

Chemical Trespass: A toxic legacy

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CHEMICAL TRESPASS: A TOXIC LEGACY

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PART 1: INTRODUCTION AND OVERVIEW

The post-war chemical revolution has resulted in global contamination. Thousands of substances have been released into the environment with few prior checks on their potential for causing long term harm. For many years, little attention was paid to what happened to these substances after they were released. However, it has now been realised that many are persistent and can cause unwanted effects in the longer term. Sometimes it is the parent molecule itself which is particularly hazardous, while in other cases, it can be a degradation product or a metabolite which is more harmful. This document highlights the particular concerns about fat soluble pollutants that are not readily broken down by metabolic processes, because these substances can be stored in body fats and build up to dangerous levels.

Predator birds, reptiles and mammals, including man, are particularly at risk, because persistent organic contaminants, along with some heavy metals, can build up in the food chain (bioaccumulate). Moreover, many of these pollutants can be passed on to offspring, either via the egg or via the placenta, at a particularly sensitive stage of their development. Mammalian offspring are potentially most at risk because further exposure to the pollutants stored in body fats occurs during breast feeding. Exposure of the foetus is related to the maternal body burden and, similarly, the exposure of a breast milk fed baby is related to the levels in a mother's adipose (fat) tissue.

Human exposure arises not only from the build up of environmental contaminants in the food chain and from exposure to contaminants in air and drinking water, but also from the direct ingestion of substances used in food packaging and in processed foods, and from the absorption through the skin of certain substances used in cosmetics. This report identifies many of the contaminants which have been found in human adipose (fat) tissue and breast milk.

The human race is now contaminated with hundreds of synthetic chemicals which would not have been found in our Victorian ancestors. Protecting our children from the legacy of these chemicals is a major challenge to modern society. Indeed, it is now recognised that the foetus can be damaged by relatively low levels of contaminants which do not affect the adult. Exposure in the womb can cause birth defects and affect our children's future ability to reproduce and their susceptibility to diseases, including cancer. Functional deficits can also be caused, such that some children may not reach their full potential. Put simple, the integrity of the next generation is at stake.

As evidence of the harmful effects of these substances has grown, the need for international agreements to reduce or eliminate discharges and losses of a dozen or so of the most persistent and toxic substances has been recognised by the United Nations.¹ However, because of their persistence, it will take many years for the risks from these substances to be eliminated. In addition, as the number of man-made chemicals has increased dramatically, there is still a threat from the numerous hazardous substances that remain in widespread use.

¹ The UNEP (United Nations Environment Programme) proposed Convention on POPs will require global controls over 12 substances at the outset including: aldrin, chlordane, DDT, dieldrin, dioxins and furans, endrin, heptachlor, HCB, mirex, PCBs and toxaphene.

The UN ECE (United Nations Economic Commission for Europe) Protocol on Persistent Organic Pollutants (POPs) under the Convention on Long Range Transboundary Air Pollution relates to 16 substances, which include the twelve listed above and polyaromatic hydrocarbons (PAHs), chlordecone, hexabromobiphenyl (HBB), and hexachlorocyclohexane (which includes lindane).

The global expansion of the organic chemical industry has been phenomenal, with total production in the 1950s estimated at around 7 million tonnes, compared to over 250 million tonnes in the early 1990s (CEC,1992). Not only the sheer volume of chemicals used, but also the number of chemicals, have increased dramatically, with perhaps around 80,000 chemicals currently in widespread use. This rapid post-war expansion in the chemical industry has certainly resulted in increased foetal exposure to many lipophilic contaminants. However, the problems associated with early-life exposure to pollutants are only now becoming a focus of attention. Rather like a snowball gathering snow as it is rolled along, mothers will pass a proportion of their contamination onto their children, who will then pick up more contamination from their own lifetime's exposure to numerous chemicals. DDT was first found in breast milk in 1950 (Laug et al.,1950), and PCBs were detected some twenty years later (Westoo and Noren; Acker and Schulte,1970). Nowadays, there is widespread contamination of mother's milk both in industrial cities, and in remote areas of the globe. Unfortunately, it has however taken many years for mankind to realise the extent to which we have contaminated our own species, and the susceptibility of developing offspring.

In humanity's rush to industrialise, wildlife throughout the world has been contaminated. Many species, including whales, seals, otters, alligators, birds and fish, have been adversely affected. However, because we are now living with so many pollutants, it is almost impossible to use field studies or epidemiological studies to ascertain which pollutants are responsible for causing which effects. This means that polluters are relatively safe from having to bear liability for perpetrating this mass chemical trespass of our bodies. Indeed, blame can only be established when pollutants cause rather specific effects, and there are clearly defined exposed and non-exposed populations, as was the case with asbestos and asbestosis and mesothelioma, and cigarettes and lung cancer. And even then, getting compensation in the courts is problematic, to say the least.

There are three overriding conclusions of this report. Firstly, over 350 contaminants have, at some time, been found in human breast milk. However, despite this, mothers should certainly not be discouraged from breast feeding. Secondly, urgent action should be taken to reduce foetal and neonatal exposure to man-made chemicals. And thirdly, substances that are persistent and able to bioaccumulate should be phased-out irrespective of their currently known toxicity, because if effects due to these substances do become evident, then it will be impossible to remedy these in the short term.

Part 2 of this report outlines the potential effects of exposure to chemical toxicants. Part 3 lists some substances and the levels that have been found in human body fats, while Part 4 identifies substances which have been detected in breast milk, and provides an indication of some of the higher concentrations that have been recorded. Part 5 looks at some of the levels of contaminants reported in breast milk from mothers living in Britain and outlines some future studies that Government departments are to oversee in the UK. Part 6 details the main conclusions of the report and makes some recommendations.

The toxic properties associated with the hundreds of chemicals that have been found contaminating the human species are numerous, and for a few of the compounds identified, some of these properties are briefly outlined in Appendix 1.

PART 2: THE POTENTIAL EFFECTS OF CONTAMINATION IN HUMANS

The foetus is particularly vulnerable to environmental toxicants, as is, to probably a slightly lesser extent, the neonate and the infant. This is because they have a greater relative exposure per kilogram of body weight and they have increased absorption and retention as their metabolism is less developed. Also, they are at a more sensitive stage of development because their cells are growing and changing rapidly, and in the foetus there is a high rate of cell production and cell division.

Given the known benefits of breast feeding, it is stressed that this report does not advocate that babies should not be breast fed. This is because breast feeding undoubtedly provides immunological and psychological advantages, and human milk is the ideal nutrient for infants. The alternative of powdered bottled milk formula may anyway also be contaminated with various pollutants. Indeed, chemicals such as phthalates, some of which possess endocrine disrupting properties, have been found in UK samples of infant formulae (MAFF, 1996; FAC, 1997). It should also be recognised that the foetus is likely to be far more sensitive than the neonate, and little can be done to avert transplacental exposure during this period if the mother is already contaminated. This report therefore reiterates the conclusion of expert committees, that on the basis of available information, the benefits of breast feeding outweigh the possible risks from chemical contaminants present in human milk.

With regard to the toxic substances in breast milk, first born infants may be at a higher risk than subsequent children, because mothers tend to excrete the largest proportion of their body burden of contaminants during their first lactation (Vaz et al., 1993). Premature and low birth weight infants may also be particularly at risk because they have less adipose tissue for the storage of lipophilic chemicals, which may mean that these chemicals are present at higher concentrations in vital organs. Heavy metals, such as lead and mercury, which may also be found in breast milk, may accumulate at different rates in the brain of premature infants (Jensen and Slorach, 1991).

The potential effects of exposure to the chemicals which are now found as contaminants in human body fat and breast milk are numerous. Some of the contaminants identified are known to have the ability to cause cancer and some are able to impair the immune system. Others, termed hormone disruptors or endocrine disrupting chemicals (EDCs), are known to interfere with the normal functioning of the bodies own hormones, or chemical messengers. It is certainly particularly worrying that animal experiments show that if early life forms are exposed to hormone disrupting substances, when they are being programmed to control and respond to the hormone signals throughout life, then a whole series of irreversible effects can occur. For example, in utero exposure to sex hormone disrupting substances can particularly compromise the ability of that offspring to reproduce later in life, while exposure to other hormone disrupting substances, such as thyroid hormone disruptors, can de-rail normal brain function. Animal experiments have shown that exposure to low doses of numerous environmental toxic agents, during the neonatal period of rapid brain growth (or brain growth spurt), can lead to disruption of adult brain function and increase the susceptibility to toxic agents in later life. In humans, this period of rapid brain growth starts during the third trimester of pregnancy and continues throughout the first two years of life (Eriksson et al., 1998).

With regard to effects on infants, exposure to hormone disrupting substances in utero has been suggested to increase the incidence of birth defects of the reproductive tract (Kallen et al., 1986;

Ansell et al.,1992; Nurminen et al.,1995; Garcia-Rodriguez,1996; Weidner et al.,1998), affect birth height (Dewailly et al.,1993) affect visual recognition and offspring intelligence (Jacobson and Jacobson,1996), and affect the sex ratio of babies born into a population (Moller,1996; Karin,1997). Furthermore, relatively high levels of some organochlorines have been associated with premature delivery (Saxena et al.,1980; Wassermann et al., 1982; Taylor et al.,1989; Fein et al., 1984), stillborn infants (Curley et al.,1969) and shortened lactation (Rogan et al.,1987; Gladen and Rogan,1995).

In women, exposure is implicated in effects such as endometriosis (Rier et al.,1995; Johnson et al.,1997) and increased breast cancer rates. However, the studies correlating the levels of organochlorine oestrogenic pollutants in human tissue with breast cancer incidence have been contradictory (Wolff et al.,1993; Adami et al.,1995; Hunter et al.,1997; Hoyer et al.,1998; see review in Lopez-Carillo et al.,1996), although none of the studies has looked at exposures in the womb and tried to correlate these with future breast cancer risk. It is, nevertheless, a reasonable hypothesis that man-made oestrogen mimicking compounds may be in part to blame for breast cancer. This is because it is well known that increased exposure to endogenous natural oestrogen, as occurs in women with early menarche, lack of breast feeding and late menopause, increases the risk of breast cancer (Henderson et al.,1988). Furthermore, recent studies have suggested that tamoxifen, an anti-oestrogenic pharmaceutical, can prevent breast cancer (BMJ, 23 May 1998). In addition, it may be that other man-made chemicals, apart from oestrogen mimicking compounds, are also partly to blame for the increased incidence of breast cancer. Some workers have found aromatic amines in breast milk and believe that these may play a role in the etiology of human breast cancer (deBruin et al.,1999).

With regard to effects on the testes, there is epidemiological evidence linking certain occupational exposures with increased risk of testicular cancer (Hardell et al.,1997). In addition, other small epidemiological studies also point to chemicals exerting effects on testicular function. Indeed, men who farm without pesticides or who eat food grown without pesticides have been found to have higher sperm concentrations (Kold Jensen et al.,1996; Abell et al.,1994). Fertility may also be affected. For example, in fruit growers, exposure to pesticides has been linked with an increase in time to pregnancy (see Health Council of the Netherlands,1997), although not all studies have shown effects on male fecundability (Larsen et al.,1998).

Decreased sperm counts have been found in men exposed in the womb to the synthetic oestrogen DES (diethylstilboestrol), as some years ago, DES was unfortunately used as a pharmaceutical medicament (Stillman,1982). This effect of oestrogen mimicking compounds is borne out by laboratory experiments on pregnant animals which show that other oestrogenic chemicals can also affect an offspring's sperm counts and sex linked behaviour traits (vom Saal et al.,1995). It is therefore a matter of considerable concern that human babies are now exposed in the womb to numerous oestrogenic pollutants which are contaminants of their mothers. The origin of testicular cancer may also be in foetal life. For example, there is some suggestion that testicular cancer and sperm count deficits may have a common cause (Moller and Skakkebaek,1999). Therefore, it is likely that exposure to some of these substances in the womb may make our children more predisposed to certain behaviours and certain diseases, including cancers in later life.

It is certainly a matter of increasing international concern that, in many industrialised countries, the incidence of hormone related cancers, such as breast cancer, prostate cancer, and testicular cancer, have all increased dramatically over the last 50 years. There are also good data to show, at least in

certain areas, an increase in birth defects of the reproductive tract, and a decline in sperm counts. Moreover, there may be in-utero and neonatal exposure to other carcinogenic substances apart from endocrine disrupting substances. It is speculated that such exposures might be implicated in the rising levels of childhood cancers, although many factors are also likely to play a part, including genetic susceptibility. Given that in the USA, childhood cancer rates appear to be increasing at the rate of approximately 1% each year (EHP, January 1998), this report argues that it would be wise to endeavour to urgently reduce in-utero exposures to substances identified as possible carcinogens.

In the general population it may be that exposure to numerous substances with additive or even possibly synergistic effects are tipping certain people over the threshold for effects, but it may be that, for some substances, there is no threshold below which effects do not occur. In addition, it is likely that there are narrow sensitive windows of exposure when certain processes are at risk, although as central nervous system (CNS) development takes place over a relatively long time period, it is likely that offspring are particularly at risk of exhibiting effects on behaviour.

People and animals living in heavily industrialised areas and consuming polluted fish at the top of the food web, such as trout and salmon, are likely to be most at risk. For example, at least 14 species of fish and fish-eating wildlife in the Great Lakes have experienced effects, including population declines and reproductive problems, which have been attributed to persistent chemical contaminants (Health Canada, 1997). In an effort to confirm the effects of simultaneous exposure to all the chemicals contaminants found in these Great Lakes fish, separate studies were undertaken. Scientists fed these contaminated fish to numerous species, including rats, coho salmon, ranch mink, and chickens, and in each case there were measurable changes in functionality or survivability (Villeneuve et al., 1981; Leatherland and Stonstegard, 1982; Heaton et al., 1991; Daly et al., 1989; Summer et al., 1991). It is therefore perhaps not surprising that several studies have indicated effects on behaviour and neuromuscular development in the offspring of fish-eating women living in the Great Lakes area.

In one particular study, intellectual impairment was correlated to prenatal exposure to PCBs and co-contaminants. Furthermore, this study highlighted that exposure to contaminants in the womb appeared to be far more important than post natal exposure from breast milk. The Jacobsons' found that women who ate contaminated fish (from Lake Michigan), for 6 years prior to pregnancy, produced babies with poorer visual recognition as compared to less exposed children (Jacobson et al., 1985). At age four, the children who had had the higher cord serum PCB levels were associated with poorer verbal and memory performance and slower information processing. Even at 11 years old, the most highly exposed children showed lower full scale and verbal IQ scores (Jacobson and Jacobson, 1997). The Jacobsons' study suggested that exposure to contaminants in the fish was linked to an increase in the proportion of children at the lower end of the normal IQ range, although there was no evidence of gross intellectual impairment. This is important, because it highlights that only very detailed studies would pick up such effects.

A study in Mexico has also provided some startling comparisons in children's development. This study suggested that compared to children with minimal pesticide exposure, children living in an area with heavy pesticide use, had decreased physical stamina, reduced memory, and amongst other effects, a reduced ability to draw a person, which was a test used to provide a non-verbal measure of cognitive ability. This study did not attempt to elucidate actual exposures, but nevertheless suggests that man-made chemicals may be causing alarming effects (Guillette et al., 1998).

Studies in Europe have also highlighted effects. For example, a study undertaken in the Netherlands, has associated pre and postnatal exposure to PCBs, dioxins and furans, to delays in psychomotor development in children (Koopman-Esseboom et al.,1996).

It could certainly be argued that more research is needed into the effects of pollutants on behaviour and brain function. For example, many environmental pollutants can alter thyroid function and it is known that the hormones secreted by this gland help coordinate the sequence of steps required for normal brain function (Porterfield,1994). Pollutants may therefore cause numerous effects, including, for example, the loss of ability to concentrate and to cope with stressful situations (Daly,1992; Lonky et al.,1996).

International agencies have already reacted to the warning bells. In June 1998, the World Health Organisation (WHO) reduced the tolerable daily intake (TDI) for dioxin like substances (which includes certain PCBs) to 1-4 picograms per kilogram body weight per day (pg/kg bw/day) from a previous level of 10pg/kg bw/day. This was in response to recent studies that had highlighted dioxin's effects on neurological development and on the endocrine system. The WHO noted that "subtle effects may already occur in the general population in developed countries at current background levels of 2-6 picograms/kilogram body weight" (WHO, Press Release, 3rd June 1998). It is also rather alarming to note that in the industrialised world, the new TDI would be far exceeded by many babies during breast feeding (see Parts 4 and 5). In the UK, for example, the latest breast milk study, in 1993-94, found intakes of two month old babies were around 170 pg TEQ/kg bw/day which dropped to around 39 pg TEQ/kg bw/day at 10 months (MAFF, June 1997). These data show that 2 month old infants receive around 40 times in excess of the WHO tolerable daily intake, while 10 month old infants receive 10 times in excess of the new WHO TDI. As of March 1999, the UK Government had still not reduced its TDI of 10pg/kg bw/day, and therefore had not come into line with the new WHO limits, but even these higher limits can be seen to be widely exceeded by breast fed infants.

BOX 2.0: SUMMARY OF THE POSSIBLE EFFECTS OF EXPOSURE TO ENDOCRINE DISRUPTING SUBSTANCES (Taken from Health Council of the Netherlands, 1997)

The *possible* effects of in utero exposure to endocrine disruptors include:-

- Abnormal development of the reproductive system, such as undescended testes and defects (hypospadias and epispadias) of the penis. Feminisation of the reproductive tract in males and masculinisation in females. Testicular cancer, and clear-cell carcinoma of the cervix or vagina. Decrease in sperm concentration and quality, and decrease in spermatogenesis.
- Abnormal development of the central nervous system, leading to neurological, cognitive, and behavioural disorders (including effects on sexual behaviour), smaller head size at birth.
- Other general developmental abnormalities, such as shorter pregnancies, lower birth weight, disturbed hormonal regulation or thyroid gland effects, arrested growth and effects on sex ratios.

The *possible* effects of exposure later in life include:-

- Abnormal functioning of the reproductive system, and disturbance of hormonal regulation. In men, this could mean impotence and loss of libido, reduced testes size and weight, decreased sperm quantity and quality and altered spermatogenesis. In females, problems with breast feeding, menstrual or menopausal problems, endometriosis, alteration in fertility and an increased rate of abortions.
- An increased incidence of cancers related to hormonal disturbance, such as breast, endometrial, prostate, testicular, ovarian, adrenal and thyroid cancers.

In a few cases, mostly due to industrial exposure, contaminants in breast milk have been implicated in causing demonstrable effects on infants in the short term. These have included perchlorethylene from a dry cleaning facility causing jaundice in the infant, and styrene exposure in a plastics factory, where several cases of inhibition of lactation were reported (Jensen and Slorach, 1991).

Accidents have also provided evidence of the harmful effects of chemicals transferred in breast milk, and a particularly tragic event happened in Turkey in the 1950s, where about 4000 people were poisoned and about 500 died due to eating bread baked with flour made from HCB-treated wheat. Many of the children under two years old, who had been breast fed by mothers who had eaten the bread, died of a condition known as pink sore.

Other cases of mass accidental poisonings have occurred. In Japan, in the 1960s, there was an incident due to PCB contaminated rice oil, and a similar incident happened in Taiwan some ten years later. In Japan, the disease □Yusho□, characterised by skin abnormalities including chloracne, was reported in babies exposed in utero and in babies exposed solely through breast milk (Jensen and

Slorach,1991, citing Yoshimura T.,1974).

Similarly, high levels of the related compounds, PBBs, were detected in Michigan residents in the early 1970s when these substances were accidentally included in animal feed. Exposed 2-4 year old children showed an inverse relationship between body burdens and developmental abilities, but it was not specified whether these body burdens were acquired in utero or from breast feeding (Jensen and Slorach,1991). The mercury poisoning incidents at Minimata in Japan in the 1960s, and in Iraq in the 1970s, are also well documented. In the later case, breast milk with around 200 ppb of mercury in whole milk was reported to be directly toxic to the infant (Jensen, 1996).

Maternal exposure to alcohol and tobacco in pregnancy are now well known to cause foetal alcohol syndrome and reduced birth weight. Similarly, in-utero marijuana exposure is reported to cause reduced body weight and head size, as well as reduced memory and verbal skills in infants and children (Nahas,1979). Other drugs are also known to cause unwanted effects in offspring, and so perhaps it should not be surprising that pollutants stored in our body fat may play a damaging role in our children's development. This is an issue which must be addressed, because even small shifts in behaviour and IQs at the population level, could cause profound economic and social consequences.

PART 3: CONTAMINANTS IN BODY FAT

Monitoring the concentrations of chemicals in air, water and soil, is not by itself an adequate means to assess the exposure of humans and wildlife. Useful additional data on which to base estimates of exposure can however be provided by identifying and quantifying the levels of toxic substances found in body fats. This serves to integrate, over time, many kinds of exposures via different media. In the long run, this information can serve as a warning system for environmental exposures, as well as provide an insight into the causes of diseases that may be related to the environmental pollutants. Furthermore, if repeated, such studies can be used to monitor trends in exposure and to evaluate the effectiveness of regulatory programs.

Data on toxic chemicals in human body fats provide incontrovertible evidence that exposure has occurred. This review identifies the substances which contaminate humans. It can thus be concluded that the human species is now exposed to hundreds of man-made pollutants. Furthermore, foetal exposure, which is related to maternal body burden, is particularly worrying.

The level of contaminants found in the adipose tissue (body fat) of older men tends to be higher than in younger men, which may be due to either the build up over time, or to exposures having been higher in the past. Women, however, tend to have significantly lower levels than males, probably because of excretion during breast-feeding. Nevertheless, this research document does not try to provide an overview of likely levels in males and females, nor in different age groups or in different regions. Rather, the aim is to identify contaminants that are likely to be present, and in some cases show the likely range of concentrations. However, as the usage of chemicals may change over time, exposures are likely to vary considerably. Furthermore, analytical procedures tend to improve, and although this leads to a more accurate picture, it often means that data are not comparable over time. In some studies, the frequency of detection is shown. This provides a useful indication of the likelihood of an individual being contaminated; although where these are composite samples, it should be noted that without some statistical manipulation, this will overestimate the chances of any one individual being contaminated.

Levels of contamination can vary considerably between populations in different areas. People living in rural areas where low input agriculture is practised will tend to be less contaminated than people from industrialised areas. However, people in the developing world are also at risk. Fat levels of DDT and its breakdown product certainly tend to be highest where it is used on crops and in homes for control of malaria (Kelce et al., 1995). For example, in 1992, Waliszewski and coworkers found average levels of DDE to be 18.9 ppm in Veracruz in the Gulf of Mexico. (Lopez-Carillo, 1996). The use of other persistent insecticides may also be relatively high in the southern-hemisphere, but in most countries relatively few data exist for the range of potential contaminants.

