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RISK ASSESSMENT AND RISK MANAGEMENT OF DIOXINS AND PCBs IN FOOD

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This document contains an appendix (Appendix A) that was initially written based on the collected information, i.e. including references. Subsequently this information was used to write a summary covering the different aspects of dioxins and PCBs.

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Summary

In this report a brief overview is given concerning PCBs and dioxins in food. Background levels and the way PCBs and dioxins enter the environment are described. In the risk assessment part of the report an evaluation of toxicity is given, the way standards for dioxins and PCBs have been determined, which analysis methods are used as well as which levels of PCBs and dioxins have been measured in various food items.
Finally, in the risk management part of this report it is tried to make clear what measures have been taken to reduce the risks related to exposure to dioxin and PCB.

Samenvatting

In dit rapport wordt in het kort een overzicht gegeven van de stand van zaken op het gebied van PCBs en dioxines in voedsel. Achtergrondblootstelling en de manier waarop deze achtergrondblootstelling ontstaat wordt besproken. In de risicobeoordeling wordt een overzicht gegeven van de toxicologische effecten, de wijze waarop een norm voor PCBs en dioxines is afgeleid, welke meetmethoden gebruikt worden en welke concentraties van PCBs en dioxines in verschillende voedingsmiddelen voorkomen.
In het risico management deel wordt inzicht gegeven in de maatregelen die genomen zijn om de risico's ten gevolge van blootstelling aan PCBs en dioxines te verminderen.

Risk assessment and risk management of dioxins and PCBs in food

Introduction

1 Dioxins and PCBs are ubiquitously present in the environment and food as contaminants. The margin between estimated human intake and doses that are considered to be safe from a toxicological point of view is small. This urges the need to evaluate maximum permitted levels for these contaminants in food, air, soil, water and other products. This report is intended to review the information concerning PCBs and dioxins, in particular focused on contamination of food.

Background and identification of the contaminants

Definition of dioxins, furans

2 Dioxins is a general name for polychlorodibenzo-p-dioxins (PCDD) and polychlorodibenzofurans (PCDF). The group of dioxins consists of 210 congeners of which 17 are particular important for the assessment of toxicity.

Definition of PCBs

3 Polychlorobiphenyls (PCB) consist theoretically of 209 compounds which can be divided into 2 main classes: the coplanar PCBs having a dioxin-like structure and toxicity, and the non-planar PCBs. In commercial products, only 130 congeners are likely to occur. Of the 209 PCB congeners there are 3 non-ortho PCBs, 8 mono-ortho PCBs and 12 di-ortho PCBs with a coplanar structure resembling 2,3,7,8-TCDD. These compounds are all substituted at the two para positions and at least 2 meta positions (see appendix I)

Origin and degree of environmental contamination with doxins

4 Dioxins are not produced commercially and have no applications. They are formed during combustion processes in, for example, waste incinerators and as unwanted by-products of industrial processes. Evaporation from chlorophenol wood preservatives, like pentachlorophenol (PCP), emission by sinter industries, the use of 2,4,5-T (a pesticide) and Agent Orange (a defoliant used in the Vietnam war), and the bleaching of paper pulp in the paper industry also contribute to the environmental contamination.

5 Dioxins enter the environment mainly by emission to air. After transport through air, they deposit on soil, vegetation, and water. Deposition occurs near the source but also, due to large range transport by air, far away from the source. Dioxins reach livestock through contaminated water, air, soil and plants, used for animal feed. Dioxins accumulate in adipose tissue and in the fat of organs.

6 In 1990 in the Netherlands the main emission occurred to the air (ca. 600 g I-TEQ/year), whereas emissions to water (4 g I-TEQ/year) and soil (3 g I-TEQ/year) were of

less importance (TEQ or toxic equivalents will be explained in more detail in paragraph 31).

7 Background levels for soil in rural areas have been reported to be 2 to 5 ng I-TEQ/kg dry matter (d.m.), for sediment in lakes and rivers 10 ng I-TEQ/kg d.m., and for air 0.01 to 0.04 pg I-TEQ/m^3. The deposition of dioxins ranges from 2-25 ng I-TEQ/m^2/year. Locally, levels may exceed these background levels.

8 In Germany concentrations of dioxins measured in soil samples ranged between 3 and 112 ng I-TEQ/kg dry matter. Levels in air at urban sites have been reported to be 0.1 pg I-TEQ/m^3 and at industrial sites 2.3 pg I-TEQ/m^3.

9 Environmental background levels of dioxins in the USA and other West-European countries are comparable to Dutch and German levels.

Origin and degree of environmental contamination with PCBs

10 PCBs were produced commercially under various product names such as Aroclor, Clophen and Kanechlor. Various types of these commercial mixtures, consisting of both coplanar and non-planar PCBs, were produced and are identified by the percentage by weight of chlorine. For example Aroclor 1254 contains 54% of chlorine.

11 PCBs have been used in the past in both open and closed systems like transformers, capacitors, electric insulation and hydraulic fluids. PCBs entered the environment by leakage from these systems. Another relatively minor way of entering the environment is by combustion processes in which PCBs are formed.

12 Total PCB levels reported for air samples in Canada, Sweden, Germany, Japan and the USA range from 2 pg to 50 ng per m^3. In soil samples taken in the UK, the Netherlands, Japan and Germany, concentrations of 1 to 50 µg/kg and for surface water samples from rivers and lakes in Germany, The Netherlands and the USA levels of 1 to 500 ng/L were found. Due to the poor solubility of PCBs in water, these compounds tend to sediment in rivers and lakes, resulting in levels of 10.6 mg to 13,4 g per kg sediment. PCB levels in sewage sludge from several European countries and the USA have been reported to range from 0.1 to 9 mg/kg dry matter, with exceptional levels of up to 750 mg per kg.

13 PCBs reach livestock trough contaminated water, air, soil and plants ,used for animal feed. PCBs accumulate in adipose tissue and in the fat of organs.

Risk assessment

Toxicological evaluation dioxin

Mechanistic considerations

14 Most toxic effects are assumed to be mediated by binding of dioxins to the intracellular *Ah*-receptor. The complex of dioxin and *Ah*-receptor is transported to the DNA of the nucleus where the expression of a number of gene products is induced. Effects on thyroid and vitamin A status may be mediated differently.

Kinetics and metabolism

15 The oral route is the predominant uptake route for dioxins. In humans, the bioavailability of dioxins from food containing fat or oil is higher than 75%. Distribution is dose and congener dependent. Elimination rates are also dose and congener dependent. Metabolism of congeners with chlorine atoms at the positions 2, 3, 7, and 8 occurs at very low rates.

In man adipose tissue is the main storage site for dioxins. Elimination of dioxins is relatively slow in humans, as demonstrated by an estimated half-life for 2,3,7,8-TCDD of 7 years. In rats, the liver is the main storage site for dioxin. A relatively short half-life (20 days) for 2,3,7,8-TCDD has been determined, but these kinetic data have been determined at much higher doses than the human kinetic data. This makes a direct comparison difficult. Dioxins can enter the mammalian fetus via the placenta.

Toxicity

16 Dioxins produce a variety of effects. These effects are species dependent, as is e.g. demonstrated by the acute toxicity; LD_{50}s vary from 0.6 µg to 5051 µg/kg bw. In practice, humans are exposed to much lower doses. Therefore, emphasis is placed on effects occurring at low doses. The Lowest Observed Adverse Effect Level (LOAEL) for TCDD in a chronic study was 0.01 µg/kg bw/day for liver tumours in female rats. The No observed Adverse Effect Level (NOAEL) based on the same study is 0.001 µg/kg bw/day. Teratogenic effects occur in mice at 0.1 µg/kg bw/day (LOAEL). The LOAEL for female reproduction toxicity as determined in a 3-generation study in rats is 0.01 µg/kg bw/day, with a NOAEL of 0.001 µg/kg bw/day. When pregnant rats were exposed to a single dose of TCDD (0.064 µg/kg bw), changes in sexual behaviour in the male offspring were observed.

Epidemiological data from human exposure to dioxins

17 Chloracne is the only effect that correlates consistently with TCDD exposure in humans. Weak associations have been reported between dioxin exposure and soft tissue carcinomas and lung cancer. Such associations have become apparent after a latency period of more than 5 years in accidentally exposed people in Seveso or after more than 20 years in occupationally exposed people. In Seveso serum levels ranged from 1770 to 10400 ppt near the accident site, with 56000 ppt as an exceptional high level. In a lower exposed region serum levels ranged from 74 to 526 ppt. However, data on exposure are scarce or unreliable. Therefore, no reliable dose-response relationships have been established. In these epidemiological studies co-exposure could not be excluded. Thus, induced effects cannot exclusively be attributed to dioxin exposure.

Determination of a TDI for 2,3,7,8-TCDD

18 In European countries, such as The Netherlands, Canada, The United Kingdom, Switzerland and Germany, TDIs for 2,3,7,8-TCDD have been established ranging from 1 to 10 pg/kg bw/day. Since this compound does not appear to be a genotoxic agent, a threshold was assumed.

19 The WHO (1990) toxicity standard for TCDD is 10 pg/kg bw/day based on liver tumours and reproductive effects. The premise for this toxicity standard is that a threshold dose exists below which no toxic effects are induced. For the determination of the TDI a pharmacokinetic model was applied to convert the NOAEL in experimental animals into a NOAEL in humans, using an internal dose concept. The resulting dose is divided by a factor

of 10 to compensate for uncertainties that are not taken into account by the pharmacokinetic model.

20 In the USA several organisations have calculated safe doses applying the Linear Multistage Model to liver tumour data observed in female rats after chronic exposure to 2,3,7,8-TCDD. These organisations regard TCDD as a complete carcinogen, which implies that no threshold exists. Based on this principle, the US-EPA has calculated a safe dose of 0.006 pg/kg bw/day, corresponding to a lifetime tumour risk of 10^{-6}.

Toxicological evaluation of PCBs

Mechanistic considerations

21 For coplanar PCBs a comparable toxic mechanism as for dioxin is assumed, based on structural similarities. The binding of coplanar PCBs to the *Ah*-receptor induces toxicity. The non-planar PCBs induce toxicity differently. The mechanism is not yet clear. In the case of certain PCBs, there are indications that hydroxy metabolites have an effect on transport proteins for vitamin A and thyroid hormones in the plasma. As such the *Ah*-receptor appears not to be involved.

Kinetics and metabolism

22 The oral route is the predominant uptake route in humans. The bioavailability of PCBs is higher than 75%. Distribution of PCBs depends on the congener. Elimination rates are low and are also congener dependent. Preferential elimination of some congeners containing 3 or 4 ortho substituents and preferential retention of congeners with 1 or 2 ortho substituents have been reported. Slow elimination rates are related to low metabolic rates. PCBs are stored in adipose tissue and in the liver. Transfer of PCBs to the fetus occurs in mammals.

