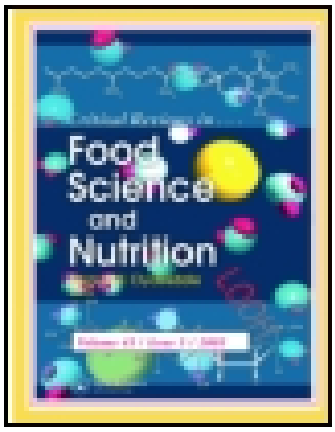

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A critical review about the human exposure to polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) through foods

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Abstract

Dioxins include polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and part of polychlorinated biphenyls (PCBs). Only the compounds that are chlorinated at the 2,3,7 and 8 positions have characteristic dioxin toxicity. PCDDs, PCDFs and PCBs accumulate in the food chain due to their high lipophilicity, high stability, and low vapor pressure. They are not metabolized easily; however their hydroxylated metabolites are detected in feces. They cause a wide range of endocrine disrupting effects in experimental animals, wildlife, and humans. Endocrine related effects of PCDDs, PCDFs and PCBs on thyroid hormones, neurodevelopment and reproductive development were referenced. In addition, some studies of contamination of foods, bioaccumulation, dietary exposure assessment, as well as challenges of scientific research in these compounds were reviewed.

Keywords: polychlorinated dibenzo-p-dioxins (PCDDs); polychlorinated dibenzofurans (PCDFs); polychlororinated biphenyls (PCBs); human exposure; occurrence in foods; bioaccumulation; methods of removal; health effects.

Contents

7. Conclusions

1. General description of PCDDs, PCDFs and PCBs

PCDDs, PCDFs, and PCBs are persistent organic pollutants (POPs) with similar chemical structure and are chemically classified as halogenated aromatic hydrocarbons (**Figure 1**). All these congeners are lipophilic and have very low water solubility, so they easily enter the food chain and accumulate in fatty tissues. Their presence in the environment is unintentional for PCDDs and PCDFs whereas PCBs are present in the environment because they were extensively produced by industry in the past and worldwide utilized (IPCS 1989; 1992).

1.1. Structure-related physical and chemical properties

Knowledge of physical and chemical properties is essential to understanding and modeling the environmental transport and transformation of organic compounds such as PCDDs, PCDFs and PCBs. The properties most important for understanding the environmental behavior of the dioxin and dioxin-like compounds appear to be octanol/water partition coefficient (Kow), octanol/air partition coefficient (Koa), water solubility (s_w), vapor pressure (P_v) and organic carbon partition coefficient (Koc) (**Table 1**).

The basic structure of PCDDs is a dibenzo-p-dioxin (DD) molecule, which is comprised of 2 benzene rings joined at their para carbons by 2 oxygen atoms. There are 8 homologues of CDDs, monochlorinated through octachlorinated. The class of PCDDs contains 75 congeners, consisting of 2 monochlorodibenzo-p-dioxins (MCDDs), 10 dichlorodibenzo-p-dioxins (DCDDs), 14 trichlorodibenzo-p-dioxins (TrCDDs), 22 tetrachlorodibenzo-p-dioxins (TCDDs), 14 pentachlorodibenzo-p-dioxins (PeCDDs), 10 hexachlorodibenzo-p-dioxins (HxCDDs), 2 heptachlorodibenzo-p-dioxins (HpCDDs), and a single octachlorodibenzo-p-dioxin

(OCDD) (Ryan et al., 1991). The general structure of the dibenzo-p-dioxins is shown in **Figure 1**. The numbers indicate the positions for chlorine substitutions, excluding, of course, positions 5 and 10. Chlorinated dioxins exist as colorless solids or crystals in the pure state. They have a low solubility in water and a low volatility. Chlorinated dioxins have an affinity for particulates and readily partition to particles in air, water, and soil. The more toxic compounds appear to be the 2,3,7,8-substituted tetra-, penta-, and hexachloro compounds (i.e., 2,3,7,8-TCDD, 1,2,3,7,8-PeCDD, 1,2,3,4,7,8-HxCDD, 1,2,3,6,7,8-HxCDD, and 1,2,3,7,8,9-HxCDD). These are also the congeners, along with OCPDD, that have the greatest tendency to bioaccumulate. One of the most toxic congeners in mammals is believed to be 2,3,7,8-TCDD; this compound has also been the most studied of the TCDD congeners.