Another population of concern is the Inuit people. Indeed, many persistent substances are redistributed to the polar regions in a process of global redistillation and some Inuit have a high dietary intake of sea food, including predator animals, which tend to be heavily contaminated. Long range transport and biomagnification in the Arctic food chain have caused human contamination levels ten to twenty times higher than in temperate regions. For example, compared to women from southern Canada, Inuit women have 4 to 5 times higher levels of DDE in their breast milk, and five to ten times higher levels of mirex, chlordane, and hexachlorocyclohexane (AMAP, 1997).

It is also interesting to note that there may be ethnic differences in sensitivity to the toxicity of certain compounds. For example, it has been reported that black males tend to have higher serum levels of total DDT than white males. Furthermore, recent studies have shown that the decline in body burdens of total DDT in the 1980s was faster in Caucasians. This suggests a difference in storage, metabolism and elimination, which might be of a genetic origin, and further highlights the need to consider the most sensitive sub-populations.

In the 1970s, workers in the US built up data-bases from world literature on the body burdens of toxic chemicals identified in human biological media and animals. These reports (available from the US National Technical Information Service (NTIS) in Springfield, Virginia) contain information on some 1300 chemicals, including drugs. However, perhaps the best data on the wide range of compounds to which people in the industrialised world may be exposed to comes from the American National Human Monitoring Program. Under this program, the National Human Adipose Tissue Survey (NHATS) was set up to establish the chronic (long-term) exposure of the general US population to toxic compounds from commercial products and environmental routes. The NHATS has now been disbanded and although the last samples were collected in 1992, the last samples to be analysed were those collected in 1987. Nevertheless, the results of the monitoring undertaken in the 1980s provide a good indication of which contaminants might now be expected to occur in the body fat of people living in industrialised nations.

In the late 1990s a new USA programme, called Body Burden 2000, was given the go-ahead. This initiative will utilise samples of blood and urine to measure the amounts of selected chemicals in people's bodies. In particular, methods to improve the exposure assessment of environmental endocrine disruptors have been developed in order to improve the base for risk assessment (NTP, 1998).

With regard to levels of contaminants in adipose tissue, the NHATS relied on samples taken from cadavers and surgical patients, who had died a sudden traumatic death. Furthermore, it excluded people who had worked with toxic chemicals, and if there was any selection bias, it was felt that the sampling may have under-represented rural populations. Owing to the amount of tissue needed to perform the analysis, samples had to be bulked together or composited, and this was done for various age groups and various geographical areas (Lordo et al., 1996).

The compounds identified in the NHATS samples of human fat taken in 1982, which were subjected to the most comprehensive analysis, are listed below in Tables 3.0 - 3.6. For some contaminants, the concentration range found in the samples is also provided in the tables. It should however be noted that, because these are composite samples, the actual concentration range in the US population would be much greater. For the substances identified using automated peak identification, as listed in Tables 3.5 and 3.6, no information is provided on concentrations. Also, some of these substances are not environmental contaminants as such, but residues of drugs. In addition, some normal chemical constituents of human tissues such as fatty acids and discrete lipids have also been picked up. Therefore, the actual number of contaminants is unknown (Stanley, 1998).

The samples taken in 1982 were first subjected to a broad scan analysis using high resolution gas chromatography / mass spectrometry to determine whether certain targeted compounds were present. Basically the semi-volatile compounds were extracted with solvents, and the volatile compounds

were purged using helium gas, although some compounds were found in both fractions.

Table 3.0: INCIDENCE AND LEVELS OF COMPOUNDS FOUND IN THE VOLATILE FRACTION IN THE NHATS SURVEY OF SAMPLES COLLECTED IN 1982 (46 composite samples)

| Compound | % +ve | Range of concentrations ng/g lipid (ppb) (wet tissue concentration) |
|---------------------------------------|-------|---|
| Chloroform | 76 | ND - 580 |
| 1,1,1- Trichloroethane | 48 | ND - 830 |
| Benzene | 96 | ND - 97 |
| Tetrachloroethane | 61 | ND - 94 |
| Toluene | 91 | ND - 250 |
| Chlorobenzene | 96 | ND - 9 |
| Ethylbenzene | 96 | ND - 280 |
| Styrene | 100 | 8-350 |
| 1,1,2,2-Tetrachloroethane | 9 | ND - 8 |
| 1,2-Dichlorobenzene | 63 | ND - 2 |
| 1,4-Dichlorobenzene | 100 | 12 - 500 |
| Xylene (exact isomers not determined) | 100 | 18 - 1,400 |
| Ethylphenol | 100 | 0.4 - 400 |
| 2-Amylfuran* | 98 | |
| Bromoheptane* | 9 | |
| Bromopentane* | 6 | |
| Butyraldehyde* | 98 | |
| Ethyl isovalerate* | 96 | |
| 1-Iodopentane* | 74 | |
| Isobutyraldehyde* | 93 | |
| Nonene* | 100 | |
| 3-Octen-2-one* | 96 | |
| Pentylalcohol* | 80 | |
| Pentylcyclohexane* | 22 | |
| Trichloroethylene* | 43 | |

Notes to Table 3.0:

ND Not detected at the limit of detection

* Compounds marked with an asterisk were identified in subsequent target compound analysis to identify previously unidentified compounds.

Table 3.1: INCIDENCE AND LEVELS OF COMPOUNDS FOUND IN THE SEMIVOLATILE FRACTION IN THE NHATS SURVEYS IN 1982 AND 1986

| COMPOUNDS | 1982 SAMPLES - 46 samples | | 1986 SAMPLES | | |
|-------------------------------|------------------------------|---------------------------------|--------------|--|---|
| | % +□ve | Range of concs ng/g lipid | % +□ve | Range of concs ng/g lipid ¹ | Average concs ng/g ^{2,3,4} |
| Dichlorobenzene | 9 | ND - 57 | 86 | ND - 279 | 103 |
| of which 1,3 | | | 0 | | |
| □ 1,4 | | | 86 | ND - 279 | 103 |
| □ 1,2 | | | 0 | | |
| Trichlorobenzene | 4 | ND - 21 | 0 | ND | |
| Naphthalene | 40 | ND - 63 | 84 | ND - 102 | 20.3 |
| Diethyl phthalate (DEP) | 42 | ND - 970 | 10 | ND - 119 | 17.2 |
| Tributyl phosphate | 2 | ND - 120 | 0 | ND | |
| Hexachlorobenzene | 76 | ND - 1,300 | 98 | ND - 199 | 55.1 |
| β-HCH | 87 | ND - 570 | 92 | ND - 581 | 184 |
| Phenanthrene | 13 | ND - 24 | 8 | ND - 13 | 5.87 |
| Di-n-butyl pththalate (DBP) | 44/50 | ND - 1,700 | 76 | ND - 132 | 60.8 |
| Heptachlor epoxide | 67 | ND - 310 | 94 | ND - 218 | 63.7 |
| trans-Nonachlor | 53 | ND - 520 | 92 | ND - 612 | 141 |
| p,p□-DDE | 93 | ND - 6,800 | 100 | 291 - 14,300 | 2,600 |
| Dieldrin | 31 | ND - 4,100 | 62 | ND - 336 | 47.7 |
| p,p□-DDT | 55 | ND - 540 | 96 | ND - 1470 | 200 |
| Butylbenzylphthalate (BBP) | 69/74 | ND - 1,700 | 72 | ND - 221 | 55.9 |
| Triphenyl phosphate | 36 | ND - 850 | 4 | ND - 276 | 29.3 |
| Di-n-octyl phthalate | 31 | ND - 850 | | | |
| Mirex | 13 | ND - 41 | 32 | ND - 51 | 10.6 |
| tris(2-Chloroethyl) phosphate | 2 | ND - 210 | 0 | | |
| Anthracene* | 2 | ND - <1 | | | |
| Biphenyl* | 20 | ND - 1 | 0 | | |
| Cymene* | 93 | ND - 5 | 80 | ND - 93 | 20.3 |
| Dibenzofuran* | 7 | ND - <1 | 0 | | |

Table 3.1 cont. INCIDENCE AND LEVELS OF COMPOUNDS FOUND IN THE SEMIVOLATILE FRACTION IN THE NHATS SURVEYS IN 1982 AND 1986

| COMPOUNDS | 1982 SAMPLES - 46 samples | | 1986 SAMPLES | | |
|--|------------------------------|------------------------------|--------------|--|---|
| | % +□ve | Range of concs ng/g lipid | % +□ve | Range of concs ng/g lipid ¹ | Average concs ng/g ^{2,3,4} |
| Limonene* | 93 | ND - 49 | 96 | ND - 660 | 254 |
| Diphenyl ether* | 91 | ND - 45 | | | |
| Safrole* | 9 | ND - 63 | | | |
| 1,2,4-Trimethylbenzene* | 95 | ND - 52 | 62 | ND - 200 | 38.1 |
| 2,6-Xylidene* | 25 | ND - 20 | | | |
| Di -2-ethylhexyl adipate* (DEHA) | 17 | ND - 165 | 10 | ND - 100 | 11.4 |
| Butyl glycol butyl phthalate* | 17 | ND - 90 | | | |
| Carbaryl* | 2 | ND - 2,325 | | | |
| o-Cresol* | 83 | ND - 290 | | | |
| m,p-Cresol* | 93 | ND - 437 | | | |
| Di-(2-ethylhexyl) phthalate* (DEHP) | 91 | ND - 941 | 78 | ND - 26,700 | 975 |
| 2,4-Diaminotoluene* | 43 | ND - 238 | | | |
| 2-Ethoxy benzaldehyde* | 13 | ND - 6 | | | |
| 4-Pentyl benzaldehyde* | 20 | ND - 6 | | | |
| 2-Phenyl phenol* ⁺ | 48 | ND - 1,099 | 24 | ND - 1,820 | 90.4 |
| Toxaphene* ⁽⁴⁾ (tested for in over 45's only) | 86 | | | | |

Notes to Table 3.1:

1. Unadjusted for surrogate recoveries
 2. Adjusted for surrogate recoveries
 3. A compound is detected within a composite sample, if the result is classified as either trace or positive quantifiable reading
 4. Prior to summarising the data, the measured concentrations for all samples with not-detected outcomes were replaced by one-half of the reported limit of detection.
- ND Not detected at the limit of detection
- * Compounds marked with an asterisk were identified in subsequent target compound analysis to identify previously unidentified compounds found in the broad scan analysis which identified the first compounds on this list.
- + This compound is suspected to be a contaminant from the adipose collection procedure
- NB Quantitative values for concentration ranges should only be regarded as estimates.

From Stanley et al., 1986 in Environmental Epidemiology edited by Frederick v Kopfler and Gunther F Craun, Lewis Publishers Inc., Michigan

This initial targeted approach to the analysis of the human fat samples, taken in the financial year of 1982, revealed the presence of some 13 volatile organic compounds, 37 semi-volatile compounds (including 10 dioxin and furans, and 8 PCBs), and 18 trace elements. These compounds are listed without an asterisk (*) in Tables 3.0 - 3.4 (Stanley, 1986). The levels of PCBs, dioxins and furans are set out in Tables 3.2 and 3.3, alongside levels found some years later for comparison of the level and frequency of contamination. However, many unidentified compounds were also noted, and so further work was carried out.

A library search trying to match the chromatographs of known compounds with the unidentified peaks was undertaken, using a technique called automated peak identification, resulting in the tentative identification of some additional 121 compounds in the volatile fraction and 177 in the two semi-volatile fractions. These compounds are listed in Tables 3.5 and 3.6, although the number of compounds listed are somewhat less because only substances with separate CAS (Chemical Abstracts Service) numbers have been included. Furthermore, several substances were identified in more than one fraction but these have only been listed once.

This automated exercise still left unidentified some 99 compounds in the volatile fraction and, similarly, some 601 unidentified compounds in the semi-volatile fraction (Onstot and Stanley, 1989). However, as previously stated, it should be recognised that not all these are contaminants, as many of the chemicals identified in the automated screening are lipid based materials, derived from the fat tissue itself (Stanley, 1998).

| Compound | 1982 SURVEY - 46 samples | | 1986 SURVEY | | |
|-----------------------|-----------------------------|-------------------------------|-------------|---------------|---|
| | % +ve | Range of detection ng/g | % +ve | Range Ng/g | Average concs ng/g ^{1,2,3} |
| Total PCBs | 83 | ND - 1,700 | | | |
| - Trichlorobiphenyl | 22 | ND - 33 | 30 | ND - 58 | 14.8 |
| - Tetrachlorobiphenyl | 53 | ND - 93 | 66 | ND - 330 | 70.1 |
| - Pentachlorobiphenyl | 73 | ND - 270 | 88 | ND - 612 | 157 |
| - Hexachlorobiphenyl | 73 | ND - 450 | 94 | ND - 1,435 | 351 |
| - Heptachlorobiphenyl | 53 | ND - 390 | 86 | ND - 1,149 | 146 |
| - Octachlorobiphenyl | 40 | ND - 320 | 44 | ND - 413 | 51.9 |
| - Nonachlorobiphenyl | 13 | ND - 300 | 26 | ND - 124 | 23.1 |
| - Decachlorobiphenyl | 7 | ND - 150 | 28 | ND - 157 | 31.1 |

| Notes to Table: | |
|------------------------|--|
| 1. | Adjusted for surrogate recoveries |
| 2. | A compound is detected within a composite sample, if the result is classified as either trace or positive quantifiable reading |
| 3. | Prior to summarising the data, the measured concentrations for all samples with not-detected |

outcomes were replaced by one-half of the reported limit of detection.

Table 3.3: INCIDENCE AND LEVELS FOUND OF PCDD AND PCDFS (DIOXINS AND FURANS) - IN THE NHATS SURVEYS IN 1982 AND 1987

| Compound | 1982 SURVEY - 46 samples (Stanley,1986) | | 1987 SURVEY - 48 samples (US,1992) | |
|--|---|--|--|--|
| | % +□ve | Range of detection pg/g (lipid adjusted concs) | % +□ve | Estimated average concentrations pg/g for nation |
| NOTE: 1982 SURVEY RESULTS ARE NOT COMPARABLE TO 1987 RESULTS | | | | |
| 2,3,78-TCDD | 76 | ND - 14 | 97 | 5.38 |
| 1,2,3,7,8-PeCDD | 91 | ND - 5,000 | 97 | 10.7 |
| HxCDD | 98 | ND - 620 | | |
| 1,2,3,4,7,8 + 1,2,3,6,7,8 | | | 100 | 75.1 |
| 1,2,3,7,8,9HxCDD | | | 97 | 11.7 |
| 1,2,3,4,7,8,9-HpCDD | 98 | ND - 1,300 | | |
| 1,2,3,4,6,7,8-HpCDD | | | 100 | 110 |
| OCDD | 100 | 19 - 3,700 | 100 | 724 |
| 2,3,7,8-TCDF | 26 | ND - 660 | 100 | 1.88 |
| 1,2,3,7,8-PeCDF | | | 14 | 0.31 |
| 2,3,4,7,8-PeCDF | 89 | ND - 90 | 95 | 9.70 |
| HxCDF | 72 | ND - 60 | | |
| 1,2,3,4,7,8 HxCDF | | | 89 | 7.42 |
| 1,2,3,6,7,8 HxCDF | | | 92 | 5.78 |
| 2,3,4,6,7,8 HxCDF | | | 18 | 0.54 |
| 1,2,3,7,8,9 HxCDF | | | 2 | 0.44 |
| 1,2,3,4,6,7,8-HpCDF | 93 | ND - 79 | 89 | 15.3 |
| 1,2,3,4,6,7,9 HpCDF | | | 4 | 0.73 |
| OCDF | 39 | ND - 890 | 30 | 2.28 |

Notes to Table 3.3:

1. ND = Not detected at the limit of detection
2. With regard to establishing trends in exposure to dioxins and furans, the FY1987 estimated national average concentrations of 2,3,7,8-TCDD; 1,2,3,4,6,7,8-HpCDD and OCDD were consistent with those established in the FY 1982 survey. However, the FY 87 estimates for many of the other dioxins and furans were significantly lower than the estimates for the FY 1982, an effect which was attributed in part to the advances in the analytical method (EPA Report 560/5-91-003). Breast milk surveys as shown in Table 4.0 provide useful estimates of trends.

Table 3.4: INCIDENCE AND LEVELS FOUND OF (18) TRACE ELEMENTS IN THE NHATS

| SURVEYS IN 1982 (9 selected composite samples) (Stanley and Stockton, 1986). | |
|--|------------------------------------|
| Compound | Reported concentrations ug/g (ppm) |
| Aluminium | ND - 4.3 |
| Boron | ND - 22 |
| Calcium | 15 - 98 |
| Iron | 3 - 36 |
| Magnesium | 6.5 - 25 |
| Sodium | 150 - 1,200 |
| Phosphorus | 130 - 220 |
| Tin | 4.6 - 15 |
| Zinc | 1.1 - 6 |
| Gold | ND - .003 |
| Bromine | .33 - 2.4 |
| Chlorine | 360 - 1,500 |
| Cobalt | .034 - .079 |
| Iodine | ND - 13 |
| Potassium | 52 - 270 |
| Rubidium | ND - .27 |
| Selenium | ND - .056 |
| Silver | ND - .38 |

A few of these residual unidentified compounds in the 1982 body fat samples were subsequently identified in a final targeted approach to determine if certain potentially significant compounds were present. This was therefore a return to the analysis of a specific list of target analytes. It resulted in the identification of 12 new additional compounds in the volatile fraction and 19 more compounds in the semi-volatile fraction. These are listed in Tables 3.0-3.1 above, marked with an asterisk (*) (Onstot and Stanley, 1989). Toxaphene was only looked for in the fat samples taken from people over 45 years old, and although the levels were not quantified, it was reported as present in 86% of the samples tested.

Table 3.5: COMPOUNDS TENTATIVELY IDENTIFIED IN THE VOLATILE ORGANIC FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987).

| COMPOUND | CAS number |
|--|------------|
| Carbon dioxide | 124-38-9 |
| 2-Methyl-butane | 78-78-4 |
| Unidentified cyclopentane | 287-92-3 |
| C3 Substituted cyclopropane | 2415-72-7 |
| 2,3-Dimethyl-hexane | 584-94-1 |
| 1,2-Diethyl-cyclobutane | 61141-83-1 |
| Alkane>C10 | 124-18-5 |
| C10 Alkane | 871-83-0 |
| 2,2,3,3-Tetramethyl-hexane | 13475-81-5 |
| Sat alkane>C11 | 6975-98-0 |
| Alkyl substituted hexane | 4292-92-6 |
| 2,2-Dimethyl-decane | 17302-37-3 |
| C13 Alkane | 17312-65-1 |
| Alkane (6-Ethyl-2-methyl-decane) | 62108-21-8 |
| Alkane (2,6,7-Trimethyl-decane) | 62185-25-2 |
| Alkane > C11 (5-(1-Methylpropyl)-nonane) | 62185-54-0 |
| C13 Alkane (2,2,7-Trimethyl-decaane) | 62237-99-4 |
| 3,3,8-Trimethyl-decane | 62338-16-3 |
| Alkane (6-Methyl-tridecane) | 13287-21-3 |
| C5 Alkane (1-Pentene) | 109-67-1 |
| 1-Hexene | 592-41-6 |
| 3-Methyl-1,4-heptadiene | 1603-01-6 |
| 1,6-Octadiene | 3710-41-6 |
| 1,3,6-Octatriene | 22038-69-3 |
| Unidentified C8H12 | 62338-00-5 |
| 1-Nonene | 124-11-8 |

| Table 3.5 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE VOLATILE ORGANIC FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987). | |
|--|------------|
| 3-Ethyl-2-methyl-1,3-hexadiene | 61142-36-7 |
| C10 ringed alkane | 464-17-5 |
| 1-Methyl-4-(1-methylethenyl)-cyclohexene | 5989-54-8 |
| 7-(1-Methylethylidene)-bicyclo(4,1,0)heptane | 53282-47-6 |
| C11 Alkene (1-Undecene) | 821-95-4 |
| C11 Alkene (1-Ethenyl-2-hexenyl-cyclopropane) | 22822-99-7 |
| Isomer of Undecen-3-yne (5-Undec-3-yne) | 74744-31-3 |
| C2 Alkyl benzene | 95-47-6 |
| C3Alkyl benzene (1-Methylethyl-benzene) | 98-82-8 |
| Propyl-benzene | 103-65-1 |
| Isomer of tetramethyl benzene (1,2,3,4-) | 488-23-3 |
| 1-Methyl-3-(1-methylethyl-) benzene | 535-77-3 |
| Naphthalene | 91-20-3 |
| 1-Ethylpropyl-benzene | 1196-58-3 |
| 3-Methyl-1-butanol | 123-51-3 |
| 1-Hexanol | 111-27-3 |
| Isomer of ethyl hexanol | 13231-81-7 |
| 2-Ethyl-1-Hexanol | 104-76-7 |
| Isomer of octanol | 111-87-5 |
| Unidentified C13H28O | 112-70-9 |
| Isomer of Octen-ol | 57648-55-2 |
| Unidentified C5H10O | 110-62-3 |
| Unidentified C6H12O | 66-25-1 |
| C7 Aldehyde | 111-71-7 |
| Nonanal | 124-19-6 |
| Decanal | 112-31-2 |
| 2-Methyl-propenal | 78-85-3 |

Table 3.5 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE VOLATILE ORGANIC FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987).

