that PCDD/F TEQ levels have decreased in the last few years in several European countries and Canada, levels in some countries such as Denmark and Finland do not show a decline. In addition, recent research in the US does not clearly show a decrease in body burden. When 4 individual blood samples were considered from 1995 (8.7 ppt TEQ), levels appeared to have decreased since the 1980s and 1992 (26 and 23 ppt TEQ respectively). Similarly, breast milk data for 5 individual samples from 1995/6 showed a decline from 20 to 8.1 ppt TEQ. However, when pooled US blood samples, (n=100), taken in 1996, Binghamton, New York, were considered, there was no declining trend in recent years, with levels in 1996 being 27.6 ppt TEQ (Schecter *et al.* 1996). The authors noted that both the above mentioned German (Furst *et al.* 1994) and US studies represented samples from among the largest collections of blood and milk in these countries. However, these results may not be completely representative of levels in the general population since the samples were not collected in a systematic fashion (Schecter *et al.* 1997b).

In summary, available research on time trends of PCDD/F levels in human milk shows that levels are not increasing in Canada, USA, and several European countries. The research indicates that levels in some of these countries has declined over the past decade but in others has remained stable. There are still uncertainties in assessing time trends of PCDD/F levels within and between studies because of possible differences in sampling strategies and analytical techniques. No data on time trends was located for developing countries.

### **PCBs**

The situation regarding PCBs is somewhat different to PCDD/Fs. The few studies available show PCB levels have remained more steady and less of a decline is apparent. A study in Sweden analysed blood samples which had been stored frozen for several years. It found PCBs declined between 1972 and 1980, but did not decline between 1985 and 1989 (Noren 1993). A study on breast milk in Germany reported that for PCB congeners 138, 153 and 180, levels appeared to remain constant from 1984 to 1989, although in the following two years results indicated a slight decline (Furst *et al.* 1994). Studies in 1988 and 1993 in the Netherlands reported no change in

calculated the average daily dose of PCDD/Fs to which an infant would be exposed after one year of breast feeding assuming the mothers milk contained 20 ppt TEQ (US EPA 1994). The figure of 20 ppt TEQ in milk is synonymous with levels in breast milk found in many industrialised countries. The calculation predicted that the average daily dose would be 60 pg TEQ/kg body weight/day. This figure exceeds the ADI of 0.006 pg/kg/day set by the US EPA by 1000-fold, and exceeds the TDI of 1-4 pg/kg/day set by WHO. A study by Schecter *et al.* (1996b) also showed that breast-feeding caused the ADI to be exceeded. The study estimated the intake of PCDD/Fs by twins who had been breast-fed for two years. The average daily TEQ intake for each twin was estimated to be 66 ppt TEQ/kg/day during the first year, and thus exceeded the ADI. It is also of note that the US EPA estimated that the range of background exposure for the general population is 1-3 pg TEQ/kg/day. This figure is similar to the WHO TDI of 1-4 pg/kg/day and greatly exceeds the ADI of 0.006 pg/kg/day proposed by the US EPA.

### **2.5.2 Arctic Regions**

People residing in Arctic regions who consume a diet rich in seafood can be exposed to relatively high levels of some organochlorine contaminants. To date, organochlorine contaminants have been documented in blood from mothers living in ten different Arctic regions as part of the Arctic Monitoring and Assessment Programme (AMAP) circumpolar study (AMAP 1997). Participating countries included Canada, Norway, Russia and Sweden. It was reported that average levels of PCDD/Fs in breast milk were similar to non-Arctic regions (10-20 ppt TEQ on an extractable fat basis). However, PCBs were elevated in some regions compared to non-Arctic regions. The highest PCB levels were found in Northwest Greenland and Nunavik, Northern Quebec.

A separate study was recently undertaken on PCDD/F and PCB blood levels in 499 Inuit adults from the Hudson Bay and Ungava Bay regions in Nunavik, Arctic Quebec (Ayotte *et al.* 1997). Inuit people residing in the region are exposed to higher than average levels of organochlorines through their traditional diet which includes large quantities of sea mammal fat. In this study, individual blood samples were pooled together into 20 samples categorised into the same age group, sex and region of residence. These samples were compared to control samples taken from residents of Southern Quebec. For PCBs, the study measured non-ortho PCB congeners (nos. 77, 126 and 169), and mono and di-ortho congeners (nos. 105, 118, 156, 157, 170 and 180). Results showed striking differences in PCB levels between the two populations. For Inuit men and women aged 18-39 residing in Nunavik, the total PCB concentration was 2.0 mg/kg lipids. This is 15-fold greater than residents of Southern Quebec where the total PCB concentration was 0.13 mg/kg. PCDD/Fs levels were also higher in Inuit residing in Nunavik. The mean concentration was 89 ppt TEQ which was 3.4-fold greater than residents of Southern Quebec (26 ppt TEQ).

PCBs were found to contribute very substantially (78%) to the total TEQ. Mono and di-ortho PCBs represented 64% of the total TEQ concentration, non-ortho congeners represented 14% while PCDD/Fs represented only 20%. This is in contrast to samples from Southern Quebec where PCDD/Fs contributed 56%, mono and di-ortho PCB congeners 24%, and non-ortho PCBs 20%.



A higher PCB contribution to the total TEQ appears to be typical for individuals who consume large amounts of species from the marine food web since such species are a high source of these chemical contaminants. For instance, a study in the Faroe islands reported the highest PCB levels were found in the breast milk of women who frequently ate whale meat/blubber. The levels of PCBs were 7 to 12 times higher than in breast milk from other European women, whereas levels of PCDD/Fs were not elevated (Grandjean *et al.* 1995). Another study in Sweden reported that fish from the Baltic Sea were a major source of PCBs in people's diets. For example, a higher fish intake was associated with higher PCB levels in blood. The PCB contribution to the total dioxin TEQ was nearly 80% among high consumers of fish (Asplund *et al.* 1994).

In 1997, the AMAP circumpolar study reported that current exposure to PCDD/Fs is at, or just below, tolerable daily intakes in most circumpolar nations. However, when dioxin-like PCBs are added to the PCDD/Fs, this pushes the total dioxin TEQ exposure well above tolerable daily intakes set by regulatory authorities (AMAP 1997). The study on Inuit women from Nunavik (Ayotte *et al.* 1997) concluded that body burdens of PCBs and dioxin-like compounds are close to those which induced adverse health effects in laboratory animals. However, the study speculated that dietary benefits from the sea-food based diet still outweigh the hypothetical risks for health.

### 2.5.3 Residence in Contaminated Environments

A study on tissue levels and health of a Native American community who reside along the St. Lawrence River in New York, US, and in Ontario and Quebec, Canada, has been continuing over the past few years. Environmental sampling has revealed high PCB contamination in regions close to the inhabitants. The source of the PCB contamination is most likely from leaks and discharges of nearby industries that occurred in the past. This is of great concern since the Mohawk community rely on local game and fish for food. The study found that Mohawk women who gave birth in 1986-89 had twice the level of total PCBs in their breast milk compared to a control group from the general population. However, Mohawk women who gave birth in 1990 did not have higher levels in their breast milk. This was most likely due to a significantly lower intake of fish by the mothers over time, probably as a result of health advice. Unfortunately, in one region, Cornwall Island, levels in breast milk remained high in mothers who have resided in the area for over 6 years. The high levels were not related to fish consumption, but only to the time of residence in the region. It was suggested that the PCB contamination in the area could be coming from several sources, and the high levels in breast milk reflected multiple exposures to the women (Fitzgerald *et al.* 1994).

Another study on a fishing population that inhabits small coastal communities along the Lower North Shore of the St. Lawrence River, Quebec, found that residents had elevated blood PCB levels which were similar to those reported previously for Inuit in the Canadian Arctic. The total TEQ for PCDD/Fs and PCBs in the fishing population was 5-fold greater than the TEQ in urban residents in the region. The study found that the high levels appeared to be due to largely to the consumption of seabird's eggs rather than fish in this area. Consumption of a single seabird egg would result in an individual exceeding the TDI set by Health Canada for both PCDD/Fs and PCBs (Ryan *et al.* 1997b).

In some areas of rural China, residents have been exposed to elevated levels of dioxins because of the spraying of a dioxin-contaminated pesticide, sodium pentachlorophenol (Na-PCP), to control the spread of snail-borne schistosomiasis. Residents of sprayed areas had higher blood levels of total PCDD/Fs (9 to 16.3 ppt TEQ) compared to residents living in areas which were not sprayed (4.8 to 6.4 ppt TEQ). In addition, levels in breast milk of mothers from the sprayed regions (5.4 ppt TEQ) were about twice those of unexposed mothers (2.6 ppt TEQ). The authors suggested that although tissue levels of the general population in China are low compared with levels in more industrialised countries, the higher levels in persons exposed to Na-PCP are cause for concern (Schechter *et al.* 1994b).

### 2.5.4 Occupational Exposure

PCBs were in widespread use from the 1930s until the 70s. Their use declined steadily thereafter as many countries throughout the world banned or severely limited their production. Only recently however, it was revealed in unconfirmed press reports that PCBs are still being manufactured in Russia (Washington Post 1998).

Main uses of PCBs included dielectrics in transformers and capacitors and as cooling fluids in hydraulic systems. Studies on health impacts of PCBs on workers at capacitor plants have been reported in the past (reviewed by Silberhorn *et al.* 1990). In 1987, workers who had been employed for 4 to 37 years at a power plant in Zagreb, in former Yugoslavia were found to have blood levels 2 to 4 times those of the general population due to their handling of PCB containing materials (Krauthacker 1990). Although PCBs are no longer deliberately manufactured, it is possible that occupational exposure may still occur in some instances because, for example, they are present in many old electrical appliances that will eventually have to be disposed of. Also, PCBs have been detected in air emissions from incinerators. One theory is that they are emitted from incinerators when PCBs are present in refuse fed to the incinerator (US EPA 1994). A recent study at a hazardous waste incinerator in Sweden found that the pattern of some PCB congeners present in workers blood was similar to the pattern found in air samples at the plant. This indicated some influence of occupational exposure in the workers although the total level of PCBs in workers was not significantly different from blood samples taken from the general population (Selden *et al.* 1997).

PCDD/Fs are produced as by-products from a wide variety of industrial processes including the production of some chlorinated chemicals, for example, chlorophenols and various pesticides, incineration of municipal and hazardous waste, various metallurgical processes, certain processes in the pulp and paper industry and the production of PVC. Consequently, there are numerous occupations where individuals could be potentially exposed to dioxins. Indeed many studies have documented elevated blood levels of dioxins in workers from several occupations, examples of which are given below. In addition, there have also been accidents which have resulted in populations being highly exposed to dioxins, such as Seveso, Italy in 1976.

### Past and present production of chlorophenols and phenoxyherbicides

Several studies have shown that occupational exposure to dioxins occurred in workers in the 1960s, 70s and 80s at factories that produced trichlorophenol (TCP), or various phenoxyherbicides such as 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and 2,4-D.



High levels of TCDD are characteristic of occupational exposure to these trichlorophenol-containing chemicals. For example, in Ufa Russia, two decades after production at a plant ceased, former workers were found to have blood levels of TCDD which were up to 10 times those of background levels in the region. Levels of other PCDD/Fs were two to three times as high as background levels (Schechter *et al.* 1992, Kruglov *et al.* 1995). A more recent analysis of blood samples taken in 1992 from some of these Russian workers showed that the levels of TCDD were about twice those of in the initial reports. In addition, even administrative workers at the plant had notably greater blood levels of PCDD/Fs than normal (Ryan *et al.* 1997a). Another study on female workers from the plant was undertaken to investigate whether their children, who are now adults, had raised blood levels as a result of exposure transplacentally and via breast feeding. Twenty years on after initial exposure from their mothers, the children were found to have TCDD levels which were 150 to 2000 times higher than the general population. In most cases, levels were higher in the children than their mother's, indicating that relatively large amounts of TCDD were transferred from mothers to the children (Schechter *et al.* 1994c).

A study of former workers from a phenoxyherbicide plant in Sweden showed that their blood contained elevated levels of TCDD and PCDD/Fs, 16-21 years after they had finished their employment with the plant. Mean levels of TCDD were 8 times higher than non-exposed persons and the total PCDD/F TEQ was over 2-fold higher (Rappe *et al.* 1994). At a herbicide plant in Germany which closed in 1984, the average TEQ for total PCDD/Fs in workers blood measured in 1988-91 was 249.5, which was 6 times higher than background levels in the general population at that time of 40.8 ppt TEQ (Papke *et al.* 1992).

Elevated dioxin levels in workers have been demonstrated to be present up to 34 years after substantial exposure. This shows the extreme persistence of dioxin in human tissues (Schechter 1998). The half-life of these chemicals in the body in human tissues has been estimated. The half-life is the time taken for the level in the body to reach half its former level. For TCDD, varying half-lives have been reported ranging from 6.9 to 11.3 years. Less is known about half-lives of the other 2,3,7,8-substituted dioxins and furans. A recent study noted that half-lives for most PCDDs were in the same order of magnitude as TCDD, and half-lives were for most PCDFs were slightly shorter (Flesch-Janys *et al.* 1994).

Occupational exposure to dioxins from the production of pentachlorophenol has been reported. Unlike the production of trichlorophenol products where high levels of TCDD occur, the production of pentachlorophenol typically results in different dioxin congeners being elevated. Studies at factories that produced pentachlorophenol in Germany (Papke *et al.* 1992), and more recently in China (Olie *et al.* 1997), have shown increased levels of dioxins in workers. In Germany, the mean level recorded in workers blood was 158.6 ppt TEQ which is over 3 times greater than the national average. The maximum and minimum levels recorded were respectively 946.5 and 31.2 ppt TEQ. At the chemical plant in China the same production process of PCP as in the Germany plant was reported to be used. However, levels of PCDD/Fs in the blood of workers are outstandingly high. In six of the workers who were tested, levels were between 1168 and 7480 ppt TEQ and in one worker the level was 22,308 ppt TEQ. The background level in Chinese general population has been reported to be 20.9 ppt TEQ.

### ***Metal Industries***

A study of metal reclamation workers in Germany found that certain PCDD/Fs were elevated in their blood. The mean value for the total PCDD/Fs was 90.2 ppt TEQ which is over twice the national average of 40.8 ppt TEQ (Papke *et al.* 1992). Another study found elevated levels of dioxins in the blood of men whose occupation involved metal burning (Menzel *et al.* 1996). A recent study in Germany found that levels of repair welders were somewhat elevated and should be further investigated. However, the greatest concern was for workers performing thermal oxygen cutting at scrap metal reclamation and demolition sites. The median blood level in these workers was 44.4 ppt TEQ, which is elevated in comparison to a value of 17.3 for the general population of Germany. Levels in the workers blood increased with time of employment, confirming there was a causal link between occupation and blood levels. The source of dioxin in this occupation was found to be due to PVC in anticorrosive paints on the metal. The authors concluded that it is necessary to exclude such exposure to workers in the future by banning PVC as a component of anticorrosive paint (Menzel *et al.* 1998).