Toxicity

23 PCB mixtures can induce cancer depending on the congener composition. Thusfar, rhesus monkeys are the most sensitive animal species for the effects of PCBs. The following experiments concern exposure of Rhesus monkeys to PCBs. Immunotoxicity is reported after chronic exposure to 5 µg/kg bw/day Aroclor 1254. The lowest dose tested of Aroclor 1248 was 90 µg/kg bw/day (chronic exposure). At this dose increased mortality rate, growth retardation, dermal effects, and embryotoxic effects were observed. In neonatal monkeys the same effects were induced and, in addition, neurological and immunological effects. Aroclor 1242 induced similar effects. The NOAEL for Aroclor 1242 is 40 µg/kg bw/day.

24 It must be noted that in most toxicological experiments commercial mixtures or individual congeners have been used to determine the NOAEL. Due to the selective metabolism and excretion of individual PCBs by food-producing animals, humans are exposed to mixtures with different congener composition. It is likely that these mixtures will have a different toxic potency and as such another NOAEL.

25 *In utero* and lactational exposure to Aroclors at a maternal dose of 6 µg/kg bw/day caused behavioural effects in neonates and infants of Rhesus monkeys. In accidentally exposed humans, comparable effects were reported at estimated doses ranging from 0.014 to 0.9 µg/kg bw/day. This dose range is a result of rough calculation of the consumption pattern of the exposed women and the concentrations of PCBs in the food products. The non-planar

dioxin-like PCBs also appear to be involved in these behavioural effects. At present it is thought that prenatal exposure has more impact than postnatal exposure by breastmilk, due to a specific sensitive period in the development of the fetus.

Epidemiological data from human exposure to PCBs

26 An increase in tumour incidence was observed in populations in Japan and Taiwan that were accidentally exposed to cooking oil contaminated with PCBs. In Japan the mean daily intake for PCBs was 157 µg/kg bw/day. Serum levels after the accident were not available. In Taiwan no daily intake estimate was available, but the total was estimated to be 0.7 to 1.8 g. Serum levels of PCBs ranged from 3 to 1156 µg/l with 44% of 613 patients had levels of 51-100 µg/l, and 28 % had levels over 100 µg/l. Co-exposure to PCDF, present in the cooking oil occurred also. Therefore, carcinogenic activity of PCBs could not conclusively be established. Besides no dose-response relationships could be determined because exposure data were scarce, and the number of deaths for pathological research to find tumours was small.

27 The earliest symptoms of high PCB exposure are dermal and ocular effects. These effects are reversible. Respiratory complaints, however, are persistent for some years. Fetal exposure to PCBs is associated with cognitive deficits in infants and young children. Since co-exposure could not be excluded, these effects could have been induced by compounds other than PCBs. Whether these effects are reversible is not clear.

Determination of a TDI for PCBs

28 No TDI for PCBs has been established yet. However a NOAEL for Aroclor 1242 is determined at 40 µg/kg bw/day in Rhesus monkeys. According to JECFA this dose can be considered as some indication for a safe dose. Since the coplanar PCBs are assumed to induce toxicity by a similar pathway as dioxins, the TEQ principle (see 31) can be used to determine the toxicity. The non-planar PCBs are not taken into account in the TEQ calculations. For these PCBs toxicity must be determined differently.

Comparison of toxicological effect induced by dioxin and PCB

29 Some effects induced by dioxins or coplanar PCBs are rather similar. The coplanar PCBs probably induce the same effects as dioxins, since these compounds also bind to the *Ah*-receptor. Neurotoxic effects, liver toxicity, epithelial effects, reproductive effects, carcinogenicity and immunotoxic effects have been reported after exposure to both dioxins and PCBs. Table 1 presents the potency of dioxins and coplanar PCBs relative to 2,3,7,8-TCDD. The reproductive effects include reduced fertility, decreased gestational period, and endometriosis.

30 Non-planar, lowly chlorinated PCBs accumulate in brain tissue, whereas dioxins and coplanar PCBs do not. PCB congeners and their metabolites may decrease plasma levels of thyroid hormones and vitamin A. Such decreases may modulate tumour promotion, developmental and behavioural changes. The *Ah*-receptor is assumed not to be involved in these processes.

Application of the TEQ-concept

31 In order to deal with the fact that environmental and biological samples in general contain complex mixtures of the different dioxins (PCDDs and PCDFs) and PCBs, the concept of toxic equivalency factors (TEFs) has been developed for risk assessment. Basically, it is assumed that the individual effects of all dioxins and PCBs acting via the *Ah*-receptor are additive. The affinity for the *Ah*-receptor of different congeners is different. The toxic potency of the various congeners is related to the receptor affinity and expressed as toxic equivalence factors (TEFs). TEFs are used to indicate the toxicity related to the most toxic congener: 2,3,7,8-TCDD.

32 Interim TEF values have been determined for individual congeners, although in practice, TEF values are depending considerably on the experimental conditions used. More weight has been given to results from semi-chronic and chronic studies with small laboratory animals like rats, mice or guinea pigs, than to those from short-term toxicity studies or *in vitro* bioassays.

33 Results from toxicity studies with single compounds and complex mixtures of PCDDs and PCDFs, support the validity of the TEF-concept for these compounds. Application of the TEFs on complex mixtures of non-, mono-, and di-ortho PCBs has been shown to overestimate the toxic potency as compared to the actually observed toxicity. In some cases antagonism or potentiation has been observed. Based on currently available information it is assumed that these kind of interactions only occur at high dose-levels and as such do not interfere with the application of the TEQ-concept at low concentrations.

34 Since only toxic effects mediated by the *Ah*-receptor are included, the TEQ-concept is not applicable to compounds, whose toxicity is not mediated via this receptor. This appears to be the case for certain non-planar PCBs.

35 Using the TEFs, analytical results are transformed into toxic equivalents (TEQ) using the formula: $\Sigma([\text{Congener}]\text{xTEF})_{\text{PCDD/F or PCB}}=\text{TEQ}$. For the interpretation of analytical data it is important to realize that different TEFs have been used by different countries (Table 1), and that only recently more general TEFs have been proposed. For dioxins the I-TEQ (International-TEQ) has been established by a working group of CCMS/NATO in 1988. The Netherlands, Canada, The United Kingdom, The United States of America, Germany and Scandinavian countries officially adopted the I-TEFs.

36 I-TEF values for dioxins range from 1 for 2,3,7,8-TCDD to 0.001 for octaCDD. PCDD and PCDF congeners without chlorine atoms at the 2, 3, 7 and 8 positions of the molecule have been assigned a TEF value of 0.

37 In a recent WHO-ECEH and IPCS consultation, WHO-TEF values have been proposed for non-, mono- and di-ortho PCBs, capable of binding to the *Ah*-receptor. TEF values range from 0.1 for 3,3',4,4',5-pentaCB to 0.00001 for 2,3',4,4',5,5'-hexaCB and 2,2',3,4,4',5,5'-heptaCB. Despite the relatively low TEF values for the mono-ortho PCBs it has been shown that these compounds might significantly contribute to the total TEQ value of e.g. fish samples because of their much higher concentrations. If WHO TEF values are used to calculate TEQ, these TEQs are called WHO-TEQ.

Methods for the analysis of dioxins and PCBs

GC/MS methods

38 Since concentrations of dioxins and coplanar PCBs in biological samples are in general in the low pg/g range, highly sensitive and specific methods are required. In the case of biological samples, the first step is a quantitative extraction of the fat, in the case of environmental samples, an exclusion with acid. After extraction an extensive clean up using successively a number of different procedures, is necessary in order to prepare sufficiently concentrated and cleaned extracts for final quantification with gas chromatography-mass spectrometry. In order to allow correction for the generally observed low recoveries, ^{13}C labelled dioxins or coplanar PCBs are added to the samples prior to extraction.

39 In two recent ring-tests, coefficients of variation for analysis of dioxins in milk powders have been shown to range from 10 to 20% both within and between laboratories. (Similar variations have been observed for coplanar PCBs at the RIKILT).

40 High resolution gas chromatography-mass spectrometry (HRGC-MS) is at present the best suited technique combining sufficient sensitivity and specifity. For environmental samples in principle both low resolution and high resolution mass spectrometry are applicable although high resolution is in favour due to higher sensitivity and better selectivity. In general laboratories active in the field of dioxin analysis perform a number of quality controls e.g. recovery of internal standard, accuracy of spiked samples and blanks. In general recoveries of the internal standards are in the range of 25% to 125%. Non planar PCBs, occurring in relatively high levels, are normally analyzed using gas chromatography with electron capture detection.

Bioassays

41 Bioassays using both mammalian cancer cell lines and freshly isolated cells have been developed. In general, these assays are based on the induction of certain cytochrome P450 enzymes (1A) as measured by an increased conversion of the substrate ethoxyresorufin into resorufin (EROD activity). Other end-points are increased CYP 1A mRNA levels, porphyria and keratinization of cells. The sensitivity of the current assays may be as low as 0.16 pg per assay. New bioassays, using recombinant DNA techniques are under development and aim at a further improvement of both the sensitivity and selectivity of the assay.

42 Major advantages of these assays are reduction in costs, the time required and the fact that in the ideal case the total TEQ-value of a sample can be estimated, without identification of all the single compounds contributing to this TEQ-value. This may include possible synergistic or antagonistic effects.

Exposure assessment

Levels of dioxins and PCBs in human food

43 Levels of dioxins in food of plant origin measured in The Netherlands have been reported to be 0.006 to 0.03 for vegetable oils and fats, 0.08-0.2 for curly kale and 0.34 pg I-TEQ/g fat for cereals. In the Netherlands, the use of vegetable oils in processed foods does not contribute significantly to the total dioxin intake.

44 Levels of coplanar PCBs have been reported to be 0.015 to 0.03 pg WHO-TEQ/g fat for vegetable oils and fats and 1 pg WHO-TEQ/g fat for cereals (The Netherlands). Mean total PCB levels measured in Germany have been reported to be 7.2 ng/g fat in vegetable oil and 6.7 ng/g fresh weight in cereals (Table 3).

45 Levels of dioxins measured in food of animal origin are 0.7-2.5 pg I-TEQ/g fat in dairy products (milk, butter, cheese), 0.4-1.8 pg I-TEQ/g fat in beef, pork and chicken meat. Concentrations in the liver appear to be substantially higher than those in meat (2 to 35-fold), varying with the animal species. In fish 2.4 to 48.7 pg I-TEQ/g fat have been found in Germany and the Netherlands and 0.02 to 1.42 pg I-TEQ/g wet weight in the UK and the USA.