| | |
|--|------------|
| Isomer of Hexenal | 6728-26-3 |
| C7 Unsat aldehyde | 18829-55-5 |
| C7 Unsat aldehyde | 57266-86-1 |
| 2,4-Heptadienal | 4313-03-5 |
| 2,4-Nonadienal | 6750-03-4 |
| Isomer of decanal | 3913-81-3 |
| Diene aldehyde | 25152-84-5 |
| Diene aldehyde | 21662-16-8 |
| C7 Ketone | 110-43-0 |
| 4-Heptanone | 123-19-3 |
| Unidentified C7H12O | 1449-49-6 |
| C8 Ketone | 106-68-3 |
| Sat Ketone | 693-54-9 |
| Isomer of octen-one | 1669-44-9 |
| 3,5-Octadien-2-one | 30086-02-3 |
| C9 Unsat ketone | 14309-57-0 |
| Dimethoxy methane | 109-87-5 |
| Propanoic acid ethyl ester | 105-37-3 |
| C5 Methyl ester | 623-42-7 |
| Propanoic acid, propyl ester | 106-36-5 |
| Pentanoic acid, methyl ester | 624-24-8 |
| C7 Methyl ester | 106-70-7 |
| 3-Methyl butanoic acid, ethyl ester | 108-64-5 |
| Propanoic acid, butyl ester | 590-01-2 |
| 2-Methyl propanoic acid, 1-methylethyl ester | 617-50-5 |
| Acetic acid, pentyl ester | 628-63-7 |
| 2-Methyl butanoic acid, ethyl ester | 7452-79-1 |

| Table 3.5 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE VOLATILE ORGANIC FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987). | |
|--|------------|
| C8 Ethyl ester | 123-66-0 |
| Acetic acid, hexyl ester | 142-92-7 |
| C8 Ester (3-Methyl butanoic acid, propyl ester) | 557-00-6 |
| C8 Ester (Butanoic acid, 1-Methylpropyl ester) | 819-97-6 |
| Octanoic acid, methyl ester | 111-11-5 |
| Hexanoic acid, 1-methylethyl ester | 2311-46-8 |
| Butanoic acid, pentyl ester | 540-18-1 |
| Hexanoic acid, 2-methylpropyl ester | 105-79-3 |
| Octanoic acid, ethyl ester | 106-32-1 |
| C10 Ester (2-Methyl-propanoic acid, hexyl ester) | 2349-07-7 |
| C11 Ester (Hexanoic acid, pentyl ester) | 540-07-8 |
| C11 Ester (4-Methyl pentanoic acid, pentyl ester) | 25415-71-8 |
| C11 (Hexanoic acid, 2-Methylbutyl ester) | 2601-13-0 |
| Isomer of octanoic acid | 2035-99-6 |
| 3-Octen-1-ol, acetate | 69668-83-3 |
| C5 Bromoalkane | 110-53-2 |
| 3-Bromo-pentane | 1809-10-5 |
| Brominated alkane >C7 | 629-04-9 |
| Dichlorobutane | 110-56-5 |
| 2-Bromo-2-Chloro-1,1,1-trifluoro-ethane | 151-67-7 |
| Isomer of ethyl-phenol | 123-07-9 |
| Unidentified C9H14O | 3777-69-3 |
| Dimethyl disulfide | 624-92-0 |
| Dimethyl trisulfide | 3658-80-8 |

Table 3.6: COMPOUNDS TENTATIVELY IDENTIFIED IN THE SEMI-VOLATILE FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987).

| COMPOUND | CAS Number |
|--|------------|
| 2,,6,10,14,Tetramethyl-hexadecane | 638-36-8 |
| 2,,6,10,14,Tetramethyl-nonadecane | 55124-80-6 |
| >C18 (2,6,10,14-Pentamethyl eicosane | 52268-60-5 |
| 1,2,4-Cyclopentatrione | 15849-14-6 |
| 12-Methyl-tridecanoic acid, methyl ester | 5129-58-8 |
| Nonanedioic acid, bis(1-methylpropyl) ester | 57983-36-5 |
| 9-Octadecenoic acid, ethyl ester | 111-62-6 |
| Methyl 2-methyl-1-(methylthio)butyl disulfide | 69078-83-7 |
| Dimethyl trisulfide | 3658-80-8 |
| Glycine, anhydride | 4202-74-8 |
| C5 Substituted naphthalene | 17334-55-3 |
| Hexahydro-4,7-dimethyl-1-(1-methylethyl) naphthalene | 483-76-1 |
| 5 Ethylidene-1-methyl-cycloheptene | 15402-94-5 |
| C30 Unsat.hydrocarbon | 111-02-4 |
| Ylangene | 14912-44-8 |
| 2-Butyl-2-octenal | 13019-16-4 |
| Unidentified C9H8O | 30844-12-3 |
| N,N-Dimethyl-3-octen-2-amine | 55956-31-5 |
| 6,10-Dimethyl-5,9-undecadien-2-one | 3796-70-1 |
| C4 Alkyl benzene | 933-98-2 |
| 2-Ethyl-1,3-dimethyl-benzene | 2870-04-4 |
| C4 Alkyl benzene (4-Ethyl-1,2 dimethyl) | 934-80-5 |
| C4 Alkyl benzene (Diethyl) | 25340-17-4 |
| C4 Alkyl benzene (Methyl (1-methylethyl)) | 25155-15-1 |
| Cylohexyl-benzene | 827-52-1 |
| C3 Alkyl benzene (1,3,5-trimethyl) | 108-67-8 |

| Table 3.6 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE SEMI-VOLATILE FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987). | |
|---|------------|
| C4 Alkyl benzene (1-Ethyl-2,3-dimethyl) | 933-98-2 |
| C5 Alkyl benzene (1-Ethyl-4-(1-methylethyl)) | 4218-48-8 |
| C3 Alkyl benzene (1-Ethyl-3-methyl) | 620-14-4 |
| C3 Alkyl benzene (1-Ethyl-2-methyl) | 611-14-3 |
| C4 Alkyl benzene (1-Ethyl-2,4-dimethyl) | 874-41-9 |
| 2-Methyl-naphthalene | 91-57-6 |
| Unidentified C10H12 | 767-58-8 |
| Unidentified C15H24 | 1461-03-6 |
| Unsat C4 alkyl benzene | 27831-13-6 |
| 2-Propenyl-benzene | 300-57-2 |
| Benzaldehyde | 100-52-7 |
| 4-Pentyl-benzaldehyde | 6853-57-2 |
| Unidentified C9H8O | 83-33-0 |
| 1-Phenyl-ethanone | 98-86-2 |
| 2,6-Bis(1,1-dimethylethyl)-4-methyl-phenol | 128-37-0 |
| 1,1'-Biphenyl)-2-ol | 90-43-7 |
| 2,2'-Methylenebis(6-(1,1-dimethylethyl)-4-methyl-phenol | 119-47-1 |
| Benzenepropanoic acid, ethyl ester | 2021-28-5 |
| 1,1'-Oxybis-benzene | 101-84-8 |
| 1-Methoxy-4-(1-propenyl)-benzene | 104-46-1 |
| C2 Alkyl benzenamine | 108-69-0 |
| 4-Methyl benzaldehyde, oxime | 3717-15-5 |
| Thiocyanic acid, phenyl ester | 5285-87-0 |
| 2,3,5-Trimethyl-1H-pyrrole | 2199-41-9 |
| Unidentified C8H7N | 120-72-9 |
| Unidentified C8H7N | 274-40-8 |
| 2-(Methylthio)-benzothiozole | 615-22-5 |

Table 3.6 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE SEMI-VOLATILE FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987).

| | |
|--|------------|
| 5-(2-Propenyl)-1,3-Benzodioxole | 94-59-7 |
| 1,4-Dioxaspiro(4,6)undec-7-ene | 7140-60-5 |
| 2,4-Dihydro-2,5-dimethyl-3H-pyrazol-3-one | 2749-59-9 |
| 5,5-Diethyl-2,4-imidazolidinedione | 5455-34-5 |
| (5Alpha)-cholest-3-ene | 28338-69-4 |
| (3Beta)-cholest-5-en-3-ol acetate | 604-35-3 |
| Cholest-5-en-3-ol (3beta) propanoate | 633-31-8 |
| Cholest-5-en-3-one | 601-54-7 |
| Cholest-5-ene | 570-74-1 |
| (5Alpha)-cholest-7-en-3-one | 15459-85-5 |
| Cholesta-3,5-dien-7-one | 567-72-6 |
| (3Beta)-cholesta-4,6-dien-3-ol benzoate | 25485-34-1 |
| Cholesterol | 57-88-5 |
| Isomer of Cholesterol | 633-31-8 |
| Pregnane (5alpha) | 641-85 |
| (3Beta)-26,27-dinoregost-5-en-3-ol benzoate | 58003-48-8 |
| 1,1-Dichloro-1-propene | 563-58-6 |
| (4-Chlorophenyl) phenyl-methanone | 134-85-0 |
| 2-Chloro-6-methyl-benzonitrile | 6575-09-3 |
| Dichlorobenzene (1,3) | 541-73-1 |
| Lindane | 58-89-9 |
| DDD | 72-54-8 |
| Isomer of decamethyl-cyclopentasiloxane | 541-02-6 |
| Octamethyl-cyclotetrasiloxane | 556-67-2 |
| Diheptylphthalate | 3648-21-3 |
| Unidentified C ₁₀ H ₂₀ | 1331-43-7 |
| C ₁₃ H ₂₂ O ₂ | 2756-56-1 |

| Table 3.6 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE SEMI-VOLATILE FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987). | |
|---|------------|
| Dodecanoic acid ethyl ester | 106-33-2 |
| Hexanedioic acid, mono(2ethylhexyl) ester | 4337-65-9 |
| Alkyl ester (15 Methyl-heptadecanoate | 57274-46-1 |
| Ethylhydrazone propionaldehyde | 7422-92-6 |
| 9-Oxo-nonanoic acid, ethyl ester | 3433-16-7 |
| 1,-Methyl-3-(1-methylethenyl)-cyclohexane | 499-03-6 |
| Trimethyl-3-cyclohexene-1-carboxaldehyde | 40702-26-9 |
| 3-Methyl-3-Buten-2-one,dimer | 54789-11-6 |
| 2,4,6-Cycloheptatriene-1-one | 539-80-0 |
| 5-Undecen-4-one | 56312-55-1 |
| 5-Ethyl-2-methyl-4-heptene-3-one | 49833-96-7 |
| Substituted cyclopentenone | 53690-92-9 |
| 2-Methoxy-2-octen-4-one | 24985-48-6 |
| 5,5-Dimethyl-3-heptyne | 23097-98-5 |
| C3-Alkyl benzene (1,3,5-trimethyl) | 95-63-6 |
| Unidentified C11H10 | 2471-83-2 |
| Unidentified C10H10O | 4411-89-6 |
| N-Methyl-1-naphthalenecarboximide | 3400-33-7 |
| Benzene propanoic acid, beta, beta, dimethyl- | 1010-48-6 |
| 2-(acetylamino)-benzoic acid, methyl ester | 2719-60-2 |
| Benzenepropanoic acid | 501-52-0 |
| Butyl decyl phthalate | 89-19-0 |
| Isomer of diheptyl phthalate | 3648-21-3 |
| Butyl phthalate, ester with butyl glycolate | 85-70-1 |
| Unidentified phthalate | |
| Methyl phenol | 95-48-7 |
| 2-Naphthalenol | 135-19-3 |

| Table 3.6 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE SEMI-VOLATILE FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987). | |
|---|------------|
| 1,3-Dimethoxy-benzene | 151-10-0 |
| 1-Phenyl-1,2-butanediol | 22607-13-2 |
| 2-Ethoxy-benzaldehyde | 613-69-4 |
| Unidentified C7H5ONS | 3774-52-5 |
| Methaqualone | 72-44-6 |
| Unidentified barbiturate | 7391-61-9 |
| Alkyl substituted pyrimidinetrione (Methobarbital) | 115-38-8 |
| Pentobarbital | 76-74-4 |
| Phenobarbital | 50-06-6 |
| Metharbital | 50-11-3 |
| 1,7-Naphthyridine | 253-69-0 |
| Isomer of dimethyl-piperidine | 695-15-8 |
| 3-Pyridinecarboxaldehyde, oxime | 51892-16-1 |
| 4,Pyridine carboxaldehyde | 872-85-5 |
| C2 Alkyl pyrazine | 108-50-9 |
| 2-Meethoxy-3-methyl-pyrazine | 2882-21-5 |
| 1,2-Benzisothiazole | 272-16-2 |
| Unidentified C7H11NS | 41981-63-9 |
| Alkyl thazole | 52414-91-2 |
| 4-Propyl-thiazole | 41981-60-6 |
| Benzodioxole | 274-09-9 |
| 4,7-Dimethyl-3(2H)-benzofuranone | 20895-45-8 |
| Unidentified C11H16O2 | 17092-92-1 |
| 5-(Butylimino)-2(5H)-furanone | 27396-39-0 |
| 2H-1-Benzopyran-2-one | 91-64-5 |
| 1,3,5-Trimethyl-1H-pyrazole | 1072-91-9 |
| Isomer of thienyl-ethanone | 1468-83-3 |

| Table 3.6 cont. COMPOUNDS TENTATIVELY IDENTIFIED IN THE SEMI-VOLATILE FRACTION IN THE NHATS SURVEY OF 1982 SAMPLES OF US HUMAN ADIPOSE TISSUE - BY AUTOMATED PEAK IDENTIFICATION (Onstot et al.,1987). | |
|---|------------|
| 1-(4-Hydroxy-3-theinyl)-ethanone | 5556-16-1 |
| 2,3,4-trimethyl thiophene | 1795-04-6 |
| 2-Methyl-5-propyl-thiophene | 33933-73-2 |
| 2-t-Butoxy-thiophene | 23290-55-3 |
| Isomer of cholest-en-ol | 62014-96-4 |
| Cholesta-5,7-dien-3-ol | 434-16-2 |
| Isomer of cholestanol | 80-97-7 |
| Methyl-cholestan-3-ol | 43217-65-8 |
| 3-(Acetoxy)-cholestan-6-one | 1256-83-3 |
| Cholestane-3,5-diol | 3347-60-2 |
| Cholestanol | 80-97-7 |
| 1-Chloro-4-(Methylsulfonyl)-benzene | 98-57-7 |
| Isomer of fluoro-methyl-benzene | 95-52-3 |
| Carbonochloridothioic acid, S-methyl ester | 2812-72-8 |
| 1,1-Dichloro-ethene | 75-35-4 |
| 4-Chloro-2-(phenylmethyl)-phenol | 120-32-1 |
| 1-Butynyl-trimethyl silane | 62108-37-6 |
| Trimethyl(1-methyl-2-propynyl)oxy-silane | 17869-76-0 |

Notes to Tables 3.5 and 3.6:

1. Tentative compound identification is based on search vs. the NBS mass spectral library. Confirmation has not been achieved by comparing retention with an authentic standard. In cases where more than one reference compound successfully matched the unknown spectrum, a general descriptive name is reported and the best ranked NBS name is provided in brackets.
2. In cases where both a general name and an NBS name is reported, the formula corresponds to the NBS name and may not be applicable to the general name.
3. In cases where both a general name and an NBS name is reported, the CAS number corresponds to the NBS name.
4. Where compounds were found in both the volatile and semi-volatile fraction, their presence is only reported in the semi-volatile fraction.
5. Only compounds with separate CAS numbers are reported.

Table 3.7: SEMI-VOLATILE COMPOUNDS IDENTIFIED BY TARGETED ANALYSIS IN THE FY1986 US SURVEY, FOR WHICH CONCENTRATIONS IN FY 1982 WERE NOT KNOWN (DINH K,1994, Volumes 1 & 2). (Compounds marked with an asterisk were, however, also identified in the FY1982 survey - and so also appear in Table 3.6)

| COMPOUNDS | % of samples +ve | Concs reported ng/g (unadjusted for surrogate recoveries) | Average concs ng/g _{1,2,3} (adjusted for surrogate recoveries) |
|---------------------------------|------------------|---|---|
| *Lindane (γ HCH) | 4 | ND - 118 | 9.01 |
| Oxy chlordane | 78 | ND - 366 | 108 |
| Tritolyl Phosphate | 2 | ND - 27.7 trace | 23.5 |
| Fluoranthene | 2 | ND - 7.2 trace | 5.39 |
| Chrysene | 4 | ND - 12.8 | 5.56 |
| Butylated hydroxy toluene (BHT) | 18 | ND - 166 | 11.4 |
| *Octamethyl cyclotetrasiloxane | 72 | ND - 180 | 45.1 |
| Isophorone | 16 | ND - 100 | 4.83 |
| Dichlorvos | 2 | ND - 60 | 3.21 |
| Chlorpyrifos | 28 | ND - 40 | 6.15 |
| Isopropalin | 10 | ND - 10 | 4.83 |
| Butachlor | 12 | ND - 200 | 8.44 |
| Nitrofen | 8 | ND - 300 | 14.1 |
| Dicofol | 6 | ND - 300 | 9.8 |
| Pentachloroanisole | 2 | ND - 10 | 4.92 |
| 2,3,4-trichloroanisole | 4 | ND - 200 | 9.64 |
| Octachloronaphthalene | 2 | ND - 20 | 5.11 |
| Benzo(a)anthracene | 26 | ND - 10 | 4.29 |
| Benzo(b)fluoranthene | 10 | ND - 30 | 3.66 |
| Benzo(k)fluoranthene | 4 | ND - 300 | 8.29 |
| 1-Nonene | 50 | ND - 800 | 108 |
| Cumene | 34 | ND - 200 | 11.4 |
| Hexyl acetate | 82 | ND - 800 | 128 |
| 1,3-Diethyl benzene | 8 | ND - 20 | 5.98 |

Table 3.7 cont. SEMI-VOLATILE COMPOUNDS IDENTIFIED BY TARGETED ANALYSIS IN THE FY1986 US SURVEY, FOR WHICH CONCENTRATIONS IN FY 1982 WERE NOT KNOWN (DINH K,1994, Volumes 1 & 2). (Compounds marked with an asterisk were, however, also identified in the FY1982 survey - and so also appear in Table 3.6)

| COMPOUNDS | % of samples +ve | Concs reported ng/g (unadjusted for surrogate recoveries) | Average concs ng/g ^{1,2,3} (adjusted for surrogate recoveries) |
|---|------------------|---|---|
| Quinoline | 8 | ND - 400 | 15 |
| Chlordane | 2 | ND - 100 | 6.65 |
| Endrin ketone | 2 | ND - 66.7 trace | 38.2 |
| *Ethyl hydrocinnamate = Benzene propanoic acid, ethylester | 2 | ND - 35.2 trace | 28 |

Notes to Table 3.7:

1. Adjusted for surrogate recoveries
2. A compound is detected within a composite sample, if the result is classified as either trace or positive quantifiable reading
3. Prior to summarising the data, the measured concentrations for all samples with not-detected outcomes were replaced by one-half of the reported limit of detection.

Four years later, in the fiscal year 1986, samples of body fat were again taken from the population and analysed for some 111 semi-volatile compounds. The compounds and concentrations found are shown in Table 3.7 and Table 3.1, where a comparison can be made with the 1982 results. However, only about 10 of the compounds and total PCBs were considered for official statistical comparison with predicted national average concentrations in the 1982, 1984 and 1986 surveys. This was because it was considered that this could only be undertaken when sufficient numbers of detectable results were available, and only 10 compounds were detected in at least 50% of the composite samples, within each survey. It should also be noted that methods of analysis, and thus precision, have changed over time; details of this can be found in the NHATS comparability study (Rogers and Chu,1992).

Table 3.8 provides a comparison of the predicted national average concentrations of these 10 substances. It also provides an estimate of the predicted national average concentrations of a further 6 compounds measured in over 50% of the samples in 1986.

Table 3.8: PREDICTED NATIONAL AVERAGE CONCENTRATIONS FOR 16 SUBSTANCES FOUND IN THE 1986 SURVEY AND COMPARISONS OF PREDICTED NATIONAL AVERAGE CONCENTRATIONS NG/G (PPB) FOR 10 SELECTED SEMIVOLATILES IN BODY FAT SAMPLES TAKEN IN THE FISCAL YEARS 1982, 1984 AND 1996 NHATS (Lordo et al.,1996).

| COMPOUNDS | 1982 | 1984 | 1986 |
|---------------------|-----------------------------|------------|------------|
| | Mean (SE) (standard errors) | Mean (SE) | Mean (SE) |
| p,p-DDT | 189 (31) | 123 (11) | 177 (20) |
| p,p-DDE | 1840 (350) | 1150 (90) | 2340 (270) |
| β -HCH | 291 (54) | 199 (24) | 157 (25) |
| Trans-nonachlor | 109 (28) | 105 (5) | 130 (15) |
| Heptachlor epoxide | 59.4 (13.4) | 68.3 (7.1) | 57.6 (4.2) |
| Hexachlorobenzene | 118 (68) | 42.9 (5.4) | 51.3 (4.0) |
| Tetrachlorobiphenyl | 15.7 (1.4) | 48.8 (5.9) | 56.4 (4.7) |
| Pentachlorobiphenyl | 78.3 (7.9) | 115 (11) | 135 (15) |
| Hexachlorobiphenyl | 176 (28) | 198 (11) | 314 (18) |
| Heptachlorobiphenyl | 84.6 (17) | 129 (10) | 125 (22) |
| Total PCBs | 407 (34.9) | 508 (19.5) | 672 (34.8) |
| Oxychlorane | - | - | 114 (7) |
| Dieldrin | - | - | 47 (17) |
| 1,4-Dichlorobenzene | - | - | 90.9 (17) |
| Naphthalene | - | - | 20.7 (11) |
| 1-nonene | - | - | 124 (41) |
| Hexyl acetate | - | - | 123 (18) |

Table 3.8 shows that exposure to p,p-DDE increased during the mid-1980s, while exposure to beta benzene hexachloride (β -HCH) decreased. PCB exposure also appeared to have increased but this might have been due to improvement in the analytical techniques (Lordo et al.,1996). Earlier studies undertaken in the late 1970s and early 1980s had shown that reduced use of PCBs, DDT, and dieldrin had resulted in lower tissue concentration of these compounds (Bailar,1995).

In the fiscal year 1987, samples of adipose tissue were again taken and this time analysed for PCDDs (chlorinated dioxins), PCDFs (chlorinated furans), brominated dioxins and brominated dibenzofurans. The brominated dioxins and furans compounds were not found to be present, but some polychlorinated and polybrominated diphenylethers (PCDEs and PBDEs) were found. These are shown in Table 3.9 (Cramer et al.,1990a & 1990b).