PCDFs are three-ringed structures, with two rings of six carbon atoms each (benzene rings) attached to the furan (**Figure 1**). Between one and eight chlorine atoms are attached to the rings. There are 135 types of PCDFs, whose properties are determined by the number and position of the chlorine atoms. PCDFs are closely related to PCDDs and PCBs. These three types of toxic compounds often occur together and PCDFs are major contaminants of manufactured PCBs. In fact, the term dioxin commonly refers to a subset of these compounds that have similar chemical structures and toxic mechanisms. This subset includes 10 of the PCDFs, as well as seven of the PCDDs and 12 of the PCBs. Less frequently, the term dioxin is used to refer to all 210 structurally-related PCDFs and PCDDs, regardless of their toxicities.

PCBs are a class of compounds formed by the chlorination of a biphenyl molecule, which is used as an antifungal food additive (Paseiro-Losada et al., 1990). There are 209 possible different positional congeners of PCBs. The physical/ chemical properties of each PCBs congener vary according to the degree and position of chlorine substitution. There are several ways to group these congeners. Six congeners, which represent about 50% of all PCB congeners in food, are called indicator PCBs (iPCBs):

PCB 28, 52, 101, 138, 153, and 180 (Sirot et al., 2012). On the other hand, based on structural characteristics and toxicological effects, PCBs are divided into dioxin-like PCBs (DL-PCBs) showing toxicological properties similar to dioxins and non dioxin-like PCBs (NDL-PCBs), which do not share the dioxin's toxic mechanism. They are regulated under to Toxic Substances Control Act in part because of their probable carcinogenicity and tendency to bioaccumulate in the food web (Kelly et al., 2007). In terms of structural relationship to toxicity, PCBs could be also classified in 2 distinct categories: coplanar or non-ortho-substituted PCBs and non coplanar or ortho-substituted PCBs. The coplanar group members have a fairly rigid structure, with the 2 phenyl rings in the same plane. This gives the molecule a structure similar to PCDDs and PCDFs, and allows it to act in the same way as these molecules as an agonist of the aryl hydrocarbon receptor (AhR) in organisms. These PCBs are considered as contributors to overall dioxin toxicity, and the term dioxin is often used interchangeably when the environmental and toxic impact of these compounds is considered. Non coplanar PCBs, with chlorine atoms at the ortho positions, have not been found to activate the AhR, and are not considered part of the dioxin group; however, studies have indicated some neurotoxic and immunotoxic effects, but at levels much higher than normally associated with dioxins, and thus of much less concern to regulatory bodies (Winneke et al., 1998)

PCBs have certain characteristics, such as persistence and low water/high lipid solubility (**Table 1**), which contribute to their ability to bioconcentrate and bioaccumulate (Robertson and Ludewig 2011).

1.2. Sources

The main sources of PCDDs and PCDFs are industrial and natural combustion processes, the massive industrial use of chlorine and a large production of chlorine-containing materials, whereas the main sources

of PCBs are associated to accidental events and environmental reservoirs (soil and sediments) after illegal disposal of contaminated material (Fernández-González et al., 2011). So, both PCDDs, PCDFs and PCBs are ubiquitous in the environment. However, their environmental levels have decreased during the last two decades as a result of the banning of PCBs and the implementation of PCDD and PCDF risk-reducing policies since the 1980s (Fattore et al., 2006).