### ***Incineration***

Municipal waste incinerators, which are commonly used to dispose of domestic waste, are known to emit dioxins. Workers may be exposed to contaminated soot and flue ash at such facilities. Studies at older types of incinerators in New York and in Germany found elevated levels of some PCDD/Fs congeners in the blood of workers (Schechter 1994). A more recent study at a municipal waste incinerator in Germany also found levels of some congeners were statistically significantly elevated (Hazel and Frankort 1996). However, another study at a modern state of the art incinerator in Germany did not find elevated levels in workers blood (Schechter *et al.* 1994). Research on workers at 3 chemical waste incinerators in Germany did not find elevated levels of dioxins in workers (Papke *et al.* 1994). A study in Finland has been conducted on workers who were involved in hazardous waste disposal. Levels of dioxins in the blood of most workers was not elevated, but certain PCDD/Fs were elevated about two-fold in some workers. Differences in blood levels between workers was not unexpected because they had jobs in different parts of the plant which could lead to varying levels of exposure (Luotamo *et al.* 1993).

### ***Production of Chlorine and PVC***

Workers involved in the production of chlorine in the chloralkali industry and in the production of vinyl chloride (VCM), a precursor of PVC, could be potentially exposed to PCDD/Fs. A recently published Swedish study found that overall levels of PCDD/Fs were not different from those of referent individuals not working in the industry. However, the distribution pattern of congeners in the workers blood was notably different to referents. Specifically, two PCDF congeners were related to work in the VCM and chloralkali industries (Hansson *et al.* 1997).

### ***Pulp and Paper Industry***

PCDD/Fs are produced as unwanted by-products when pulp and paper is bleached with chlorine-based chemicals. Studies which investigated occupational exposure to PCDD/Fs at pulp and paper mills in Finland and the US, found that levels of the compounds in workers blood were not statistically significantly elevated. (Rosenberg *et al.* 1994, Tepper *et al.* 1995).



## Summary

From the above information, it appears that occupational exposure to dioxins that resulted in extremely elevated levels in workers, such as production of TCP and phenoxy-herbicides, may no longer occur because of increased safety standards and the closure of some chlorophenol and herbicide plants. Nevertheless, it is also apparent that there are occupations that continue to expose workers to dioxins and may result in increased body burdens. Given this fact, and given the high number of occupations involving potential exposure to dioxins, it could be considered that there is currently a paucity of data concerning occupational exposure to dioxins. For example, there is little information in published scientific literature for the handling of hazardous wastes, production of PVC, spraying phenoxy or chlorophenol based pesticides, and more studies are required to investigate certain processes in the metal industry. Of further and perhaps greater concern, is the very limited data available for developing countries where industrial standards may be lower than currently employed in western nations. For instance, the case of production of PCP at a plant in China illustrates that workers at this factory are exposed to exceedingly high levels of dioxins.

## 2.6 Relevance to Human Health

### Infants

It is of great concern that ADIs set for PCDD/Fs are exceeded by breast-fed infants in developed countries. As previously mentioned (section 1.3.2), infancy is a critical period in development and guidelines for the intake of organochlorines should not be exceeded (Quinsey *et al.* 1996).

The relevance for health of infants exceeding ADIs is however not known. Consequently attempts have been made to estimate risks to infant health due to intake of PCDD/Fs during breast feeding, by better characterising their exposure to the chemicals. Mathematical models are used to estimate the body burden of the infant. The body burden can then be compared to estimated body burdens in laboratory animals, or body burdens in humans at which a particular health effect is known to occur (eg. Rogan and Ragan 1994, Ayotte *et al.* 1994). Such comparisons between animal and human data are deemed reasonable since many studies have noted that health effects induced by TCDD occur at similar doses in most animal species. Therefore, the dose of TCDD that produces a particular effect in experimental animals might be expected to be similar to the dose which causes the same effect in humans (DeVito *et al.* 1995).

One study has estimated health risks to Inuit infants since Inuit breast milk has been found to contain high levels of PCBs (Ayotte *et al.* 1994). Based on levels in Inuit breast milk, the maximum estimated body burden an infant would be likely to attain was a concentration of 264 ng/kg in adipose tissue. This figure does not exceed NOAELs recorded for cancer and reproductive effects in rats. However, this exposure to Inuit infants is close to exposure at which other adverse health effects occurred in laboratory animals. For example, the exposure is 4.6 times lower than adverse reproductive effects which occurred on male rats exposed to TCDD *in utero* and during lactation. Using such methods to estimate health risks to infants can thus provide an indication that for some infants there is only a small margin of safety

between their exposure and exposure which is known to cause effects in laboratory animals. This itself is obviously of great concern, and becomes more so when it is considered that human sensitivity to a particular effect may vary between individuals.

Direct investigations of the potential health impacts to infants resulting from *in utero* and lactational exposure to PCDD/Fs and PCBs, rather than estimating health risks, has come from epidemiology studies. Several studies of highly exposed infants, and infants exposed to current background levels of PCDD/Fs have shown associations between PCDD/F and/or PCB exposure and various subtle effects on nervous system function and changes in immune system cells (see Allsopp *et al.* 1997)

### Adults

A recent study estimated body burdens in experimental animals that produced effects on health, and body burdens in humans which have been associated with health effects. The study compared these results to body burdens of the general population (DeVito *et al.* 1995). Cancer in animals was found to occur at body burdens of 944-137 000 ng TCDD/kg body weight and non-cancer effects at 10-12,500 ng/kg. The average human body burden in the general US population was estimated to be 13 ng TEQ/kg body weight, and in highly exposed persons ranging from 96-7000 ng TEQ/kg body weight. For several health effects, body burdens in the general population were found to be similar to, or within an order of magnitude of the body burdens in experimental animals. For instance, experiments in which animals have been exposed to TCDD show that one of the most sensitive targets for TCDD toxicity is the immune system. Immune alterations, including altered lymphocyte subsets in marmosets and enhanced viral susceptibility in mice, have been reported at body burdens equivalent to human background exposures, although the clinical significance of such parameters is not known. Presently, it is still unknown whether levels of dioxins in the general adult population are causing effects on human health (DeVito *et al.* 1995), but the fact that tissue levels in the general population are close to those known to cause health effects in animals is of great concern.

## 2.7 Polychlorinated diphenyl ethers (PCDEs) and polybrominated dibenzo-p-dioxins and dibenzofurans (PBDD/Fs)

Aside from PCDD/Fs and PCBs, there are other dioxin-like compounds found in human tissues. Over 100 phenolic organohalogenated substances were detected in a recent analysis of human blood, including chlorinated, brominated and mixed chlorobrominated phenols, hydroxylated and dihydroxylated PCB metabolites (Wehler *et al.* 1997).

Polybrominated dibenzo-p-dioxins (PBDDs) and dibenzofurans (PBDFs) as well as mixed brominated and chlorinated phenols, are structurally similar to PCDD/Fs. They are formed as by-products of combustion processes such as incineration, but PBDD/Fs are also used as flame retardants. They have been identified as potential environmental pollutants. Like PCDD/Fs, these chemicals are thought to exert biological effects through the Ah receptor. They have similar, if not identical, biological effects to PCDD/Fs. It has been proposed that the TEQ system could also be applied to the PBDD/Fs. There are however only limited data on the presence of these compounds in biological tissues (Mennear and Lee 1994). In addition to PBDD/Fs, there are many other environmental contaminants, mostly organohalogenes,



which have the potential to cause adverse effects through the Ah receptor mechanism. These chemicals may contribute in addition to the dioxin-like toxicity of chemical mixtures in biological tissues. However, their toxicity is not represented by the TEQ system (Giesy *et al.* 1994).

One study reported that PBDD/Fs were either not detectable, or were present at low concentrations (less than 20 ppt on a lipid basis), in human breast milk samples from Swedish women (Wiberg *et al.* 1992). The authors suggested that these compounds are of minor concern for human health, whereas PCDD/Fs, present at higher concentrations, are a more serious environmental problem. Nevertheless, it is of concern that PBDD/Fs add to the body burden of dioxin-like compounds in humans, and that less is known about their toxicity than other PCDD/Fs. In addition, exposure to PBDD/Fs may be an occupational problem. For example, workers could be exposed in plastic and textile industries which produce or manufacture goods that are treated with brominated flame retardants. One study on resin production, which involved extrusion blending of polybutyleneterephthalate with decabromodiphenylether, found this process lead to the formation of PBDD/Fs. Research on workers employed in this process reported that blood levels of PBDD/Fs in these individuals correlated well with the amount of time they had been employed and therefore exposed (Zober *et al.* 1991).

Polychlorinated diphenyl ethers (PCDEs) are chemicals that are generated from combustion sources and from chlorophenol preparations. A recent study has monitored the levels of PCDEs in Finnish human adipose tissue and in fish tissue from various species. The study found four PCDE congeners in human adipose tissue (estimated TEQ < 3 ppt, on an extractable fat basis). Similar levels were detected in Canadian and US human tissue samples in separate studies. The researchers concluded that the most likely sources of these compounds in the Finnish environment is from wood preservative, and in human tissue is from consuming fish (Koistinen *et al.* 1995). PCDEs have also been detected in human milk in Germany and recently in human blood in Sweden. Although levels of these chemicals are two orders of magnitude lower than PCB levels, the study suggested that the relevance of the PCDE levels is unknown, since too few toxicological studies have been performed to date on these chemicals (Wehler *et al.* 1997).

### 3. DICHLORODIPHENYL TRICHLOROETHANE (DDT) and DICHLORODIPHENYL DICHLOROETHANE (DDE)

#### 3.1 Introduction

Since the 1940s DDT has been widely used throughout the world to combat agricultural pests, indoor insects, and in sanitation campaigns against malaria. Its use has been totally banned in developed countries, due to its persistent, bioaccumulative properties, adverse impacts on wildlife and suspected effects on humans. However, DDT remains in use in some developing countries. The WHO currently recommends the use of DDT for malarial outbreaks, although public health experts do not uniformly endorse its use. DDT targets adult insects and cannot kill larvae. Resistance of insects to DDT has occurred world-wide (Lopez-Carillo *et al.* 1996, Rivero-Rodriguez *et al.* 1997).

DDT and its metabolites DDE and DDD are commonly found in human tissue samples, and have been reported as being the most widespread contaminant in human milk (Jensen and Slorach 1991). In many countries, despite being banned several years ago, DDT compounds continue to be found in human tissues, demonstrating the remarkable biological persistence of this chemical (Sonawane 1995). The isomers *p,p'*-DDT and *p,p'*-DDE can be detected in breast milk. Levels of the *o,p'*-DDT and *p,p'*-DDD isomers are much lower, such that *p,p'*-DDT and *p,p'*-DDE are the major contributors to the total sum of DDT compounds (DDT + DDE + DDD). In humans, levels of DDT and DDE in blood serum have been found to increase with increasing age (ASTDR 1997).

Countries where very high levels of DDT and DDE are found in human tissue are those where DDT is still used in agriculture or to control vector-borne diseases such as malaria. Despite the undesirable properties of DDT, it is used in developing countries primarily due to cost-benefit efficacy and broad spectrum toxicity (Nair *et al.* 1996). In India, it is used both in agriculture and in vector control programmes. As a result, the environment suffers high contamination with DDT and there are elevated levels in human tissues (Kashyap *et al.* 1994).

#### 3.2 Levels in Breast Milk

Tables 3a and 3b list the concentration of DDT compounds found in human milk in various countries and tables 3c and 3d show *p,p'*-DDE levels. DDT is generally reported as *p,p'*-DDT and sometimes as total DDT.

The studies showed that DDE is a very widespread contaminant of human milk. It was present in virtually all samples of breast milk that were tested from many different countries. For instance, most studies reported DDE contamination in 100% samples, and 3 reported it in 96, 97 and 99% of samples. DDT was also found to be present in breast milk from all countries, although the proportion of samples containing *p,p'*-DDT was less than for *p,p'*-DDE. The number of samples which contained *p,p'*-DDT ranged from 21.5% in Spain to over 95% in several countries.

Jensen and Slorach (1991) reported large differences in human tissue levels of DDT and DDE between different countries. Elevated levels were found in south-eastern US, southern and eastern Europe, and in developing countries. Studies presented in tables 3a-d in the present report, also showed that by far the highest DDT and DDE levels were evident in developing countries. These included some countries in South America, Asia and Africa. The studies also showed that relatively high levels were apparent in eastern Europe and in a few western European countries. The lowest levels were evident in some western and north-western European countries and the US.

The highest DDT and DDE levels were present in India (DDT 13.1 ppm and DDE 12.5 ppm) and Zimbabwe (DDT 9.07 and DDE 13.6 ppm). High levels of DDT, over 1 ppm, were also apparent in Kenya (3.73 ppm), Mexico (1.27 ppm), Nigeria (2.27 ppm) Turkey (2.35 ppm), South Vietnam (4.7 ppm) and Egypt. High levels of DDE were also reported for some of these countries. Those with DDE levels around and over 2.5 ppm included Brazil (2.53 ppm), Kenya (2.95 ppm), Mexico (5.01 ppm), Thailand (3.61 ppm), Turkey, (2.4 ppm), and South Vietnam (6.7 ppm). Note that



levels reported for Thailand and South Vietnam are based on a limited number of samples, but nevertheless reflect the fact that DDT was used in sanitation campaigns at the time of study (Schechter *et al.* 1989).

Several countries were reported to have p,p'-DDE levels around 1 to 2 ppm, including Australia (0.96 ppm), Faroe Islands (2.01 ppm), France (2.18 ppm), former East Germany (1.13 ppm), Italy (2.2 ppm), Jordan (2.04 ppm), Kazakstan (1.96 ppm), Nigeria (1.33 ppm), Russia (1.26 ppm) Slovak Republic (1.66 ppm). Concentrations lower than 1 ppm were evident in the USA and some European countries, Netherlands, Norway, Spain, Sweden, UK.

Considering the contribution that different DDT compounds make to the total sum of DDT in breast milk (i.e. DDT + DDE + DDD), it is apparent that DDE is the greatest contributor in western countries. Thus DDE levels are much higher than DDT levels in breast milk in such countries, which is clearly evident in tables 3a-d. However, in developing countries where DDT is still in use, DDE has been found to contribute less to the total, around 50%, whilst DDT compounds contribute more (Kalra *et al.* 1994). Detection of p,p'-DDT in human tissue and human milk samples indicates recent exposure to the parent compound, whereas p,p'-DDE represents chronic exposure (Quinsey *et al.* 1995, Rivero-Rodriguez *et al.* 1997). Thus higher levels of p,p'-DDT in breast milk samples from developing countries is most likely caused by the continued use of DDT and therefore continued exposure to the compound in these regions (Kalra *et al.* 1994).

Marked regional differences in levels of DDT and DDE in human milk are apparent in countries where DDT is still in use. For instance a study in India found that women residing in areas Fairdkot, where DDT is used in cotton-growing, had higher breast milk levels of DDT and DDE than women living in the urban community of Ludhiana where use of pesticides is less (Kalra *et al.* 1994).