A subsequent study of samples collected in Sweden 1995-1997 also concluded that, mainly due to

exposure through the food chain, human beings are now contaminated with ng/g concentrations of PBDEs in adipose tissue. TetraBDE was found in all samples in the range 0.6-98.2ng/g (Lindsrom et al.,1998). Similarly, a study by de Boer and co-workers, looked for an association between the levels found in body fat and the time spent watching TV, because these substances are used as flame retardants in TV casings (de Boer et al.,1998). The levels they found in a 21 year old Israeli man are detailed in bottom three rows of Table 3.9, and these are the congeners which have subsequently been found to dominate in adipose tissue and breast milk. These studies suggest that exposure can arise both due to food chain contamination and due to leaching from consumer product.

| Compound | % +ve | Concentration in pg/g (ppt) |
|--|---|------------------------------------|
| Hexachloro-diphenylether (HxCDE) | 94 | ND - 20 |
| Heptachloro-diphenylether (HpCDE) | 85 | ND - 70 |
| Octachlor-diphenylether (OCDB) | 96 | ND - 200 |
| Nonachloro-diphenylether (NCDE) | 100 | 30-2000 |
| Decachloro-diphenylether (DCDE) | 21 | ND-20 |
| Hexabromo diphenylether (HxBDE) | 72 | ND - 1000 |
| Heptabromo diphenylether (HeptaBDE) | 100 | 1 - 2000 |
| Octabromo diphenylether (OBDE) | 60 | ND - 8000 |
| Nonabromo diphenylether (NBDE) | | detected |
| Decabromo diphenylether (DBDE) | 60 | ND-700 |
| 2'4'2'4' Tetrabromo diphenylether (TetraBDE) | 21 yr male TV □addict□ from Israel (de Boer, 98) | 2000 |
| 2'4'5'2'4' Pentabromo diphenylether (PeBDE) | | 4000 |
| unknown Pentabromo diphenylether (PeBDE) | | 1000 |

Studies elsewhere have shown that polyaromatic hydrocarbons (PAHs) may also be ubiquitous low level contaminants. A study undertaken some years ago by Obana and co-workers in Japan looked at the levels of these substances in body fat taken from ten people. The levels found are reported in Table 3.10, and it appears that most of the subjects exhibited low level contamination with some of these substances (Obana et al.,1981). It should also be noted that some PAHs were found in the US surveys.

| Compound | % +ve | Range found in 10 people |
|-----------------------|--------------|---------------------------------|
| anthracene | 90 | ND - 575 |
| pyrene | 100 | 590 - 2700 |
| benz(a)anthracene | 0 | - |
| benzo(e)pyrene | 100 | 30 - 150 |
| benzo(b)fluoranthene | 100 | 56 - 260 |
| benzo(k)fluoranthene | 90 | ND - 48 |
| benzo(a)pyrene | 90 | ND - 59 |
| benzo(g,h,i)perylene | 100 | 13 - 110 |
| dibenz(a,h)anthracene | ND | - |

Pentachlorophenol (PCP), which has been used as a wood preservative, has also been found in human adipose tissue at levels of 4-250 ppb, along with its palmitic acid ester (Ansari, 1985).

In addition, several compounds used as synthetic fragrances are now found in humans. Nitro musk compounds and polycyclic musk compounds have been identified as contaminants which are likely to be ubiquitous human contaminants (Rimkus et al.,1994). Muller and colleagues analysed adipose tissue taken from 15 Swiss people, and found the range of contamination with musk xylene and musk ketone to be similar to that found by Rimkus and co-workers (see Table 3.11). Some polycyclic musk compounds were also monitored and these are all shown in Table 3.11.

The concentrations of musk xylenes and musk ketones found in the fat of 19 men and 13 women in Germany are shown in table 3.12, where it can be seen that the average level of musk xylene found in the women (86ng/g) was twice that of the men (42ng/g). These synthetic musk compounds are used as fragrances in cosmetics and detergents. Some exposure may be due to food chain contamination and some may arise from dermal absorption; these results suggest that dermal absorption is certainly important. The levels of the non-nitro benzenoid musk substances (that is the polycyclic musks) found in human adipose tissue are of particular concern because few toxicological data are available (Muller et al.,1996).

Muller also looked at the levels of nonylphenol, octylphenol, and their ethoxylates in 25 samples of human adipose tissue, and although some nonylphenol and octylphenol were detected, this was within the analytical background levels which could not be eliminated. These results therefore suggested that these substances are not typically found in human fat (Muller,1997).

However, another study which looked at the levels of nonylphenol and octylphenol in women's body fat, recorded levels of octylphenol in the parts per billion range. It is interesting to note that this study also looked for the presence of bisphenol A, butylated hydroxyanisole, endosulfan and hydroxylated PCBs, although these were not found at levels above the limit of detection.

However, in agreement with the earlier US studies, this study also highlighted the presence of some phthalates (Schafer et al., 1997). Furthermore, all the substances present were found both in samples of endometrium and in the women's body fat.

Nevertheless, although it seems that nonylphenol and bisphenol A are not found stored in adipose tissue, it may be that foetal exposure still occurs due to perhaps food contact materials leaching into the diet. For example, a study has reported both bisphenol A and nonylphenol in human placental cord at the level of nanograms per gram of wet tissue (Takada et al., 1999).

However, it has been tentatively questioned whether all compounds with phenolic groups would be picked up in all analyses. It might be that current methods of extraction need to be improved, as such compounds might be firmly bound in fat. This effect similarly means that the analysis of certain compounds in breast milk might also be hampered.

The polychlorinated terphenyls (PCTs) are another group of chemicals which have been detected in human fat. For example, a study in the Netherlands recorded levels of 0.5ppm and 0.8ppm in two samples of adipose tissue (Freudenthal and Greve, 1973). They are of particular concern because they are considered to have PCB like properties.

| Compound | | Conc. in ng/g lipid (Muller et al., 1996) Switzerland | Conc. in ng/g lipid (Rimkus et al., 1994; Rimkus & Wolf 1996) Germany |
|---|----------------------|---|---|
| N I T R O | Musk xylene | 6.7-288 | 5-220 |
| | Musk ketone | <1-173 | 15-220 |
| | Musk ambrette | <1-67 | |
| | Musk moskene | <1-42 | |
| | Musk tibetine | <1 | |
| P O L Y C Y L I C | Celestolide (ADBI) | 0.12-3.5 | ND-3 |
| | Galoxolide (HHCB) | 12-171 | 28-189 |
| | Fixolide (AHTN) | 1-23 | 8-33 |
| | Phantolide (AHDI) | | ND-5 |
| | Traseolide (ATII) | | ND-10 |
| | Versalide (ATTN) | | ND |

| Sample No | Concentrations in MEN ng/g fat | Concentrations in WOMEN ng/g fat |
|-----------|--------------------------------|----------------------------------|
|-----------|--------------------------------|----------------------------------|

| | Age | Musk Xylene | Musk Ketone | Age | Musk Xylene | Musk Ketone |
|----|-----|-------------|-------------|-----|-------------|-------------|
| 1 | 48 | 50 | 10 | 77 | 140 | 10 |
| 2 | 30 | 20 | 10 | 32 | 110 | 40 |
| 3 | 74 | 90 | 30 | 49 | 60 | 50 |
| 4 | 56 | 60 | 20 | 44 | 40 | 20 |
| 5 | 59 | 90 | 30 | 49 | 80 | 20 |
| 6 | 38 | 50 | 20 | 67 | 150 | 220 |
| 7 | 27 | 60 | 20 | 68 | 130 | 20 |
| 8 | 48 | 20 | 30 | 55 | 50 | 10 |
| 9 | 51 | 70 | 30 | 62 | 20 | 10 |
| 10 | 56 | 40 | 10 | 80 | 40 | 20 |
| 11 | 61 | 60 | 20 | 51 | 30 | 10 |
| 12 | 68 | 40 | 10 | 51 | 50 | 10 |
| 13 | 74 | 20 | 30 | 54 | 220 | 10 |
| 14 | 76 | 40 | 20 | | | |
| 15 | 87 | 40 | 10 | | | |
| 16 | 43 | 30 | 10 | | | |
| 17 | 46 | 50 | 20 | | | |
| 18 | 50 | 20 | 20 | | | |
| 19 | 66 | 50 | 30 | | | |

With regard to the levels of contamination of body fat in the UK population, a number of studies have been undertaken since the early 1960s. However, unfortunately these relate to relatively very few compounds. Samples taken in 1995-1997 were investigated for the presence of just eleven organochlorine pesticides, and Table 3.13 summarises these results.

In the UK study, as in the US study, it should be recognised that any one person may be contaminated with many pollutants. For example, in the UK, it was found that 201 out of the 203 people sampled had multiple residues, and hence were contaminated with between 2-7 of the eleven contaminants monitored.

| Table 3.13: LEVELS OF ORGANOCHLORINE CONTAMINANTS IN THE UK HUMAN ADIPOSE TISSUE OBTAINED IN 1995-1997 (203 samples) (taken from Annual Report of the Working Party on Pesticide Residues: 1996, published by MAFF,1997) | | |
|---|--------------|---|
| COMPOUND | % +ve | Range of concentrations ng/g lipid |
| Chlordane (as oxychlordane) | 53 | ND - 100 |
| DDT as pp'-DDT,o,p'-DDT,p,p'-TDE and p,p'- | 99 | ND - 9,300 |

| | | |
|-------------------------|------|----------------------------|
| DDE | | |
| Dieldrin | 59 | ND - 100 |
| β -HCH | 98.5 | ND - 800 |
| γ -HCH | 3 | ND - 1,900 |
| Heptachlor as epoxide | 30 | ND - 50 |
| Hexachlorobenzene (HCB) | 93.5 | ND - 200 |
| Aldrin | 0 | ND (Limit of detection 10) |
| Endrin | 0 | ND (Limit of detection 10) |
| Alpha-HCH | 0 | ND (Limit of detection 10) |
| Endosulfan | 0 | ND (Limit of detection 10) |

PART 4: CONTAMINANTS IN BREAST MILK²

Lactating women may be exposed to numerous chemicals from various sources, including food, water, air, and cosmetics. Direct contact with the pollutant in both the occupational and household environments may be an important determinant of the residue levels found, but in many cases, dietary habits also play a major role. For example, several studies have indicated that eating contaminated fish may be one of the most important dietary factors influencing the levels of DDT and PCBs in human milk. Such exposure does not have to be recent, because persistent compounds can be stored in body fats for several years. Levels of organochlorines in breast milk are therefore not very dependant on dietary intakes at the time, due to the dominating effect of mobilisation from body fat stores.

Despite the fact that the levels of certain contaminants in breast milk exceed the levels set as tolerable daily intakes, because of the known benefits from breast feeding, experts still recommend that this is continued. Levels of many organochlorine compounds are now less than in the 1980s when mothers in some regions in Germany were advised to breast feed for only a few months, and hence, this recommendation was rescinded many years ago (Rimkus,1998). Indeed, in many countries, including the UK, the levels of several organochlorine pesticides in breast milk have declined significantly. In Canada, for example, in the last 30 or so years, the total DDT levels found in breast milk have decreased by about 30 fold (Health Canada,1997). However, other contaminants have now also been found. Therefore, this report argues that there is a need to fully evaluate the levels and potential effects of exposure to all the contaminants in breast milk, and to reduce this contamination as soon as possible.

At birth, newborn infants are already contaminated by toxic chemicals due to transplacental exposure of the foetus. Furthermore, there is evidence to suggest that placental transfer may be more important, despite the fact that some studies have indicated that the transfer of several persistent pollutants across the placenta is much smaller than the transfer via milk. This is because exposure is occurring at an earlier and a more sensitive period (Jacobson and Jacobson,1996).

In females, lactation is the most important route of elimination for persistent organochlorine substances which have been stored in adipose tissue. For example, in mice, the entire body burden of persistent organohalogens may be transferred to suckling offspring during a period of a few weeks, although as mice milk contains far more fat than human milk, such findings can not be directly extrapolated to humans (Jensen and Slorach,1991). However, the bulk of the contamination of mammalian offspring at weaning can certainly arise from breast milk. For example, at weaning, about 98% of a seal's residues were accumulated from maternal milk (Addison and Stobo,1993).

²Much of the data used in this report is taken from a 1991 review publication by Jensen and Slorach entitled Chemical Contaminants in Human Milk. Where this is the case, the reference used in the text of this report will refer the reader to this review and not to the original research paper.

There is usually a good correlation between the levels of most persistent organohalogenes in whole breast milk and the levels found in adipose tissue. When calculated on a fat basis, these are generally similar, although as milk is taken to have a fat content of around 3.5% fat, adipose tissue levels are around 30 times higher as compared to whole milk. However, for chemicals with a high affinity to the liver, such as dioxins, this may not hold true (Jensen and Slorach, 1991).

The levels of contaminants in breast milk can either be expressed as the amount in whole milk, or the amount found in the milk fat. However, since the concentration of fat in milk from an individual donor can fluctuate during a single feeding occasion, and during the day and between days, there is no definitive figure by which these values can be interchanged. Also, during the lactation period, the amount of fat in the milk decreases. Therefore, in many studies, the percentage of milk fat is actually measured and can be used to interchange how the data are presented. Where the fat content is not known (since whole milk contains in the order of 1.8-4.8% fat), to convert the concentration found in whole milk to the concentration in milk fat for comparison, multiplying by a figure between 20-55 should provide a range within which the concentration found in milk fat occurs. Some workers suggest that multiplying the concentration in whole milk by 21 to 28 provides a range which equates reasonably well with the contamination in milk fat (Jensen and Slorach, 1991). The World Health Organisation have used an assumed fat content figure of 3.5%. This means that to convert the concentration in whole milk to the concentration in milk fat would require multiplying by 28.

If residue concentrations are presented on the basis of the amount in extractable fat, the variations are smaller than if they are calculated on a whole milk basis. Therefore, comparisons between levels in different areas and over time are best made on the basis of measured levels in breast milk fat.

The contaminants found in breast milk are predominantly lipophilic, but if a chemical readily binds to milk proteins, as do some heavy metals, such as lead, cadmium, and mercury, then that chemical is also likely to be found in milk. For heavy metals, it seems that placental and lactational transfer may be of about the same order.

In conclusion, it can be seen that compounds which are lipophilic, biologically stable, un-ionized and have a low molecular weight are readily transferred from mother to infant during breast feeding. However, in principle, most chemicals can be transferred by lactation. The amount transferred depends on the structure of the chemical to some extent, with the more highly chlorinated PCBs being transferred more easily than the less chlorinated PCBs, and PCBs being more easily transferred than furans.

Much of the data on contaminants found in breast milk relate to the levels of dioxin and PCBs. In 1996, the World Health Organisation (WHO) published the results of studies undertaken in several countries. These detailed the levels of PCDDs (dioxins), PCDFs (furans) and PCBs in breast milk samples taken in 1987-1988 and subsequently in 1992-1993. In 17 countries, analysis was performed on pooled samples from at least 10 mothers, but in the Netherlands and Denmark the analysis was performed on individual samples (WHO, 1996).

Women living in different regions have been found to have relatively higher body burdens of specific component groups, such as dioxins, furans, dioxin-like PCBs, and indicator PCBs, although, for example, the sample from the Hudson Bay region in Canada contained relatively high levels of all compounds investigated. High levels of PCBs have also been detected in a woman living close to

municipal waste incineration plant (Jensen, 1996), and near to contaminated waste sites in New Bedford Harbor, USA. In the latter case, mean levels of 320ng/g milk fat were recorded (maximum 2,071 ng/g milk fat for subject without known occupational exposure) (Korrick and Altshul,1998). Inuit eating food from the sea have also been found to have high levels. This highlights the build up of contaminants in the food chain and the role of global distillation in redistributing pollutants to the colder polar regions. It is also interesting to note that a study by Furst and colleagues in Germany detected higher levels of dioxins in mothers living in houses with open fires (Jensen,1996).

Besides some particular regions, generally higher levels of dioxins and furans were observed in both Belgium and the Netherlands. Table 4.0 shows the trends in certain areas and indicates that in general, the levels of dioxins, furans, and PCBs tend to be higher in industrialised countries (Jensen and Slorach,1991). A full breakdown of the levels of the different congeners found in UK breast milk was detailed in the WHO report published in 1996. Unfortunately the results were subsequently found to be inaccurate (Harrison,1998), and are therefore not reproduced in this report.

It seems that the levels of PCDDs and PCDFs are not typically increasing. Moreover, several countries have significantly decreased exposure over this time. However, for the indicator PCBs (those with IUPAC numbers 28, 52, 101,138, 153, 180), the trend is unclear due to less reliable analytical methods in the first of the two studies.

Despite the downward trend in exposure to dioxins and furans, safety margins are considered to be less than when the results of the earlier survey were considered (WHO,1996). This is because new research has suggested effects at lower levels of exposure than previously suggested. It is also now thought to be more appropriate to group the toxicity of PCDDs and PCDFs along with some dioxin-like PCBs (to give a composite toxicity equivalent or TEQ) (see under dioxins in Appendix 1 for explanation of TEQ).

The World Health Organisation (WHO), after having lowered its TDI for dioxin like substances from 10pg TEQ/kg bw/day to 1-4 pg (WHO Press Release, 3rd June 1998), was still sticking to its earlier assessment, undertaken in 1987, of the merits of breast feeding. Thus, the WHO maintains that,

"despite the presence of PCBs, PCDDs and PCDFs in human milk, breastfeeding should be encouraged and promoted on the basis of convincing evidence of the benefits of human milk to the overall health and development of the infant " (WHO,1996)

Nevertheless, the WHO noted,

"several studies have demonstrated that persistent neurobehavioural, reproductive, and endocrine alterations can be observed in experimental animals following in utero and lactational exposure to PCBs, PCDDs and PCDFs. The lowest observable adverse effect levels (LOAELs) for developmental, neurobehavioural and reproductive endpoints, based on body burdens of TEQs in animals, may be in the range of current background human body burdens in certain segments of the population" (WHO,1996).

There are 75 possible (PCDDs) polychlorinated dibenzo-p-dioxins and 135 possible polychlorinated dibenzofurans (PCDFs). At least 17 PCDDs and PCDFs (dioxins and furans) have been detected in human milk (WHO,1996).

Of the 209 PCB congeners, more than 70 have been detected in human milk samples, with relatively more of the higher chlorinated ones being found (Jensen and Slorach,1991). Methylsulphone metabolites have also been detected in human milk, generally at around one twentieth of the PCB concentration.

Apart from PCBs and dioxins, another chemical frequently detected is DDT, which was the first environmental chemical detected in human breast milk. In the 1980s, typical average background levels found were around 0.03ppm (30ppb) total DDT in whole milk and 1ppm in milk fat. However, in some developing countries with high usage of DDT, levels 10 to 100 times higher have been found (Jensen and Slorach,1991). For example, in Guatemala in 1970-71 over 100ppm DDT in milk fat was found, and this was thought to be due to indoor spraying to prevent malaria. Similarly, for example, DDE at 0.594 ppm was found in total breast milk Mexico City in 1995, whilst 5.02 ppm was found in total breast milk in tropical Mexico (where spraying for malaria had been undertaken) (Lopez-Carillo,1996).

Monitoring the levels of chemicals in human milk can provide data to estimate both the mother's exposure and the offspring's daily intake. Also, the ratio of a metabolite, such as p,p'-DDE, to the parent molecule, p,p'-DDT, can also give an indication of whether exposure is recent and direct. Apart from metabolites of DDT, by-products of its manufacture are also found as human contaminants. Tris(4-chloro-phenyl)methanol (TCPM) is a persistent chemical which has been found by Rahman and colleagues in breast milk taken from Swedish mothers. The bulk of this appears to have arisen due to its formation as a by-product in the manufacture of DDT, as only a limited amount was produced commercially (Swedish EPA,1998).

The levels of the cyclodiene pesticides found in breast milk are typically lower than the levels of DDT. On occasion, the following substances have been detected: aldrin, dieldrin, endrin, heptachlor and its epoxide, chlordane, oxychlordane, and trans-nonachlor, although the reports of aldrin and heptachlor are difficult to understand because theoretically these compounds should be transformed to their stable metabolites in living organisms (eg. heptachlor to heptachlor epoxide and aldrin to dieldrin). In the 1980s, typical average background levels of dieldrin and heptachlor epoxide were around 0.05ppm in milk fat. High levels of dieldrin were found in breast milk in Australia in the early 1970s, which was presumed to be due to the use of aldrin against termites. Iraq and Uruguay also reported high levels of dieldrin in the 1980s and 1970s respectively (Jensen and Slorach,1991).

Table 4.0: COMPARISON OF THE RESULTS FROM THE FIRST AND SECOND ROUND OF WHO-COORDINATED EXPOSURE STUDIES ON HUMAN MILK (WHO, 1996)

| COUNTRY | AREA | TEQ (PCDD/F)(pgTEQ/gfat) | | Sum of marker PCBs ng/gfat | |
|-------------|------------------------|--------------------------|----------------------|----------------------------|---------------------------|
| | | 1988 (No of samples) | 1993 (No of samples) | 1988 (No of samples) | 1993 (No of samples) |
| Austria | Viena | 17.1 ⁽⁵⁴⁾ | 10.7 ⁽¹³⁾ | | 381 ⁽¹³⁾ |
| | Tulln | 18.6 ⁽⁵¹⁾ | 10.9 ⁽²¹⁾ | | 303 ⁽²¹⁾ |
| Belgium | Brabant | 33.7 | 20.8 ⁽⁸⁾ | 558 ⁽¹²⁾ | 275 ⁽⁸⁾ |
| | Liege | 40.2 | 27.1 ⁽²⁰⁾ | 609 ⁽²¹⁾ | 306 ⁽²⁰⁾ |
| | Brussels | 38.8 ⁽⁵⁴⁾ | 26.6 ⁽⁶⁾ | | 260 ⁽⁶⁾ |
| Croatia | Krk | 12.0 ⁽¹⁴⁾ | 8.4 ⁽¹⁰⁾ | 500 ⁽¹⁴⁾ | 218 ⁽¹⁰⁾ |
| | Zagreb | 11.8 ⁽⁴¹⁾ | 13.5 ⁽¹³⁾ | 450 ⁽⁴¹⁾ | 219 ⁽¹³⁾ |
| Denmark | Several regions/cities | 17.8 ⁽⁴²⁾ | 15.2 ⁽⁴⁸⁾ | 830 ⁽¹⁰⁾ | 209 ⁽⁴⁸⁾ |
| Finland | Helsinki | 18.0 ⁽³⁸⁾ | 21.5 ⁽¹⁰⁾ | 150 ⁽³⁸⁾ | 189 ⁽¹⁰⁾ |
| | Kuopio | 15.5 ⁽³¹⁾ | 12.0 ⁽²⁴⁾ | 203 ⁽³¹⁾ | 133 ⁽²⁴⁾ |
| Germany | Berlin | 32.0 ⁽⁴⁰⁾ | 16.5 ⁽¹⁰⁾ | | 375 ⁽¹⁰⁾ |
| | Northrhine-Westphalia | 31.6 ⁽⁷⁹⁾ | | 762 ⁽¹⁴³⁾ | |
| Hungary | Budapest | 9.1 ⁽¹⁰⁰⁾ | 8.5 ⁽²⁰⁾ | | 61 ⁽²⁰⁾ |
| | Scentes | 11.3 ⁽⁵⁰⁾ | 7.8 ⁽¹⁰⁾ | | 45 ⁽¹⁰⁾ |
| Netherlands | rural area | 37.4 ⁽¹³⁾ | | 416 ⁽¹⁰⁾ | |
| | urban area | 39.6 ⁽¹³⁾ | | 392 ⁽¹⁰⁾ | |
| | all regions | 34.2 ⁽¹⁰⁾ | 22.4 ⁽¹⁷⁾ | 272 ⁽⁹⁶⁾ | 253 ⁽¹⁷⁾ |
| Norway | Tromso | 18.9 ⁽¹¹⁾ | 10.1 ⁽¹⁰⁾ | 562* ⁽¹⁰⁾ | 273(536*) ⁽¹⁰⁾ |
| | Hamar | 15.0 ⁽¹⁰⁾ | 9.3 ⁽¹⁰⁾ | 507* ⁽¹⁰⁾ | 265(483*) ⁽¹⁰⁾ |
| | Skien | 19.4 ⁽¹⁰⁾ | 12.5 ⁽¹⁰⁾ | 533* ⁽⁸⁾ | 302(468*) ⁽¹⁰⁾ |
| UK | Birmingham | 37.0 | 21 ⁽²⁰⁾⁺ | | 129 ⁽²⁰⁾ |
| | Glasgow | 29.1 | 21 ⁽²³⁾⁺ | | 131 ⁽²³⁾ |

Notes to Table 4.0:

- In calculating sums of the six marker PCBs and the levels expressed as toxic equivalents, data are shown assuming not detected values are equal to zero.
 - Numbers in parenthesis in superscript font are the number of samples
- * Analysed using packed column technique. To compare results between first and second round some samples were re-analysed using (old) packed column technique.
- + denotes that values are not as published in WHO report, but are values from re-analysis as published in Food Surveillance Information Sheets 88 (1996) and 105 (1997)

Chlordane is a pesticide used against termites in the US, but it has not been used much in Europe. Oxychlordane is the stable metabolite, while cis- and trans-nonachlor and gamma-chlordene are stable impurities. Chlordane and cis-nonachlor are rarely found in human milk but oxychlordane and trans-nonachlor have been detected in some countries. Levels in breast milk from European women are low, and mostly below detection limits, while high levels of oxychlordane have been found in Mexico and the USA, with average concentration of around 0.08ppm in fat in the mid 1970s (Jensen and Slorach,1991).