46 Higher levels have been measured in the Netherlands in horse meat and game, in beef of animals pasturing on 2,4,5-T treated rangelands in the USA (up to 66 pg I-TEQ/g fat) or in dairy products and meat of cows grazing in the vicinity of waste incinerators (up to 13 pg/g milk fat and 18 pg/g fat in meat).

47 In the Netherlands the intake of dioxins from animal fat used for manufacturing processed foods is estimated to be 27% of total intake (not including butter and cheese).

48 Total PCB levels measured in food of animal origin were 10-200 ng/g fat in dairy products (Germany, Japan, the Netherlands, the United Kingdom, the USA), and 7-500 ng/g fat in meat products (Italy, Germany, the Netherlands, Sweden). In fish from the North Sea and the North Atlantic levels of 10 to 200 ng/g fresh weight have been measured, in fish from the Baltic Sea levels of 340 ng/g fresh weight. Certain fish species (eel) or fish products (fish liver and fish oil) contain much higher levels of PCBs, even up to 10 mg/kg. Coplanar PCBs have been determined in Dutch dairy products to be around 2 pg WHO-TEQ/g fat (Table 3).

49 In a recent study in the Netherlands dioxin and PCB levels were measured in milk samples from about 200 women. Mean levels were 31 pg I-TEQ and 35 pg WHO-TEQ PCBs per gram fat for respectively dioxins and PCBs. In the paper reporting about the WHO-meeting on PCB TEFs, the data from one Swedish sample are used to show the impact of the new TEF-values. In this sample, dioxin and PCB levels are respectively 20.6 and 21 pg I-TEQ cq. WHO-TEQ/g fat. In the USA, mean levels of 16 pg I-TEQ dioxins/g fat were reported (42 women), in Germany 32 pg I-TEQ dioxins/g fat (728 women). Maximum and minimum levels differed from these mean concentrations by a factor of 2 to 5.

50 In general it can be concluded that concentrations of dioxins and PCBs in food for human consumption are highest in food products of animal origin.

Intake by humans

51 The daily human exposure to dioxins and PCBs has been estimated in a number of industrialized countries, like Sweden, the USA, the Netherlands, Germany, Canada, Norway, the UK and Italy. In the Netherlands, the total dioxin intake was estimated by combining dioxin levels in food with food consumption data obtained from a survey with about 6000 persons. This pattern and those used for estimating the dioxin intake in some other countries are depicted in Table 4.

52 In general it can be concluded that more than 90% of the human exposure to dioxins and PCBs occurs through the diet, with food of animal origin being the predominant source. The average daily exposure for adults to dioxins from food varies from 1 to 2 pg I-TEQ/kg body weight. In Italy, a range of 4-7.5 pg EPA-TEQ/kg body weight has been reported.

53 For breast fed infants, the daily intake of dioxins has been estimated to range from 100 to 200 pg I-TEQ/kg bw, assuming a body weight of 4.5 kg, a milk consumption of 800 ml/day, a milk fat content of 3.5% and average dioxin concentrations of 16-31 pg I-TEQ/g fat. As such the daily intake exceeds the tolerable daily intake of 10 pg I-TEQ/kg bw. However, the breast-feeding period covers a relatively short period in life, in contrast to the life-time exposure on which the TDI is based. JECFA, Dutch Health Council and WHO have evaluated PCBs and breastmilk and recommend the use of breastmilk. Further information is needed to evaluate the consequences of this high exposure.

54 Since levels in TEQ of coplanar PCBs are similar to those of dioxins (35 pg WHO-TEQ/g fat), intake of these compounds may be in the same order of magnitude. The intake of total PCBs by breast-fed infants in EC countries has been estimated to range from 3 to 11 µg/kg bw per day.

55 Other sources and pathways, like air, soil, drinking-water and non-food, are of minor importance. Estimates of the daily intake of dioxins from these sources are 0.04-0.06 pg I-TEQ/kg bw from air, 0.01 pg I-TEQ/kg bw from soil, less than 0.01 to 0.05 pg I-TEQ/kg bw from drinking water and 0.15 pg I-TEQ/kg bw from packaging.

56 For the Dutch population the intake of total PCBs through inhalation has been estimated to be about 36 ng/day. Levels of PCBs in drinking water range from 0.1 to 0.5 ng/l. At a daily water consumption of 2 L for adults, the PCB intake by drinking water would range from 0.2 to 1.0 ng per day and as such contribute only slightly to the total human exposure.

Risk management

Population at risk

57 A relatively high intake has been reported for the fetus and for breast-fed infants. Toxic effects due to fetal exposure to dioxins and PCBs have been reported. Since these effects occur at low doses, fetuses are considered as a group at risk. In certain areas dioxin and PCB concentrations in fish are relatively high. Lake Michigan is e.g. contaminated with PCBs. If populations in these area are major fish consumers, these populations might be at risk.

Residue limits in food

Dioxins

58 Based on the TDI and the food consumption patterns, residue limits can be set for certain food products. In the Netherlands, a residue limit for dioxins in dairy products has been set at 6 pg I-TEQ/g fat. Initially this limit was established by combining an average food consumption pattern with the former TDI of 4 pg I-TEQ per kg bw per day. In this standard,

all 17 dioxin congeners are taken into account via the TEQ-concept. It was subsequently estimated that this residue limit guarantees that less than 1% of the Dutch population will exceed the new TDI of 10 pg/kg bw/day. In Germany and the UK level of respectively 5 pg I-TEQ/g milk fat and 17.5 pg I-TEQ/g milk fat (0.7 ng I-TEQ/kg whole milk) are used as action levels, without legal implementation

PCBs

59 The maximum levels of total PCBs in food products are based on a daily consumption of 0.5 to 1 g animal fat per kg bw, a NOAEL for monkeys of 40 µg/kg bw/day, divided by a factor of 100 because of uncertainties with respect to human toxicity, and the concentration of PCBs on a fat basis. Thus the maximum acceptable level of total PCB in food will range from 0.5 to 1 mg/kg animal fat.

Policy

Dioxins

60 Reduction of emission by waste incinerators is the general policy measure in various countries. In The Netherlands at the first of january 1995 all municipal waste incinerators (MWI) must meet the legal emission standard of 0.1 ng I-TEQ/m^3. This standard is also used in Germany. Ban of the use of pentachlorophenol and measures concerning the bleaching of paper are other important instruments to reduce the exposure. Monitoring programs exist to check and control the exposure. In The Netherlands a food quality standard exists for dioxins in cow's milk, which is 6 pg I-TEQ/g milk fat.

PCBs

62 The most important regulatory measure has been the OECD ban of the use of PCBs in open systems in the early 1970s and in new equipment in the early 1980s. PCB exposure monitoring programs exist in several countries. Some countries have established maximum levels for PCB in food items. Table 2 presents these levels. Data on PCB levels in food in other countries were not available.

Policy Costs

Dioxins

61 To meet the new emission standards, waste incinerator companies in The Netherlands had to built new installations. The costs for these installations vary between 65 and 90 guilders per ton of waste. The new installations produce far less dioxins. For example the MWI in the Lickebaert area was adjusted to reduce the dioxin emission after dioxin levels exceeded the milk standard of 6 pg I-TEQ/g milk fat in 1989. In 1994 the dioxin concentration in cow's milk have decreased to less than 6 pg I-TEQ/g milk fat.
It is estimated that in the year 2000 the emission of dioxins trough MWIs to air will have decreased from 400 g I-TEQ/year (1991) to 2-4 g I-TEQ/year. It is estimated that in the year 2000 the total emission to air will have decreased from 600 g I-TEQ/year to 125 g I-TEQ/year. The Dutch government payed 17.5 million guilders as a financial compensation to farmers who had to destroy milk with dioxin levels over 6 pg I-TEQ/g milk fat.

PCBs

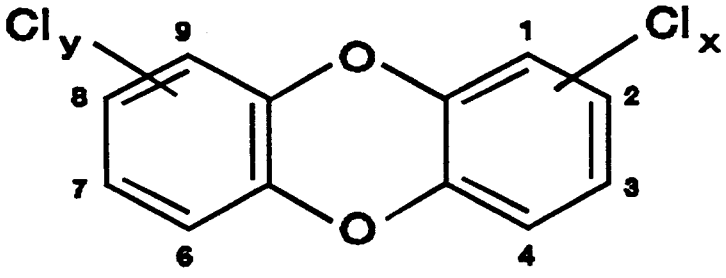
63 Since the OECD ban of PCBs in open systems and new equipment, the PCB levels in the environment have decreased in The Netherlands. Also in breast milk of Dutch women PCB levels have decreased. In Scandinavian countries a similar trend was reported, i.e. a decrease of PCBs in blood and fat. In 1980 the Dutch government has compensated 47 million guilders for the removal or destruction of transformers and capacitors. Other costs concerning PCB policy were not available.

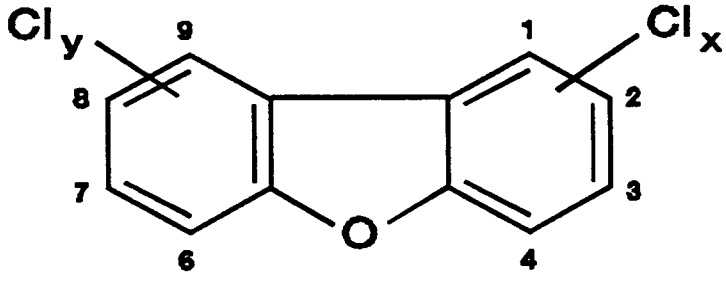
64 For dioxins different policies exist in various countries. Some countries have established maximum levels for food products to protect public health, while others have not. It can be imagined that trade barriers arise in such a case; for example some countries might restrict the import of milk when the toxicity standard in the export country is much higher. Information on this item, however, is not available.

Policy concerning other environmental pollutants

65 The assessment approach concerning dioxins and PCBs deviates from that for other environmental contaminants. For example the TEQ principle is not applied to compounds other than dioxins, and certain PCBs. The pharmacokinetic approach to determine a TDI is rarely applied to other contaminants. In general, the NOAEL is divided by a safety factor which usually is 100, resulting in a TDI.

Appendix I
General structures of dioxins (PCDDs and PCDFs) and PCBs.