Regional differences relating to DDT usage are also evident in other countries. For instance, aerial spraying of DDT is carried out in the Kariba area of Zimbabwe in tsetse fly vector control programmes. As shown in the tables 3a-d breast milk levels of DDT and DDE are considerably higher Kariba (9.07 and 13.60 ppm) than the national average breast milk levels (1.33 and 4.49 ppm), (Chikuni *et al.* 1997). Similarly, in a tropical region of Mexico, higher DDT and DDE levels were found in human milk in suburban areas of Veracruz than in urban areas. This was reported to be due to the spraying of DDT in suburban areas for malarial control which resulted in inhalation of DDT vapours by mothers, causing extensive exposure and eventual elimination in breast milk. Levels of DDT and DDE in breast milk respectively were 0.422 and 2.709 ppm in urban Veracruz versus 2.460 and 8.253 ppm in the suburban area (Waliszewski *et al.* 1996). In non-agricultural and non-tropical areas of Mexico, such as Mexico city, DDT is still found to accumulate in human tissues but to a lesser degree. For example, in Mexico city, mean breast milk levels of p,p'-DDE were reported to be 0.594 ppm (Lopez-Carillo *et al.* 1996). This is 10-fold lower than human breast milk in the tropical area of Veracruz, mean 5.017 ppm.

In Kazakstan, average DDE levels were 1.96 ppm, but in rural areas the figure was higher, 3.3 ppm. This was possibly because of its persistence in the food chain, since its use on cotton crops was curtailed in the 1970s. In a region by the Aral Sea, the ratio of DDT to DDE was elevated which suggested recent exposure to the parent

compound, possibly from pesticide-laden dust blowing from the dry lake bed (Hooper *et al.* 1997). A recent study conducted on the health of children who are living in areas close to the Aral Sea, found they had high blood levels of DDT compounds. The levels were 20 times higher than children living in Stockholm, Sweden (Jensen *et al.* 1997).

The AMAP study of maternal blood levels of POPs in Arctic countries found particularly high levels of DDT and DDE in north-western Russia. Levels of DDT were about 3 to 20 times higher than levels in other countries (Gilman *et al.* 1997). It was suggested that these very high levels could be either due to significant uses of the pesticide in this region or to significant amounts in the food supply. The study found somewhat elevated levels in Greenland and Canada. It was noted that levels of certain POPs in Arctic regions were consistent with the relative amounts consumed in traditional foods, especially where marine mammals were a large part of the diet.

### 3.3 Time Trends

In countries where DDT has been banned, the body burden of this pesticide and its metabolites have declined with time in recent years. Studies on breast milk have reported a downward trend in levels of DDT compounds in Canada, USA, Australia, several European countries including Spain, UK, Norway and Sweden, and Turkey (respectively, Mes 1994, Sonawane 1995, Stevens *et al.* 1993, Hernandez *et al.* 1993, Dwarka *et al.* 1995, Johnsen *et al.* 1994, Atuma *et al.* 1998, Cok *et al.* 1997).

For a few countries, including Australia, USA, Canada and Norway, data is available from the 1970s, and shows a general decrease in breast milk levels of DDT from this time until the 1990s. Recent studies have presented figures which also illustrate the decline in DDT levels. For example, in the UK, a p,p'-DDE level of 1.6 ppm was recorded in 1979/80, and in 1989/91 the level was 4 times lower, 0.4 ppm. This represents a 75% drop in levels. It reflects the withdrawal of DDT from agricultural use in the UK and prohibition of the compound in the European Community (Dwarka *et al.* 1995). In Norway, total DDT levels are estimated to have fallen by 75% between 1982 and 1991 (Johansen *et al.* 1994). In Sweden levels also fell between 1986 and 1990, but DDE levels increased slightly between 1990 and 1994. The authors did not offer an explanation of this increase (Atuma *et al.* 1998). Studies carried out in Canada indicate a decline in breast milk levels of DDT compounds from 1967 to 1986 (Mes 1994). Total DDT was estimated to decline by 64% between 1986 and 1992 in Canada (Newsome *et al.* 1995). Similarly, studies in the province of Quebec, Canada, show that levels in 1988/90 were 61% lower than levels reported 10 years previously (Dewailly *et al.* 1996). In Australia, studies showed a progressive decrease in total DDT levels between 1974 and 1991. Levels fell by about 33% between 1980 and 1991 (Stevens *et al.* 1993).

In non-western or developing countries little information was available in recent literature to determine whether levels of DDT had fallen at all in the past few years. In Iran, a survey of adipose tissue levels in 1991/2, noted that levels had fallen from those recorded 1974-6 and were now equivalent to levels found in most western countries (Burgaz *et al.* 1995). One report of blood levels of DDT in Gujarat state, India, reported that lower levels than had been found previously, indicating a lowered usage of DDT in this region (Kashyap *et al.* 1994). In Mexico, studies on adipose



tissue levels of DDT do not appear to indicate a decline in levels (Lopez-Carillo *et al.* 1996).

### 3.4 Highly Exposed Populations

#### 3.4.1 Nursing Infants

A recent study showed that maternal DDE levels were significantly reduced as a result of lactation. The study monitored a woman's blood and breast milk levels of DDE during a 2.5 year period while she nursed twins. Levels in breast milk decreased considerably over time from 0.246 to 0.0459 ppm milk fat (Schechter *et al.* 1996c).

An ADI of 20 ug/kg/day was set in 1994 for any combination of DDT, DDD plus DDE (WHO 1997). Table 11 shows the estimated concentrations of DDT, DDD plus DDE in breast milk fat and whole milk which should not be exceeded if an infants intake is not to exceed the ADI. Table 3e shows the total sum of DDT compounds for different countries. Comparison of the estimated levels which should not be exceeded (table 11), with mean levels of DDT compounds in breast milk reported for different countries (table 3e), reveals that estimated infant intakes are close to the ADI in several countries. Estimated intakes exceed the ADI in Kenya, Mexico, Nigeria and Thailand. The highest exceedances are for India and Zimbabwe, where in some regions, estimated infant intakes are over 6-fold higher than the ADI.

#### 3.4.2 Occupational Exposure

Occupational exposure to DDT can result in very high tissue levels of DDT and DDE compounds. A study in Veracruz, Mexico, investigated adipose tissue levels of DDT compounds in a group of workers whose occupation involved spraying houses with DDT and other pesticides to control malaria vectors (Rivero-Rodriguez *et al.* 1997). Comparisons were made with the general population of Veracruz state for whom adipose tissue levels may reflect direct exposure to the sanitation campaigns and exposure through diet, (mean p,p'-DDT concentration of 1.34 ppm, p,p'-DDE, 14.1 ppm and total DDT 15.65 ppm fat), (Waliszewski *et al.* 1995). Adipose tissue levels of total DDT in the workers who sprayed DDT were found to be 6-fold higher than levels the general population (mean p,p'-DDT 31.0 ppm fat, p,p'-DDE 60.98 ppm fat, and total DDT 104.48 ppm fat), (Rivero-Rodriguez *et al.* 1997)

### 3.5 Relevance to Human Health

Numerous animal studies have been carried out on DDT, but human data is more limited. The central nervous system is a major target organ in humans and animals. Studies in humans have reported symptoms of hypersensitivity to contact, tremors, and convulsions following occupational exposure or ingestion at high doses. Such effects have also been observed in laboratory animals following oral administration of DDT (ASTDR 1997).

Animal studies have shown that the liver and reproductive system could be potential target organs in humans. Several adverse effects on the liver have been demonstrated in animals. In humans, alteration of liver enzymes in occupationally exposed humans has been associated with DDT exposure, although there is no evidence whether the liver damage this reflects is irreversible. No human studies have indicated

reproductive toxicity associated with DDT exposure. Animal studies however, show that long-term, low level exposure to DDT results in decreased fertility, stillbirths, and increased foetal mortality (ASTDR 1997). DDT and DDE have also been identified as endocrine-disrupting chemicals (see Allsopp *et al.* 1997). For instance, DDT was shown to cause estrogenic effects in laboratory animals (eg. Bustos *et al.* 1988). DDE was shown to be anti-androgenic in laboratory studies and caused effects in laboratory animals consistent with this mechanism (Kelce *et al.* 1995). It has been suggested that the endocrine-disrupting properties of DDT, and possibly other chemicals, may be responsible for adverse effects on the reproductive systems of wild alligators in Lake Apopka, Florida (Guillette *et al.* 1994).

Studies on animals have reported immunotoxic effects of DDT. It has been suggested that immune responses observed in animals may be indicative of effects in humans subjected to long-term, low level exposure (ASTDR 1997).

Exposure to DDT *in utero* or in newborns has been shown to cause developmental neurotoxicity in animals such as effects on behaviour. The levels of DDT that cause behavioural changes in mice are comparable to levels to which human infants have been exposed. It is not certain whether effects from DDT exposure could occur from exposure via breast milk in human infants (ASTDR 1997).

Studies on animals have demonstrated that long-term DDT exposure can cause cancer including lymphomas, and liver and adrenal tumours. It has been suggested that studies conducted on occupational exposure to DDT in humans are not conclusive of an association between exposure and the development of cancer because of inadequacies in the studies (ASTDR). One study on occupational exposure has however suggested a link between exposure and pancreatic cancer (Garabrant *et al.* 1992, see Allsopp *et al.* 1995).

Recent studies on women in the US and Mexico found that women with higher levels of DDT in their breast milk lactated for shorter time periods than women with lower levels. It was suggested that DDE, and possibly other estrogenic chemicals could be contributing to declines in the duration of lactation that are evident throughout the world (Gladden and Rogan 1995).

## 4. HEXACHLOROBENZENE (HCB)

### 4.1 Introduction

HCB has a variety of sources including its previous use as a fungicide for seed grain. It is produced as an unwanted by-product or impurity in the manufacture of chlorinated solvents, other chlorinated compounds, such as vinyl chloride, and several pesticides. It is also produced as a by-product in waste streams of chlor-alkali plants and wood preserving plants, and in fly ash and flue gas effluents from municipal waste incineration. Its main source in the environment today is from the manufacture of pesticides (Foster 1995, ATSDR 1997).



## 4.2 Levels in Breast Milk

Levels of HCB in breast milk from different countries reported on a lipid and on a whole milk basis are shown in tables 4a and 4b respectively. The tables indicate that HCB is a widespread contaminant of human milk. In all except three countries, Spain, Brazil and Egypt, HCB was found in greater than 90% of the samples tested. HCB is found in human milk in countries such as India, where it was never used as a fungicide, and where the highest levels are detected in industrialised regions (see Thomas and Colborn 1992).

A previous review of data on levels of HCB in breast milk observed that the average world-wide background concentration was about 0.1 ppm (Jensen and Slorach, 1991). Studies presented in table 4a show that the majority of countries have levels around 0.04 to 0.2 ppm. Falling into this category are Australia, Kazakstan, Turkey, Mexico and European countries France, Germany, Netherlands, Italy, Norway and Sweden. Among these countries, northern European countries Norway and Sweden, and Mexico have levels at the lower end of the range. Another South American country, Brazil, also had relatively low levels, 0.02 ppm. Other countries with comparatively low levels of around 0.02 ppm or less, were Canada, Spain, UK, and in Asia, South Vietnam and Thailand. The highest levels of HCB were reported for Jordan (0.29 ppm, median), Perth in Australia (0.411 ppm), and eastern European countries, the Czech Republic (0.639 ppm), and Slovakia (0.829 ppm). Researchers suggested that particularly high HCB levels in human milk in Slovakia may be caused by its use in agriculture and its formation during the manufacture of chlorinated solvents (Kocan *et al.* 1995).

The AMAP study of maternal blood levels of POPs in Arctic countries reported that HCB levels were significantly elevated in some Arctic regions, in particular, Greenland. It was noted that the patterns of certain POPs in maternal tissue were consistent with the relative amounts of traditional food consumed, especially where marine mammals formed a large amount of the diet (Gilman *et al.* 1997).

## 4.3 Time Trends

A few studies in developed countries have reported a decline in levels of HCB in blood and milk in recent years. A study in Denmark observed that levels in breast milk in 1993 had fallen to less than half the value measured in 1986 (Hilbert *et al.* 1996). Similarly, in Norway levels decreased by about 50% between 1986 and 1991 (Johansen *et al.* 1994). Statistically significant declines in breast milk were also reported to occur in Sweden between 1981 (mean 0.096), 1986 (0.057), and 1990 (0.037), (Vaz *et al.* 1993). A study of the general population in Barcelona, Spain, revealed that blood levels in 1993 (range 0.7 to 19.7, mean 4.13 ng/ml) were significantly lower than levels found in the same population in 1986 (range 1.6 to 94.2, mean 11.09 ng/ml), (To-Figueras *et al.* 1995).

Studies which have reported information on trends of HCB levels, appear to be those where HCB levels are now relatively low, that is northern Europe and Spain. No specific data on trends in countries where HCB levels are comparatively high were found in the recent literature.

## 4.4 Highly Exposed Populations

### 4.4.1 Nursing Infants

HCB is transferred from mother to foetus through the placenta, and can readily pass to the nursing infant through breast milk. One study measured a significant drop in breast milk HCB concentrations throughout 98 days of lactation (see Thomas and Colborn 1992). A study on a woman in Sweden observed that maternal HCB levels were significantly reduced by lactation. Levels of HCB during her first pregnancy (0.12 ppm) were higher than in her second pregnancy (0.06 ppm) and third pregnancy (0.04 ppm). This was due to excretion of the compound from her body during lactation and transfer to the foetus during her pregnancies (Vaz *et al.* 1993). Experiments in laboratory rats have also shown that HCB is passed to young through milk. Lactation resulted in the maternal body burden being reduced by 15-20% (see ATSDR 1997).

A temporary ADI value of 0.6 ug/kg/day was set for HCB in 1976 but withdrawn in 1978. In pesticide evaluations published by WHO (1997), a tentative ADI of 0.6 ug/kg/day is given, and this is considered below any dosage rate known to be harmful. Table 11 shows the ADI for HCB and the estimated concentrations of HCB in breast milk fat and whole milk which should not be exceeded if an infants intake is not to exceed the ADI. Comparison of the estimated levels which should not be exceeded with mean levels of HCB in breast milk reported for different countries (tables 4a and b), indicates that the mean breast milk levels exceed the ADI in several countries. These include Australia, Czech Republic, Egypt, France, Eastern and Western Germany, Italy, Russia and the Slovak Republic. The highest exceedances of the ADI are for the Czech Republic and Slovak Republic for which the mean values exceed the ADI by around 6 and 8 fold.

A recent study in Australia provided information on actual rather than estimated infant intakes of HCB from breast milk. It found that about a quarter of infants in the study received daily intakes of HCB from breast milk which exceeded the ADI. Some intakes were 48 times in excess of the ADI. In a few cases, the intakes approached the NOAELs in animals that are used as a basis for ADIs (Quinsey *et al.* 1995 and 1996).