The levels of organochlorine pesticides in breast milk can be seen to typically exceed the levels of dioxins found in breast milk by several orders of magnitude. However, dioxins are extremely toxic substances, therefore cause concern even at low levels of contamination. As an example, a recent study of 124 women from Kyushu in Japan, which was undertaken from 1994 to 1997, found that in breast milk, the average dioxin concentration was 0.96 parts per trillion (= pg/g), while the average concentration of HCH was 17.1 parts per billion (= ng/g), DDT was 13.9 ppb, chlordane was 3.2ppb, heptachlor-epoxide was 0.18 ppt and dieldrin was 0.17 ppb. From these figures it can be seen that the pesticide concentrations were around 200 to 17,000 times higher than those of dioxin (Nagayama,1998).

Technical grade hexachlorocyclohexane (HCH), which is actually a mixture of different isomers including alpha-HCH, beta-HCH, delta-HCH and gamma-HCH, is no longer used as a pesticide in the UK nor in several other countries. However, gamma-HCH (lindane) is still used as a pesticide in the UK and elsewhere, and lindane may contain traces of β -HCH, which is also formed as a by-product of its manufacture. In human milk samples, it is the β -HCH which predominates because this is the most persistent and bioaccumulating isomer. In general, HCH levels in most European countries are low and have averaged around 0.2ppm in fat, although higher levels have been found in Czechoslovakia, France, and Italy. Parts of Asia, particularly in India and China, have much higher levels of β -HCH, with averages around 6ppm (ranging from 0.89-19ppm) in milk fat in China in the 1980s (Jensen and Slorach,1991).

Table 4.1: MAN-MADE CHEMICAL CONTAMINANTS FOUND IN HUMAN BREAST MILK AND SOME CONCENTRATIONS RECORDED (data from Jensen and Slorach,1991)

| COMPOUND | | Typical levels | | High values recorded | |
|---|-----|------------------------|----------------------|------------------------|----------------------|
| | | Whole milk ug/kg (ppb) | Milk Fat mg/kg (ppm) | Whole milk ug/kg (ppb) | Milk Fat mg/kg (ppm) |
| PCDDs and PCDFs | 17 | See Table 4.0 and 5.2 | | | |
| PCBs | >70 | | | See Table 4.0 | |
| PCB methylsulfone metabolites | Yes | | | | |
| DDT total - includes isomers of DDT and DDE and DDD | 5 | 30 | 1 | | >100 Guatemala 70/71 |
| TCPM (tris(4-chlorophenyl)methanol) | | | | | Sweden 1990s |
| Dieldrin | Yes | | 0.05 | 68 | 1.78 Australia 71/72 |
| Aldrin | Yes | | | | 0.76 Kenya 1983/84 |
| Endrin | Yes | | | 19 Italy 76/77 | 0.77 FRG 1981 |
| Heptachlor | Yes | | | 39 Spain □79 | 11.7 Spain 1979 |
| Heptachlor epoxide, | Yes | | 0.05 | 210 1971 Guatemala | 2.05 USA 1975 |
| Chlordane | Yes | | 0.08 USA | | >2 Mexico and Iraq |
| Oxychlordane, | Yes | | | | |
| Cis-nonachlor | Yes | | | | |
| Trans-nonachlor | Yes | | | 34 Iraq 1983/84 | 3.75 Finland 84/85 |
| α-HCH | Yes | | 0.2 Europe | 160 Punjab 1979 | 2.25 Turkey 1984/5 |
| β- HCH | Yes | | | 900 GDR 1971 | 19 Beijing 1982 |
| γ-HCH | Yes | | | 80 Spain 1973 | 3.79 FRG 1981/3 |
| total HCH | Yes | | | 325 India 1979 | 7.83 Turkey 1984/5 |

Table 4.1 cont. MAN-MADE CHEMICAL CONTAMINANTS FOUND IN HUMAN BREAST MILK AND SOME CONCENTRATIONS RECORDED

| Compound | Found | Typical levels | | High values recorded | |
|---|-------|------------------|----------------|------------------------|-------------------------|
| | | Whole milk ug/kg | Milk Fat mg/kg | Whole milk ug/kg | Milk Fat mg/kg (ppm) |
| HCB | Yes | | 0.1 | 224 Salonikki | 19 Salonikki 74/75 |
| Polychlorinated Terphenyls (PCTs) | Yes | | 0.02 Japan | Few measurements | |
| Polybrominated Biphenyls (PBB) | Yes | | | | 92 Michigan 1973 |
| 1,4-Dichlorobenzene | Yes | | | 35 1981 Yugoslavia | |
| 1,2-Dichlorobenzene | Yes | | | 98 1981 New Jersey | |
| 1,3-Dichlorobenzene | Yes | | | <5 mean □81 Yugoslavia | |
| 1,2,3-Trichlorobenzene | Yes | | | 10 1981 Yugoslavia | |
| 1,2,4-Trichlorobenzene | Yes | | | 6 Canada □82 | |
| 1,3,5-Trichlorobenzene | Yes | | | 3 1981 Yugoslavia | |
| 1,2,3,4-Tetrachlorobenzene | Yes | | | 3 1981 Yugoslavia | |
| 1,2,3,5-Tetrachlorobenzene + 1,2,4,5-Tetrachlorobenzene | Yes | | | 5 1981 Yugoslavia | |
| | Yes | | | | |
| Pentachlorobenzene | Yes | | | 3 1981 Yugoslavia | |
| Pentachlorophenol | Yes | | | 2.83 FRG □79/81 | 0.8 1983 Netherlands |
| Polychlorinated naphthalenes PCNs | Yes | | | | 3ppb USA <1989 |
| Bis (2,3,3,3-tetrachloropropyl)ether (S241) | Yes | | | 3.8 Tokyo 1979 | 0.032 (mean) Tokyo 1979 |
| Mirex | Yes | | | 0.6 Canada □77 | 0.25 USA 1978/80 |

Table 4.1 cont. ORGANIC CONTAMINANTS FOUND IN HUMAN BREAST MILK AND SOME CONCENTRATIONS RECORDED

| Compound | | Found | Typical levels | | High values recorded | |
|--|-----------------|-------|---|----------------|---------------------------|----------------------|
| | | | Whole milk ug/kg | Milk Fat mg/kg | Whole milk ug/kg (ppb) | Milk Fat mg/kg (ppm) |
| Toxaphene | | Yes | | | | 0.1 Sweden □84 |
| PAHs | | 14 | | | See Table 4.2 | |
| Malathion | | Yes | | | 1.88ppm ave. Taiwan 74/75 | |
| DDVP | | Yes | | | 0.1ppm Taiwan 74/75 | |
| Aromatic amines | o-toluidine | Yes | 0.04 | | 0.26 Canada 1998 | |
| | aniline | Yes | 0.36 | | 5.8 Canada 1998 | |
| | N-methylaniline | Yes | 0.55 | | 7.44 Canada 1998 | |
| Lead, Cadmium, Mercury | | 3 | | | See Table 4.3 | |
| Metaphos ¹ | | Yes | | | 100ug/l -1988 Kazakhstan | |
| Carbophos ¹ | | Yes | | | 220ug/l -1988 Kazakhstan | |
| TCM-3 ¹ | | Yes | | | 13 -1988 Kazakhstan | |
| Bi-58 ¹ | | Yes | | | 230ug/l -1988 Kazakhstan | |
| Saturn ¹ | | Yes | | | 500ug/l -1988 Kazakhstan | |
| Propanide ¹ | | Yes | | | 2.5ug/l -1992 Kazakhstan | |
| Thiodane ¹ Kaltin KLT A 30 (chlorobiphenyl) | | Yes | These are listed as pesticides, found in central Asian breast milk, but their proper names are not given. Thiodane might be endosulfan, as endosulfan is marketed as Thiodan. | | | |

Notes to Table 4.1:

- ¹ Taken from Lederman 1996. See glossary for alternative names.
- Background levels are shown only when numerous studies are available, and generally refer to what was considered to be background in the 1980s.
- The column headed □high values recorded□ generally records the highest level found in any sample in surveys undertaken in several countries. Where only one study was found, the highest level found in any sample is recorded. Only when stated do these values refer to mean or average levels in a study.

Hexachlorobenzene (HCB) has been used as a fungicide, but it can also occur as an impurity in other pesticides and as a by-product of manufacture. An unfortunate poisoning incident took place in Turkey in the late 1950s, when 4000 people became ill after eating bread baked with flour made from HCB treated wheat. Some of the breast fed infants died of the condition known as pink sore, and the HCB levels were determined to be around 700ppb in the whole milk of one affected mother (corresponding approximately to 15-20ppm in the milk fat). High levels have also been recorded in eastern Europe, and in Greece (where they averaged around 7ppm in milk fat and ranged up to 19 ppm, which may be in the toxic range). In general, however, average background levels were around 0.1ppm in milk fat in the 1980s (Jensen and Slorach,1991).

Polychlorinated terphenyls (PCTs) have similar properties as PCBs. They have been detected in human adipose tissue in the Netherlands, and in a Japanese study, they have been detected in human milk fat at an average level of 0.02ppm which was 1/60 of that of PCBs in the same sample (Jensen and Slorach,1991).

Polybrominated biphenyls (PBBs) have been recorded in human milk from Michigan residents, where a pollution incident occurred due to the contamination of animal feed with a mixture of PBB flame retardants. Directly exposed farmers' wives recorded the highest levels of contamination at up to 92ppm in milk fat (Jensen and Slorach,1991).

Several chlorobenzene compounds have been detected in human breast milk (as shown in Table 4.1). Although there is generally a lack of data on the extent of contamination with these pollutants, there have been a few studies done in Canada, US, and Yugoslavia (Jensen and Slorach,1991). A UK study of the levels of chlorobenzenes in food found most occurrences were in animal and fish products which reflects the tendency of these products to bioaccumulate (MAFF,1998). The potential sources of chlorobenzene compounds are outlined in Appendix 1. It should certainly be a matter of concern that 1,4-dichlorobenzene, a compound which has been used as a deodorant block in toilets and nappy buckets, has been found in human breast milk. Indeed, this compound has been listed as a cancer causing agent in animals.

Pentachlorophenol (PCP) has been detected in human milk from Upper Bavaria in the Federal Republic of Germany (FRG), the Netherlands, and Sweden, where the levels in Stockholm seemed to peak in the mid-1970s. Contamination may derive from the use of PCP itself, or from the formation of PCP when HCB is metabolised (Jensen and Slorach,1991).

Polychlorinated naphthalenes (PCNs), used in lubricants and insulating fluids, have been found in breast milk surveys undertaken in Sweden and Los Angeles.

Bis(2,3,3,3-tetrachloropropyl)ether (S241) has been found in breast milk in Japan, where it is used with pyrethrum insecticides against mosquitoes. Similarly, mirex is an organochlorine flame retardant and pesticide which has been used to control ants in the US (Jensen and Slorach,1991), and this has been found in human milk samples from Canada and the US.

Toxaphene (camphechlor) is another organochlorine pesticide which is a persistent global pollutant that can be transported long distances in air currents. For example, despite little use in Sweden, it has been found in Swedish wildlife and human milk samples.

Therefore, many organochlorine chemicals have been found in human breast milk. However, in the industrialised world the levels appear to have reduced in recent decades, and the levels of organochlorine pesticides now tend to be higher in the developing countries.

Apart from organohalogen compounds, other less persistent organic compounds, such as some organophosphorous pesticides, have also been found in breast milk. Their presence may therefore reflect more recent exposure. For example, malathion, an organophosphate pesticide which has been used as a DDT substitute against malaria, has been found in milk from Taiwan, along with another pesticide DDVP (Jensen and Slorach,1991). Several organophosphate pesticides were also detected in a study of breast milk in Kazakhstan, and these are also shown in Table 4.1. In the UK, some investigation of the levels of organophosphate pesticides in breast milk was also undertaken, but none were found above the limit of detection (see Part 5).

Polyaromatic hydrocarbons have been found in breast milk samples from Germany. At least 14 PAHs have been detected, including the potentially cancer causing benz(a)pyrene and benz(a)anthracene (Jensen and Slorach,1991). This group of substances includes initiating and promoting carcinogens, and so it is impossible to set a TDI for such a group of substances. Nevertheless, some researchers consider that the infant is unlikely to be at risk from an intake of benzo(a)pyrene at 1ng/kg bw/day (determined from 800 mls of milk containing 6.4 ng/kg being fed to an infant weighing 5kg) (Somogyi and Beck,1993). However, it is interesting to note that in rats, PAHs cause liver tumours when given to newborn animals but not when given to adults. It might be conjectured that it is the rate of cell proliferation in the infant which increases the likelihood of cancer. Some PAHs are also known to be hormone disrupting compounds (see Lyons,1997).

Table 4.2: AVERAGE LEVELS AND RANGES OF PAHS IN 10 SAMPLES OF HUMAN MILK FROM AHRENSBURG,FRG (published 1984) (taken from Jensen and Slorach,1991).

| Polyaromatic Hydrocarbons (14 PAHs in total) | PAH levels in ng/kg or ppt in whole milk | |
|--|--|--------|
| | Mean | Range |
| Benzo(b)naphtho(2,1-d)thiophene | 8.7 | 3-31 |
| Benzo(ghi)fluoranthene + | 5.7 | 3-10 |
| Benzo(c)phenanthrene | | |
| Benz(a)anthracene | 1.0 | 3-21 |
| Chrysene + | 47.8 | 14-195 |
| triphenylene | | |
| Benzo(a)fluoranthenes (b+j+k) | 16.4 | 8-36 |
| Benzo(e)pyrene | 16.3 | 8-25 |
| Benzo(a)pyrene | 6.5 | 3-10 |
| Perylene | 4.6 | 3-10 |
| Indeno(1,2,3-cd)pyrene | 8.3 | 3-10 |
| Anthanthrene | 4.6 | 3-10 |

Another worrying group of chemicals which have been detected in human breast milk are the nitro musk and polycyclic musk compounds. These compounds are widely used in detergents and cosmetics, as synthetic substitutes for natural musk fragrance derived from musk deer. It is thought that dermal absorption may be an important exposure route, but because of their lipophilic nature, these chemicals also have an environmental route of exposure via the food chain. Studies by Rimkus and colleagues in Germany have highlighted that these substances are now probably ubiquitous contaminants in breast milk. In the breast milk of all 15 women studied, musk xylene and musk ketone were present, and musk ambrette and musk moskene were detected in a few fat samples at low levels (Rimkus et al., 1994). The polycyclic musk compounds, HHCB, AHTN and ADBI were also found in breast milk and these are all shown in Table 4.3 (Rimkus and Wolf, 1996). However, although AHDI, ATII and ATTN were found in a few samples of adipose tissue, these were not found in the samples of breast milk which were taken from different people. The chemical names of these compounds are listed in the glossary of abbreviations.

TABLE 4.3: LEVELS OF SYNTHETIC MUSK COMPOUNDS DETECTED IN HUMAN BREAST MILK AND SUBSTANCES ARISING FROM UV SUN SCREENS (Rimkus et al.,1994; Rimkus and Wolf, 1996)

| Compound | Cas Number | Concentration in milk fat (ug/kg fat) |
|--|------------|--|
| Musk Xylene | 81-15-2 | 10-190 |
| Musk Ketone | 81-14-1 | 5-90 |
| Musk ambrette | 83-66-9 | |
| Musk moskene | 116-66-5 | |
| HHCB | 1222-05-5 | 16 - 108 |
| AHTN | 1506-02-1 | 11 - 58 |
| ADBI | 13171-00-1 | 1 - 18 |
| Benzophenone-3 ¹ | 131-57-7 | ND - 417 (present in 4 out of 6 samples) |
| Octyl Methoxycinnamate ¹ OMC | 5466-77-3 | ND - 47 (present in 2 out of 6 samples) |

Notes to Table:

- ¹ Compounds found in breast milk in Germany, arising from their use in UV sun screens (Hany and Nagel, 1995, Deutsche Lebensmittelrundschau 91, p341-345 from Schlumpf,1999)

In the same way, substances used in UV sun screens have been found to arise in breast milk, probably, at least in part, due to their absorption through the skin (Schlumpf,1998). These are shown in the bottom two rows of Table 4.3. This should be a particular concern because test tube tests indicate that benzophenone and octyl methoxycinnamate (OMC) are potential endocrine disruptors, as they are active in-vitro (Schlumpf,1999).

Three lipophylic UV sun filters, 3,4-methyl-benzylidene-camphor (MBC), homo-menthyl salicylate (HMS) and octyl-methoxycinnamic acid have been found at high levels in fish. It would therefore be wise to see if these were also found in humans. MBC has been found to be estrogenic in the E-screen and in the uterotrophic assay, and in 1999, OMC was also being tested in the uterotrophic assay (Schlumpf, 1999 &1999b). UV filter chemicals are used to protect the skin from UV radiation, but are increasingly added to cosmetics such as bubble bath, hair sprays, beauty creams and so forth. Another compound used in sun screens, octyl methyl p-amino benzoic acid was also able to induce proliferation in the E-screen, but no information was found as to whether this might be present in human breast milk (Schlumpf, 1999).

The fact that polybrominated diphenyl ethers (PBDEs) have been found in adipose tissue, underlines their likely ubiquitous presence in breast milk, and indeed studies in Germany and Sweden confirm this. Table 4.4 illustrates the levels found in mothers from Uppsala county Sweden, nursing their first child. From this it can be seen that the observed median was 3.4 ng/g in milk fat, which is about one hundred times less than that found for PCBs, although the maximum level found was similar to the levels of the commonly found PCBs. The mean fat content of the milk was 3.2%.

Another study of mothers in Stockholm also showed that PBDE-47 (ie. tetrabromobiphenylether)

was the predominant congener in all the samples, accounting for about 60-70% of the total amount. This study also looked at time trends and showed that there had been continuous and dramatic increase in the levels of these contaminants from 1972-1997. The sum of the concentrations of PBDE congeners increased from 72 to 4010 pg/g fat during the 20 years up to 1997 (Meironyte et al.,1998). Given the toxicity profile of these substances, and the possible effects of these compounds on the thyroid hormone system, it is argued that measures should be put in place to reduce future exposures.

Table 4.4: LEVELS OF PBDEs IN BREAST MILK IN SWEDEN
(Taken from Darnerud et al.,1998)

| COMPOUND | pg PBDEs/g fat of breast milk | | | | pg PBDEs/g in breast milk | | | |
|-------------------------------------|-------------------------------|--------|------|-------|---------------------------|--------|-----|-----|
| | mean | median | min | max | mean | median | min | max |
| PBDE-47 (2,2',4,4'-tetraBDE) | 2516 | 1830 | 331 | 16100 | 77 | 58 | 8 | 358 |
| PBDE-99 (2,2',4,4',5-pentaBDE) | 717 | 442 | 181 | 4470 | 24 | 16 | 4 | 222 |
| PBDE-100 (2,2',4,4',6-pentaBDE) | 475 | 340 | 60 | 5140 | 14 | 10 | 1.5 | 114 |
| PBDE-153 (2,2,4,4',5,5'-hexaBDE) | 648 | 478 | 255 | 4320 | 19 | 14 | 8 | 96 |
| PBDE-154 (2,2,4,4',5,6'-hexaBDE) | 70 | 60 | 30 | 270 | 2.1 | 1.5 | 1.5 | 6 |
| sumPBDEs | 4452 | 3373 | 1139 | 28170 | 137 | 102 | 28 | 628 |

Further industrial chemicals have recently been found in human breast milk. Aromatic amines, used in numerous industrial processes including in the production of plastics (eg. polyurethane foams), dyes, pesticides and pharmaceuticals, were found in breast milk by David Jospehy and co-workers of Guelph University at levels up to 7.44ppb. A number of amines, such as aniline, N-methylaniline, and o-toluidine were reported. Concern was expressed particularly at the level of o-toluidine which was found at concentration of up to 0.26ppb, because of possible links to mammary cancer (DeBruin et al.,1999). Environmental sources of aromatic amines include tobacco smoke, but no significant difference was found in the levels of smokers compared to non-smokers. Some industrial sources were thus also suggested. Furthermore, exposure to such sources was considered to be possibly relatively recent because the less lipophilic monocyclic aromatic amines have relatively short half lives.

Other German investigators have found that residues of other substances can get into milk from cosmetics. The use of contaminated raw materials, such as lanolin, have been identified as a source (Jensen,1996).

With regard to metal contamination of human breast milk, both inorganic and organic metal compounds are found, but unlike the lipophilic pollutants these are not associated with the milk fat.

Average background levels of lead in breast milk from industrialised countries were probably between 5 and 20ppb, with higher levels being found in areas with heavy traffic. However, with the introduction of unleaded petrol, lead emissions have rapidly declined in many countries. Also, it is interesting to note that lead levels in breast milk tend to be lower than in some powdered milk formulas. Cadmium has also been found on occasion. Similarly to lead, it seems to be more bioavailable when found in milk as compared to other foods. Average background levels of cadmium are thought to be less than 2ppb, although ten times higher levels have been quoted (Jensen and Slorach,1991). Smokers tend to have twice the level of cadmium in their breast milk as compared to non- smokers (Jensen,1996).