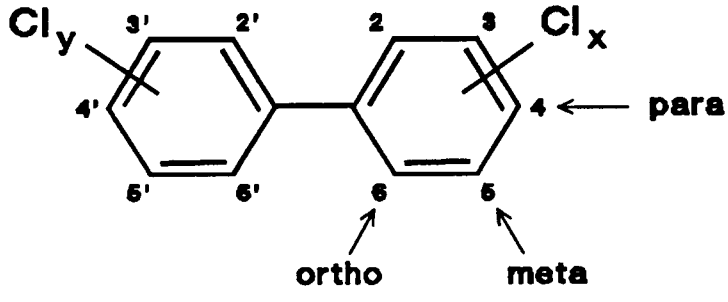


Table 1 Overview of various TEF values

Congener	IUPAC number	FHO (BGA) 1984	Nordic 1989	Safe	EPA*	i-TEF	range	
							in vivo	in vitro
2,3,7,8-tetraCDD		1.0	1.0	1.0	1.0	1.0		
1,2,3,7,8-pentaCDD		**0.1**	0.5	0.5	0.5	0.5	0.053-0.59	0.07-0.64
1,2,3,6,7,8-hexaCDD		0.1	0.1	0.1	**0.04**	0.1	0.015-0.16	0.005-0.5
1,2,3,7,8,9-hexaCDD		0.1	0.1	0.1	**0.04**	0.1	0.016-0.14	0.009
1,2,3,4,7,8-hexaCDD		0.1	0.1	0.1	**0.04**	0.1	0.013-0.24	0.05-0.13
1,2,3,4,6,7,8-heptaCDD		**0.001**	0.01	0.01	**0.001**	0.01	0.0076	0.003
OctaCDD		0.001	0.001	0.001	**0.0**	0.001	>0.0013	0.0006
2,3,7,8-tetraCDF		0.1	0.1	0.1	0.1	0.1	0.016-0.17	0.006-0.43
2,3,4,7,8-pentaCDF		**0.1**	0.5	0.5	**0.1**	0.5	0.12-0.8	0.11-0.67
1,2,3,7,8-pentaCDF		**0.1**	**0.01**	**0.1**	**0.1**	0.05	0.018-0.9	0.003-0.13
1,2,3,4,7,8-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	0.038-0.18	0.013-0.2
2,3,4,6,7,8-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	0.017-0.097	0.015-0.1
1,2,3,6,7,8-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	--	0.037-0.048
1,2,3,7,8,9-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	--	--
1,2,3,4,6,7,8-heptaCDF		0.01	0.01	0.1	**0.001**	0.01	0.22	--
1,2,3,4,7,8,9-heptaCDF		0.01	0.01	**0.1**	**0.001**	0.01	0.20	--
OctaCDF		0.001	0.001	0.001	**0.0**	0.001	--	--
3,3',4,4',5-pentaCB	126		0.1	0.1		0.1		
3,3',4,4',5,5'-hexaCB	169		0.01	**0.05**		0.01		
3,3',4,4'-tetraCB	77		0.0005	**0.01**		0.0005		
2,3,4,4',5-pentaCB	114		0.0005	**0.0002**		0.0005		
2,3,3',4,4',5-hexaCB	156		**0.001**	**0.0004**		0.0005		
2,3,3',4,4',5'-hexaCB	157		**0.001**	**0.0003**		0.0005		
2,3,3',4,4'-pentaCB	105		0.0001	**0.001**		0.0001		
2,3',4,4',5-pentaCB	118		0.0001	0.0001		0.0001		
2',3,4,4',5-pentaCB	123		0.0001	**0.00005**		0.0001		
2',3,3',4,4',5,5'-heptaCB	189					0.0001		
2,2',3,3',4,4',5-heptaCB	170					0.0001		
2,3',4,4',5,5'-hexaCB	167					0.00001		
2,2',3,4,4',5,5'-heptaCB	180					0.00001		

* Until 1989 EPA used these TEFs including TEFS for non-2,3,7,8 substituted PCDDs and PCDFs (other tetraCDDs 0.01, other pentaCDDs 0.005, other hexaCDDs 0.0004, other heptaCDDs 0.00001, other tetraCDFs 0.001, other pentaCDFs 0.001, other hexaCDFs 0.0001 and other heptaCDFs 0.00001).

** Figures printed in bold are different from the I-TEFs and WHO-TEFs for dioxins and PCBs respectively.

Table 2 PCBs levels that are permitted in food items in Sweden, The Netherlands, Canada and Finland

Sweden (CX/FAC 91/Sweden 5)
Maximum Permitted Levels for PCBs in Food on fat basis

Meat	0.2	mg/kg
Milk	0.05	mg/kg
Butter and Cheese	0.1	mg/kg
Eggs	0.1	mg/kg
Fishery Products	2.0	mg/kg
Liver of cattle	2.0	mg/kg
Liver of pigs	2.0	mg/kg
Fish liver	5.0	mg/kg
Salmon	5.0	mg/kg

The Netherlands
Dutch Guideline Levels for PCBs in food on fat basis
March 91 Codex (CX/FAC 90/20)

Milk and Dairy products	0.5	mg/kg
Meat and Meat products	1	mg/kg
Poultry meat	1	mg/kg
Eggs	1	mg/kg
Freshwater fish	2	mg/kg
Fish liver, fish oil	5	mg/kg (total)
Other fishery products	1	mg/kg (total)
Finished animal feed	0.05	mg/kg (total)

Finland (CX/FAC 90/20)
Finnish regulations for maximum PCB levels

Fish and fish preparations (except fish liver)	2.0	mg/kg
PCB 28	0.6	mg/kg
PCB 52	0.1	mg/kg
PCB 101	0.2	mg/kg
PCB 118	0.2	mg/kg
PCB 138	0.2	mg/kg
PCB 153	0.2	mg/kg
PCB 180	0.2	mg/kg
Other PCBs	0.6	mg/kg

Canada (CX/FAC 94/23)
Guidelines for PCB in foods in Canada

Meat-Beef-fat basis	0.2	ppm
Eggs-whole egg less shell	0.1	ppm
Poultry-fat basis	0.5	ppm
Fish-edible portion	2.0	ppm

Table 3 Dioxin and PCBs in various food items

Food item	Dioxin range/level pg I-TEQ/g fat	PCBs range/level pg WHO-TEQ/g fat	Total PCB ng/g fat
Plant origin			
vegetable oil/fat	0.006-0.03	0.015-0.03	7.2
curly kale	0.08- 0.2*		
cereals	0.34	1	6.7^
Animal origin			
dairy products	0.2-2.5	2	10-200
milk			
butter			
cheese			
meat	0.4-1.8		20-500
beef			
fat			
pork			
chicken			
Fish products	2.4-48.7		10-200^
eel			< 10 #
Human products			
milk	16-31	16-35	

* pg I-TEQ/g fresh weight
^ ng/g fresh weight
# mg/kg

Table 4 Daily Human intake

food item	NL		FRG		Canada	USA
	total (g)	fat (g)	total (g)	fat (g)	total (g)	total (g)
dairy	370	10.0	184	18.0	444	266
cheese	29	8.7	33	5.2		
eggs	16	1.6			29	25
meat	116	21.2	112	28.6	95	90
fish	8	0.8	15	1.8		18
vegetable oils	48	33.5	23	19.0		
Dioxin intake	157 pg I-TEQ/day		85 pg FHO-TEQ/day		92 pg I-TEQ/day	100 pg I-TEQ/day

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Risk assessment and risk management of dioxins and PCBs in food and food production

1 Background and identification of the contaminants

1.1 Definition of dioxins

Dioxins is a general name for polychlorodibenzo-p-dioxins (PCDD) and polychlorodibenzofurans (PCDF). The group of dioxins consists of 210 congeners of which 17 are important for the assessment of toxicity.

1.2 Definition of PCBs

The polychlorobiphenyls (PCB) consist theoretically of 209 compounds which can be divided into 2 main classes: the coplanar PCBs (non- and mono-orthochloro) having a dioxin-like toxicity and the non-planar PCBs. In commercial mixtures, however, only about 130 congeners are present consisting of coplanar PCBs as well as non planar PCBs (Safe, 1990)

Of the 209 PCB-congeners, there are 3 non-ortho PCBs, 8 mono-ortho PCBs and 12 di-ortho PCBs with a coplanar structure resembling 2,3,7,8-TCDD. These compounds are all substituted at both para positions and at least 2 meta positions (see Fig I).

1.3 Origin and degree of environmental contamination with dioxins

Dioxins are not produced commercially and have no applications. They are formed during combustion processes and as unwanted by-products of industrial processes. Dioxin sources are Municipal Waste Incinerators (MWI), Hospital Waste Incinerators (HWI), and Chemical Waste Incinerators (CWI). In The Netherlands the main source (2/3 of the total emission into air) are the Municipal Waste Incinerators (MWI).

Dioxins enter the environment by evaporation from chlorophenol based wood preservatives sinter industry, metal reclaiming industry, paper pulp industry in bleaching processes, the production of pesticides like 2,4,5-T, the use of Agent Orange (a defoliant) during the Vietnam war also have contributed to contamination of the environment with dioxins.

Dioxins enter the environment mainly by emission to air. After emission to the air, dioxins deposit finally on soil, vegetation, and in water. Since dioxins are predominantly emitted to air, deposition can occur near its source or, due to transport by air, away from its source.

Dioxins reach livestock through contaminated air, water, soil and vegetables and then accumulate in adipose tissue.

In 1990 in The Netherlands the main emission was to the air (ca. 600 g I-TEQ/year), whereas emissions to water (4 g I-TEQ/year) and soil (3 g I-TEQ/year) were less important (Liem *et al.*, 1993). TEQ (=toxic equivalents) are used to indicate the toxicity of a dioxin mixture, related to the most toxic congener: 2,3,7,8-TCDD; 1 g TEQ means that the mixture is as toxic as 1 g 2,3,7,8-TCDD. (The TEQ-principle is explained in section 3.4)

Background levels for soil in rural areas have been reported to be 2-5 ng I-TEQ/kg dry matter, for sediment in water 10 ng I-TEQ/kg d.m., for air the background ranges from 0.01-0.04 pg I-TEQ/m^3 and the deposition of dioxins ranges from 2-25 ng I-TEQ/m^2/year. Locally, levels may exceed these background levels (Liem *et al.*, 1993).

In Germany concentrations of dioxin in soil samples from forest, grassland and plowland

were 112, 30, and 3 pg I-TEQ/g dry matter, respectively (Rotard, 1991). Mean concentrations of dioxin at rural and industrial sites are 6 and 251 pg I-TEQ/g dry matter, respectively (Rappe and Kjeller, 1987).

Environmental background levels of dioxins in other western countries are comparable to the Dutch and German background levels.

1.4 Origin and degree of environmental contamination with PCBs

PCBs were produced commercially under various product names such as Aroclor, Clophen and Kanechlor. Various types of these mixtures, consisting of both coplanar and non-planar PCBs, were produced and were indicated by their percentage of chlorine. For example Aroclor 1254 contains 54% of chlorine.