### 4.4.2 Occupational Exposure

There are several occupations which could result in exposure to HCB, although there appear to be few recent studies in the literature which document tissue levels in workers. Several studies in the 1970s found elevated levels of HCB in blood of persons occupationally exposed to this compound. Workers at a carbon tetrachloride and perchloroethylene production facility had plasma levels of 0.223 ppm. Workers involved in the manufacture of chlorinated solvents had blood levels ranging from 0.0055 to 1.121 ppm (mean 0.310 ppm) in 1974, and 0.022 to 0.467 ppm (0.170 mean) in 1977. Pesticide sprayers applying HCB contaminated dimethyltetrachloroterephthalate (DCPA) had mean plasma levels of 0.040 ppb (see ASTDR 1997).

More recently, two studies on occupational exposure to HCB have been conducted in Sweden. HCB is released by the use of hexachloroethane for hydrogen removal (degassing) in molten aluminium. A study on tissue levels in workers in Swedish aluminium foundries noted that this process was banned a few years ago due to the



release of HCB. The study found that the mean level of HCB in workers blood, 2 to 4 years on after the process had been banned, was elevated to a level 4 times higher than in workers who were not exposed to the process (0.313 vs 0.066 ppm), (Selden *et al.* 1994).

In another study, workers at hazardous waste incineration plants were investigated since they are exposed to many chemicals including organochlorines. Levels of HCB in blood samples from workers were significantly elevated, by almost two-fold (0.063 vs 0.035 ppm) (Selden *et al.* 1997).

#### 4.5 Relevance to Human Health

A wide range of toxic effects due to HCB exposure have been reported in experimental animals, including porphyria and other liver effects, skin lesions, neurological effects, altered enzyme levels and several types of cancer. Adverse effects on reproduction and development and on the immune system have also been reported. In humans, much of the information on adverse effects of HCB is derived from an incident which occurred in Turkey in the late 1950s, when people ate breads made from HCB-treated wheat. About 500 people were fatally poisoned during the incident and about 4000 became sick. Infants died who were breast fed by HCB exposed mothers. Exposure to HCB was not quantified in follow up research of the incident, but analysis of human milk reported a level of 0.51 ppm in exposed and 0.07 ppm in unexposed women. (This level is in the same order of magnitude as levels in human milk found in eastern European countries today). Elevated levels of HCB in human milk were still found in the region 20 to 30 years after the accident. Adverse health effects to adults from the contamination included skin lesions due to altered porphyrin metabolism. Many developmental effects were evident in children who survived the incident such as skin, neurologic and orthopedic abnormalities (Sonawane 1995, ATSDR 1997).

Liver toxicity appears to be the most sensitive effect caused by chronic HCB exposure in adult animals and humans. In humans, chronic exposure to HCB at the incident in Turkey caused hepatic porphyria. More recently, several studies in north-east Spain have reported high levels in human adipose in populations residing in areas polluted by organochlorines. A link between HCB contamination and the high and variable incidence of porphyria cutanea tarda has been hypothesised (Enriquez de Salamanca *et al.* 1990).

Another health effect of HCB is immunotoxicity. A review of animal data noted that immune dysfunction occurs at lower doses than those associated with most other toxic effects. It was suggested that this may be an area of concern for human exposure to HCB (ASTDR 1997). The chemical also causes various reproductive toxicities in adult female animals, including ovarian and menstrual cycle effects, reduced gestational viability and fertility. Alteration of levels of hormones has been reported including reproductive hormones progesterone and oestradiol, as well as thyroid hormones. Studies in animals found effects on the ovary at levels only two orders of magnitude higher than HCB levels in the general human population. Considering evidence available from animal studies, it has been suggested that HCB represents a concern to ovarian function in humans. It may also have the potential of advancing ovarian failure and menopause onset (Foster 1995).

HCB is known to cross the placenta and be transferred via breast milk to young and causes various developmental effects in animals. In humans, there are no specific studies on the impacts of HCB on development *in utero*, although a number of developmental abnormalities were reported in children before they reached puberty, following their accidental exposure to HCB at the poisoning incident in Turkey (ATSDR 1997).

HCB is known to cause multiple tumour types in laboratory animals when given orally, including cancers of the liver, parathyroid, thyroid and bile duct. Animal studies suggest that HCB has the potential to cause cancer in humans and it is considered a probable human carcinogen. No malignant tumours have been reported in humans following HCB exposure, although liver cancers, in association with porphyria, have been reported in several human studies (ASTDR 1997). A recent study has reported an excess of soft tissue sarcoma and thyroid cancer in a small population with elevated serum HCB levels living near an organochlorine manufacturing factory (Grimalt *et al.* 1994). The serum levels were 5 to 6-fold higher than baseline levels which have been reported for the general population of Barcelona Spain (To-Figueras *et al.* 1995). It was suggested that since these baseline levels refer to a very large human population, the toxic risk to the general population does not seem negligible. The study noted that the range of serum levels reported for the general population of Barcelona cannot be considered safe with the relation to the possible long term effects of HCB, and further efforts to reduce exposure and intake through the food chain should be encouraged.

## 5. HEXACHLOROCYCLOHEXANES

### 5.1 Introduction

Technical grade hexachlorocyclohexane (HCH) is an insecticide, which is comprised of a mixture of different isomeric forms of HCH. The approximate isomer content is alpha-HCH (53-70%), beta-HCH (3-14%), gamma-HCH (11-18%), delta-HCH (6-10%), others (3-10%). The insecticide lindane is the common name for the gamma isomer. It is produced by purification of the technical HCH mixture (see Thomas and Colborn 1992).

Although lindane and technical grade HCH have been banned or severely restricted in many countries they are still widespread use. In India, DDT and HCH together contribute to more than 70% of the total pesticide consumption (Nair *et al.* 1996). Most of the HCH used in India is for agricultural purposes and around 10% is consumed in vector control programs (Kashyap *et al.* 1994). Lindane is also used in many western countries in medications including shampoo for head lice.

Quantitatively, the most important isomers are alpha-, beta-, and gamma-HCH. Bioaccumulation of these chemicals in tissues of some animals has been recorded, although the alpha and gamma isomers do not concentrate highly through the foodchain. The beta-isomer is however more persistent (Johnston 1989). Human intake of HCH compounds is largely through food consumption (Toppari *et al.* 1995). Alpha, beta and gamma-HCH isomers have been recorded in human breast-milk with the beta-isomer being the most ubiquitous. The generally less widespread nature of the alpha and gamma isomers in comparison to beta-HCH is due to the more rapid



clearance of these isomers from the body (National Research Council 1993). Like many persistent organochlorines, HCH levels in the body have been found to increase with age (ASTDR 1997).

## 5.2 Levels in Breast Milk

Levels of alpha-, beta- and gamma-HCH in breast milk from different countries reported on a lipid and on a whole milk basis are shown in tables 5a and 5b respectively. All three isomers are detectable in breast milk from different countries in these studies. Beta-HCH is very persistent and this is reflected in the widespread occurrence of the isomer. It was found in 90 to 100% of samples tested where data was available. The percentage of alpha and gamma isomers in samples was more variable between different countries. For instance gamma-HCH was detected in 17% of samples in Canada, but in 80 to 100% of samples in France, Turkey and India. The differences probably reflect where lindane was still in use.

In general, beta-HCH is not only more widespread in breast milk than alpha and gamma-HCH, but it is also present in higher concentrations. This is again a result of the persistent nature of beta-HCH and the more rapid clearance from the body of alpha and gamma-HCH. The levels of both beta and gamma-HCH vary widely between different countries, by more than two orders of magnitude.

Exceptionally high levels of beta-HCH in breast milk were evident in India (4.37-8.83 ppm). In a previous review, Jensen and Slorach (1991) noted that the average concentration of HCH was 6 ppm in India and in China. In the present review, very high levels of beta-HCH were also evident in Kazakstan (2.21 ppm) and Russia (1.58 ppm). High levels of beta-HCH, ranging from 0.5 to 1.0 ppm, were observed in two South American countries, Brazil (0.9 ppm) and Mexico (0.56 ppm), and in Turkey (0.52). Below this, levels ranging from 0.1 to 0.5 ppm were found in France, Australia, Jordan, and two Asian countries, South Vietnam and Thailand. The lowest levels, below 0.1 ppm, were recorded in US, Canada, Spain, Germany, UK and the Czech Republic. For gamma-HCH, the highest levels were also apparent in India and Kazakstan.

Regional differences in breast milk levels within a country were reported for India. Levels of alpha-, beta- and gamma-HCH were found to be around twice as high in an agricultural area compared to an urban area in Punjab (Kalra *et al.* 1994).

Information on levels of HCH compounds was located in the literature for several but not all western European countries, US, Canada, and a few Asian and Latin American countries. With the exception of Jordan, data on Middle eastern regions was lacking and no studies were found on Africa.

The AMAP study on maternal blood levels of POPs in Arctic countries recently reported very high levels of beta-HCH in north-western Russia. Levels of 0.225 ppm were recorded which are around 25 times greater than blood levels in Norway and Sweden. It was suggested that the high levels were either a result of significant uses of HCH in the region, or significant amounts in the food supply (Gilman *et al.* 1997).

## 5.3 Time Trends

A gradual decrease in the levels of beta-HCH were reported to occur in breast milk samples from Sweden between the mid 1970s and 1985 (Noren 1993), and between 1981, 1986 and 1990 (Vaz *et al.* 1993). In Canada, a small decrease was documented between 1986 (0.69 ppb whole milk) and 1992 (0.55 ppb whole milk) (Newsome *et al.* 1995). Some reduction in levels was also evident in the US between 1970 and 1983 (see ASTDR 1997).

## 5.4 Highly Exposed Populations

### 5.4.1 Nursing Infants

Maternal levels of HCH are reduced during lactation. For example, levels of beta-HCH were shown to decrease during three pregnancies of a Swedish woman due to transplacental transfer and excretion through lactation. The levels in breast milk in during the first pregnancy were 0.088 ppm, the second 0.058 ppm and the third 0.038 ppm (Vaz *et al.* 1993).

No ADI has been set for beta-HCH, but a temporary ADI of 1 ug/kg/day was set for gamma-HCH (lindane) in 1997 (WHO 1997). Table 11 shows estimated concentrations of lindane in breast milk fat and whole milk that should not be exceeded if an infant's intake is not to exceed the ADI. Comparison of the estimated levels which should not be exceeded with mean levels of lindane in breast milk reported for different countries (table 5a and b), indicates that the mean breast milk levels exceed the ADI in two countries, namely India and Jordan. By far the greatest exceedance of the ADI is for India. An infants estimated intake of lindane from breast milk in India, based on mean levels in breast milk fat, exceeds the ADI by up to 12 times.

### 5.4.2 Occupational Exposure

Workers may be exposed to HCH compounds at manufacturing plants and during agricultural usage. Alpha-, beta- and gamma-HCH have been detected in the blood and adipose tissue of individuals occupationally exposed to HCH in pesticide formulation (ASTDR 1997)

## 5.5 Relevance to Human Health

In studies on laboratory animals, many health effects following exposure to HCH have been documented (ASTDR 1997), and beta and gamma-HCH were found to have oestrogen-like effects (see Toppari *et al.* 1995, Thomas and Colborn 1992). A review of toxicological information suggested that the possible human health effects associated with exposure to HCH are adverse hematological effects, liver and kidney effects, immunological, neurological and reproductive effects and cancer (ASTDR 1997).

A number of health effects in humans have been recorded following occupational exposure. These studies were conducted during or prior to the 1980s. Health effects include blood disorders in individuals exposed to gamma-HCH at work or in homes, where HCH vaporisers were operated; increased liver enzymes in workers exposed to



technical grade HCH principally by inhalation in a pesticide formulating plant: several neurological effects including abnormal EEG, vertigo, headaches, seizures and convulsions in individuals occupationally exposed to gamma-HCH, and in individuals exposed accidentally or intentionally to large amounts of gamma-HCH by ingestion; and, alterations of reproductive hormones in men occupationally exposed to HCH and gamma-HCH. Alpha-, beta-, gamma- and technical grade HCH are carcinogenic in laboratory animals. It has been proposed that animal data suggests that liver cancer may be of potential concern to human individuals exposed to HCH isomers for prolonged periods of time (ASTDR 1997).

The relevance of current background levels of HCH compounds to the health of the general population is difficult to assess from current toxicological data.

## 6. DIELDRIN, ALDRIN AND ENDRIN

Chlorinated cyclodienes are noted to be both environmentally persistent and among the more toxic pesticides. Despite restriction of their production in recent years in some countries, residues of these pesticides continue to be reported as being present in human tissues. The chlorinated cyclodiene pesticides include aldrin, dieldrin, chlordane, oxychlordane, heptachlor and heptachlor epoxide.

### 6.1 Introduction

Dieldrin, aldrin and endrin are very persistent insecticides that have been banned in many countries but remain in use in some developing countries. Dieldrin is a metabolite of aldrin that persists in adipose tissue (Sonawane *et al.* 1995). Several studies have detected dieldrin in human milk. Aldrin and endrin have also been found in human milk, although the data are very limited.

### 6.2 Levels in Human Milk

Levels of dieldrin in breast milk from different countries reported on a lipid basis are shown in tables 7a. The available data showed that the occurrence of detectable concentrations of dieldrin in human milk was variable ranging from 5% in Jordan to 100% in Australia.

A previous review reported that the average level of dieldrin in human milk was 0.05 ppm on a lipid basis (Jensen and Slorach 1991). Similar levels were noted in the present report, which showed that levels in the majority of countries were between 0.01 and 0.1 ppm. Higher levels were reported for Victoria in Australia (0.159 ppm), France (0.19 ppm), USA (0.541), Iraq (1 ppm) and Uruguay (1 ppm). The lowest levels, below 0.01 ppm, were present in Canada, Russia, Spain, and South Vietnam. Levels of dieldrin in human milk world-wide are thus highly variable between countries ranging by more than two orders of magnitude from 1.0 to less than 0.01 ppm.

Very few studies were found on levels of aldrin and endrin in human milk. Endrin levels were reported for France (table 7b), and aldrin levels for Australia, France and Turkey (table 7c). Aldrin was found to be present in 75% of samples in France, 88% in Turkey, but only 5% in Australia. Levels were similar, 0.02 to 0.047 ppm, in all

three countries. A study in Mexico reported that aldrin was not detected in human milk (Waliszewski *et al.* 1996). The AMAP study of maternal blood levels of POPs in Arctic countries did not report elevated levels of aldrin in Canada, Greenland, Sweden, Norway, Iceland or Russia (Gilman *et al.* 1997).

### 6.3 Time Trends

In recent years, levels of dieldrin in human milk have decreased according to reports from some countries. A study in Sweden reported a gradual decline in levels between 1972, shortly after most uses were banned and 1985 (Noren 1993). A study in Denmark reported a steady decline between 1982 and 1993 (Hilbert *et al.* 1996). Research in Canada noted a decline in levels between 1986 and 1992 (Newsome *et al.* 1995).

### 6.4 Highly Exposed Populations

#### 6.4.1 Nursing Infants

An ADI of 0.2 ug/kg/day has been set for endrin and a value of 0.1 ug/kg/day has been set for dieldrin combined with aldrin (WHO 1997). Estimated concentrations of dieldrin, aldrin and endrin in breast milk fat and whole milk which should not be exceeded if an infants intake is not to exceed the ADI are given in table 11. Levels of endrin in breast milk were only located in the scientific literature for France. The mean breast milk level in this study is slightly greater than the ADI for endrin.