Specifically, the most important sources of dioxins include (IPCS 1989): contaminated commercial chemical products, such as PCBs and chlorinated phenols and their derivatives (Bremmer et al., 1993); incineration of sewage sludges (Öberg et al., 1992) and municipal, hazardous, and hospital wastes (Rappe 1994); automobile operation (Ballschmiter et al., 1986; Bingham et al., 1989); fossil fuel combustion; overheating and emissions from fires involving PCBs; disposal of industrial wastes resulting from processes such as the production of chlorophenols and their derivatives, chlorophenol wood treatment, use of PCB fluids in electrical equipment, and wastes from pulp and paper processing (Beck et al., 1989; Wiberg et al., 1989).

The first studies conducted to measure ambient air levels of PCDDs and PCDFs were performed in the early 90s owing to the low detection limits required to quantify the expected low concentrations of specific congeners of PCDDs and PCDFs. The obtained data from these studies have indicated fairly comparable PCDD and PCDF levels in Europe, Japan and USA. Besides, higher PCDD and PCDF concentrations have been found close to known sources and in urban areas (Wevers et al., 1993; Bolt and de Jong 1992; Prinz et al., 1990; König et al., 1993; Broman et al., 1991; Tysklind et al., 1993; Duarte-Davidson et al., 1994; Hunt and Maisel 1990; Sugita et al., 1993; and Taucher et al., 1992). However, in other studies high PCDD and PCDF levels have been found in vehicle tunnel air as a result of emissions from cars (Rappe et al., 1988; Oehme et al., 1991; Wevers et al., 1992). Besides, high indoor air PCDD and PCDF levels were found in houses by Balfanz et al. (1993) using particle board that had been coated with PCBs.

With regard to current sources of PCB release, volatilization from landfills containing transformer, capacitor and other PCB-wastes; sewage sludge, spills and dredge spoils; and improper or illegal disposal to open areas are included. PCB pollution could occur during the incineration of industrial and municipal waste due to that most municipal incinerators are not effective in destroying PCBs. Besides, explosions or overheating of transformers and capacitors may release significant amounts of PCBs into the local environment. More recently, Hu and Hornbuckle (2010) detected PCB congeners, such as PCB 11, in azo and phthalocyanine pigments, which are commonly used in paint, inks, textiles, paper, cosmetics, leather, plastics, food and other materials.

Council Directive 85/467/EC restricted the use and marketing of PCBs in the EU, but some European countries (Sweden) had even banned the use of PCBs more early. Nowadays, PCBs are widely spread due to their large presence in transformers and capacitors in which they are used as dielectric fluids, as well as in building material, carbon less copy paper, lubricants, surface coatings, adhesives, plasticizers and inks, among other uses. In this sense, Council Directive 96/59/EC established that Member States had to invent a detailed plan about disposal of the relevant PCB wastes and the decontamination/disposal of relevant equipment containing these pollutants (IPCS 1992).

An inhalation route of exposure could predominate in some specific situations, such as certain occupational exposures or people residing or working in contaminated buildings and in large cities. In contrast to foodborne PCBs, airborne PCBs are lower chlorinated, more volatile and subject to metabolic attack. So, the impact of exposures to airborne PCBs is an issue to take into account for those individuals who are occupationally exposed, for persons living near contaminated sites (Ulaszewska et al., 2011), for workers or students who stay in contaminated buildings, and especially for the young, the socio-economically disadvantaged and medically-underserved or nutritionally-deficient populations.

On the other hand, PCBs can be converted to PCDFs under pyrolytic conditions. Thus, the uncontrolled burning of PCBs can be an important source of hazardous PCDFs. Therefore, the destruction of PCB-contaminated waste should be carefully controlled, especially with regard to the burning temperature, residence time, and turbulence (IPCS 1992).

1.3. Analytical methods

In recent years, several high-profile contamination crises have raised concerns over dioxin levels in a variety of food products. The principal steps in the analytical methods used for the determination of PCDDs, PCDFs and DL-PCBs use to include several steps, such as sampling, spiking with surrogate standards, pre-treatment, extraction, clean-up, spiking with recovery standard and separation, identification and quantification. This methodology is based on the isotopic dilution technique and therefore, different internal standards labeled with ^{13}C must be added to the sample before any sample treatment (Eljarrat and Barceló 2002).