PCBs have been used in the past in both open and closed systems like capacitors, transformers, electric insulation and hydraulic fluids. PCBs entered the environment by leakage from these systems and from waste disposal. Another relatively minor way of entering the environment is by combustion processes in which PCBs are formed (CCRX, 1991). Air levels range from 0.002 to 15 ng /m^3 (Rappe and Kjeller, 1987).

PCBs reach livestock like dioxins and they also accumulate in adipose tissue.

2 Risk assessment

2.1 Toxicological evaluation dioxin

2.1.1 Mechanistic considerations

2,3,7,8-TCDD (TCDD) is the most studied and most toxic congener of the dioxin family. Toxicity of other congeners of dioxins is expressed in TCDD equivalents according to the Toxicity Equivalence Factor (TEF) concept (see paragraph 3.4). 2,3,7,8-TCDD is assumed to cause toxicity by binding to the intracellular *Ah*-receptor (*A*ryl *h*ydrocarbon receptor) in experimental animals as well as in humans. The *Ah*-TCDD complex is translocated into the nucleus and stimulates among others the formation of the cytochrome P450 1A family which is considered the most sensitive effect (Banbury meeting, 1990). Most other toxic effects induced by 2,3,7,8-TCDD are assumed also to be mediated by the *Ah*-receptor. It is suggested, however, that effects of TCDD on thyroid hormones and vitamin A are not necessarily receptor mediated (Ahlborg *et al.*, 1992b). Furans are not discussed separately because the toxic mechanism and toxic effects are comparable with the toxic mechanism of PCDDs.

2.1.2 Kinetics and metabolism

The oral route is the predominant uptake route. The absorption after oral uptake of mixtures of dioxins is matrix-dependent. The bioavailability is higher than 75%, if animals are exposed to dioxin in oil. The absorption of dioxin congeners from breast milk is more than 90% (McLachlan, 1993).

Metabolism of 2,3,7,8-TCDDs occurs at low rates and the metabolites are less toxic than the parent compound (Mason and Safe, 1986). The half-life of dioxin in the body is species and congener dependent. For humans 2,3,7,8-TCDD half-life is estimated to be 7 years (Michalek *et al.*, 1992) and in rats 20 days (Abraham *et al.*, 1988). Only dioxin congeners

substituted at the positions 2, 3, 7, and 8 show long retention times. In humans dioxins are mainly stored in adipose tissue (Poiger and Schlatter, 1986; Ryan *et al.*, 1985), while in rats they are mainly stored in the liver. The storage and elimination in the liver is dose dependent.

Transfer of dioxins to the fetus occurs in pregnant mammals.

2.1.3 Toxicity

Animal sensitivity to dioxin varies. The oral Lethal Dose for 50% of the population (=LD_{50}) of guinea pigs is 0.6 µg/kg bw and for hamsters 5051 µg/kg bw (Liem *et al.*, 1993). Induction of microsomal liver enzymes is considered the most sensitive effect. In rats the no-observed-adverse-effect-level (NOAEL) was determined at 0.001 µg/kg bw/day in a chronic carcinogenicity study (Kociba, 1978). There is insufficient evidence for genotoxicity of 2,3,7,8-TCDD. Kociba *et al.* (1978) found liver tumours in female rats only. Hormonal influences are assumed since Lucier *et al.* (1991) found that ovariectomy exerts a protective effect against liver carcinomas in female rats .

Teratogenic effects (cleft palate) occurred in mice at 0.1 µg/kg bw/day. Rats showed embryotoxic effects at 2,3,7,8-TCDD levels that were already toxic to the mother.

In a 3-generation reproduction study with rats, Murray *et al.* (1979) established a NOAEL at 0.001 µg/kg bw/day while at 0.01 µg/kg bw/day female reproductive effects were found. Rier *et al.* (1993) found an association between TCDD exposure and endometriosis in Rhesus monkeys. Four years exposure to 5 ppt and 25 ppt in the feed resulted, 10 years afterwards, in an endometriosis incidence of 33% in the control group, and 43% and 71%, in the dose groups, respectively.

A single dose of 0.064 µg/kg bw 2,3,7,8-TCDD, which was the lowest dose in the dose range, to pregnant rats on day 15 of gestation induced male reproductive defects in adolescent rats and affected sexual behaviour (Mably *et al.*, 1991, 1992). Occurrence of postnatal exposure was not excluded. Recently it was demonstrated that the reproductive system of the rat male is more sensitive to *in utero* exposure than to lactational exposure (Bjerke and Peterson, 1994). *In utero* exposure to TCDD did not affect sexual behaviour in rats. (Bjerke and Peterson, 1994).

2,3,7,8-TCDD induces thymic atrophy in several animal species. From limited studies with monkeys it appeared that reproductive and dermal effects occur at lower doses than effects on the immune system (Liem *et al.*, 1993).

2.1.4 Epidemiological results after exposure to dioxins

Chloracne is the only effect that can be related consistently to 2,3,7,8-TCDD exposure in humans. In an American cohort of people who produced chemicals contaminated with TCDD Fingerhut *et al.* (1991) found positive correlations between 2,3,7,8-TCDD exposure and lung cancer and soft tissue carcinomas. These correlations were found in a cohort with a latency period of more than 20 years and an exposure for more than one year. Comparable results were found by Manz *et al.* (1991) in a similar German cohort. A positive correlation between duration of exposure and concentration of exposure and cancer mortality rate was found in both studies.

In patients from the Seveso accident Bertazzi *et al.* (1993) also found, an increased soft tissue carcinoma incidence, with a latency period of more than 5 years. Besides, the incidence of other tumour types were also increased. Breast cancer was below expectations and a clear decrease in endometrial cancer was observed. The dioxin exposure levels in this study ranged

from 15.5 to 580 $\mu g/m^2$ in the highest exposed area (Zone A). Serum levels of dioxin ranged from 1770 to 10400 ppt in adults. In a 4 year old boy 56000 ppt has been measured.

In zone B, the area around zone A exposure levels were below 50 $\mu g/m^2$. In the serum the following levels have been reported ranging from 74 to 526 ppt. In zone R where low and pathy contamination was observed, levels were below 5 $\mu g/m^2$. No serum levels have been reported by Bertazzi.

Despite positive correlations still insufficient data are available to conclude that dioxins are carcinogenic, because uncertainty exists about exposure levels and possible co-exposure.

2.1.5 Determination TDI 2,3,7,8-TCDD

Two approaches exist to determine a toxicological standard for TCDD. The US-EPA treats TCDD as a complete genotoxic carcinogen, whereas most other countries and WHO assume a threshold for TCDD. In the case of genotoxicity the 10^{-6} risk is determined (lifetime risk). In the case of a threshold effect a tolerable daily intake (TDI) is established.
For the determination of both standards the study by Kociba *et al.* (1978) was used.

Countries such as Canada, Germany, The Netherlands, Switzerland, and the United Kingdom determined TDIs ranging from 1-10 pg TCDD/kg bw/day (Banbury meeting, 1991). A TDI of 10 pg/kg bw/day was established by the WHO in 1990 (WHO/EURO, 1991) and is supported by several countries like the Scandinavian countries and The Netherlands. The determination of the TDI by the WHO is based on the following factors. First, it is assumed that human sensitivity to dioxin is less or equal to that of experimental animals. The No-Observed-Adverse-Effect-Level (NOAEL) of 1 ng/kg bw/day is based on reproduction toxicity (Murray *et al.*, 1979) as well as liver toxicity in rats (Kociba *et al.*, 1978). Pharmacokinetics was taken into account to convert the NOAEL in experimental animals to a NOAEL in humans. This resulted in a human internal dose of 100 pg TCDD/kg bw/day. An extrapolation factor of 10 was applied because of uncertainties that were not taken into account by the pharmacokinetic model, resulting in a TDI of 10 pg/kg bw/day. For other congeners no individual TDI could be established, but the TEF concept can be used to determine exposure and toxicity.

In the USA 10^{-6} lifetime risks were established at: 0.0572 pg/kg bw/day on a dose per body weight basis (US-FDA, 1983), 0.0276 pg/kg bw/day based on liver concentration (US-CDC, 1984) and 0.006 pg/kg bw/day on dose per surface basis (US-EPA, 1986). In all cases the linearised multistage model was used.

2.2 Toxicological evaluation of PCBs

2.2.1 Mechanistic considerations

The coplanar congeners are assumed to induce toxic effects by binding to the *Ah* receptor. The non-planar PCBs induce toxicity by a different mechanism which is not clear. Some non-coplanar PCBs are suggested to induce "phenobarbital"-like drug metabolising enzymes and to induce toxicity accordingly (Safe, 1994). In addition, there is clear evidence for the interference of dioxins and PCBs with the metabolism of vitamin A and thyroid hormones. In the case of certain PCBs, there are indications that hydroxy metabolites have an effect on transport proteins for vitamin A and thyroid hormone in the plasma (Brouwer and van den Berg, 1986).

2.2.2 Kinetics and metabolism

The oral route is the predominant uptake route for humans. Up to 90% is absorbed by the gastrointestinal tract (IPCS, 1993). Once absorbed the PCBs are stored mainly in adipose tissue and in the liver (IPCS, 1993). The disposition of PCBs in tissues is congener dependent. More highly chlorinated PCBs show higher tissue/blood partitioning coefficient (IPCS, 1993). Metabolic and elimination rates depend on the animal species and the number and position of chlorine atoms. Preferential elimination of some congeners containing 3 or 4 ortho substituents and preferential retention of PCBs with 1 or 2 ortho substituents has been reported (IPCS, 1993). Half-lifes of some congeners of PCBs in mice range from 0.9 (3,4,3',4'-TCB) to 9.2 (2,4,2',4'-TCB) days (IPCS, 1993). Human half-life for 2,4,5,2',4'-PCB and 2,3,4,3',4'-PCB were 9.8 and 7.8 months, respectively (IPCS, 1993). Cross-placental transport of PCBs has been noted (IPCS, 1993).

2.2.3 Toxicity

Most toxicological experiments are conducted with either commercial mixtures with specific compositions or with individual congeners. However, redistribution in the environment or preferential concentration of some congeners in for example food result in different mixtures inducing possibly different toxicity profiles (Ahlborg *et al.*, 1992).