Since there are very few studies which provided breast milk levels of both dieldrin and aldrin, data on dieldrin only (table 7a) and aldrin only (table 7c) are considered separately. Comparison of the estimated levels which should not be exceeded with mean levels of dieldrin in breast milk reported for different countries (table 11), indicate that the mean breast milk levels exceed the ADI in several countries. These include Australia, Brazil, Eastern Germany, Jordan, Thailand, UK, USA and Uruguay. The highest exceedances of the ADI are for Iraq, Uruguay and one study in Brazil, which all exceed the ADI by greater than 50 times. When data on aldrin alone is considered, the ADI for dieldrin + aldrin is exceeded 1-2 fold for countries where studies were available, that is Australia, France and Turkey.

A study in Australia provided specific information on actual rather than estimated infant intakes of dieldrin from breast milk. It found that dieldrin was detected in 43% of samples tested. Of these, 88% would have resulted in doses exceeding the ADI (Quinsey *et al.* 1995).

## 7. HEPTACHLOR AND HEPTACHLOR EPOXIDE

### 7.1 Introduction

Heptachlor is a constituent of technical-grade chlordane, approximately 10% by weight. Heptachlor epoxide (HE) is an oxidation product of heptachlor and of chlordane. Technical-grade heptachlor usually consists of 72% heptachlor and 28% impurities such as trans-chlordane, cis-chlordane, and nonachlor. Heptachlor has been used for the control of termites, ants and soil insects in cultivated and uncultivated



soils, and for the control of household insects. The general population is primarily exposed to heptachlor and heptachlor epoxide through diet (ASTDR 1997).

## 7.2 Levels in Breast Milk

Levels of heptachlor and heptachlor epoxide in breast milk from different countries reported on a lipid and on a whole milk basis are shown in tables 6a, 6b and 6c,6d respectively. The occurrence of heptachlor and HE in human milk varied from country to country. For example, the percentage of samples positive for heptachlor varied between 33% in Spain to 89% in Australia. The percentage positive for HE varied from 17% in Brazil to 92% and 95% in Spain and France respectively. Studies prior to 1990 in the US showed that between 25% and 100% of human milk samples contained heptachlor and HE (see Sonawane 1995).

A previous review of levels of heptachlor and heptachlor epoxide in breast milk, reported that average levels world-wide were 0.05 ppm. High levels were recorded for Spain (2.5 ppm) and Italy (0.48 ppm). Heptachlor epoxide was also elevated in Belgium, Israel and Guatemala (Jensen and Slorach 1991). In the US, levels were reported to range from 0.035 to 0.13 ppm (see Sonawane 1995). In the present review, similar high levels were not reported for HE. Levels in most countries, including Spain, were below 0.05 ppm. Exceptions were Australia (0.061 ppm) and France (0.097 ppm). For heptachlor, however, a very high level was reported in Jordan (0.7 ppm). All other countries had levels below 0.05 ppm.

It should be noted that data on levels of heptachlor and heptachlor epoxide in human milk in different countries were quite limited. Published studies were only found for ten countries. This included a few European countries, Turkey, Egypt, Canada, Russia and Brazil. No studies were located for Asian countries.

## 7.3 Time Trends

Little data was published on time trends of heptachlor. One study in Canada however reported a decline of about 70% in human milk levels of heptachlor epoxide between 1986 and 1992 (Newsome *et al.* 1995).

## 7.4 Highly Exposed Populations

### 7.4.1 Nursing Infants

An ADI of 0.1 ug/kg/day was set for heptachlor and heptachlor epoxide in 1994 (WHO 1997). Table 11 shows the estimated concentrations of heptachlor and HE in breast milk fat and whole milk which should not be exceeded if an infant's intake is not to exceed the ADI. Comparison of the estimated levels which should not be exceeded with mean levels of heptachlor and HE in breast milk reported for different countries (table 6a-d), indicate that the mean breast milk levels exceed the ADI in several countries. These include Australia, France, Germany, and Jordan.

A study in Spain which estimated intakes of dieldrin from breast milk reported that the mean levels of heptachlor and HE did not exceed the ADI. However, 11.7% of samples that contained the chemicals exceeded the ADI (Hernandez *et al.* 1993).

A study in Australia provided specific information on actual rather than estimated infant intakes of heptachlor from breast milk. It found that heptachlor was present in less than one third of samples which were tested, but levels in all these samples exceeded the ADI (Quinsey *et al.* 1995).

### 7.4.2 Occupational Exposure

Workers involved in the manufacture of heptachlor, and in its application are at risk of exposure to heptachlor (ASTDR 1997). However, the available data on exposure of workers to heptachlor appears to be very limited.

## 7.5 Relevance to Human Health

Animal studies have identified heptachlor as being a toxic to the central nervous system. It is likely that the nervous system is also a target system in humans. Signs of neurotoxicity have been reported in humans following exposure to technical-grade chlordane, which contains between 6 and 30% heptachlor. However, these effects cannot be solely attributed to heptachlor. Animal studies also show that heptachlor causes toxicity to the liver, and indicate that the liver would be a target organ in humans. Studies show that heptachlor may affect the male and female reproductive systems in animals. Only limited human data are available on reproductive and developmental toxicity in humans and these are inconclusive (ASTDR 1997).

## 8. CHLORDANE

### 8.1 Introduction

Technical grade chlordane is a mixture of alpha and gamma-chlordane and *trans*-nonachlor (Quinsey *et al.* 1995). Its uses were mainly as a field crop insecticide and in the control of termites. It is extremely persistent in the environment. It has been reported to persist in some soils for over 20 years, and is known to bioconcentrate in the food web (ASTDR 1997).

Chlordane is metabolised in humans and in most other organisms to two persistent epoxides: heptachlor epoxide and oxychlordane. Food is the most significant source of exposure to chlordane and these metabolites. Indoor air can also be an important source of exposure to technical chlordane where it has been used as a pesticide in homes (Dearth and Hites 1991). Chlordane vaporises gradually in treated homes for over ten years (ASTDR 1997). It was used widely for termite control in homes the US for between 1960 and 1988. Its use in the US has now stopped, but exposure continues since it has a half-life in the environment of 5 and possibly 15 years (Dearth and Hites 1991). The US EPA estimated that, up to 1988, 1.3 to 1.8 million people per year in the US were exposed to cyclodiene termiticides, as occupants of newly treated buildings. They also estimated that about 30 million buildings in the US had been treated for termites with these chemicals, resulting in the exposure of over 80 million people (ASTDR 1997).



## 8.2 Levels in Human Milk

Jensen and Slorach (1991) reported that chlordane was found more frequently in human milk in the US than elsewhere. The average level in breast milk world-wide was 0.08 ppm although the highest levels (> 2ppm) were found in Mexico and Iraq. In this report, data for different countries are shown in table 8. Comparisons between different countries are difficult, because of the varying ways in which levels were reported, for example, as alpha-chlordane, gamma-chlordane or oxychlordane. With the exception of an oxychlordane value of 0.13 ppm for Victoria, Australia, levels of chlordane and oxychlordane were all below the previous reported average value of 0.08 ppm. This included studies in Canada, France, Japan, Russia, Thailand, USA and South Vietnam.

The AMAP study on maternal blood levels of POPs in Arctic countries reported that levels of chlordane metabolites were significantly elevated in Greenland and Canada where communities relied on a seafood diet which included sea mammals (Gilman *et al.* 1997). For example, levels of oxychlordane were 0.0608 and 0.0278 ppm in blood lipid in Greenland and Canada respectively. These levels were much greater than levels in other countries, for instance 0.0019 and 0.0037 in Sweden and Norway respectively.

## 8.3 Time Trends

A review of data on chlordane in 1991 concluded that the levels of chlordane compounds in people are not declining. For instance, mean adipose tissue levels found in a US study in 1986-88 were 0.048, 0.088 and 0.12 ppm for heptachlor epoxide, oxychlordane, and trans-nonachlor respectively. These results showed no apparent decline from a previous study, the National Human Adipose Tissue monitoring program from 1974-1982 where the levels of the compounds were 0.07-0.09, 0.09-0.12, and 0.06-0.14 ppm. Thus, with the exception of heptachlor epoxide which may also be coming from other sources, following ten years of regulation in the US, there had been no measurable decline in levels of chlordane compounds at this time (Dearth and Hites 1991).

## 8.4 Highly Exposed Populations

### 8.4.1 Nursing Infants

An ADI of 0.5 ug/kg/day was established for chlordane in 1994 (WHO 1997). Table 11 shows the estimated concentrations of chlordane in breast milk fat and whole milk that should not be exceeded if an infants intake is not to exceed the ADI. While some studies on levels of chlordane in breast milk have recorded levels of oxychlordane, others have reported on the alpha and gamma isomers (see table 8). Data is only available for a few countries, but none of these exceeded the ADI.

### 8.4.2 Exposure in Treated Buildings/Occupational Exposure

A study in Japan showed that the concentration of chlordane and oxychlordane in the milk fat of women living in chlordane treated houses (0.0138 ppm and 0.0336 ppm respectively), was much higher than in breast milk of women who were not exposed in this way (0.0036 and 0.0193 ppm). Several occupations may lead to chlordane

exposure including its manufacture, formulation, shipping, storage, application, and disposal (see ASTDR 1997).

## 9. TOXAPHENE

### 9.1 Introduction

Toxaphene is a trade name for an insecticide which consists of a mixture of at least 177 separate components, the major constituents being chlorobornanes. More than half a million metric tons of toxaphene has been produced since the mid-1940s. These production figures are almost comparable to those of PCBs. It is estimated that 80-90% of all toxaphene produced has been used in cotton growing. In addition, fisheries managers in Canada and the US have applied toxaphene as a fish poison to rid lakes of undesirable fish. As a result of the large scale production of toxaphene, its bioaccumulative properties and its high toxicity to fish, this pesticide may be considered a threat to the aquatic ecosystem to the same extent as PCBs (de Boer and Wester 1993).

Toxaphene is a global pollutant distributed by long-range transport on air currents. It is bioconcentrated by marine organisms to high levels, and appears to biomagnify through aquatic food chains (ASTDR 1997). Toxaphene has hardly been used in western Europe. Nevertheless, exposure through the foodchain is possible in countries where toxaphene has not been used. For example, concentrations of toxaphene in cod, hake and haddock from the North Sea were found to exceed the German tolerance standard for levels in food by 2-8 fold. High concentrations are also evident in Baltic fish due to the use of toxaphene in eastern Europe. The highest concentrations have been detected in fish from Canadian and Arctic waters, in which levels are at least a factor of 10 higher than in North Sea fish (de Boer and Wester 1993).

### 9.2 Levels in Breast Milk

Few studies have monitored the level of toxaphene constituents in human tissues, blood or milk (see table 9). Comparisons between different studies are difficult because of differences in analytical methods. One study on 16 human breast milk samples from Nicaragua, Central America, found that levels were high (2.0 mg/kg lipid weight) in comparison with levels in Finnish breast milk (0.005-0.5 mg/kg) and Swedish breast milk 0.1 mg/kg (de Boer and Wester 1993). This is probably a reflection of the continued use of toxaphene in Nicaragua.

### 9.3 Highly Exposed Populations

#### 9.3.1 Nursing Infants

Nursing infants can be exposed to toxaphene via breast milk. However, estimates of risks to nursing infants is complicated because the identified congeners were usually partially metabolised and there is little information on the toxicity of such congeners (ATSDR 1997). No ADI has been proposed for toxaphene.



### 9.3.2 Other Groups

Occupational exposure to toxaphene is possible during the manufacture or application of the pesticide. Other groups with potentially high exposure to toxaphene include arctic indigenous people who rely on a seafood diet and consume aquatic mammals. In some countries, individuals residing near to hazardous waste disposal sites contaminated with toxaphene may be more highly exposed. In addition, infants and young children who are given vitamin supplements from cod liver oil could have a higher exposure to toxaphene (ASTDR 1997).

### 9.4 Relevance to Health

Animal studies have shown that short and long-term exposure to toxaphene is toxic to the liver and kidney. It has been suggested that individuals exposed to toxaphene may be at risk for compromised liver and kidney function and liver injury. Long term exposure to toxaphene can also result in neurotoxic effects in humans and animals. Laboratory rats which were exposed *in utero* and via lactation to toxaphene had slight changes in motor function and behaviour. Toxaphene can also cause cancer in animals and this evidence suggests that it may also be carcinogenic in humans (ATSDR 1997).

## 10. MIREX

### 10.1 Introduction

About 75% of mirex that was produced was used as a fire retardant additive, while 25% was used as a pesticide. It was used as a fire retardant additive in various coatings, plastics, rubber, paint, paper and electrical goods. *Uses of mirex as an insecticide included fire ant control in USA, leaf cutter ants in South America, harvester termites in South Africa, mealybugs in pineapples in Hawaii, and yellowjacket wasps in the USA.* Although mirex was banned in the USA in 1976, its *release into the environment* continues from waste disposal sites. Mirex is very *persistent* in the environment and bioaccumulates and biomagnifies in aquatic and terrestrial food chains (ASTDR 1997).

### 10.2 Levels in Breast Milk

Research on levels of mirex in human tissues appears to be very limited. A few studies found traces of mirex in human milk from North America (see Sonawane 1995). The AMAP study on maternal blood levels of POPs in Arctic countries found that levels were highly elevated in Greenland (0.0091 ppm blood lipid), and somewhat in Canada (0.0045 ppm), in comparison with other countries in the study. For example, levels in Sweden, Norway, Iceland and Russia were between 0.001 and 0.002 ppm. It was noted that patterns of certain POPs found in maternal blood samples are consistent with relative amounts consumed in traditional foods, particularly where marine mammals form a large part of the diet (Gilman *et al.* 1997).

## TABLES

Tables 1 and 2 show levels of PCDD/Fs and PCBs in human blood/milk/adipose tissue. Tables 3 to 9 show levels of organochlorine pesticides in human milk.

For tables on organochlorine pesticides, the data are presented in separate tables showing levels in human milk measured on a lipid basis, and levels in human milk measured on a whole milk basis. For data presented on a whole milk basis, figures reported in studies as per kg or g weight of milk are shown as ppm, and figures reported as per litre are left unchanged. These figures approximate to ppm.

In tables 1 to 10, n represents the number of samples taken. For tables 3 to 9 on organochlorine pesticides, the date that samples were taken in each study are given where this information was available. In tables 1 to 10, values denoted \* are the median rather than the mean.

**Table 1a**  
Mean Blood Levels of PCDD/Fs, 1980-91

	USA n=100	Germany n=85	North Vietnam (Hanoi) n=32	South Vietnam (Dong Nai) n=33	Guam n=10	Soviet Union (St. Petersburg) n=50	Soviet Union (Baikal City) n=8
PCDD/F TEQ	41	42	10	49	32	17	18

Table 1a shows mean blood levels of PCDD/Fs (total TEQ, ppt, lipid) for general populations in various countries, 1980-91.