Sampling and extraction

Sampling, sample preparation and analytical detection procedures are very important for determination of PCDDs, PCDFs and DL-PCBs in foodstuffs. The general criteria were established in the European Commission Directive 2002/69/EC that establishing the sampling methods and the methods of analysis for the official control of dioxins and the determination of dioxin-like PCBs in foodstuffs, although this regulation was later repealed by Commission Regulation (EC) No. 1883/2006. Nowadays, as a result of the application of new maximum levels for NDL-PCBs and also to provide a harmonization at Union level, the

current provisions are set in Commission Regulation (EU) No. 252/2012 laying down methods of sampling and analysis for the official control of levels of dioxins, DL-PCBs and NDL-PCBs in certain foodstuffs and repealing Commission Regulation (EC) No. 1883/2006. Thereby, the PCDD, PCDF and PCB congeners that have to be controlled due to their toxicological concern are 17 PCDDs, PCDFs and 12 DL-PCBs with assigned Toxic Equivalent Factors (TEFs) in Appendix to Annex III in Commission Regulation (EU) No. 252/2012.

Commission Regulation (EU) No. 252/2012 establishes that a screening method of analysis with widely acceptable validation and high throughput can be used to identify the samples with significant levels of PCDDs, PCDFs and DL-PCBs. The levels of PCDDs, PCDFs and DL-PCBs in these samples need to be determined by a confirmatory method of analysis. It is therefore appropriate to establish appropriate requirements for the screening method making sure that the false-compliant rate with respect to maximum levels is below 5 % and strict requirements for the confirmatory methods of analysis. Furthermore, confirmatory methods allow the determination of levels also in the low background range. That is important for to follow time trends, exposure assessment and for the re-evaluation of maximum and action levels.

Samples intended for the official control of the levels of PCDDs, PCDFs, DL-PCBs and NDL-PCBs in foodstuffs shall be taken according to the methods described in Annex II of Commission Regulation (EU) No. 252/2012, and aggregate samples thus obtained shall be considered as representative of the lots or sublots from which they are taken. On the other hand, the sampling method applied shall ensure that the aggregate sample is representative for the lot or sublot that is to be controlled. For this, Commission Regulation (EU) No. 252/2012 in Annex II establishes a sampling plan in which specifies several indications about division of lots into sublots, number of incremental samples, special provisions for the sampling of lots containing whole fishes of comparable and/or different size and weight, and sampling at retail stage.

For PCDDs, PCDFs and DL-PCBs, the lot is accepted, if the result of a single analysis performed by a screening method with a false-compliant rate below 5 % indicates that the level does not exceed the respective maximum level of PCDDs, PCDFs and the sum of PCDDs, PCDFs and DL-PCBs as laid down in Commission Regulation (EC) No 1881/2006; or if the result of a single analysis performed by a confirmatory method does not exceed the respective maximum level of PCDDs and PCDFs, and the sum of PCDDs, PCDFs and dioxin-like PCBs as laid down in Commission Regulation (EC) No 1881/2006 taking into account the measurement uncertainty.

Several laboratories applied soxhlet technique using toluene/ethanol, toluene/acetone, hexane and cyclohexane, although their main drawbacks are time-consuming (>48 h) of refluxing with cold solvent and considerable solvent consumption, to extract PCDDs, PCDFs and PCBs from animal feedingstuffs, such as (Eppe et al., 2004). Moreover, other classical extraction techniques used for the analysis of PCDDs, PCDFs were liquid/liquid extraction, solid-phase extraction (SPE), semi-permeable membrane devices (SPMD), or the more recent pressurized fluid extraction (Reiner et al., 2006).