Critical endpoints for risk assessment of PCB exposure in test animals are cancer, immunotoxicity and behavioural effects. In a long-term bioassay with a daily dose of 5 mg/kg bw of the commercial mixtures Aroclor 1260 or Clophen A60 tumours were found in rats. Aroclor 1254 did not induce tumours at various dose levels (25, 50, 100 ppm). PCBs are not genotoxic and there is no conclusive evidence for tumour initiating activity, but there is some evidence that supports the promotional activity of highly chlorinated PCBs (IPCS, 1993)

Long-term exposure to 5 µg/kg bw/day of Aroclor 1254 induced changes in immunological endpoints in Rhesus monkeys (IPCS, 1993). The lowest tested dose for Aroclor 1248 was 90 µg/kg bw/day. This dose already induced effects. Increased mortality rate, growth retardation, alopecia, acne, swelling of the eyelids, liver toxicity, embryo toxicity and epithelial effects were observed (IPCS, 1993). Neonatal monkeys showed also similar effects, but also neurotoxic and immunotoxic effects were induced.

Behavioural effects (hyperactivity and impaired learning ability) have been reported for Rhesus monkey infants exposed to Aroclors via lactation and *in utero* (Bowman *et al.*, 1978, 1981). The mothers of these monkey infants were dosed with 6 µg/kg bw/day. Similar effects were found in rats, mice and quails. In humans comparable effects were measured in infants from mothers exposed to PCBs (Jacobson *et al.*, 1990ab). Rough calculation of the maternal dose resulted in a dose between 0.014 and 0.9 µg/kg bw/day that induced neurotoxic effects in neonates. Transplacental exposure appear to be more hazardous than postnatal exposure (IPCS, 1993).

Aroclors were not teratogenic in rats and non-human primates during the organogenesis at a dose that induced fetotoxicity and maternal toxicity. It is suggested (Seegal *et al.*, 1990) that an association exists between *in utero* exposure to PCBs and developmental deficits in infants and young children. In monkeys exposed to 8 and 30 ppm Aroclor 1016 in the feed, ortho substituted PCBs accumulated in fetal brain tissue and caused a decrease of dopamine levels (Seegal *et al.*, 1990).

2.2.4 Epidemiological results after exposure to PCBs

In some epidemiological studies humans exposed occupationally to commercial mixtures

of PCBs increased tumour incidences of liver and biliary tract were found (IPCS, 1993). However, PCB contaminated food usually has a congener composition different from commercial mixtures. This implies that maybe other effects are induced by PCB contaminated food.

In a contamination accident, cooking oil (Yusho and Yucheng incident) was contaminated with PCBs but also PCDFs. The daily intake of PCBs the Japanese patient was estimated at 157 µg/kg bw/day. Serum levels of PCBs were not available. For Taiwanese patients the total intake of PCBs was estimated at 0.7 to 1.8 g. Serum levels of PCBs after the accident ranged from 3 to 1156 µg/l; 44% of 613 patients had levels from 50 to 100 µg/l and 28 % had blood levels over 100 µg/l.

In the exposed population an increase in tumour incidence was found. Increased mortality due to malignant neoplasms in lung, liver, trachea and bronchi was seen in males after 12 years only. It could not be concluded that PCBs induced carcinogenicity because of the contamination with PCDFs. Besides no dose-response relationships could be established because exposure data were scarce and the number of deaths for pathological research was small.

The earliest symptoms were ocular and dermal effects. Most patients suffered from chronic bronchitis-like disturbances that persisted for several years. Neurological effects became apparent several years after exposure, while early symptoms like chloracne gradually disappeared. Decreased sensory nerve and motor nerve conduction velocity was found one year after exposure. Blood levels were 39.3 ± 16.6 µg PCB/l. Two years after exposure there were no correlations between PCB blood concentration and neurological effects. Exposure to contaminated cooking oil also induced endocrine, hepatotoxic, immunotoxic and respiratory effects (Ahlborg *et al.*, 1992b)

Children of exposed mothers were smaller at birth compared to non-exposed children. Dermal lesions and poorer performance on standardised intelligence tests were observed in these children (Ahlborg, 1992b, Jacobson *et al.*, 1990ab). Fetal exposure to PCBs caused more health effects than infant exposure. Prenatal exposure to PCBs is associated with cognitive deficits in infants and young children (Jacobson *et al.*, 1990, 1992) particularly effects concerning short-term memory and cognitive processing efficiency. However, co-exposure could not have been excluded in this study. Long term implications are presently unclear.

2.2.5 Determination of TDI for PCBs

The coplanar PCB induce effects comparable to those of 2,3,7,8-TCDD according to a similar mechanism. As for dioxins the TEF principle is used. On a recent WHO meeting (Derks *et al.*, 1994) TEFs for these PCBs were established (WHO-TEF). Most non-planar PCBs are not considered herein.

The US-EPA (1990) established a drinking water toxicity standard at 0.005 µg Aroclor 1260/l corresponding to a life-time cancer risk of 10^{-6}. In 1990 and 1993 the FAO/WHO evaluated PCB toxicity but did not determine a TDI. However, it was concluded that the monkey was the most sensitive animals species. In this species a NOAEL of 40 µg/kg bw/day was established for Aroclor 1242 (IPCS, 1993).

2.3 Comparison of toxicological effect induced by dioxin and PCB

Effects induced by dioxins or coplanar PCBs are rather similar. The coplanar PCBs probably induce the same effects as dioxin, since these compounds are assumed to bind to the *Ah*-receptor. Neurotoxic effects, liver toxicity, epithelial effects, reproductive effects,

carcinogenicity and immunotoxic effects have been reported. The reproductive effects include endometriosis (Rier *et al.*, 1993 and Campbell *et al.*, 1985), reduced fertility, and decreased gestational period.

Non-planar, lowly chlorinated and non-dioxin like PCBs accumulate in brain tissue, whereas dioxins and coplanar PCBs do not (Seegal *et al.*, 1990). PCB congeners and metabolites can decrease plasma thyroid hormones and vitamin A levels (Ahlborg *et al.*, 1992b). Such decreases may modulate tumour promotion and developmental and neurobehavioural changes (Ahlborg *et al.*, 1992b).

2.4 Application of the TEQ-concept

In order to deal with the fact that environmental and biological samples in general contain complex mixtures of the different PCDDs, PCDFs and PCBs, the concept of toxic equivalency factors (TEFs) has been developed for risk management. Basically, it is assumed that the individual toxic effects by all dioxins and planar PCBs are induced by binding to the Ah-receptor. However, since the affinity of different congeners for the Ah receptor and also the toxic potential is different, toxic equivalence factors (TEFs) have been determined, showing the relative potential of a certain PCDD, PCDF or PCB as compared to the most toxic congener 2,3,7,8-TCDD. It is also assumed that effects via the Ah-receptor are additive.

Single interim TEF values have been determined for dioxins and PCBs, although in practice, TEF values are depending on the experimental conditions used (Safe 1991 and 1994). More weight has been given to results from semi-chronic and chronic studies with small laboratory animals like rats, mice or guinea pigs, than to those from short-term toxicity studies or *in vitro* bioassays.

Results from toxicity studies with single compounds and complex mixtures of PCDDs and PCDFs, support the application of the TEF concept for these compounds. Application of the TEF concept on complex mixtures of non-, mono-, and di-ortho PCBs has been shown to overestimate the toxic potency as compared to the actually observed toxicity. This is thought to be due to the fact that the TEF-concept does not take into account possible antagonistic (or synergistic) effects of PCBs alone or in combination with PCDDs and PCDFs. Furthermore, considerable species-differences have been observed. Based on currently available information it is however assumed that these kind of interactions might only occur at high dose-levels and as such do not interfere with the application of the TEF-concept at low concentrations (Ahlborg *et al.* 1992).

One must be aware that the TEQ-concept must not be applied to pathways which are not mediated by the Ah-receptor, e.g. non-planar PCBs, since the TEQ-concept is based on the affinity for a dioxin congener to the Ah-receptor.

Using the TEF approach, analytical results are transformed into toxic equivalents (TEQ) using the formula: $\Sigma([\text{Congener}]\text{xTEF})_{\text{PCDD/F or PCB}}=\text{TEQ}$. For the interpretation of analytical data it is important to realize that different TEFs have been used by different countries (Table 1), and that only recently more general TEFs have been proposed.

I-TEF values for dioxins range from 1 for 2,3,7,8-TCDD to 0.001 for octaCDD. PCDD and PCDF congeners without chlorine atoms at the 2, 3, 7 and 8 positions of the molecule have been assigned a TEF value of 0 (NATO/CCMS, 1988, Safe, 1991). The TEFs for dioxins are officially adopted by the United States, the United Kingdom, The netherlands, Canada, Germany and the Scandinavian countries.

On a recent WHO-ECEH and IPCS consultation, WHO-TEF values have been proposed

for non-, mono- and di-ortho PCBs, capable of binding to the Ah-receptor (Ahlborg *et al.*, 1994). TEF values range from 0.1 for 3,3',4,4',5-pentaCB to 0.00001 for 2,3',4,4',5,5'-hexaCB and 2,2',3,4,4',5,5'-heptaCB. Despite the relatively low TEF values for the mono-ortho PCBs it has been shown that these compounds might significantly contribute to the total TEQ concentrations of e.g. fish samples regarding their much higher concentrations.

Thusfar, the application of TEF values for PCBs is far less general than those of dioxins and is still a matter of discussion in many countries.

2.5 Methods for the analysis of dioxins and PCBs

2.5.1 GC/MS methods

Since concentrations of dioxins and coplanar PCBs in biological samples are in general in the low pg/g range, highly sensitive and specific methods had to be developed (Fürst 1984 and 1989, Liem *et al.* 1990, Maier *et al.* 1994). In the case of biological samples, the first step is a quantitative extraction of the fat, in the case of environmental samples, an exclusion with acid. After extraction an extensive cleanup using successively a number of different procedures, is necessary in order to prepare sufficiently concentrated and cleaned extracts for final quantification with gas chromatography-mass spectrometry. In order to allow correction for the generally observed low recoveries, ^{13}C labelled dioxins or coplanar PCBs are added to the samples prior to extraction.

High resolution gas chromatography-mass spectrometry (HRGC-MS) is at present the best suited technique combining sufficient sensitivity and specifity. For environmental samples in principle both low resolution and high resolution mass spectrometry are applicable although high resolution is in favour due to higher sensitivity and better selectivity. The mass spectrometric methods are in general based on United States Environmental Protection Agency protocols (Tondeur, 1987). In general laboratories active in the field of dioxin analysis perform a number of quality control e.g. recovery of internal standard, accuracy of spiked samples and blanks. In general recoveries of the internal standards are in the range of 25% to 125%. General aspects and recommendations are formulated by a group of experts and published (Maier *et al.* 1994).