Source: Schecter (1994)

**Table 1b**  
Mean Blood Levels of PCDD/Fs, 1996

	Gaza n=39	Palestinian West Bank n=20	Israel (Jerusalem) n=50	USA (New York) n=100
PCDD/Fs TEQ	8.44	16.91	26.64	26.84

Table 1b shows mean blood levels of PCDD/Fs (total TEQ, ppt, lipid) for general populations in various countries in 1996

Source: Schecter (1994)



**Table 1c**  
Mean Adipose Tissue Levels of PCDD/Fs, 1980s

	USA n=15	Germany n=4	China n=7	Japan n=6	Canada n=46	North Vietnam n=26	South Vietnam n=41
PCDD/F TEQ	24	69	18	38	36	4	30

Table 1c shows mean adipose tissue levels of PCDD/Fs (total TEQ, ppt, lipid) for general populations in various countries (1980s)

Source: Schecter (1994)

**Table 1d**  
Mean Breast Milk Levels of PCDD/Fs, 1980s

	USA n=43	Germany n=185	Japan n=6	Canada n=200	Pakistan n=7
PCDD/Fs TEQ	20	27	27	26	13

	North Vietnam (Hanoi) n=30	South Vietnam (Da Nang) n=11	Thailand n=10	Cambodia n=8	Russia n=23
PCDD/Fs TEQ	9	34	3	3	12

Table 1d shows mean breast milk levels (pooled) of PCDD/Fs (total TEQ, ppt, lipid) for general populations of various countries (1980s).

Source: Schecter et al. (1997)

**Table 2a**  
Mean Levels of PCDD/Fs and Dioxin-like PCBs, 1987/88 and 1992/3

COUNTRY	AREA	No. SAMPLES IN POOL (n) in		ppt TEQ [PCDD/F] 1987/88	ppt TEQ [PCDD/F] 1992/3	ppt TEQ [dioxin-like PCBs] 1992/93
		1987/88	1992/3			
Albania	Tirana		10		4.8	2.3
	Librazhd		10		3.8	1.7
Austria	Vienna (urban)	54	13	17.1	10.7	11.7
	Tulln (rural)	51	21	18.6	10.9	12.4
	Brixlegg (industrial)		13		14.0	19.0
Belgium	Brabant Wallou		8	33.7	20.8	7.4
	Liege		20	40.2	27.1	4.7
	Brussels		6	38.8	26.6	7.8
Canada	Maritimes	19	20	15.6	10.8	4.1
	Quebec	34	20	18.1	13.4	6.8
	Ontario	76	20	17.6	18.1	7.7
	Prairies	31	20	19.4	14.6	3.2
	British Columbia	23	20	23.0	15.7	3.5
	Canada (all provinces)		100		14.5	5.3
	Gaspe		12		23.2	12.7
	Basse Cote- Nord		4		14.6	25.4
	Ungave Bay		4		14.3	14.1
	Hudson Bay		5		20.9	21.3
Croatia	Krk	14	10	12.0	8.4	6.1
	Zagreb	41	13	11.8	13.5	8.0
Czech Republic	Kladno		11		12.1	6.0
	Uherske Hradiste		11		18.4	9.8
Denmark	7 different cities	42	48	17.8	15.2	4.5
Finland	Helsinki	38	10	18.0	21.5	4.6
	Kuopio	31	24	15.5	12.0	2.4
Germany	Berlin	40	10	32.0	16.5	11.7
Hungary	Budapest	100	20	9.1	8.5	1.7

	Scenes	50	10	11.3	7.8	1.4
Lithuania	Palanga (coastal)		12		16.6	20.4
	Vilnius city (urban)		12		13.3	20.5
	Anykshchiai (rural)		12		14.4	20.7
Netherlands	mean of 17 individual samples	10	17	34.2	22.4	11.3
Norway	Tromso (coastal)	11	10	18.9	10.1	19.5
	Hamar (rural)	10	10	15.0	9.3	10.4
	Skien/Porsgrunn (industrial)	10	10	19.4	12.5	9.5
Pakistan	Lahore		14		3.9	2.3
Russian Federation	Arkhankeisk		1		15.2	8.6
	Karhopol		1		5.9	4.9
Slovak Republic	Michalovce		10		15.1	13.3
Spain	Bizkaia		19		19.4	10.6
	Gipuzkoa		10		25.5	8.2
Ukraine	Kiev nr.1		5		11.0	15.0
	Kiev nr.2		5		13.3	11.5
United Kingdom	Birmingham		20	37.0	17.9	4.3
	Glasgow		23	29.1	15.2	4.0

Table 2a shows the mean levels of PCDD/Fs and dioxin-like PCBs (total TEQ, ppt, lipid) in pooled breast milk samples from different countries studied by WHO in 1987/88 and 1992/3.

Footnote: Sum TEQ of dioxin-like PCBs presented in the table equates to the sum of non-ortho PCBs TEQ (nos 77, 126, 169) plus the sum of mono-ortho PCBs (nos 105 and 118). Units of ppt TEQ fat are equivalent to pg TEQ/g fat.

Source: WHO (1996)

**Table 3a**  
Mean Levels of DDT in Breast Milk on a lipid basis

Country/Year of Study	Number of samples	% samples Positive	DDT Compound Measured	Mean Concentration of DDT Compound (ug/g fat or ppm)	Reference
<b>Australia</b>					
Perth, 1991	128	100%	DDT	0.8 (median)	Stevens et al. 1993
Victoria	60	97%	p,p'DDT	0.225	Quinsey et al. 1995
<b>Belarus</b>					
6 different regions			sum DDT (p,p-DDE + p,p'DDT)	0.672	Barkatina et al. 1998
<b>Brazil</b>					
Ribeirao Preto Region, Sao Paulo 1983/4	30	100%	total DDT (p,p'DDT + p,p'DDE)	0.862	Matuo et al. 1992
Porto Alegre, (capital of the state of Rio Grande do Sul - an agricultural region)	30	73%	p,p'-DDT	0.12	Beretta and Dick 1994
<b>Canada</b> 1992					
Samples from several regions across the country	497	99%	p,p'-DDT	0.0221	Newsome et al. 1995
<b>Czech Republic</b>					
Prague	17		Total DDT (p,p'-DDE + p,p'DDT)	0.998	Schoula et al. 1996
<b>Faroe Islands</b>					
4 individual 9 pooled		100%	p,p'-DDT	0.159	Abraham et al. 1995
				0.064	
<b>France</b> 1990					
	20	85%	DDT	0.044	Bordet et al. 1993



**Table 2b**  
**Mean Levels of PCDD/Fs in Breast Milk, 1990s**

Country/ Year Samples Taken	Number of Samples	ppt TEQ [PCDD/Fs]	Reference
<b>Estonia</b> Tarto & Tallinin 1991	12	17.5 (Nordic)	Mussalo-Rauhamaa and Lindstrom 1995
<b>France</b>	15	20.1	Gonzalez et al. 1993
<b>Faroe Islands</b>	4 individual samples 9 pooled samples	6.7 9.5	Abraham et al. 1995
<b>Finland</b> Helsinki & Kuopio 1986-88	69	16.9 (Nordic)	Mussalo-Rauhamaa and Lindstrom 1995
<b>Israel</b> Jerusalem 1996	1	10.19	Schechter et al. 1997
<b>New Zealand</b> urban rural	38	16.5 18.1	Bates et al. 1994
<b>Norway</b> Hamar, Skien & Tromso 1987	30	17.1 (Nordic)	Mussalo-Rauhamaa and Lindstrom 1995
<b>Palestinian West Bank</b> near Bethlehem 1996	5	6.46	Schechter et al. 1997
<b>Spain</b>	13	13.31	Gonzalez et al. 1993
<b>Sweden</b> Sundsvall, Umea, Goteborg, Borlange 1987	40	22.4 (Nordic)	Mussalo-Rauhamaa and Lindstrom 1995
<b>Russia</b> Murmansk, northern Russia, 1993	30	15.8	Polder et al. 1996
<b>USA</b> New York, 1996	5 individual samples 100 pooled samples	8.13 27.6	Schechter et al. 1997 Schechter et al. 1996

Table 2b shows mean levels of PCDD/Fs (total TEQ, ppt, lipid) in pooled breast milk samples from different countries in studies published in the 1990s.

Footnote: (Nordic) denotes that the Nordic TEQ system was used and not the International TEQ system.

<b>Germany</b> Eastern Germany (former GDR) 1990-91	497		p,p'-DDT	0.134	Alder et al. 1994
West Germany 1990-91	>1000		p,p'-DDT	0.061	
Lower Saxony, 1992/3	156	99%	Total DDT	0.38 (median)	Schlaud et al. 1995
<b>India</b> Punjab: Ludhiana (urban)	40	100%	p,p'-DDT	7.18	Kalra et al. 1994
Fairidkot (agricultural region with high pesticide use for cotton)	58	100%	p,p'-DDT	13.81	
<b>Italy</b> Rome, Milan, Florence and Pavia.			DDT	0.15	Larsen et al. 1994
<b>Jordan</b> Amman 1989/90	59	100%	p,p'-DDT	0.45 (median)	Alawi et al. 1992
<b>Kazakstan</b> Southern Kazakstan 1994	75	99%	p,p'-DDT	0.3	Hooper et al. 1997
<b>Kenya 1994</b>			p,p' DDT	3.73	Heyce 1994
			sum DDT (p,p-DDE + p,p' DDT)	6.99	
<b>Mexico</b> Veracruz, a tropical region, 1994/5	43	100%	p,p'-DDT	1.271	Waliszewski et al. 1996



<b>Nigeria</b> 1986			p,p'-DDT	2.27	Atuma and Vaz 1986
			sum DDT (p,p'-DDE + p,p'-DDT)	3.83	
<b>Norway</b> Oslo, 1991	28		sum DDT (sum of all DDT, DDE and DDD isomers)	0.338	Johansen et al. 1994
<b>Russia</b> Kola Peninsula, northern Russia, 1993	30		p,p'-DDT	0.178	Polder et al. 1996
5 different regions, 1988/89	24		p,p'-DDT	0.387	Schechter et al. 1990
<b>Slovak Republic</b> 1993/4	50		p,p'-DDT	0.126	Kocan et al. 1995
<b>Spain</b> Madrid 1991	51	21.5%	p,p'-DDT	0.012	Hernandez et al. 1993
<b>Sweden</b> Uppsala 1990	13		p,p'-DDT	0.03	Vaz et al. 1993
<b>Thailand</b> Bangkok 1985-87	3		p,p'-DDT	0.731	Schechter et al. 1989
<b>Turkey</b> Manisa in west and Van in east Turkey 1995/6	104	44%	p,p'-DDT	0.10	Cok et al. 1997
			sum DDT (1.115 x p,p'-DDE + p,p'-DDT)	2.357	
Kayseri region 1988 (an agricultural area with previous heavy use of organochlorine pesticides)	51	96%	p,p'-DDT	0.410	Ustunbas et al. 1994

<b>UK</b> Samples from England, Ireland, Scotland and Wales 1989-91	193		p,p'-DDT	<0.02	Dwarka et al. 1995
<b>USA</b> New York 1985-87	7		p,p'-DDT	0.023	Schechter et al. 1989
<b>South Vietnam</b> Ho Chi Minh City 1985-87	7		p,p'-DDT	4.70	Schechter et al. 1989
<b>Zimbabwe</b> 1994			p,p'-DDT	1.33	Chikuni et al. 1997
			sum DDT (p,p'-DDE + p,p'-DDT)	6.50	
Kariba area 1994 (where DDT is in use)	39		p,p'-DDT	9.07	
			sum DDT	25.26	

Table 3a shows the mean levels of DDT in breast milk on a lipid basis (ppm) for various countries.



**Table 3b**  
**Mean Levels of DDT in Breast Milk on a Whole Milk Basis**

Country/Year of Study	Number of samples	% samples Positive	DDT Compound Measured	Concentration of DDT Compound (ppm)	Reference
<b>Belarus</b> 6 different regions	-		sum DDT (p,p'-DDE + p,p'-DDT)	0.0226 mg/l	Barkatina et al. 1998
<b>Brazil</b> Ribeirao Preto Region, Sao Paulo 1983/4	30	100%	p,p'-DDT	0.006	Matuo et al. 1992
<b>Canada</b> 1992 Samples from several regions across the country	497	99%	p,p'-DDT	0.00064	Newsome et al. 1995
<b>Egypt</b> Cairo, 1987	31	80.6%	p,p'-DDT	0.0175	Dogheim et al. 1991
20 different regions 1993	60	49%	p,p'-DDT	0.00293	Saleh et al. 1996
Cairo, 1994	11	71%	p,p'-DDT	0.00933	Dogheim et al. 1996
<b>India</b> Dehli	25	92%	p,p'-DDT	0.158 mg/l	Nair et al. 1996
<b>Punjab:</b> <b>Ludhiana</b> (urban)	47	100%	p,p'-DDT	0.141	Kalra et al. 1994
Fairidkot (agricultural region with high pesticide use for cotton)	82	100%	p,p'-DDT	0.313	

<b>Poland</b> different regions,	industri- al area 158		DDT	5.5 ug/l	Czaja et al. 1997
	less in- dustrial areas 199			2.8 ug/l	
Samples from different regions of the country	253		p,p'-DDT	0.00285 mg/l	Czaja et al. 1997b
<b>Spain</b> Madrid 1991	51	21.5%	p,p'-DDT	0.0004	Hernandez et al. 1993
<b>UK</b> Samples from England, Ireland, Scotland and Wales 1989-91	193		p,p'-DDT	<0.0001	Dwarka et al. 1995

Table 3b shows the mean levels of DDT in breast milk on a whole milk basis (ppm) for various countries.