Mercury tends to be found at lower levels than lead and cadmium, with average background levels less than 1ppb. A Swedish study detected higher levels of mercury in human milk as compared to cow's milk, with the highest values detected in fish eaters. Around 20% of the total mercury content was in the form of the more toxic methylmercury. Mothers living in other coastal areas, eating tuna, swordfish, or marine mammals, such as whales and seals, have also been found to have high mercury levels in their milk. Grandjean and colleagues working in the Faroe Islands, noted increased mercury in infant hair which depended on the duration of breast feeding (Jensen,1996). Some recorded values, as cited in the review publication by Jensen and Slorach, are shown in Table 4.4.

| Area and Year | Arithmetic mean in ug/kg or ppb (range in brackets) | | |
|--|---|-------------------|--------------|
| | Lead | Cadmium | Mercury |
| Background levels industrial countries | 5-20 average | <2 | <1 |
| UK, Glasgow,1977 | 20.7 median | - | - |
| UK, London, 1980 | 4 (<1.9-8.6) | 0.5 (<0.3-1.1) | - |
| Japan, Minimata, 1968 | - | - | 63 |
| Spain, Madrid,1981 | - | - | 9.5 (0.9-19) |
| FRG, Hamburg, 1983 | 13.5 | 24.6 | - |
| Rumania, polluted city | 420 | - | - |
| Lublin, Poland, 1980/1 | 26 (10-110) | 4 (1-9415) | 2 (0.4-225) |

Volatile and less persistent organic substances have also been found in breast milk. Pellizzari and colleagues detected around 200 volatile organic compounds (190) in milk from women living in four urban areas in the USA. The results are shown in Table 4.5. These sites were chosen as places where there was a high probability of emissions of various halogenated pollutants. Indeed, the study undertaken in order to evaluate the possibility of using breast milk in studies of populations living near industrial plants. Many volatile contaminants were present in these mothers, and the table shows the results for 8 analysis of the most contaminated samples, out of a total 42 samples. The

actual levels of these contaminants in the breast milk were not determined. However, the mere presence of carbon tetrachloride, tetrachloroethylene, chloroform, benzene, dichlorobenzene (1,4), and methylene chloride, all found in most of the samples, is worrying. Indeed, these have been listed as causing cancer in animals, although differences in metabolism may mean that these substances do not necessarily pose a similar hazard to man.

For a number of substances, the levels in breast milk have been monitored where exposure in occupational settings has occurred. For example, tetrachloroethylene or "perc" was detected in a woman's breast milk after she had visited her husband at a dry cleaning factory. The levels of perc were 10ppm after 1 hour and 3ppm after 24 hours, and this was thought to be the cause of her baby developing jaundice. Similarly, methylene chloride, 1,2-dichloroethane (ethylene dichloride), carbon disulphide, petroleum solvents, and halothane (2-bromo-2-chloro-1,1,1-trifluoroethane) have all been detected in the milk of women exposed occupationally. Furthermore, in women exposed to petroleum solvents in the rubber industry, and in women exposed to styrene, it seems that such exposure may be associated with inhibition of lactation.

Several other metals and trace elements have been detected in milk, and these are shown in Table 4.7. Trace elements in minute quantities are necessary for growth, and so these substances cannot be considered contaminants, unless they are found at levels in excess of "natural" levels. Occupational exposure to these environmental chemicals may result in higher levels.

Nitrosamines may also occasionally be found in human milk, and these may arise after a meal high in nitrates, such as smoked bacon, although some contamination may originate from consumer articles such as plastics and rubber (Braybrook, 1998). Nitrate is a natural component of human milk at concentrations around 1-3 mg/kg, but nitrites would not normally be detected, unless bacteria were present (Somogyi and Beck, 1993). However, for the purposes of this report, many of the substances found in breast milk are not counted as chemical contaminants because they are of natural origin or derived from a self-inflicted source. For example, aflatoxin M and ochratoxin A, arising from fungal contamination of food, may very occasionally be detected in breast milk, and other mycotoxins may also be present. Also, alcohol, caffeine, and nicotine have been found, and the latter can arise even from passive smoking (Jensen and Slorach, 1991). Similarly, pharmaceutical drugs can also pass into breast milk, but this report is primarily focussed on man-made environmental contaminants, and so these contaminants are not included in Table 4.1. A review of the effects of certain drugs in breast milk can be found in an article published by the American Academy of Pediatrics in 1994.

Table 4:6: VOLATILE COMPOUNDS FOUND IN HUMAN BREAST MILK AND THE PERCENTAGE OF THE (8) SAMPLES IN WHICH THEY WERE RECORDED (taken from Pellizzari et al., 1982).

| COMPOUND | %+ve | COMPOUND | %+ve |
|-------------------------|------|--------------------------------|------|
| Chlorodifluoromethane | 12.5 | α -furfuryl alcohol | 25 |
| Chlorotrifluoromethane | 50 | 2-ethyl-1-hexanol phenol | 12.5 |
| Dichlorodifluoromethane | 25 | 2,2,4-trimethyl penta,1,3-diol | 12.5 |
| Chloromethane | 25 | α -terpineol | 12.5 |
| Chloroethane | 25 | acetic acid | 25 |
| Trichlorofluoromethane | 87.5 | decanoic acid | 12.5 |
| Dichloroethylene | 12.5 | sulphur dioxide | 12.5 |
| Freon 113 | 100 | carbon disulphide | 100 |
| Methylene chloride | 100 | dimethyl disulphide | 75 |
| Chloroform | 87.5 | carbonyl sulphide | 12.5 |
| 1,1,1-trichloroethane | 100 | nitromethane | 12.5 |
| carbon tetrachloride | 62.5 | $C_5H_6N_2$ | 12.5 |
| Trichloroethylene | 100 | $C_5H_8N_2$ | 12.5 |
| Chloropentane | 25 | $C_4H_4N_2O$ | 12.5 |
| Dibromochloromethane | 12.5 | methyl acetamide | 12.5 |
| Tetrachloroethylene | 87.5 | benzonitrile | 37.5 |
| Dichloropropene | 12.5 | methyl cinnoline | 12.5 |
| Chlorobenzene | 62.5 | vinyl propionate | 37.5 |
| Chlorohexane | 50 | ethyl acetate | 12.5 |
| Iodopentane | 12.5 | ethyl-n-caproate | 12.5 |
| 3-methyl-1-iodobutane | 25 | isoamyl formate | 12.5 |
| Chloroethylbenzene | 12.5 | methyl decanoate | 12.5 |
| Dibromodichloromethane | 12.5 | ethyl decanoate | 12.5 |
| Chlordecane | 12.5 | dimethyl ether | 12.5 |
| Trichlorobenzene | 12.5 | dihdropyran | 25 |
| Acetaldehyde | 50 | 1,8-cineole | 12.5 |
| methyl propanal | 25 | furan | 12.5 |

Table 4.6 cont. VOLATILE COMPOUNDS FOUND IN HUMAN BREAST MILK AND THE PERCENTAGE OF THE (8) SAMPLES IN WHICH THEY WERE RECORDED

| COMPOUND | %+ve | COMPOUND | %+ve |
|----------------------|------|---------------------------------|------|
| n-butanal | 75 | tetrahydrofuran | 12.5 |
| methylbutanal | 25 | methyl furan | 25 |
| crotonaldehyde | 12.5 | methyl tetrahydrofuran | 12.5 |
| n-pentanal | 87.5 | ethylfuran | 25 |
| n-hexanal | 100 | dimethylfuran | 12.5 |
| furaldehyde | 25 | 2-vinylfuran | 12.5 |
| n-heptanal | 87.5 | furaldehyde | 22.5 |
| benzaldehyde | 100 | 2-n-butylfuran | 12.5 |
| n-octanal | 37.5 | 2-pentylfuran | 87.5 |
| phenyl acetaldehyde | 12.5 | methylfuraldehyde | 12.5 |
| n-nonanal | 75 | furyl methyl ketone | 12.5 |
| methyl furaldehyde | 12.5 | α -furfuryl alcohol | 25 |
| n-decanal | 25 | benzofuran | 37.5 |
| n-undecanal | 25 | C ₃ H ₈ | 12.5 |
| n-dodecanal | 12.5 | C ₄ H ₁₀ | 75 |
| acetone | 100 | C ₅ H ₁₂ | 100 |
| methyl ethyl ketone | 62.5 | C ₆ H ₁₄ | 100 |
| methyl propyl ketone | 25 | C ₇ H ₁₆ | 87.5 |
| methyl vinyl ketone | 12.5 | C ₈ H ₁₈ | 87.5 |
| ethyl vinyl ketone | 50 | C ₉ H ₂₀ | 100 |
| 2-pentanone | 50 | C ₁₀ H ₂₂ | 87.5 |
| methyl pentanone | 25 | C ₁₁ H ₂₄ | 87.5 |
| methyl hydrofuranone | 12.5 | C ₁₂ H ₂₆ | 87.5 |
| 2-methyl-3-hexanone | 12.5 | C ₁₃ H ₂₈ | 37.5 |
| 4-heptanone | 12.5 | C ₁₄ H ₃₀ | 37.5 |
| 3-heptanone | 50 | C ₁₅ H ₃₂ | 25 |
| 2-heptanone | 75 | C ₃ H ₆ | 25 |

Table 4.6 cont. VOLATILE COMPOUNDS FOUND IN HUMAN BREAST MILK AND THE PERCENTAGE OF THE (8) SAMPLES IN WHICH THEY WERE RECORDED

| COMPOUND | %+ve | COMPOUND | %+ve |
|--|------|---|------|
| methyl heptanone | 25 | C ₄ H ₈ | 62.5 |
| furyl methyl ketone | 12.5 | C ₅ H ₁₀ | 37.5 |
| Octanone | 25 | C ₆ H ₁₂ | 100 |
| Acetophenone | 100 | C ₇ H ₁₄ | 100 |
| 2-nonanone | 50 | C ₈ H ₁₆ | 100 |
| 2-decanone | 12.5 | C ₉ H ₁₈ | 87.5 |
| alkylated lactone | 12.5 | C ₁₀ H ₂₀ | 75 |
| Phthalide | 12.5 | C ₁₁ H ₂₂ | 75 |
| C ₄ H ₆ O | 12.5 | C ₁₂ H ₂₄ | 12.5 |
| C ₄ H ₈ O | 25 | C ₁₃ H ₂₆ | 12.5 |
| C ₅ H ₁₀ O | 62.5 | isoprene | 12.5 |
| C ₆ H ₈ O | 12.5 | C ₅ H ₈ | 25 |
| C ₆ H ₁₀ O | 25 | C ₆ H ₁₀ | 12.5 |
| C ₄ H ₆ O ₂ | 12.5 | C ₇ H ₁₂ | 37.5 |
| C ₆ H ₁₂ O | 25 | C ₈ H ₁₄ | 37.5 |
| C ₇ H ₁₂ O | 50 | C ₉ H ₁₆ | 50 |
| C ₇ H ₁₀ O | 25 | C ₁₀ H ₁₈ | 25 |
| C ₇ H ₁₄ O | 25 | C ₁₂ H ₂₂ | 12.5 |
| C ₆ H ₆ O ₂ | 12.5 | cyclopentane | 75 |
| C ₈ H ₁₄ O ₂ | 12.5 | methylcyclopentane | 75 |
| C ₈ H ₁₆ O | 25 | cyclohexane | 62.5 |
| C ₇ H ₈ O ₂ | 25 | ethyl methyl cyclohexane | 12.5 |
| C ₇ H ₁₀ O ₂ | 12.5 | C ₁₀ H ₁₄ isomers | 12.5 |
| C ₉ H ₁₈ O | 37.5 | C ₁₀ H ₁₆ isomers (other) | 50 |
| C ₈ H ₆ O ₂ | 12.5 | limonene | 100 |
| C ₁₀ H ₁₂ O ₂ | 12.5 | methyl decalin | 12.5 |
| C ₁₀ H ₁₄ O | 12.5 | α-pinene | 12.5 |

Table 4.6 cont. VOLATILE COMPOUNDS FOUND IN HUMAN BREAST MILK AND THE PERCENTAGE OF THE (8) SAMPLES IN WHICH THEY WERE RECORDED

| COMPOUND | %+ve | COMPOUND | %+ve |
|--|------|-------------------------|------|
| C ₁₀ H ₁₆ O | 25 | camphene | 12.5 |
| C ₁₀ H ₁₈ O | 37.5 | camphor | 12.5 |
| C ₁₀ H ₂₀ O | 25 | benzene | 100 |
| C ₁₀ H _{12.5} O ₂ | 12.5 | toluene | 100 |
| C ₉ H ₈ O ₂ | 12.5 | ethylbenzene | 100 |
| C ₁₁ H ₂₀ O | 12.5 | xylene | 100 |
| C ₁₀ H ₁₀ O ₂ | 12.5 | phenyl acetylene | 12.5 |
| Methanol | 12.5 | styrene | 100 |
| Isopropanol | 100 | benzaldehyde | 100 |
| 2-methyl-2-propanol | 12.5 | C3-alkylbenzene isomers | 100 |
| n-propanol | 12.5 | C4-alkylbenzene isomers | 75 |
| 1-butanol | 37.5 | methyl styrene | 25 |
| 1-pentanol | 50 | dimethyl styrene | 62.5 |
| Dichlorobenzene | 100 | C5-alkylbenzene isomers | 25 |
| C6-alkylbenzene isomers | 12.5 | naphthalene | 75 |

Table 4.7: TYPICAL BACKGROUND CONCENTRATIONS OF TRACE ELEMENTS IN HUMAN MILK (in ppb) (Taken from Jensen and Slorach,1991)

| | | | |
|------------|---------|-----------|---------|
| Aluminium | 300 | Antimony | 1-4 |
| Arsenic | 0.2-2 | Barium | 30 |
| Boron | 70 | Bromine | 100 |
| Cesium | 70 | Chromium | 0.8-1.5 |
| Cobalt | 0.1-1 | Copper | 180-310 |
| Fluorine | 7-50 | Iodine | 50-70 |
| Iron | 350-720 | Manganese | 3-6 |
| Molybdenum | 0.3-3 | Nickel | 15 |
| Rubidium | 700 | Selenium | 10-25 |
| Silicon | 300 | Strontium | 100 |
| Tin | 0.4 | Titanium | 100 |
| Vanadium | 0.1-5 | | |

In conclusion, excluding tobacco, alcohol, cannabis, pharmaceutical drugs, fungal and nitrate derived contaminants, and trace elements, over 350 contaminants (including some 87 congeners of dioxins and PCBs and some 190 volatile compounds) have been detected in human breast milk. Of course, many more contaminants will actually be present in human breast milk, because, in theory, potentially any of the contaminants found in a female's adipose tissue (which includes several endocrine disrupting chemicals, such as some phthalates) can be transferred to breast milk.

World Health Organisation experts have considered the risks posed by exposure to dioxin-like compounds, and over time have had to reduce the tolerable daily intakes they have proposed. This is because more data on the undesirable health effects of these substances have become available. Other substances which have been found in breast milk are known to be able to cause cancer in animals, while others can cause developmental effects. However, for many of the substances found in breast milk there is a lack of data on their potential long term effects. Thus, the risks these substances pose to the health and well being of our children can not be assessed. Furthermore, there has been little or no evaluation of the long-term risks posed to infants from the simultaneous exposure to the numerous contaminants that may now be found in breast milk. This report therefore recommends that urgent measures should be implemented in order to reduce the exposure of new born infants to chemical contaminants.

PART 5: LEVELS OF CONTAMINANTS IN UK BREAST MILK

The levels of organochlorine pesticides and dioxin-like compounds in UK breast milk appear to be declining, but there is certainly no room for complacency. As of 1999, the latest available breast milk surveys showed UK infants to be consuming dioxin-like compounds at concentrations well in excess of the levels set as tolerable daily intakes (TDIs). Similarly, some UK infants were also exceeding the TDI for dieldrin-like compounds. In addition, the full range of contaminants was not known, as until the late 1990s, UK surveys had focussed on a very limited range of substances, most of which had been banned for many years.

The UK intakes of dioxin-like substances probably give the most cause for concern, despite the fact that surveys carried out under the auspices of the World Health Organisation (WHO) indicate that the levels of these substances fell in the years 1988 to 1993. Dioxin-like substances include dioxins, furans, and certain PCBs, and the reductions in dioxin and furans levels, and some PCBs, are shown in Table 4.0, which provides a comparison, over time, of the levels found in the UK and elsewhere. Table 5.0 shows the levels of dioxins and dioxin-like PCBs found in breast milk in pooled UK samples taken from women living in three UK cities in the late 1980s and early 1990s.

| | 1987-1988 | | 1993-1994 | | |
|----------------------|------------|---------|------------|-----------|-----------|
| | Birmingham | Glasgow | Birmingham | Glasgow | Cambridge |
| Dioxins | 37 | 29 | 21 | 21 | 24 |
| PCBs | - | - | 10 | 12 | 10 |
| Dioxins +PCBs | - | - | 31 | 33 | 34 |
| Fat content | 2.8% | 3.4% | 3.1% | 3.4% | 3.2% |

Based on a knowledge of the average milk consumption at various ages, the mean intakes of dioxins and PCBs at various ages can be calculated, and these are shown in Table 5.1

From the 1993/4 survey data it has therefore been estimated that UK intakes of dioxin-like compounds in breast fed infants are equivalent to 170 picograms of the most toxic dioxin per kilogram body weight per day at 2 months and 39pg TEQ/kg bw/day at 10 months. Comparing this with the WHO Tolerable Daily Intake (TDI) of 1- 4 pg/kg bw/day, as set in June 1998, it can be seen that these levels are some 42 times in excess of the TDI for a 2 month old child, and that a 10 month old infant is estimated to receive around 10 times the TDI (MAFF, 1997). As of March 1999, the UK Government had not reduced its TDI of 10pg/kg bw/day to come into line with the new WHO TDI, but it can be seen that even this higher value is widely exceeded by breast fed infants

| Table 5.1: ESTIMATED UK INFANT DIETARY INTAKES OF DIOXINS AND PCBS FROM HUMAN BREAST MILK (taken from MAFF,1997) | | | | |
|---|---|---|-------------|-------------------------|
| Age | Mean milk consumption by nursing infants | Mean intakes via human milk (pg TEQ/kg bw/day) | | |
| months | g/kg bw/day | Dioxins | PCBs | Dioxins and PCBs |
| 2 | 160 | 110 | 58 | 170 |
| 3 | 140 | 100 | 51 | 150 |
| 4 | 124 | 88 | 45 | 130 |
| 5 | 103 | 73 | 37 | 110 |
| 6 | 79 | 56 | 29 | 84 |
| 7 | 63 | 44 | 23 | 67 |
| 8 | 42 | 30 | 15 | 45 |
| 10 | 37 | 26 | 13 | 39 |

However, because the TDI is based on lifetime exposure, and because of convincing evidence of the benefits of breast feeding to the overall health and development of the infant, experts still recommend that breast feeding should be encouraged.

The dioxin, furan and PCB congeners detected in UK milk during the latest WHO survey in 1993 are shown in Table 5.2, which also outlines their toxic equivalency factors (TEFs). However, the actual levels published in the WHO report are not restated in this report as the initial analysis was considered to be inaccurate (Harrison,1998).

Kevin Jones and co-workers screened for 50 PCB congeners in 115 Welsh breast milk samples and detected 24 congeners in most samples. Furthermore, their study suggested the unlikelyhood of a substantial decrease in the concentrations of PCBs in human milk over the last decade. These workers also looked at DDT and related compounds. The levels they found were indicative of exposure to DDT contaminants through food, rather than through direct contact with this compound (Duarte-Davidson et al.,1994). The sum of these DDT compounds were in the range 0.3-71.4 ng/g (mean 11 ng/g of whole milk (equivalent to 0.04-6.7 µg/g fat)(mean 0.49 µg/g fat) .

| Table 5.2: PCDDS, PCDFS AND PCBS DETECTED IN HUMAN MILK IN THE UK, AND THEIR TOXIC EQUIVALENCY FACTORS (WHO, 1996) | |
|---|-------|
| DIOXINS AND FURANS in pg/g fat | TEF |
| 2,3,7,8-TCDD | 1 |
| 1,2,3,7,8-PeCDD | .5 |
| 1,2,3,4,7,8-HxCDD | .1 |
| 1,2,3,6,7,8-HxCDD | .1 |
| 1,2,3,7,8,9-HxCDD | .1 |
| 1,2,3,4,6,7,8-HpCDD | .01 |
| 1,2,3,4,6,7,8,9-OCDD | .001 |
| 2,3,7,8-TCDF | .1 |
| 1,2,3,7,8-PeCDF | .05 |
| 2,3,4,7,8-PeCDF | .5 |
| 1,2,3,4,7,8-HxCDF | .1 |
| 1,2,3,6,7,8-HxCDF | .1 |
| 1,2,3,7,8,9-HxCDF | .1 |
| 2,3,4,6,7,8-HxCDF | .1 |
| 1,2,3,4,6,7,8-HpCDF | .01 |
| 1,2,3,4,7,8,9-HpCDF | .01 |
| 1,2,3,4,6,7,8,9-OCDF | .001 |
| DIOXIN-LIKE PCBS in pg/g fat | |
| PCB 77 | .0005 |
| PCB 126 | .1 |
| PCB 169 | .01 |
| PCB 105 ng/g fat | .0001 |
| PCB 118 ng/g fat | .0001 |

| Table 5.2 cont: PCDDS, PCDFS AND PCBS DETECTED IN HUMAN MILK IN THE UK, AND THEIR TOXIC EQUIVALENCY FACTORS (WHO, 1996) | |
|---|--------|
| MARKERS and OTHER PCBS IN NG/G FAT | |
| PCB 28 | |
| PCB 138 | |
| PCB 153 | |
| PCB 180 | |
| PCB 60 | - |
| PCB 74 | - |
| PCB 156 | .0005 |
| PCB 157 | .0005 |
| PCB 167 | .00001 |
| PCB 189 | .0001 |

Levels of organochlorine pesticides in UK breast milk have declined since the 1960, and this is shown in Table 5.3. Also, in the survey in 1996-1997, a number of other pesticides were sought but not found. These included: chlordane, endosulfan, endrin, alpha-HCH, heptachlor, phorate, chlorpyrifos-methyl, fenitrothion, diazinon, chlorpyrifos, chlorfenvinphos, pirimiphos-ethyl, pirimiphos-methyl, propetamphos, and triazophos. However, perhaps it is not surprising that the last ten substances on this list were not found as organophosphate pesticides tend to be less persistent. Chlordane was not found in this survey of breast milk, and neither was oxychlordane (WPPR, 1998), despite the fact that chlordane had been picked up in over half the samples in the 1995-97 UK survey of body fat. Therefore, it would still be useful to continue monitoring levels in breast milk

From the data, the intake of organochlorine contaminants by breast fed babies can be very approximately calculated on the assumption that at around 2 months of age, the average infant weight is around 5kg and the infant consumes around 800g of milk per day. On this basis, in 1989-91, the babies receiving the most contaminated milk would have been receiving in excess of the (WHO JMPR 1994) provisional tolerable daily intake (PTDI) of 0.1ug/kg bw/day for total aldrin and dieldrin. The TDI for a 5kg child would thus be 0.5ug, and the infant would have received 4µg per day, which is 8 times the TDI (Dwarka et al., 1995). Unfortunately, in the 1996-1997 survey, the most exposed infant received even more, that is 5.6 4µg per day, which is 11 times the TDI.