International ring-tests have been organized to determine the intra and inter-laboratory variation in the analysis of dioxins in fly-ash and milk. In a recent study organized by BCR, reference milk powders were prepared with three different concentrations of dioxins. Mean levels of dioxins as determined by the eleven different laboratories were 0.82, 2.53 and 3.98 pg I-TEQ/g milk powder, with corresponding interlaboratory coefficients of variation of 17, 10 and 11% (Schimmel *et al.* 1994). Similar variations were observed within the laboratories. Similar CVs were observed in another study organized by the WHO (De Jong *et al.* 1993).

Non planar PCBs, occurring in relative high levels, are normally analyzed using gas chromatography with electron capture detection.

2.5.2 Bioassays

Bioassays using both mammalian cancer cell lines and freshly isolated cells have been developed, in generally based on the induction of cytochrome P450 1A enzyme(s), measured by an increased conversion of the substrate ethoxyresorufin into resorufin (EROD activity). Other end-points are increased 1A mRNA levels, porphyria and keratinization of cells. The sensitivity of the current assays may be as low as 0.16 pg per assay. New bioassays are under development using recombinant DNA techniques, aiming at a further improvement of both

the sensitivity and selectivity of the assay.

A major advantage of these assays are the reduction in the costs, the required time and the fact that in the ideal case the total TEQ-value of a sample can be estimated, without identification of all the single compounds contributing to this TEQ-value. This may include possible synergistic or antagonistic effects.

2.6 Exposure assessment

2.6.1 Levels of PCDD and PCB in human food

Levels of dioxins in food of plant origin have been reported to be 0.006 to 0.03 pg I-TEQ/ g fat for vegetable oils and fats, 0.08-0.2 pg I-TEQ/g wet weight for curly kale and 0.34 pg I-TEQ/g fat for cereals.

In the same food items, levels of PCBs have been reported to be 0.015 to 0.03 for vegetable oils and fats and 1 pg WHO-TEQ/g fat for cereals. Total PCB levels have been reported to be 7.2 ng/g fat in vegetable oil and 6.7 ng/g (fresh weight) in cereals (Table 3).

Levels of dioxins measured in food of animal origin are 0.7-2.5 pg I-TEQ/g fat in dairy products (milk, butter, cheese), 0.4-1.8 pg I-TEQ/g fat in beef, pork and chicken meat and 2.4-48.7 pg I-TEQ/g fat in fish. Higher levels have been measured in The Netherlands in horse meat and game, in beef of animals pasturing on 2,4,5-T treated rangelands in the USA (up to 66 I-TEQ/g fat) or in dairy products and meat of cows grazing in the vicinity of waste incinerators (up to 13 pg/g milk fat and 18 pg/g fat in meat). In line with the storage function of liver, concentrations in this organ appear to be substantially higher than those in meat (2 to 35-fold), varying with the animal species (Table 3).

Total PCB levels measured in these products were 10-200 ng/g fat in dairy products, 20-500 ng/g fat in meat products and 10-200 ng/g fresh weight in fish. Certain fish species (eel) or fish products (fish liver and fish oil) contain much higher levels of PCBs, even up to 10 mg/kg. Dioxin-like PCBs have been determined in Dutch dairy products to be ar ɔund 2 pg WHO-TEQ per gram fat (Table 3).

in a recent study in The Netherlands dioxin and PCB levels were measures in human milk sample obtained from about 200 women. Mean levels were 31 pg I-TEQ and 35 pg WHO-TEQ PCBs per gram fat for respectively dioxins and PCBs. In the USA mean levels of 16 pg I-TEQ/g fat were reported (42 women), in germany 30 pg I-TEQ/g fat (112 women) (Beck *et al.*, 1994). Maximum and minimum levels differ from these mean concentrations by a factor 2 to 5.

In general it can be concluded that concentrations of dioxins and PCBs in food for human consumption are highest in food products of animal origin.

2.6.2 Intake by humans

The daily human exposure to dioxins and PCBs has been estimated in a number of industrialized countries, like Sweden, the USA, The Netherlands, Germany, Canada, Norway, the UK and Italy (Table 4). In general it can be concluded that more than 90% of the human exposure to dioxins and PCBs occurs through the diet, with food of animal origin being the predominant source. The average daily exposure for adults to dioxins from food varies from 1 to 2 pg I-TEQ/kg body weight. In the case of Italy a range of 4-7.5 pg/kg bw has been reported, however, these TEQs are expressed in EPA-TEQs, thus, difficult to compare with the I-TEQ.

For breast fed infants the daily intake has been estimated to be between 100 to 200 I-

TEQ/kg fat. Assuming an infant of 4.5 kg, with a milk consumption of 800 ml, a milk fat content of 3.5% and average dioxin concentrations of 16-31 pg I-TEQ/g fat. As such the daily intake exceeds the tolerable daily intake of 10 pg I-TEQ/kg bw. However, the breast-feeding period covers a relatively short period in life, in contrast to the life-time exposure on which the TDI is based. Although the concentration of PCBs and dioxins are relatively high in breastmilk, WHO, JECFA and the Dutch Health Council recommended the use of breastmilk.

Since levels of dioxin-like PCBs are similar to those of dioxins (16-35 WHO-TEQ/g fat), intake of these compounds may be in the same order of magnitude (100-220). The intake of total PCBs by breast-fed infants in EC countries has been estimated to range from 3 to 11 µg/kg bw per day, compared with 0.12-0.3 µg/kg bw for bottle-fed infants in Denmark.

Other sources and pathways, like air, soil, drinking-water and non-food, are of minor importance. Estimations of the daily intake of dioxins from these sources are 0.04-0.06 pg I-TEQ/kg bw from air, 0.01 pg I-TEQ/kg bw from soil, less than 0.01 to 0.05 pg I-TEQ/kg bw from drinking water and 0.15 pg I-TEQ/kg bw for packaging.

For the Dutch population the intake of total PCBs through inhalation has been estimated to be about 36 ng/day. Relatively high levels of PCBs in drinking water (2 ng/L), has been calculated to contribute 0.04 µg/kg bw to the total PCB concentration in the body.

3 Risk management

3.1 Population groups with increased exposure

An increased intake has been reported for the fetus and during breast feeding (see above). In addition fish consuming populations may be at higher risk due to relatively high concentrations of dioxins and PCBs in certain areas.

3.2 Residue limits in food

3.2.1 Dioxins

Based on the TDI and the food consumption patterns, residue limits can be set for certain food products. In The Netherlands, a residue limit for dioxins in dairy products has been set to 6 pg I-TEQ/g fat. Initially this limit was based on an average food consumption pattern, the former TDI of 4 pg I-TEQ per kg bw per day and all 17 dioxin congeners. It was subsequently estimated that this residue limit guarantees that less than 1% of the Dutch population will exceed the new TDI of 10 pg/kg bw/day.

3.2.2 PCBs

The maximum levels of total PCB in food products are based on a daily animal fat consumption of 0.5 to 1 g/kg bw, the NOEL for monkeys divided by a factor of 100 and the concentration of PCBs on fat basis. Based on these assumptions the food items may contain maximally 0.5-1 mg total PCB/kg fat.

3.3 Policy

3.3.1 Dioxins

In most European countries the policy towards dioxins is oriented to reduce the emission of dioxin from waste incinerators. Austria, Germany, The Netherlands, and Scandinavian coun-

tries have a standard for dioxin emission from new incinerators set at 0.1 ng I-TEQ/m^3 (Dioxin, 1993). Japan has a target value for waste incinerators of 0.5 ng I-TEQ/m^3 (Kimura, Dioxin 1994). In the USA, UK (Codex CX/FAC 91/11), and Sweden (CX/FAC 91/11 CRD13) besides the regulation of emission by incinerators, pulp and paper industry is also subject to dioxin reducing regulation. Since it was found that bleached carton contained dioxins which can migrate into carton packed food, Sweden and UK now use unbleached milk cartons (CX/FAC 90/20). Canada and USA try to reduce dioxin content of carton by technological adjustments in bleaching. Dioxin monitoring programs exists in several countries to control and check dioxin levels.
In The Netherlands milk containing more than 6 pg I-TEQ/g milk fat has to be collected and destroyed. If these contaminated cows are used for consumption, fat and organs must be destroyed too (Liem *et al.*, 1993). In Germany 5 pg I-TEQ/g milk fat is used as "orientation" value (Schulz, 1993).
The production and use of pentachlorophenol (PCP), and 2,4,5-T has been banned in several European countries like The Netherlands (Van Zorge and Liem, Dioxin 1994) and Germany (Schulz, 1993). In the US a reduction of the use of PCP is ordered (US-EPA, 1994). The use or production of PCP is banned or restricted because PCP can be contaminated with dioxins. PCP is used a wood preservative.

3.3.2 PCBs

In 1973 the OECD recommended to restrict the flow of PCBs into the environment. Since then 24 OECD countries have restricted the manufacture, sales, import, export, and use of PCBs and established a labelling system for these compounds for disposal measures. Austria, EU countries, Scandinavian countries and the USA banned the use of PCBs in new equipment in the early 1980s. In 1995 the use of all PCBs will be terminated in Scandinavian countries (Johansson and Ahlborg, Dioxin 93).

It is also advised to monitor contamination in foodstuffs. Sweden, Finland, Canada and The Netherlands have established maximum levels for several food items (Table 2).
In countries such as Germany, Sweden and in The Netherlands it is recommended that PCB content should not exceed 0.5-1 mg/kg fat if the product is consumed in amounts of 0.5-1 g/kg bw/day. Concerning food, in Sweden pregnant women are advised to avoid frequent fat fish consumption. In addition, for lactating women dieting is not recommended as dioxin levels may increase under dieting condition.

3.4 Policy Costs

3.4.1 Dioxins

The waste incinerator companies were forced by law to improve their installations to meet the new emission standard. In The Netherlands the costs for such an installation costs vary between 65 and 90 guilders per ton waste (35-45% of the total investments of a new installation relate to the techniques required to meet the emission standard). The Dutch government payed 17.5 million guilders as a financial compensation to farmers who had to destroy milk with levels over 6 pg I-TEQ/ g milk fat. Indications of costs made by other countries were not available.

The total dioxin emission to air in The Netherlands was estimated to have decreased from approximately 960 g I-TEQ per year in 1989 to 484 g I-TEQ/year in 1991 (Koning *et al.*, 1993). It is estimated that in the year 2000 air emission of dioxin will have decreased to 125

g I-TEQ/year, emission to the soil will drop to 0.2 g I-TEQ (3 g I-TEQ/year in 1990). The emission to water will remain 4 g I-TEQ/year. (Liem *et al.*, 1993). The emission of dioxins by MWIs will have decreased by then from 400 g I-TEQ/year in 1991 to 2-4 g I-TEQ/year.