**Table 3c**  
**Mean Levels of DDE in Breast Milk on a Lipid Basis**

Country/Year of Study	Number of samples	% samples Positive	DDE Compound Measured	Concentration of DDE Compound (ppm)	Reference
<b>Australia</b> Victoria	60	100%	p,p'-DDE	0.96	Quinsey et al. 1995
<b>Brazil</b> Porto Alegre, (capital of the state of Rio Grande do Sul - an agricultural region)	30	100%	p,p'-DDE	2.53	Beretta and Dick 1994



<b>Canada</b> 1992 Samples from several regions across the country	497	100%	p,p'-DDE	0.222	Newsome et al. 1995
Quebec 1988- 90	536	100%	p,p'-DDE	0.34	Dewailly et al. 1996
<b>Faroe Islands</b>	4 indi- vidual 9 pooled	100%	p,p'-DDE	2.010 0.981	Abraham et al. 1995
<b>France</b> 1990	20	100%	DDE	2.183	Bordet et al. 1993
<b>Germany</b> Eastern Germany (former GDR) 1990-91	497		p,p'-DDE	1.130	Alder et al. 1994
West Germany 1990-91	>1000		p,p'-DDE	0.589	
<b>India</b> Punjab: Ludhiana (urban)	40	100%	p,p'-DDE	10.0	Kalra et al. 1994
Fairidkot (agricultural region with high pesticide use for cotton)	58	100%		12.85	
<b>Italy</b> Rome, Milan, Florence and Pavia			DDE	2.2	Larsen et al. 1994
<b>Jordan</b> Amman 1989/90	59	100%	p,p'-DDE	2.04 (median)	Alawi et al. 1992
<b>Kazakstan</b> southern Kazakstan 1994	76	100%	p,p'-DDE	1.960	Hooper et al. 1997
<b>Kenya</b> 1994			p,p'DDE	2.95	Heyce 1994
<b>Mexico</b>	43	100%	p,p'-DDE	5.017	Waliszewski et

Veracruz, a tropical region, 1994/5					al. 1996
<b>The Netherlands</b>	10		p,p'-DDE	0.705	Dagnelie et al. 1992
<b>Nigeria</b> 1986			p,p-DDE	1.33	Atuma and Vaz 1986
<b>Russia</b> Kola Peninsula, northern Russia, 1993	30 24		p,p'-DDE p,p'-DDE	1.269 1.408	Polder et al. 1996 Schechter et al. 1990
5 different regions, 1988/89					
<b>Slovak Republic</b> 1993/4	50		p,p'-DDE	1.667	Kocan et al. 1995
<b>Spain</b> Madrid 1991	51	100%	p,p'-DDE	0.6041	Hernandez et al. 1993
<b>Sweden</b> Uppsala 1990	13		p,p'-DDE	0.35	Vaz et al. 1993
<b>Thailand</b> Bangkok 1985-87	3		p,p-DDE	3.610	Schechter et al. 1989
<b>Turkey</b> Manisa in west and Van in east Turkey 1995/6	104	100%	p,p'DDE	2.013	Cok et al. 1997
Kayseri region 1988 (an agricultural area with previous heavy use of organochlorin e pesticides)	51	100%	p,p'-DDE	2.389	Ustunbas et al. 1994
<b>UK</b> Samples from England, Ireland, Scotland and Wales 1989- 91	193	99%	p,p'-DDE	0.40	Dwarka et al. 1995



<b>USA</b> New York 1985-87	7		p,p-DDE	0.541	Schechter et al. 1989
<b>South Vietnam</b> Ho Chi Minh City, 1985-87	7		p,p-DDE	6.70	Schechter et al. 1989
<b>Zimbabwe</b> 1994 mean national level			p,p'-DDE	4.49	Chikuni et al. 1997
Kariba area 1994 (only area in Zimbabwe where DDT is still in use)	39		p,p'DDE	13.60	

Table 3c shows the mean levels of DDE in breast milk on a lipid basis (ppm) for various countries.

**Table 3d**  
Mean Levels of DDE in Breast Milk on a Whole Milk Basis

Country/Year of Study	Number of samples	% samples Positive	DDE Compound Measured	Concentration of DDE Compound	Reference
<b>Brazil</b> Ribeirao Preto Region, Sao Paulo 1983/4	30	100%	p,p'-DDE	0.019	Matuo et al. 1992
<b>Canada</b> 1992 Samples from several regions across the country	497	100%	p,p'-DDE	0.00678	Newsome et al. 1995
<b>Egypt</b> Cairo, 1987	31	97%	p,p'DDE	0.03886	Dogheim et al. 1991
20 different regions, 1993	60	100%	p,p'-DDE	0.02137	Saleh et al. 1996
Cairo, 1994	11	100%	p,p'-DDE	0.1	Dogheim et al. 1996

<b>India</b> Dehli		96%	p,p'-DDE	0.672 mg/l	Nair et al. 1996
<b>Punjab:</b> Ludhiana (urban)	47	100%	p,p'-DDE	0.196 mg/l	Kalra et al. 1994
Fairidkot (agricultural region with high pesticide use for cotton)	82	100%		0.277 mg/l	
<b>Poland</b> different regions,	industrial area 158		p,p'-DDE	0.0254 mg/l	Czaja et al. 1997
	less industrial areas 199			0.0275 mg/l	
Samples from different regions of the country	253		p,p'-DDE	0.0252 mg/l	Czaja et al. 1997b
<b>Spain</b> Madrid 1991	51	100%	p,p'-DDE	0.0187	Hernandez et al. 1993
<b>UK</b> Samples from England, Ireland, Scotland and Wales 1989-91	193	99%	p,p'-DDE	0.009	Dwarka et al. 1995

Table 3d shows mean levels of DDE in breast milk on a whole milk basis (ppm) for various countries



**Table 3e**  
**Levels of Total DDT in Breast Milk**

Country	Sum DDT Compounds	Reference
Australia Victoria	0.225+0.96 = 0.321	Quinsey et al. 1995
Belarus	0.672	Barkatina et al. 1998
Brazil	0.12 +2.53 = 2.65	Beretta and Dick 1994
Canada	0.0221+0.222 = 0.244	Newsome et al. 1995
Czech Republic	0.998	Schoula et al. 1996
Faroe Islands	0.064+0.981 = 1.045	Abraham et al. 1995
France	0.044+2.183 = 2.227	Bordet et al. 1993
Eastern Germany	0.134+ 1.130 = 1.264	Alder et al. 1994
West Germany	0.061+0.589 = 0.65	Schlaud et al. 1995
India Ludhiana	7.18+10.0 = 17.18	Kalra et al. 1994
Fairidkot	13.81+12.85 = 26.66	
Italy	0.15+2.2 = 2.35	Larsen et al. 1994
Jordan	0.45+2.04 = 2.49 (median)	Alawi et al. 1992
Kazakstan	0.3+1.96 = 2.26	Hooper et al. 1997
Kenya	6.99	Heyce 1994
Mexico	1.271+5.017 = 6.288	Waliszewski et al. 1996
Nigeria	3.83	Autuma and Vaz 1986
Norway	0.338	Johansen et al. 1994
Russia	0.178+1.269 = 1.447	Polder et al. 1996
Slovak Republic	0.126+1.667 = 1.793	Kocan et al. 1995
Spain	0.012+0.604 = 0.616	Hernandez et al. 1993
Sweden	0.03+0.35 = 0.38	Vaz et al. 1993
Thailand	0.731+3.61 = 4.341	Schechter et al. 1989
Turkey	2.357	Cok et al. 1997
UK	0.02+0.4 = 0.42	Dwarka et al. 1995
USA	0.023+0.541 = 0.564	Schechter et al. 1989
South Vietnam	4.7	Schechter et al. 1989
Zimbabwe National average	6.50	Chikuni et al. 1997
Kariba region	25.26	

Table 3e shows levels of total DDT in breast milk on a lipid basis (ppm) from various countries. The data is either the sum total of DDT compounds as presented in a study, or the sum of p,p'-DDT plus p,p'-DDE. The data was compiled from tables 3a and 3c.

**Table 4a**  
**Mean Levels of HCB in Breast Milk on a Lipid Basis**

Country/Year of Study	Number of samples	% samples Positive	Mean Concentration of HCB (mg/kg fat, or ppm)	Reference
Australia Perth, 1991	128	100%	0.10 (median)	Stevens et al. 1993
Victoria 1993	60	98%	0.411	Quinsey et al. 1995
Brazil Porto Alegre, (capital of the state of Rio Grande do Sul - an agricultural region)	30	63%	0.02	Berretta and Dick 1994
Canada 1992 Samples from several regions across the country	497	100%	0.0145	Newsome et al. 1995
Czech Republic Prague	17		0.639	Schoula et al. 1996
Faroe Islands	4 individual 9 pooled		<0.1	Abraham et al. 1995
France 1990	19	100%	0.147	Bordet et al. 1993
Germany Eastern Germany (former GDR) 1990-91	497		0.167	Alder et al. 1994
West Germany 1990-91	>1000		0.218	
Lower Saxony, 1992/3	156	99%	0.223 (median)	Schlaud et al. 1995



<b>Italy</b> Rome, Milan, Florence and Pavia			0.18	Larsen et al. 1994
<b>Jordan</b> Amman 1989/90	59	93%	0.29 (median)	Alawi et al. 1992
<b>Kazakstan</b> southern Kazakstan 1994	76	100%	0.091	Hooper et al. 1997
<b>Mexico</b> Veracruz, a tropical region, 1994/5	43	100%	0.047	Waliszewski et al. 1996
<b>The Netherlands</b>	10		0.083	Dagnelie et al. 1992
<b>Norway</b> Oslo, 1991	28		0.041	Johansen et al. 1994
<b>Russia</b> Kola Peninsula, northern Russia, 1993	30		0.129	Polder et al. 1996
5 different regions, 1988/89	24		0.245	Schechter et al. 1990
<b>Spain</b> Madrid 1991	51	67.8%	0.0008	Hernandez et al. 1993
<b>Slovak Republic</b> 1993/94	50		0.829	Kocan et al. 1995
<b>Sweden</b> Uppsala 1990	13		0.037	Vaz et al. 1993
<b>Thailand</b> <b>Bangkok</b> 1985-87	3		0.007	Schechter et al. 1989

<b>Turkey</b> Manisa in west and Van in east Turkey 1995/6	104	96%	0.050	Cok et al. 1997
Kayseri region 1988 (an agricultural area with previous heavy use of organo- chlorine pesticides)	51	96%	0.084	Ustunbas et al. 1994
<b>UK</b> Samples from England, Ireland, Scotland and Wales	193		0.02	Dwarka et al. 1995
<b>USA</b> New York 1985-87	7		0.022	Schechter et al. 1989
<b>South Vietnam</b> Ho Chi Minh City 1985-87	7		0.003	Schechter et al. 1989

Table 4a shows the mean levels of HCB in breast milk on a lipid basis (ppm) for various countries

**Table 4b**  
**Mean Levels of HCB in Breast Milk on a Whole Milk Basis**

Country/Year of Study	Number of samples	% samples Positive	Mean Concentration of HCB (mg/kg whole milk or ppm)	Reference
Canada 1992 Samples from several regions across the country	497	100%	0.00044	Newsome et al. 1995
Egypt Cairo, 1987	31	10%	0.01167	Dogheim et al. 1993
Poland various regions	industrial area 158		0.0016 mg/l	Czaja et al. 1997
	less industrial areas 199		0.0022 mg/l	
Samples from different regions of the country	253		0.002 mg/l	Czaja et al. 1997b
UK Samples from England, Ireland, Scotland and Wales	193		<0.001	Dwarka et al. 1995

Table 4b shows the mean levels of HCB in breast milk on a whole milk basis (ppm) for various countries

**Table 5a**  
**Mean Levels of HCH Compounds in Breast Milk on a Lipid Basis**

Country/Year of Study	Number of samples	% samples Positive	Compound Measured	Concentration of HCH Compound (mg/kg fat, or ppm)	Reference
Australia Victoria 1993	128		a-HCH	0.071	Quinsey et al. 1995
	60		B-HCH	0.345	
			g-HCH	0.108	
Belarus Samples from 6 different regions			sum a-HCH + B-HCH	0.417	Barkatina et al. 1998
Brazil Ribeirao Preto Region, Sao Paulo 1983/4	30	30.7%	gamma-HCH	0.0344	Matuo et al. 1992
Porto Alegre, capital of the state of Rio Grande do Sul - an agricultural region where pesticides are extensively used	30	80%	a-HCH	0.04	Beretta and Dick 1994
	25	100%	B-HCH	0.9	
	30	50%	g-HCH	0.02	
Canada 1992 Samples from several regions across the country	497	93%	B-HCH	0.0226	Newsome et al. 1995
		17%	g-HCH	0.00103	
		14%	a-HCH	0.00031	
Czech Republic Prague	17		B-HCH	0.071	Schoula et al. 1996
Faroe Islands	4 individual 9 pooled		B-HCH	<0.04	Abraham et al. 1995



<b>France</b> 1990	20	85% 100% 100%	a-HCH B-HCH g-HCH	0.052 0.287 0.037	Bordet et al. 1993
<b>Germany</b> Eastern Germany (former GDR) 1990-91	497		a-HCH B-HCH g-HCH	0.0008 0.083 0.0098	Schlaud et al. 1995
<b>West</b> Germany 1990-91	>1000		a-HCH B-HCH g-HCH	<0.01 0.075 0.016	
Lower Saxony, 1992/3	156	97% 10%	B-HCH g-HCH	0.045 0.016	
<b>India</b> Dehli	61	51% 95% 90%	a-HCH B-HCH g-HCH	1.83 8.83 2.31	Banerjee et al. 1997
Punjab: Ludhiana (urban)	40	98% 100% 80%	a-HCH B-HCH g-HCH	0.65 4.37 0.21	Kalra et al. 1994
Fairidkot (agricultural region with high pesticide use for cotton)	58	100% 100% 91%	a-HCH B-HCH g-HCH	1.76 8.20 0.41	

<b>Jordan</b> Amman 1989/90	59	55.9% 100% 37.3%	a-HCH B-HCH g-HCH	0.12 (median) 0.40 0.23	Alawi et al. 1992
<b>Kazakstan</b> southern Kazakstan 1994	74 76	98% 100%	a-HCH B-HCH	0.078 2.210	Hooper et al. 1997
<b>Mexico</b> Veracruz, a tropical region, 1994/5	43	40% 100% 52%	a-HCH B-HCH g-HCH	0.018 0.561 0.022	Waliszewski et al. 1996
<b>Norway</b> Oslo, 1991	28		sum a + B + gamma HCH. (B- HCH accounted for 93% of the sum)	0.036	Johansen et al. 1994
<b>Russia</b> Kola Peninsula, northern Russia, 1993	30		sum HCH (of which 99% is B- HCH)	0.858	Polder et al. 1996
5 different regions, 1988/89	24		a-HCH B-HCH g-HCH	0.129 1.589 0.0094	Schechter et al. 1990
<b>Spain</b> Madrid 1991	51	68.6% 85.7% 64.7%	a-HCH B-HCH g-HCH	0.0342 0.235 0.0105	Hernandez et al. 1993
<b>Sweden</b> Uppsala 1990	13		B-HCH	0.02	Vaz et al. 1993
<b>Thailand</b> Bangkok 1985-87	3		a-HCH B-HCH g-HCH	0.001 0.119 0.003	Schechter et al. 1989



Turkey Manisa in west and Van in east Turkey 1995/6	104				Cok et al. 1997
Kayseri region 1988 (an agricultural area with previous heavy use of organochlorine pesticides)	51	75%	a-HCH	0.096	Ustunbas et al. 1994
	19	100%	B-HCH	0.522	
	51	97%	g-HCH	0.156	
UK Samples from England, Ireland, Scotland and Wales	193		B-HCH	0.08	Dwarka et al 1995
			g-HCH	<0.02	
USA New York 1985-87	7		a-HCH	0.001	Schecter et al. 1989
			B-HCH	0.020	
			g-HCH	0.002	
South Vietnam Ho Chi Minh City 1985-87	7		a-HCH	0.003	Schecter et al. 1989
			B-HCH	0.221	
			g-HCH	0.023	

Table 5a shows the mean levels of HCH compounds in breast Milk on a lipid basis (ppm) for various countries.