For lindane, in both the 1989-1991 and the 1996-97 surveys the intakes of the breast fed babies were within the (WHO JMPR 1997) temporary TDI of 1ug/kg bw/day set in 1997 (ie. 5µg per day for a 5kg child), as the worst exposed infant in the earlier survey would have received around 4µg per day, whilst the most exposed infant in the 1996-97 survey received 1.6µg per day.

Similarly, in the latest survey the intake of DDT compounds by the most exposed child was just within the (WHO JMPR 1994) provisional TDI of 0.02mg/kg, which for a 5kg child would equate to

0.1 mg/day, as the most exposed 5kg child would have ingested around 0.08mg/day

Table 5.3: COMPARISON OF MEAN AND RANGE OF LEVELS OF ORGANOCHLORINE COMPOUNDS IN UK BREAST MILK OVER TIME (in mg/kg)

| Compound | 1963-64 ^(19 samples) ¹ | 1979 -1980 ^(102 samples) ² | | 1989-1991 ^(193 samples) ³ | | 1996-1997 ^(168 samples) ⁶ |
|----------|--|--|----------|---|------------------|---|
| | Whole milk | Whole milk | Milk Fat | Whole milk | Milk Fat | Whole milk |
| β-HCH | not measured | 0.007 | 0.22 | 0.002 ND-0.009 | 0.08 ND-0.99 | ND-0.030 |
| γ-HCH | .013 0.007-0.03 ⁵ | 0.007 | 0.25 | <0.001 ND-0.005 | <0.02 ND-0.16 | ND-0.002 (mean = 0.001) |
| Dieldrin | 0.006 0.001-0.01 | 0.002 ND-0.01 ⁵ | 0.08 | <0.001 ND-0.005 | 0.03 ND-0.43 | ND-0.007 (mean = <0.001) |
| pp□-DDE | 0.073 0.04-0.1 | 0.041 ND-0.2 | 1.6 | 0.009 ND-0.04 | 0.4 ND-1.72 | Sum of ppDDE + DDT |
| pp□DDT | 0.045 0.02-0.075 | 0.003 ND-0.04 | 0.11 | <0.001 ND-0.021 | <0.02 ND-0.72 | ND-0.1 |
| HCB | not measured | 0.004 ND-0.01 | 0.14 | <0.001 ND-0.005 | 0.02 ND-0.22 | ND-0.01 |
| PCBs | not measured | 0.02 ND-0.1 | 0.5 | <0.01 ND-0.05 | 0.5 ND-2 | See table 5.1 above |

Notes to Table 5.1

1. Egan H, Goulding R, Roburn J Tatton J, 1965, Organochlorine pesticide residues in human fat and milk, British Medical Journal, Volume 2, p66-69.
2. Collins G B, Holmes D C and Hoodless R A, Organochlorine pesticide residues in human milk in Great Britain 1979-1980, Human Toxicology, Volume 1, p425-431.
3. Dwarka S, Harrison D J, Hoodless R A, Merson G H J, 1995, Human and Experimental Toxicology, Volume 14, p451-455.
4. Working Party on Pesticide Residues, 1992, Annual Report of the Working Party on Pesticide Residues 1991, MAFF, London.
5. Working Party on Pesticide Residues, 1992, Report of the Working Party on Pesticide Residues 1988-1990, Food Surveillance Paper 34, MAFF, London.
6. Working Party on Pesticide Residues, 1998, Annual report of the Working Party on Pesticide Residues: 1997, MAFF, London.

It should however be recognised that breast milk is likely to be contaminated with more than one pollutant, which may act on similar biochemical pathways. For example, in the 1996-1997 survey multiple residues (2-5 compounds) were found in 75 of the 168 samples, that is in around half the samples.

In mid-1998 the UK Government signalled its intention to investigate further the extent of UK breast milk contamination. It invited tenders to undertake the pilot phase of a project which would entail taking and analysing breast milk samples from individual mothers, and archiving them as well as related information.

The chemicals of interest included, in the order of priority set by the UK Government Departments:-

- (1) dioxins, furans and PCBs
- (2) phytoestrogens, endogenous hormones, synthetic hormones
- (3) phthalates and their metabolites
- (4) organochlorine pesticide residues
- (5) lead, mercury, aluminium, antimony, arsenic, cadmium, chromium, cobalt, copper, nickel, selenium, tin, zinc
- (6) ochratoxin A
- (7) bisphenol A

This research programme was set up because concern had been expressed that exposure during infancy to some chemical contaminants in the diet may “have an adverse effect on subsequent development and health”.

The UK Government was seeking to understand i) the factors underlying the differing levels of the list of substances in samples of breast milk taken from various mothers ii) what, if any, were the effects on the subsequent development and health of infants exposed to particular amounts of chemicals of interest in human milk, and particularly whether PCBs and dioxins had an impact on neurological development and thyroid status iii) how effective were the abatement measures introduced to reduce emissions to the environment in reducing human exposure (ARCHV22B.DOC).

In addition, a study to determine the levels of PAHs in UK breast milk, which had been due to commence in 1997 (Tahourdin,1996), was still on the cards. However, as of mid-1998 this had still not started and “uncertainty over the availability of samples” of breast milk meant that the starting and completion date for this part of the survey were still uncertain, although the part of the study to evaluate the PAH levels in bottled infant milk had gone ahead (Harrison N,1998).

PART 6: MAIN CONCLUSIONS AND RECOMMENDATIONS

General conclusions and recommendations

1. This report highlights that several hundred man-made chemicals have been found as contaminants in human body fat, and many of these can be passed on to babies at a particularly sensitive stage in their development, via the placenta and during lactation.
2. There is convincing evidence of the benefits of breast feeding to the overall health and development of the infant, and therefore this practice should still be encouraged, despite the concerns raised by this report.
3. Many of the contaminants found in breast milk are inherently toxic, especially the organochlorines and heavy metals, and these chemicals may exert effects on the developmental, neurobehavioural, reproductive, and the immune system. Also, several of the contaminants found in breast milk are suspected human carcinogens. Furthermore, there is a lack of data on the chronic effects of many of the over three hundred and fifty contaminants which have been found in human breast milk, and this makes the potential long term effects very difficult to assess.
4. Urgent action should be taken to reduce exposures, particularly to substances which can cross the placenta and/or which can be found in breast milk.
5. The levels of contaminants found in humans certainly give no room for complacency. For example, infants in the UK (and elsewhere) are still exposed to dioxin-like compounds and dieldrin-like compounds at levels in excess of those set as tolerable daily intakes (TDIs), despite the recorded decline in the levels of these substances.
6. Compounds which are persistent and bioaccumulative should be considered undesirable, irrespective of their toxicity, and should therefore be considered for phase-out. This is because the long term effects of these chemicals on species at the top of the food chain are difficult, if not impossible, to predict from limited short term toxicity tests on a few selected species. Also, if effects do become evident, then due to the persistent and bioaccumulative nature of these substances, it will be impossible to reverse these effects in the short term.
7. Toxicity tests should be developed and imposed in legislation, in order to identify chemicals with endocrine disrupting effects.
8. In particular, behavioural effects seem to occur at lower exposure levels than structural deformities, and therefore new toxicity tests need to be developed and implemented in order to identify chemicals which can exert neurodevelopmental effects, and to determine the lowest levels which can cause such effects.
9. New substances with endocrine disrupting effects should be banned from entry onto the market (except for pharmaceuticals).

10. Chemicals which are currently on the market, which are found to have endocrine disrupting effects, should be prioritised for review, and exposures should be eliminated or reduced to the lowest levels practicable on a precautionary basis, taking into account the potential for simultaneous exposure to numerous substances with interactive effects.
11. It is a matter of concern that when the risks posed by existing substances are evaluated, it is usually only the risk posed by exposure to a single substance in isolation that is considered, and this should be rectified. Therefore, when estimating “safe” exposure levels, the interactive effects of all the substances to which there is concurrent exposure should be considered.
12. Tests are therefore needed to determine the “mixture effects” of the substances to which the foetus and neonate are commonly exposed. For example, in the USA, the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) has recommended that tests should be done to determine the toxicity of the mixtures of contaminants commonly found in breast milk (4-49).

Future research on foetal and neonatal exposures and effects

13. With regard to quantifying in-utero exposures, consideration should be given to monitoring the level of contaminants in blood lipids, as these can provide a good indication of the amounts of the lipophilic substance in circulation. Also, compared to taking fat samples, taking samples of blood is relatively easy.
14. Further studies are needed on the possible long term health hazards to infants from the transplacental exposure to pollutants, and from the intake of contaminated breast milk. The long term effects of exposure to chemical pollutants can only be clarified by continued surveillance. Particular consideration should be given to studies encompassing the analysis and data banking of placental cord blood, and the subsequent analysis of breast milk of these infants, coupled with epidemiological studies on the development of these children, so that any effects noted can be evaluated with respect to both in-utero and post-natal exposures.
15. Research is needed on the ability of certain toxic substances, including carcinogens (and their active metabolites) to cross the placenta. Also, more research is needed to fully understand the metabolic changes that occur during pregnancy and how these can affect the accumulation of toxic substances in the mother, or the production of toxic metabolites. In addition, the metabolic capacity of the placenta and the neonate need to be evaluated because a number of metabolic pathways responsible for bioactivation or detoxification are thought not to be present in the foetus, and are less developed in an infant.
16. Consideration should also be given to evaluating all the hormonally active substances found in breast milk, and those believed to cross the placenta. Identifying and quantifying the potency of the total oestrogenic component, and the total anti-androgenic component, would provide valuable data on in-utero and neonatal exposures to man-made endocrine disrupting compounds (EDCs).

National surveillance and international co-ordination

17. National governments should, if possible, initiate programmes to monitor human contamination in their countries, in order to provide an integrated assessment of exposures to toxic chemicals, particularly foetal and neonatal exposures. Such national programmes should be co-ordinated internationally, and a central data repository set up and maintained. The aim should be to monitor representative populations throughout the globe.
18. Within this report it has not been possible to review the potential hazards posed by the numerous substances which have been found, or which might be expected to be found in humans. However, it is recommended that this is done by national and/or international committees of experts, at least on a rough and ready basis. This would enable substances, which might be expected to pose the greatest risk, including those for which there was little information on the degree of contamination, to be prioritised for relevant further study, for example, as to their typical levels and routes of exposure. This is because such data would be invaluable in helping determine and prioritise effective control programmes.
19. In the UK, for example, in order to effectively target a national monitoring programme, it is recommended that an expert committee should be set up to oversee the programme and make recommendations as to its scope, on an on-going basis. Such an expert committee for human exposure surveillance, should be comprised of scientists working on the effects of toxic substances, representatives from the Environment Agency and environmental NGOs, and scientists from Government departments.
20. There should be an investigation of the extent of human breast milk contamination. Breast milk should be analysed for a wide range of contaminants, in order to effectively target policies for reducing early-life exposures. As numerous factors influence the accumulation of pollutants, including diet, occupation, and place of residence, breast milk should be taken from a wide range of individuals, including those living near to certain industrial sites. It is recommended that women nursing their first child are sampled in order to compare levels over time in milk from mothers residing in different geographical areas.
21. In breast milk, in addition to the usual range of organochlorine compounds, such as total DDT, dieldrin-like substances, chlordane (+ oxychlordane and nonachlor), HCH compounds, heptachlor (+ epoxide), HCB, and dioxins, furans and PCBs, consideration should be given, in particular, to determining levels of the following substances:-

PAHs, PBDEs, aromatic amines, musk xylene, musk ketone, polycyclic musk compounds, bisphenol A, octylphenol, benzophenone³, octyl-methoxycinnamic acid (OMC), 3,4-methylbenzylidene camphor (MBC), homo-menthylsalicylate (HMS), phenyl phenol, PCP (including palmitic ester), DEHA, and various phthalates and their monoesters (including DEHP, DBP and BBP), as well as lead, mercury, and cadmium.

Also, in view of their ability to bioaccumulate and their potential additive effects with PCBs, consideration should also be given to analysing the levels of PCNs and PCTs in breast milk,

although in most areas these might be expected to be low or non detectable due to the relatively low volumes used as compared to the PCBs. The levels of mirex and toxaphene should also be determined in areas with relatively high historical usage, or where transboundary transfer is likely to occur.

It is also argued that in view of the recently discovered oestrogenic activity of butylparabens and the potential for dermal exposure (Routledge et al., 1998), then the possibility that this substance might be found as a contaminant in humans should be investigated. Furthermore, in view of the oestrogenicity of nonylphenolic substances, it would be useful to verify that these are not present in body fat and breast milk, particularly as these have now been found in the umbilical cord (Takada et al., 1999).

In addition, it is recommended that more attention should be paid to the possible effects from in-utero and neonatal exposure to volatile contaminants, and therefore consideration should be particularly also given to analysing breast milk for the following substances:-

Benzene, styrene, toluene, xylene, acetaldehyde, carbon tetrachloride, chloroform, methylene chloride (dichloromethane), trichloroethylene, tetrachloroethylene (perchloroethylene), carbon disulphide, and the chlorobenzenes (particularly 1,4-dichlorobenzene and 1,2,4,5-tetrachlorobenzene) - in certain targeted locations.

22. Many substances may be metabolised to, or contaminated with, other toxic substances, and this should be given due consideration in any monitoring programme. For example, seals have been found to be contaminated with pentachloroanisole, mono-bromo-PCBs, and bis(chlorophenyl)sulphone (BCPS). Pentachloroanisole is thought to be formed by metabolism of HCB or PCP, mono-brom-PCBs are thought to arise from contamination of chlorine gas with small quantities of bromine, and BCPS may arise due to its use in paints and plastics, or from its unintentional production during the manufacture of certain pesticides (Swedish EPA, 1988).

Similarly, the palmitic ester of PCP has been detected in adipose tissue, but no data were found on potential levels in breast milk (Jensen and Slorach 1991).

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APPENDIX 1

Aromatic amines

Aromatic amines are used in the manufacture of plastics (including polyurethane foams), dyes, pesticides, and pharmaceuticals. N-methylaniline, o-toluidine, aniline have been found in milk, and concern was noted because of possible links to breast cancer (DeBruin et al.,1996).

Benzophenone 3

Benzophenone 3 or 2-hydroxy-4-methoxy benzophenone (Cas 131-57-7) has been identified as a constituent in some sun-screens. It is oestrogenic in the E screen (Schlumpf).

Bisphenol A (BPA) and Tetrabromobisphenol A

Bisphenol A is the monomer used in polycarbonate plastics. Small amounts have been found to leach from some dental sealants and from the inside linings of certain cans used for food. It has been shown to be oestrogenic both in-vitro in the E-screen (Krishnan et al.,1993) and in-vivo (see review by Ben and Steinmetz,1998). Furthermore, it shares similarities in structure, metabolism and action with diethylstilboestrol (DES).

Also, Vom Saal and co-workers have reported that a dose of 2ng/g body weight (2ppb) of BPA permanently increased the size of the prostate and preputial glands and reduced the size of the epididymides in male mice exposed in-utero on gestation days 11-17. In addition, they also found a decrease in the efficiency of sperm production at 20ng/g (20ppb) (vom Saal et al.,1998; Nagel et al., 1997). However, as of April 1999, this work using low doses had not been able to be repeated by workers funded by industry.

At a concentration of 10^{-7} M, in an amphibian test system using *Xenopus laevis*, bisphenol A caused effects on sexual development. Exposure during larval development caused an increased number of female phenotypes, and this was believed to be due to the oestrogenic activity of BPA (Kloas et al.,1999).

Tetrabromobisphenol A is a very widely used flame retardant, which if used in its reacted form with epoxyresins is probably largely prevented from leaching out. However, in certain plastics, it is used purely as an additive, and in this form it may leak into the environment (Swedish EPA, 1998).

Butylhydroxyanisole

This compound increased breast cancer cell proliferation in mammalian cell lines, and also stimulated transcriptional activity of the oestrogen receptor at concentrations between 10^{-5} and 10^{-4} M. In studies on the trout oestrogen receptor this was able to reduce the binding of tritiated 17β oestradiol to the oestrogen receptor, although whether this inhibitory effect was due to direct competition was not known.(Harries et al.,1995). At a concentration of 10^{-7} M, in an amphibian test system using *Xenopus laevis*, butylhydroxyanisole caused effects on sexual development. Exposure of larvae during development resulted in an increased number of female phenotypes compared to controls, and this was taken to indicate an in vivo oestrogenic effect (Kloas et al.,1999). BHA is used as an antioxidant in foods (E320).

Butylated hydroxytoluene

This stimulated transcriptional activity of the oestrogen receptor at concentrations greater than 10^{-4} M, but was not able to reduce the binding of tritiated 17β oestradiol to the trout oestrogen receptor (Harries et al.,1995). It is used as an antioxidant in food (E321), petrol products, rubbers, plastics and soaps

Chlordane

Technical chlordane is actually a mixture of more than 26 compounds, and impurities include cis- and trans-nonachlor and γ -chlordane. It is important in termite control, and oxychlordane is its stable metabolite.

Chlordane can induce enzyme production and disrupt endocrine control (AEA, 1994). Its major effects are on

the liver and the nervous system (AMAP, 1997), and a particular concern is that it may cause immune function impairment. A Swedish study suggests that exposure to chlordane compounds and PCBs may be associated with a higher risk of contracting non-Hodgkins lymphoma (NHL). Tissue levels in patients with NHL had significantly higher levels of trans-nonachlor, cis-nonachlor, oxy-chlordane nonachlor, and total chlordanes as compared to control subjects (Hardell et al., 1996).

Chlorinated paraffins (CPs)

These have been used as additives as plasticisers and lubricants in metal working fluids. The short chain CPs (10-13 carbon atoms) with a high degree of chlorination are bioaccumulating and toxic (Swedish EPA, 1998). Some CPs have been found to affect the thyroid system, and reduce the level of thyroxine (see Olsson et al., 1998).

Chlorobenzenes

There are 12 chlorobenzene compounds, monochlorobenzene, three dichlorobenzenes, three trichlorobenzenes, three tetrachlorobenzenes, pentachlorobenzene, and hexachlorobenzene (HCB) (MAFF, February 1998).

The chlorobenzenes are found in industrial discharges, in emissions from incinerators, and in sewage sludge, from where they can get into vegetables. As the number of chlorine atoms increase, they have an increasing tendency to bioaccumulate and become more persistent (MAFF, February 1998).

Hexachlorobenzene (HCB) was previously used as a fungicide, but is no longer approved in the UK. However, it is commonly used in the manufacture of aromatic fluorocarbons, chlorinated solvents and synthetic tyres (NRA, 1991). HCB is toxic to the immune system and carcinogenic in animals, and is capable of enzyme induction and endocrine disruption (AEA, 1994)

Apart from HCB, all the chlorobenzenes have industrial uses, mostly as intermediates in the production of pesticides and dyes (MAFF, February 1998). Monochlorobenzene is also used as a solvent, 1,3-dichlorobenzene (ortho) as a bactericide, and 1,4-dichlorobenzene (para) is used in mothballs and toilet blocks. 1,2,3-Trichlorobenzene is widely used as a solvent and as a lubricant and coolant in electrical installations and glass tempering (NRA, 1995). The higher chlorobenzenes are used in dielectric fluids. Pentachlorobenzene is also an impurity in and degradation product of HCB.

There is sufficient evidence for the carcinogenicity of 1,4-dichlorobenzene in experimental animals, and a report has suggested a possible association between leukemia and exposure to dichlorobenzenes. Similarly there is sufficient evidence that HCB causes cancer in experimental animals (US DHSS, 1994).

Chloroform

Trichloromethane or chloroform is an industrial solvent, but the ocean is also a major source of natural chloroform. It is used in the chemical synthesis, as a fumigant and in the manufacture of anaesthetics. Production in the EU was estimated to be 50,000 tonnes per year in 1988 (NRA, 1995). It is carcinogenic in animals.

Cresol

This is used as a disinfectant, parasiticide, local antiseptic, and in photographic developing solutions and in the manufacture of explosives.

DDT (Dichlorodiphenyl trichloroethane) and DDE

DDT is a pesticide, which although no longer used in many countries, still has extensive use to prevent malaria. In the body, and in the environment, DDT is converted to DDE, and both substances accumulate in animal fat, and can be transferred to the foetus via the placenta. These substances are very persistent and are therefore frequently found as contaminants in human breast milk, even in the UK where usage has been banned for several years.

DDT and DDE can have a range of effects on reproduction, development, and the nervous system, and in addition DDT is known to be able to cause cancer in animals.

DDT and DDE are both endocrine disrupting chemicals (EDCs), with both oestrogenic and anti-androgenic activity. For example, pp' and op'DDT and pp' and op'DDE are oestrogenic, while pp-DDE is also anti-androgenic (Soto et al.,1995; Kelce et al.,1995).

It has been suggested that breast milk with DDE at levels of 4µg/g fat can suppress reflexes in newborn infants, and similar levels have been correlated with restricted duration of breast feeding, although neither of these studies provided conclusive evidence that DDE was to blame (see AMAP,1997).

WWF has called for a global ban on the production and use of DDT by 2007 at the latest (WWF,1999b).

1,2-Dichloroethane

This is used in the synthesis of vinyl chloride and 1,1,1-trichloroethane and trichloroethene (NRA,1995). It is used as a solvent, a fumigant, and as a dispersant for plastics and elastomers such as synthetic rubber. There is sufficient evidence for its carcinogenicity in animals (US DHHS, 1995)

Di-2-ethylhexyl adipate (DEHA)

This is a plasticiser which has been used to impart flexibility in PVC film used in packaging food. In animal experiments, adverse effects on sperm have been noted.

Dioxins

Dioxins is the term given to the 75 possible polychlorinated dibenzo-p-dioxins (PCDDs). One particular dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is thought to be particularly toxic, and toxic equivalent factors (TEFs) have been derived to express the toxicity of other dioxins, furans and certain dioxin-like PCBs, relative to TCDD. This is to allow an assessment of the potential toxicity of complex mixtures of dioxins, furans and PCBs and to compare them with a tolerable daily intake (TDI) expressed as a toxic equivalent (TEQ) of TCDD per kilogram body weight per day. Multiplication of the concentration of a compound by its TEF gives a TEQ. The use of TEFs is justified because these compounds appear to act by a common mechanism, that is by binding to a specific cellular receptor, the Ah-receptor (MAFF,1997).