3.4.2 PCBs

Since the OECD ban of PCBs in open systems and new equipment, the PCB levels in the environment have decreased in The Netherlands (CCRX, 1990). Also in breast milk of Dutch women PCB levels have decreased (CCRX, 1992). In Scandinavian countries a similar trend is found (Ahlborg *et al.*, 1992). Patterson *et al.* (1994) showed a decrease of PCBs in blood and fat. The Dutch government has compensated 47 million guilders for the removal or destruction of transformers and capacitors in the 1980s. Data on costs concerning PCB policy in other countries were not available.

OECD countries have a policy concerning PCBs. For dioxin different policies exist in various countries. Some countries have established toxicity standards to protect public health, while others have not. It can be imagined that trade barriers arise in such a case; for example some countries might restrict the import of milk when the toxicity standard in the export country is much higher. Information on this item, however, is not available.

3.5 Policy concerning other environmental pollutants

The policy concerning dioxins and PCBs deviates from that for other environmental contaminants. For example the TEF concept is not applied to compounds other than dioxins, and some PCBs. The pharmacokinetic approach to determine a TDI is rarely applied to other contaminants. In general, the NOAEL is divided by a safety factor which usually is 100, resulting in a TDI.

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Fig I
General structures of dioxins PCDDs, PCDFs and PCBs.

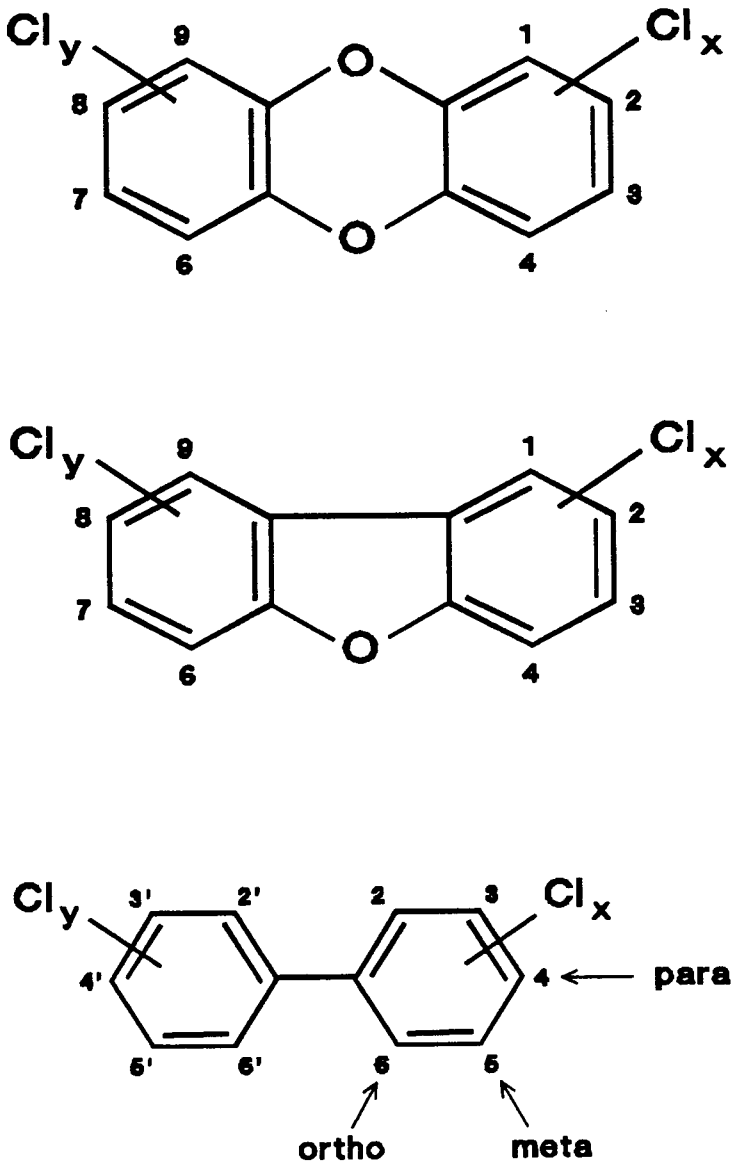

Table 1 Overview of various TEF

Congener	IUPAC number	FHO (BGA) 1984	Nordic 1989	Safe	EPA*	i-TEF	range	
							in vivo	in vitro
2,3,7,8-tetraCDD		1.0	1.0	1.0	1.0	1.0		
1,2,3,7,8-pentaCDD		**0.1**	0.5	0.5	0.5	0.5	0.053-0.59	0.07-0.64
1,2,3,6,7,8-hexaCDD		0.1	0.1	0.1	**0.04**	0.1	0.015-0.16	0.005-0.5
1,2,3,7,8,9-hexaCDD		0.1	0.1	0.1	**0.04**	0.1	0.016-0.14	0.009
1,2,3,4,7,8-hexaCDD		0.1	0.1	0.1	**0.04**	0.1	0.013-0.24	0.05-0.13
1,2,3,4,6,7,8-heptaCDD		**0.001**	0.01	0.01	**0.001**	0.01	0.0076	0.003
OctaCDD		0.001	0.001	0.001	**0.0**	0.001	>0.0013	0.0006
2,3,7,8-tetraCDF		0.1	0.1	0.1	0.1	0.1	0.016-0.17	0.006-0.43
2,3,4,7,8-pentaCDF		**0.1**	0.5	0.5	**0.1**	0.5	0.12-0.8	0.11-0.67
1,2,3,7,8-pentaCDF		**0.1**	**0.01**	**0.1**	**0.1**	0.05	0.018-0.9	0.003-0.13
1,2,3,4,7,8-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	0.038-0.18	0.013-0.2
2,3,4,6,7,8-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	0.017-0.097	0.015-0.1
1,2,3,6,7,8-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	--	0.037-0.048
1,2,3,7,8,9-hexaCDF		0.1	0.1	0.1	**0.01**	0.1	--	--
1,2,3,4,6,7,8-heptaCDF		0.01	0.01	0.1	**0.001**	0.01	0.22	--
1,2,3,4,7,8,9-heptaCDF		0.01	0.01	**0.1**	**0.001**	0.01	0.20	--
OctaCDF		0.001	0.001	0.001	**0.0**	0.001	--	--
3,3',4,4',5-pentaCB	126		0.1	0.1		0.1		
3,3',4,4',5,5'-hexaCB	169		0.01	**0.05**		0.01		
3,3',4,4'-tetraCB	77		0.0005	**0.01**		0.0005		
2,3,4,4',5-pentaCB	114		0.0005	**0.0002**		0.0005		
2,3,3',4,4',5-hexaCB	156		**0.001**	**0.0004**		0.0005		
2,3,3',4,4',5'-hexaCB	157		**0.001**	**0.0003**		0.0005		
2,3,3',4,4'-pentaCB	105		0.0001	**0.001**		0.0001		
2,3',4,4',5-pentaCB	118		0.0001	0.0001		0.0001		
2',3,4,4',5-pentaCB	123		0.0001	**0.00005**		0.0001		
2',3,3',4,4',5,5'-heptaCB	189					0.0001		
2,2',3,3',4,4',5-heptaCB	170					0.0001		
2,3',4,4',5,5'-hexaCB	167					0.00001		
2,2',3,4,4',5,5'-heptaCB	180					0.00001		

* Until 1989 EPA used these TEFs including TEFS for non-2,3,7,8 substituted PCDDs and PCDFs (other tetraCDDs 0.01, other pentaCDDs 0.005, other hexaCDDs 0.0004, other heptaCDDs 0.00001, other tetraCDFs 0.001, other pentaCDFs 0.001, other hexaCDFs 0.0001 and other heptaCDFs 0.00001).

Table 2 Maximum Permitted Levels for PCBs in Food
Sweden (CX/FAC 91/Sweden 5)

Meat	0.2	mg/kg
Milk	0.05	mg/kg
Butter and Cheese	0.1	mg/kg
Eggs	0.1	mg/kg
Fishery Products	2.0	mg/kg
Liver of cattle	2.0	mg/kg
Liver of pigs	2.0	mg/kg
Fish liver	5.0	mg/kg
Salmon	5.0	mg/kg

Dutch Guideline Levels March 91 Codex (CX/FAC 90/20)

Milk and Dairy products	0.5	mg/kg (fat-based)
Meat and Meatproducts	1	mg/kg (fat-based)
Poultry meat	1	mg/kg (fat based)
Eggs	1	mg/kg (fat-based)
Freshwater fish	2	mg/kg
Fish liver, fish oil	5	mg/kg
Other fishery products	1	mg/kg
Finished animal feed	0.05	mg/kg

Finland (CX/FAC 90/20)
Finnish regulations for PCB maximum levels

Fish and fishpreparations (except fish liver)	2.0	mg/kg
PCB 28	0.6	mg/kg
PCB 52	0.1	mg/kg
PCB 101	0.2	mg/kg
PCB 118	0.2	mg/kg
PCB 138	0.2	mg/kg
PCB 153	0.2	mg/kg
PCB 180	0.2	mg/kg
Other PCBs	0.6	mg/kg

Canada (CX/FAC 94/23)
Guidelines for PCB in foods in Canada

Meat-Beef-fat basis	0.2	ppm
Eggs-whole egg less shell	0.1	ppm
Poultry-fat basis	0.5	ppm
Fish-edible portion	2.0	ppm

Table 3 Dioxin and PCBs in various food items

Food item	Dioxin range/level pg I-TEQ/g fat	PCBs range/level pg WHO-TEQ/g fat	Total PCB ng/g fat
Plant origin			
vegetable oil/fat	0.006-0.03	0.015-0.03	7.2
curly kale	0.08- 0.2*		
cereals	0.34	1	6.7^
Animal origin			
dairy products	0.2-2.5	2	10-200
milk			
butter			
cheese			
meat	0.4-1.8		20-500
beef			
fat			
pork			
chicken			
Fish products	2.4-48.7		10-200^
eel			< 10 #
Human products			
milk	16-31	16-35	

* pg I-TEQ/g fresh weight
^ ng/g fresh weight
\# mg/kg

Table 4 Daily Human intake

food item	NL		FRG		Canada	USA
	total (g)	fat (g)	total (g)	fat (g)	total (g)	total (g)
dairy	370	10.0	184	18.0	444	266
cheese	29	8.7	33	5.2		
eggs	16	1.6			29	25
meat	116	21.2	112	28.6	95	90
fish	8	0.8	15	1.8		18
vegetable oils	48	33.5	23	19.0		
Dioxin intake	157 pg I-TEQ/day		85 pg FHO-TEQ/day		92 pg I-TEQ/day	100 pg I-TEQ/day