Table 5b  
Mean Levels of HCH Compounds in Breast Milk on a Whole Milk Basis

Country/Year of Study	Number of samples	% samples Positive	Compound Measured	Concentration of HCH Compound (mg/kg whole milk, or ppm)	Reference
Belarus Samples from 6 different regions			sum a-HCH + B-HCH	0.0142	Barkatina et al. 1998
			B-HCH	0.00071 (0.71 ppb)	Newsome et al. 1995
Canada 1992 Samples from several regions across the country	497	93%	B-HCH	0.00071 (0.71 ppb)	Newsome et al. 1995
		17%	g-HCH	0.00004 (0.04 ppb)	
		14%	a-HCH	0.00001 (0.01 ppb)	
Egypt Cairo, 1987	31	51.6%	a-HCH B-HCH g-HCH	0.00279 0.01337 0.00072	Dogheim et al. 1991
20 different regions, 1993	60	95%	g-HCH	0.00842	Saleh et al. 1996
Cairo, 1994	11	64% 82% 0 82	a-HCH B-HCH g-HCH Total HCH	0.00314 0.1912 <0.0010 0.19344	Dogheim 1996
Germany Lower Saxony, 1992/3	156	97%	B-HCH	0.045	Schlaud et al. 1995
		10%	g-HCH	0.016	
India Dehli	25	100%	a-HCH	0.045mg/l	Nair et al. 1996
		28%	B-HCH	0.198 mg/l	
		100%	g-HCH	0.084 mg/l	
Dehli	61	51%	a-HCH	0.08	Banerjee et al. 1997
		95%	B-HCH	0.24	
		90%	g-HCH	0.06	
Punjab: Ludhiana (urban)	47	98%	a-HCH	0.015	Kalra et al. 1994
		100%	B-HCH	0.09	



Fairidkot (agricultural region with high pesticide use for cotton)	82	80%	g-HCH	0.004	
		100%	a-HCH	0.031	
		100% 91%	B-HCH g-HCH	0.188 0.011	
<b>Poland</b> industrialised and less industrialised areas, 1995/6??	357		a-HCH	0.00055 mg/l	Czaja et al. 1997
Samples from different regions of the country	253		B-HCH	0.003 mg/l	Czaja et al. 1997b
			g-HCH	0.00045 mg/l	
			a-HCH	mean 0.0006 mg/l	
<b>Spain</b> Madrid 1991	51	68.6%	a-HCH	0.001	Hernandez et al. 1993
		85.7%	B-HCH	0.0072	
		64.7%	g-HCH	0.0003	

Table 5b shows the mean levels of HCH compounds in breast milk on a whole milk basis (ppm) for various countries

**Table 6a**  
Mean Levels of Heptachlor in Breast Milk on a Lipid Basis

Country/Year of Study	Number of samples	% samples Positive	Mean Concentration of Heptachlor (mg/kg fat, or ppm)	Reference
<b>Australia</b> Perth, 1991	128	89%	0.02 (median)	Stevens et al. 1993
<b>Germany</b> Lower Saxony, 1992/3	156	74%	0.022 (median)	Schlaud et al. 1995

<b>Jordan</b> Amman 1989/90	59	68%	0.70 (median)	Alawi et al. 1992
<b>Spain</b> Madrid 1991	51	33.3%	0.0044	Hernandez et al. 1993
<b>Turkey</b> Kayseri region 1988 (an agricultural area with previous heavy use of organochlorine pesticides)	32	38%	0.198	Ustunbas et al. 1994

Table 6a shows the mean levels of heptachlor in breast milk on a lipid basis (ppm) for various countries

**Table 6b**  
Mean Levels of Heptachlor in Breast Milk on a Whole Milk Basis

Country/Year of Study	Number of samples	% samples Positive	Mean Concentration of Heptachlor (mg/kg whole milk or ppm)	Reference
<b>Australia</b> Perth, 1991	128	89%	0.02 (median)	Stevens et al. 1993
<b>Egypt</b> Cairo, 1987	31		mean 1.0 ppb whole milk, range 1.0-1.0 ie. the compound was detectable	Dogheim et al. 1991
<b>Spain</b> Madrid 1991	51	33.3%	0.1 ng/g	Hernandez et al. 1993

Table 6b shows the mean levels of heptachlor in breast milk on a whole milk basis (ppm) for Various Countries.



**Table 6c**  
**Mean Levels of Heptachlor Epoxide in Breast Milk on a Lipid Basis**

Country/Year of Study	Number of samples	% samples Positive	Concentration of Heptachlor Epoxide (mg/kg fat, or ppm)	Reference
<b>Australia</b> Victoria	60	30%	0.061	Quinsey et al. 1995
<b>Brazil</b> Porto Alegre, capital of the state of Rio Grande do Sul - an agricultural region where pesticides are extensively used	30	17%	0.02	Beretta and Dick 1994
<b>Canada</b> 1992 Samples from several regions across the country	497	68%	0.00377	Newsome et al. 1995
<b>France</b> 1990	20	95%	0.097	Bordet et al. 1993
<b>Germany</b> Eastern Germany (former GDR) 1990-91	497		0.008	Alder et al. 1994
West Germany 1990-91	>1000		0.014	
<b>Russia</b> 5 different regions, 1988/89	24		0.0118	Schechter et al. 1990
<b>Spain</b> Madrid 1991	51	92.1%	0.0311	Hernandez et al. 1993

<b>Turkey</b> Kayseri region 1988 (an agricultural area with previous heavy use of organochlorine pesticides)	32	16%	0.011	Ustunbas et al. 1994
Van in east and Manisa in west Turkey 1995/6	104	96%	0.072	Cok et al. 1997

Table 6c shows the mean levels of heptachlor epoxide in breast milk on a lipid basis (ppm) for various countries.

**Table 6d**  
**Mean Levels of Heptachlor Epoxide in Breast Milk on a Whole Milk Basis**

Country/Year of Study	Number of samples	% samples Positive	Concentration of Heptachlor Epoxide (mg/kg whole milk, or ppm)	Reference
<b>Canada</b> 1992 Samples from several regions across the country	497	68%	0.00011	Newsome et al. 1995
<b>France</b> 1990	20	95%	0.097	Bordet et al. 1993
<b>Spain</b> Madrid 1991	51	92.1%	0.0009	Hernandez et al. 1993

Table 6d shows the mean levels of heptachlor epoxide in breast milk on a whole milk basis (ppm) for various countries.



**Table 7a****Mean Levels of Dieldrin in Breast Milk on a Lipid Basis**

Country/Year of Study	Number of samples	% samples Positive	Mean Concentration of dieldrin (mg/kg, or ppm)	Reference
<b>Australia</b> Perth, 1991	128	100%	0.05 (median)	Stevens et al. 1993
Victoria	60	43%	0.159	Quinsey et al. 1995
<b>Brazil</b> Ribeirao Preto Region, Sao Paulo 1983/4	30	3%	1.31	Matuo et al. 1992
Porto Alegre, capital of the state of Rio Grande do Sul - an agricultural region where pesticides are extensively used	30	83%	0.07	Beretta and Dick 1994
<b>Canada</b> 1992 Samples from several regions across the country	497	94%	0.00978	Newsome et al. 1995
<b>France</b> 1990	20	55%	0.19	Bordet et al. 1993
<b>Germany</b> Eastern Germany (former GDR) 1990-91	497		0.042	Alder et al. 1994
West Germany 1990-91	>1000		0.009	
Lower Saxony, 1992/3	156	66%	0.014 (median)	Schlaud et al. 1995
<b>Iraq</b>			1.00	Jensen and Slorach 1991

<b>Jordan</b> Amman 1989/90	59	5%	0.05	Alawi et al. 1992
<b>The Netherlands</b>	10		0.013	Dagnelie et al. 1992
<b>Russia</b> 5 different regions, 1988/89	24		<0.002-0.003	Schechter et al. 1990
<b>Spain</b> Madrid 1991	51	11.7%	0.0039	Hernandez et al. 1993
<b>Thailand</b> Bangkok 1985-87	3		0.069	Schechter et al. 1989
<b>Turkey</b> Kayseri region 1988 (an agricultural area with previous heavy use of organochlorine pesticides)	32	19%	0.0067	Ustunbas et al. 1994
<b>UK</b> Samples from England, Ireland, Scotland and Wales 1989-91	193		0.03	Dwarka et al. 1995
<b>USA</b> New York 1985-87	7		0.541	Schechter et al. 1985-87
<b>Uruguay</b>			1.00	Jensen and Slorach 1991
<b>South Vietnam</b> Ho Chi Minh City	7		0.004	Schechter et al. 1989

Table 7a shows the mean levels of dieldrin in breast milk on a lipid basis (ppm) for various countries



**Table 7b**  
**Mean Levels of Endrin in Breast Milk on a Lipid Basis**

Country/Year of Study	Number of samples	% samples Positive	Concentration of Endrin (mg/kg fat, or ppm)	Reference
France 1990	20	40%	0.058	Bordet et al. 1993

Table 7b shows the mean levels of endrin in breast milk on a lipid basis (ppm) for France.

**Table 7c**  
**Mean Levels of Aldrin in Breast Milk on a Lipid Basis (ppm)**

Country/Year of Study	Number of samples	% samples Positive	Concentration of Aldrin (mg/kg fat, or ppm)	Reference
Australia Victoria 1993	60	5%	mean 0.02	Quinsey et al. 1995
France 1990	20	75%	0.024	Bordet et al. 1993
Turkey Kayseri region 1988 (an agricultural area with previous heavy use of organochlorine pesticides)	32	88%	mean 0.047	Ustunbas et al. 1994

Table 7c shows the mean levels of aldrin in breast milk on a lipid basis (ppm) for various countries.

**Table 8.**  
**Mean Levels of Chlordane in Breast Milk on a Lipid Basis**

Country/Year of Study	Number of samples	% samples Positive	Concentration of Chlordane (CL) Compound (mg/kg fat, or ppm)	Reference
Australia Perth, 1991	128	17%	median <0.01 mg/kg fat,	Stevens et al. 1993
Victoria	60	80%	oxychlordane 0.13	Quinsey et al. 1995

Canada National survey 1987			g-CL 0.008 a-CL 0.019	see Dearth and Hites 1991
Indigenous people			g-CL 0.003 a-CL 0.012	
Canada 1992 Samples from several regions across the country	497	2%  11%	g-CL 0.00016  a-CL 0.00021	Newsome et al. 1995
France 1990	20	90%  40%	a-CL 0.078  g-CL 0.006	Bordet et al. 1993
Japan 1986			a-CL 0.0031 g-CL 0.0012	Dearth and Hites 1991
Russia Kola Peninsula, northern Russia, 1993	30		sum CL 0.059	Polder et al. 1993
5 different regions, 1988/89	24		oxychordane 0.0056	Schechter et al. 1990
Thailand Bangkok 1985-87	3		oxychlordane 0.005	Schechter et al. 1989
USA New York 1985-87	7		oxychlordane 0.006	Schechter et al. 1989
South Vietnam Ho Chi Minh City 1985-87	7		oxychlordane 0.003	Schechter et al. 1989

Table 8 shows the mean levels of chlordane in breast milk on a lipid basis (ppm) for various countries.



**Table 9**  
Mean Levels of Toxaphene in Breast Milk on a Lipid Basis (ppm)

Country/Year of Study	Number of samples	% samples Positive	Concentration of toxaphene mg/kg fat, or ppm	Reference
Honduras	1		1.4	Boer and Webster 1993
Finland			0.05-0.5	Pyysalo and Antervo 1985
Netherlands	1		0.65	Boer and Webster 1993
Nicaragua 1993	16	100%	2.0	Boer and Webster 1993
Sweden			0.1	Vaz and Blomkvist 1985

Table 9 shows the mean levels of toxaphene in breast milk on a lipid basis (ppm) for various countries.

**Table 10**  
Summary of Mean Levels of Organochlorine Pesticides in Breast Milk on a Lipid Basis (ppm)

Country	p,p'DDT	p,p'DDE	Dieldrin	HCB	HE	B-HCH	g-HCH
Australia Victoria	0.225	0.96	0.159	0.411	0.061	0.345	0.108
Belarus (sum)	0.672						
Brazil Sao Paulo Porto-Algre	0.12	2.53	1.31 0.07	0.02	0.02	0.9	0.0344 0.02
Canada	0.0221	0.222	0.00978	0.0145	0.00377	0.0226	0.001
Czech Republic (sum)	0.998			0.639		0.071	
Faroe Islands	0.064	0.981		<0.1		<0.04	
France	0.044	2.183	0.19	0.147	0.097	0.287	0.037
Germany	0.38 *		0.14*	0.223*	0.014	0.045	0.016
India Dehli						8.83	2.31
Ludhiana	7.18	10.0				4.37	0.21
Fairidkot	13.81	12.85				8.20	0.41
Italy	0.15	2.2		0.18			

Jordan	0.45*	2.04*	0.05*	0.29*		0.40	
Kazakstan	0.3	1.96	nd	0.091	nd	2.210	0.23
Kenya	3.73	2.95					
Mexico	1.271	5.017		0.047		0.561	0.022
The Netherlands		0.705	0.013	0.083			
Nigeria	2.27	1.33					
Norway (sum)	0.338			0.041			
Russia Kola Peninsula 5 different regions	0.178	1.269		0.129			
	0.387	1.408	<0.002-3.0	0.245	0.0118	1.589	0.0094
Slovak Republic	0.126	1.667		0.829			
Spain	0.012	0.6041	0.0039	0.0008	0.0311	0.235	0.0105
Sweden	0.03	0.35		0.037		0.02	
Thailand	0.731	3.610	0.069	0.007		0.119	0.003
Turkey Mania, Van Kayseri	0.1 0.41	2.01 2.389		0.05 0.084	0.011	0.522	0.156
	<0.02	0.40	0.03	0.02		0.08	<0.02
UK	0.023	0.541	0.026	0.022		0.020	0.002
USA	4.70	6.70	0.004	0.003		0.221	0.023
South Vietnam							
Zimbabwe national av. Kariba	1.33 9.07	4.49 13.60					

Table 10 shows a summary of information compiled in this report on the mean levels of several organochlorine pesticides in human breast milk from various countries.

Foonote: For DDT, (sum) denotes the total of DDT compounds measured including DDE.

Source: see tables 3a, 3c, 4a, 5a, and 6c.



**Table 11.**

ADIs set by WHO (1997) and estimated approximate level of organochlorines in breast milk which should not be exceeded if the ADI is not exceeded.

Pesticide	ADI (WHO) mg/kg body weight	Level in milk which should not be exceeded if the ADI is not to be exceeded	
		mg/kg whole milk	mg/kg fat
EDDT	0.02	0.133	3.80
HCB	0.0006	0.004	0.11
Lindane ( $\gamma$ HCH)	0.001	0.0066	0.19
Dieldrin + aldrin combined	0.0001	0.00066	0.019
Endrin	0.0002	0.0013	0.038
Heptachlor	0.0001	0.00066	0.019
Heptachlor epoxide	0.0001	0.00066	0.019
Chlordane	0.0005	0.0033	0.095

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