Dioxins are very persistent in the environment and are produced during various combustion processes and are also unwanted by-products in the manufacture of certain chemicals. The main source of dioxins in the diet are milk and dairy products, fish and fish oils, and meat and animal fats (MAFF,1997).

In animals, the most sensitive endpoints for dioxin exposure are endometriosis, cognitive effects, effects on sperm counts and female urogenital malformations, and immunotoxic effects. As outlined in the main report, exposure to PCBs has been linked with effects on intelligence, and thus dioxins and PCBs are associated with persistent neurobehavioural, reproductive, and endocrine alterations. Also, one particular dioxin (TCDD) is listed by the International Agency for Research on Cancer as a known human carcinogen.

Ethyl isovalerate

This is used as a flavouring agent in confectionary and beverages.

Furans

There are some 135 possible polychlorinated dibenzofurans (PCDFs). They are found as contaminants in certain chlorinated compounds, and like dioxins, they are also formed in combustion processes. For toxicity evaluations, they are grouped together with certain dioxins and PCBs, and to do this a (TEF) Toxic Equivalency Factor is determined (see TEQs in Glossary).

Hexachlorocyclohexane (HCH)

See under lindane

Limonene

Found in oils of lemon and orange. It has a lemon like smell and is used as a solvent in the manufacture of resins and as a wetting and dispersing agent.

Lindane and Hexachlorocyclohexane isomers

Technical grade hexachlorocyclohexane (HCH) is a mixture of different isomers including alpha-HCH, beta-HCH, delta-HCH and gamma-HCH, which is also used as a pesticide (lindane) in its own right. Beta-HCH is the most persistent and bioaccumulating isomer. Lindane has a weak oestrogenic effect (Jensen and Slorach, 1991), and can affect the liver, the nervous system, the kidneys, the reproductive system and possibly the immune system (AMAP, 1997). There is also sufficient evidence for the carcinogenicity of technical grade and α -HCH, and limited evidence for β - and γ -HCH (US DHHS, 1994).

Methylene chloride (Methylene dichloride)

This also goes under the name of dichloromethane or DCM (CAS: 75-09-2). It is used in industrial and DIY paint stripping formulations, as a solvent, as a secondary blowing agent in polyurethane manufacture, and in certain aerosols. If exposure occurs it is well distributed around the body, including the brain, and in pregnant women, it can be transferred across the placenta, although it is believed to have a short half life in the body. In animals it is carcinogenic, but the 1996 review of the International Programme on Chemical Safety (EHC Document 164), has concluded that because of metabolic differences, this chemical will not cause cancer in humans.

However, it could be argued that there is a need to fully evaluate the potential neurodevelopmental effects (such as effects on cognitive development) of DCM, particularly as it is a central nervous system depressant, and many home users, including pregnant and nursing women, will be exposed when carrying out paint stripping operations.

Mirex

This is a pesticide which is susceptible to long range transport. It can affect the liver, the kidneys, the eyes and thyroid, and is toxic to the developing foetus (see AMAP, 1997). Mirex is also carcinogenic in animals.

Musks - synthetic nitro and polycyclic musk compounds

Synthetic musk fragrances, especially nitro musks and polycyclic musk compounds are used as substitutes for natural musk, and are added to cosmetics and detergents. In 1988, Barbetta and co-workers estimated global production of synthetic musk compounds to be about 7000 tonnes per year, of which 61% were polycyclic musks, 35% were nitro musks and 3-4% were macrocyclic musks (Muller, 1997). Nitro musks are being replaced in many cases with polycyclic and macrocyclic musks.

Environmental contamination can particularly arise from the use of nitro musk compounds as perfumes in detergents. Musk xylene, musk ketone, HHCB, AHTN accumulate in fish, and AHTN has also been found to accumulate in mussels and shrimps (Brunn and Rimkus, 1997) (see also glossary of abbreviations).

One study of 60 cosmetic products and 41 detergents by Sommer and colleagues found that 53% of the samples contained nitro musks, with musk xylenes being present mainly in detergents and musk ketones in cosmetics. In order to understand which parameters affect the nitro musks levels in humans and milk, extensive examination of more samples, combined with detailed questionnaires are needed.

Musk ambrette has been shown to have neurotoxic and mutagenic effects, and in a long term study reported by Maekawa and co-workers musk xylene was found to be carcinogenic (see Rimkus et al., 1994). Certainly, it is known that trinitrotoluene, which is structurally related to musk xylene, can cause carcinogenic effects.

However, further studies are urgently needed to determine the long term toxicity of these substances (Brunn and Rimkus,1997).

In Japan, it is interesting to note that because of its high bioaccumulation potential, musk xylene has had voluntary restrictions on its usage imposed since 1982 (Rimkus et al.,1994).

With regard to the polycyclic musks, ATTN has been shown to cause behavioural effects and neuropathological changes in rats exposed dermally, but Muller has reported that the use of this was discontinued by industry in 1978. Few data are available on the other polycyclics, although HHCB and ADBI have caused increased liver weights (Muller et al.,1996).

Nonyl and Octyl phenol

Nonyl phenol is the persistent breakdown product of nonylphenol ethoxylate detergents. It is also used as an additive in certain plastics, as is octyl phenol (Routledge et al.,1998). Both compounds can exert oestrogenic action in animals, with octyl phenol being the most potent (Boockfor and Blake 1997; Harries et al.,1995).

Parabens (Alkyl hydroxy benzoates)

These compounds have been used as preservatives in the pharmaceutical products for many years. They preserve fats, proteins, oils, and gums in skin care products, perfumes, toothpastes, soaps, and some sun-screen products, and appear to be found in the majority of cosmetics applied to the skin. Although not active orally, butyl paraben (butyl hydroxy benzoate) has been found to be weakly oestrogenic by subcutaneous injection, as it gave a dose dependent positive uterotrophic response when tested in the rat. It was, however, considered to be about 100,000 times less potent than 17β oestradiol (Routledge et al.,1998). In receptor binding assay, butyl paraben was able to compete with oestradiol for binding to the rat oestrogen receptor, with an affinity approximately 5 orders of magnitude lower than diethylstilboestrol and between 1 and 2 orders of magnitude less than nonylphenol. In in-vitro tests with the yeast assay, the four most widely used parabens (methyl, ethyl, propyl and butyl) were also found to be weakly oestrogenic. Furthermore, this in-vitro oestrogenic activity was inhibited by 4-hydroxy tamoxifen, showing that these substances act via the oestrogen receptor (Routledge et al.,1998).

Pentyl alcohol

This is used as a solvent.

Phenyl phenol

Soto has reported that para-phenyl phenol is a full oestrogen agonist, and that meta, and to a lesser extent, ortho-phenyl phenol, are partial agonists. Para-phenyl phenol is used in the rubber industry and in the manufacture of resins. Ortho-phenyl phenol is used in the rubber industry, in fungicides and in disinfectants. Phenyl phenol is reported to be a widely used ingredient for indoor applications (Soto, IBC conference May1997, London; Sonnenschein and Soto,1998). However, care should be taken in interpreting the data shown in this report as some ortho phenyl phenol is suspected to originate from the sample collection procedure (Onstot and Stanley,1989).

Phthalates (including DEHP, DBP, and BBP)

Diethyl hexyl phthalate (DEHP) has extensive use as a plasticiser, imparting flexibility into plastics. It has been identified as a testicular and reproductive toxicant, and can cause effects on the oestrus cycle (Heindel et al.,1989; Eagon et al.,1994; Davis et al.,1989).

DBP is also used as a plasticiser, and is used in PVC and many other household articles. It appears to act as an anti-androgen as it impaired the androgen dependent development of the reproductive tract in male offspring of female rats dosed at 250, 500 and 750 mg/kg/day throughout pregnancy and lactation up until offspring were 20 days old. The epididymis was absent or underdeveloped in 9, 50 and 71% of offspring when examined at

100 days old at the 250, 500 and 750 mg/kg/day dose levels respectively. Similarly hypospadias occurred in 3, 21, and 43 % of males exposed at the different dose levels and ectopic or absent testes were noted in 3, 6, and 29% of males (Mylchreest et al., 1998). An earlier NTP continuous breeding study had revealed increased sensitivity in F₁ male rats as compared to the F₀ generation, which indicates that altered male reproductive development was due to in utero, neonatal and/or pubertal exposure of the F₁ generation (NTP, 1991; Wine et al., 1997).

These studies suggest that DBP produces changes in reproductive organ development by an anti-androgenic endocrine mediated mechanism, in which effects on follicle stimulating hormone (FSH) are believed to play an important part.

Phthalates decrease the responsiveness of the Sertoli cells in the testis to FSH stimulation and hence the Sertoli cells may be the primary site of toxicity as receptors for FSH are specific to these cells in the testis (Mylchreest et al., 1998).

BBP (Butyl benzyl phthalate) has an oestrogenic effect in human breast cancer cells, as does DBP. Similarly, BBP has also been shown to affect spermatogenesis and cause adverse effects on the testes (for summary see Olsson et al., 1998)

Polyaromatic hydrocarbons (PAHs)

Polyaromatic hydrocarbons (PAHs) are formed during the burning of coal, oil, gas, wood, tobacco, rubbish, and other organic substances. They are also present in coal tars, crude oil, and petroleum products, such as creosote and asphalt. PAHs are ubiquitous environmental contaminants, and one particular PAH, benzo(a)pyrene (BaP), is considered an indicator of such contamination because it usually occurs in mixtures of PAHs. There are some natural sources, such as forest fires and volcanoes, but PAHs mainly arise from combustion-related or oil-related man-made sources. Human exposure also arises from barbecued and smoked foods. Only a few PAHs are used by industry in medicines and to make dyes, plastics and pesticides.

Some studies suggest that PAHs can affect the immunocompetence of wildlife and humans. Also, some of these substances are carcinogenic and some are hormone disruptors. In humans, exposure to PAHs in cigarette smoke has been associated with reduced fertility and low birth rate of offspring (see Lyons, 1997)

Polybrominated biphenyls (PBBs)

Polybrominated biphenyls were used as flame retardants. People exposed to accidental contamination in Michigan had skin reactions, neurological changes, abnormal liver function and immunological changes and the children affected have also shown behavioural changes (KEMI and SNV, 1991).

Polybrominated diphenylethers (PBDEs)

Polybrominated diphenyl ethers (PBDEs) are used as flame retardants. They are also known as polybrominated biphenyl ethers (PBBEs), which may also be abbreviated PBDPEs. They essentially took over from PBBs, and are primarily used as fire retardants in resins and polymers, with extensive use in the plastics, textile, building, and numerous other industries (Cramer et al., 1990). For example, electronic appliances, such as computer and TV casings, frequently contain these flame retardants (Meironyte et al., 1998).

The PBDE products commercially available today consist primarily of the highly brominated compounds, with world production dominated by the decabrominated diphenyl ether with the maximum 10 bromine atoms. Other PBDE products consist of mixtures with an average of 5 (pentabrominated diphenyl ether) or 8 bromine atoms (octabrominated diphenyl ether). However, it is the tetra and pentabromodiphenyl ether (with 4 and 5 bromine atoms) that have the greatest ability to bioaccumulate, and the PBDE congeners that are found in the largest amounts in environmental and human samples are 2,2',4,4'-tetrabromobiphenyl ether (PBDE 47) and 2,2',4,4',5-pentabromobiphenylether (PBDE 99 or PeBDE) (Eriksson et al., 1998).

These PBDEs have been found in sediments, fish, marine mammals, human adipose tissue and breast milk. The worry is that the higher brominated compounds may eventually be broken down to these forms in the environment (Swedish EPA, 1998).

PBDEs can affect the thyroid hormone system, and cause reduced thyroxin (T4) levels in rodents. The precise mechanism is not yet known with certainty, although proposed mechanisms include induction of UDP-glucuronyl transferase, interference with T4 transport proteins and increased T4 excretion, and direct effects on the thyroid gland leading to decreased T4 synthesis. Indeed, it may be that several mechanisms may operate together (Hallgren and Damerud, 1998). In man, thyroid hormone disruption has also been reported in workers exposed to PBBs and PBDEs (including decabrominated diphenyl ether) (see Olsson et al., 1998).

In mice exposed to PBDE in the first few weeks of life, neurotoxic effects were induced in the adult animal, and both PBBE 47 and 99 induced permanent changes in motor behaviour, and this disruption worsened with age. In addition, learning and memory functions in the adult animal were affected (Eriksson et al., 1998). A WWF briefing on PBDEs is available from Panda House, Godalming (see Lyons, 1999).

Polychlorinated biphenyls (PCBs)

Polychlorinated biphenyls are a group of 209 related compounds which differ in the number and pattern of chlorine atoms attached to the biphenyl molecule. PCBs are resistant to degradation in the environment and can build up in the food chain. Some PCBs have dioxin-like effects and are therefore grouped as contaminants (see under dioxins).

Several PCB mixtures are known to be able to cause cancer in animals, and PCBs have been implicated in effects on the liver, reproduction, infant birth weight, neurobehavioural development, and the immune system. (AMAP, 1997).

PCBs have been used in the UK since the early 1930s as dielectric fluids in transformers and capacitors, but their manufacture has been banned in the UK and all existing PCBs must be taken out of use and destroyed by the end of 1999 (FSD, 1997). The main source of PCBs in the diet are milk and dairy products, fish and fish oils, meat and animal fats (MAFF, 1997).

Polychlorinated diphenylethers (PCDEs)

Polychlorinated diphenyl ethers (PCDEs), which are also known as polychlorinated biphenylethers (PCBPEs) are usually associated with dioxins and furans as by-products in the production of chlorinated compounds, such as pesticides, wood preservatives, and other commercial products (Cramer et al., 1990). They are, for example, found as contaminants in technical grade pentachlorophenol (PCP).

Polychlorinated naphthalenes

The PCNs were predecessors to the PCBs, and were used in the same types of applications, and in limited amounts as a timber preservative. They have also been found as contaminants in PCB products. They are no longer made in Europe, but some usage may still occur (Swedish EPA, 1998). In 1997, British Telecom were reported to have significant stocks in the UK (ENDS 267, April 1999).

PCNs they have been found in Arctic fish and air, as well as in humans, birds, fish, water, air, and sediments in North America and Europe. Some are considered to have dioxin-like toxicity.

Polychlorinated terphenyls (PCTs)

Polychlorinated terphenyls are related to PCBs. They were used as plasticisers, hydraulic fluids and in investment casting waxes, and they had some usage in precision engineering and as flame retardants.

In the EU, usage of PCTs is now regulated by Council Directive 96/59/EC, and the commitment made at the September 1992 Ministerial Meeting of the Oslo and Paris Commission (PARCOM Decision 92/3) on the

phasing out of PCBs and hazardous PCB substitutes (see Explanatory Note to UK draft PCB regulations 15 February 1999). EU countries are therefore committed to phase out all PCBs and PCTs and to destroy all identifiable remaining stocks by the end of 1999 at the latest

These substances were used throughout Europe and probably world wide, although total usage in the UK is estimated to be in the region of tens of tonnes rather than hundreds of tonnes (Short, 1999). This should be compared to the 8,000 tonnes of PCBs which were still awaiting disposal in the UK in 1993 (DETR,1993). The PCTs are suspected of causing similar environmental damage as the PCBs (Swedish EPA).

Safrole

In 1983 in the USA, this was listed as an ingredient in over 100 over-the-counter drug formulations, generally for application on the skin but occasionally for oral administration. It has been listed as an animal carcinogen.

Styrene

Styrene is produced in vast quantities worldwide, but it does occur naturally in some foods such as fruits, vegetables, nuts, beverages, and meats. It is used extensively, for example, in polystyrene, rubber, plastic, insulation, pipes, car parts, food containers, and carpet backing. Inhaling high levels of styrene is most likely to cause effects on the nervous system, but there is a paucity of information on the health effects from swallowing styrene. The International Agency for Research on Cancer has determined that styrene is possibly carcinogenic to humans, as studies in animals that breathed or swallowed styrene suggested it was weakly carcinogenic.

Some years ago, Zlobina and co workers reported evidence of disruption of the menstrual cycle and the appearance of a hypermenstrual syndrome in occupationally exposed women (Brighton et al.,1979). More recently, Mutti and co-workers described neuroendocrine effects, including effects on prolactin levels, consistent with the hypothesis that styrene exposure reduces the dopaminergic modulation of pituitary secretion (Mutti et al.,1984).

However, a Japanese study on styrene trimers, dimers, and monomer has concluded no significant binding to the oestrogen or androgen receptor, and no inhibition of testosterone production in Leydig cells, and no oestrogen like alteration in the uterus and vagina of young adult female. This study on the effects of styrene compounds on the sex hormones, led them to conclude that these compounds do not have any endocrine disrupting effects (Nobuhara et al.,1998), but it should be noted that this study only related to the sex hormone disrupting properties of these compounds.

The toxicity of styrene was recently reviewed by the Working Group of the EU Scientific Committee for Food (MAFF, Food Surveillance Information Sheet, no 38), and they reported their intention to recommend to the Commission that there should be a ban on styrene in oven ware due to unacceptably high migration (Synoptic Document 4th September 1998).

Tetrachloroethylene

Tetrachloroethylene (or perchlorethylene □perc□) is a solvent which was used extensively in the dry cleaning industry and in the manufacture of paint remover. It may also be formed when water is chlorinated (NRA,1995). Tetrachloroethylene causes cancer in animals.

1,1,1-Trichloroethane

This is used as an industrial solvent and cleaning agent, with no natural sources (NRA,1995)

Trichloroethylene

This is widely used as a solvent in industry, and it is also used in anaesthetics. It has no natural sources (NRA,1995).

Toluene

Toluene is used in the manufacture of dyes, explosives, and other organic compounds. It is a solvent for paints, lacquer, and resins, and is also found in vehicle exhaust emissions.

Toxaphene

Also known as camphechlor, this mixture of chemicals is used as a pesticide. High doses of toxaphene can affect the nervous system, the kidneys, and the liver, while longer term exposure can affect the adrenals, the immune system and the developing foetus (see AMAP, 1997). Toxaphene is also a hormone disruptor which binds to the oestrogen receptor, and is listed as an animal carcinogen.

GLOSSARY OF TERMS AND ABBREVIATIONS

| | |
|-----------|---|
| ADBI | 1-(6-(1,1-dimethylethyl)-2,3-dihydro-1,1-dimethyl-1H-inden-4-yl)ethanone Trade names Celestolide, Crysolide |
| AHDI | 1-(2,3-dihydro-1,1,2,3,3,6-hexamethyl-1H-inden-5-yl)-ethanone Trade name Phantolide |
| AHTN | 1-(5,6,7,8-tetrahydro-3,5,5,6,8,8-hexamethyl-2-naphthalenyl)-ethanone Trade names Tonalide, Fixolide |
| ATII | 1-(2,3-dihydro-1,1,2,6-tetramethyl-3-(1-methyl-ethyl)-1H-inden-5-yl)-ethanone Trade name Traseolide |
| ATTN | 1-(3-ethyl-5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-ethanone Trade name Versalide |
| BBP | Butyl benzylphthalate |
| Bi-58 | o,o-dimethyl methylcarbomoyl-methyl-phosphorodithioate |
| Carbophos | succinic acid, mercapto-diethyl ester, S-ester with o,o-dimethyl phosphorodithioate |
| DBP | Di-n-butylphthalate |
| DDT | Dichlorodiphenyl trichloroethane or 1,1,1-trichloro-2,2'-bis(p-chlorophenyl) ethane |
| DDE | Dichlorodiphenyl dichloroethane - principal metabolite of DDT |
| DEHA | Diethylhexyl adipate |
| DEHP | Di (2-ethylhexyl) phthalate |
| dioxins | A generic term for polychlorinated dibenzo-p-dioxins (PCDDs) |
| DPMI | 1,2,3,4,5,6,7-hexahydro-1,1,2,3,3-pentamethyl-4H-inden-4-one Trade name Cashmeran |
| EDC | Endocrine Disrupting Chemical |
| HCB | Hexachlorobenzene |
| HCH | Isomers of hexachlorocyclohexane, (including lindane, γ HCH) |
| HHCB | 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta(g)-2-benzopyran Trade names Galaxolide, Abbalide, Pearlide |
| HMS | Homo-menthylsalicylate (a UV screen) |
| MBC | 3,4-methyl-benzylidene camphor (a UV screen) |
| Metaphos | Phosphorothioic acid, or o,o dimethyl o-(p-nitrophenyl) ester |
| OMC | Octyl-methoxy-cinnamic acid (a UV screen) |
| PAHs | Polyaromatic hydrocarbons |
| PBDEs | Polybrominated diphenyl ethers |
| PCBs | Polychlorinated biphenyls |
| PCNs | Polychlorinated naphthalenes |
| PCP | Pentachlorophenol |
| PCT | Polychlorinated terphenyls |
| Propanide | n-(3,4-dichlorophenyl) propanamide |
| Saturn | Carbamic acid, diethylthio-S-(p-chlorobenzyl) ester |
| TCDD | 2,3,7,8-tetrachlorodibenzo-p-dioxin |
| TCM-3 | Trichlorometaphos -3 or phosphorothioic acid, o-ethyl o-methyl o-(2,4,5-trichlorophenyl) ester |
| TDI | Tolerable Daily Intake is an estimate of the amount, expressed on a body weight basis, of a contaminant which can be ingested every day over a whole lifetime without appreciable health risk. |
| TEQ | Toxic Equivalents is a concept that has been developed to express the toxicity of a "dioxin-like" compound in terms of the equivalent amount of TCDD. It relies on evidence which suggests a common mechanism of action of dioxins and PCBs based on binding of these compounds to a specific cellular receptor, the Ah-receptor. The available toxicological and biological data for dioxins and PCBs is used to generate a set of weighting factors, called |

Toxic Equivalency Factors (TEFs) each of which expresses the toxicity of the "dioxin-like" compound in terms of the equivalent amount of TCDD. The TEQ is derived by multiplying the concentration of a compound by its TEF. The toxicity of any mixture, relative to TCDD is taken to be the sum of the TEQs for each of the compounds of interest. The approach has limitations due to a number of assumptions, not least that the effects of the components of a given mixture are additive (FSD, No 105,1997).

WHO World Health Organisation

WHO JMPR Inventory of International Programme on Chemical Safety and other WHO pesticide evaluations and summary of toxicological evaluations performed by the Joint Meeting on Pesticide Residues (JMPR). The document WHO/IPCS 98.1 lists TDIs and ADIs.

UNITS

mg = 10^{-3}

ug = 10^{-6}

ng = 10^{-9}

pg = 10^{-12}

mg/g milligrams per gram or parts per thousand

μg/g micrograms per gram or parts per million (ppm)

ng/g nanograms per gram or parts per thousand million or parts per billion (ppb)

pg/g picograms per gram or parts per million million or parts per trillion (ppt)

μg/kg micrograms per kilogram or parts per billion (ppb)