However, new improved techniques have been developed in the last years, such as supercritical fluid extraction (SFE), accelerated solvent extraction (ASE) and microwave-assisted extraction (MAE). In this way, SFE uses a gas above the critical point to extract analytes from the matrix and their main advantages are that that the extracting gas can be evaporated as well as that solvent disposal is not required (Reiner et al., 2006). ASE systems offer a high level of automation although only one extraction at a time can be conducted, while MAE systems can perform several simultaneous extractions, but the main drawback of ASE and MAE is the high investment cost of these types of systems. Both of them have been tested by several laboratories for PCDDs, PCDFs and PCBs extraction, and these tests led to the conclusion that ASE and MAE are very attractive alternatives to conventional Soxhlet extractions due to considerable

reductions in extraction time, solvent consumption, energy and generated waste (Eljarrat and Barceló 2002; Eppe et al., 2004; Reiner et al., 2006).

Clean-up

Normally, the obtained extracts usually contained interfering substances so that a clean-up step was indispensable, based on solid-liquid adsorption chromatography using a combination of different adsorbents, such as modified silica, florisil, alumina and several types of carbon columns, but this procedure is time- and labor-consuming. Eppe et al. (2004) and Reiner et al. (2006) confirmed the use of these adsorbents materials to clean-up PCDDs, PCDFs and PCBs. Therefore, automated clean-up systems were developed based on the use of pressurized column chromatographic procedures, which were able to process automatically several samples simultaneously. On the other hand, immunoaffinity chromatography (IAC) has been investigated to simplify PCDD, PCDF and PCB clean-up. These columns have been generated from anti-dioxin and anti-PCB antibodies and shown to bind these pollutants selectively from samples. This IAC method was quite more fast and selective as well as less solvent-consuming than traditional clean-up. However, the main limitations of IAC methodologies were the lack of selectivity for all 17 toxic congeners and the incompatibility with high-fat matrices (Eljarrat and Barceló 2002).

Reiner et al. (2006) reviewed advances in analytical techniques for PCDDs, PCDFs and PCBs. In this sense, these authors highlighted that multicolumn automated systems like the Fluid Management System (FMS) automated Power Prep system were used in several applications, including water and food, and the addition of a pressurized liquid extraction (PLE) interface previous to this system allows the sample to be

extracted and cleaned-up in the same automated run. In this way, an alternative method used an automated gel permeation chromatographic (GPC)/carbon system, in which GPC removed co-extractives (such as lipids) from the extract and, later, this extract was treated with activated carbon to separate planar from non-planar compounds. Moreover, these researchers cited other alternative techniques such as an automated microwave solvent extraction system (MASE) coupled to a liquid chromatograph, and a modified PLE extraction cell in which the sample matrix was inserted above activated carbon. All these techniques were developed to remove most interference from the sample extract, but a considerable number of interferences often remain in the cleaned sample extracts because many compounds have similar physical and chemical properties.

Identification and quantification

Sample preparation and analysis for the official control of the levels of PCDDs, PCDFs, DL-PCBs and NDL-PCBs in foodstuffs listed in Section 5 of the Annex to Regulation (EC) No. 1881/2006, later amended by Commission Regulation (EU) No. 1259/2011, shall be carried out in accordance with the methods set out in Annex III and IV to Commission Regulation (EU) No. 252/2012, in which are specified all requirements for methods of analysis used for this purpose.

Specifically, monitoring for the presence of PCDDs, PCDFs and DL-PCBs in foodstuffs may be performed with two different goals: (i) selection of those samples with levels of PCDDs, PCDFs and DL-PCBs that exceed the maximum levels, or the action levels. This approach may involve a screening method allowing cost-effective high sample- throughput, thus increasing the chance to discover new incidents with high exposure and health risks of consumers. Screening methods may comprise bioanalytical methods and

GC/MS methods. Their application should aim at avoiding false-compliant results. The concentration of PCDDs, PCDFs and the sum of PCDDs, PCDFs and DL-PCBs in those samples with significant levels needs to be determined/confirmed by a confirmatory method; and (ii) determination of the levels of PCDDs, PCDFs and DL-PCBs in food samples in the range of low background levels. This is important in order to follow time trends, exposure assessment of the population and to build a database for possible re-evaluation of action and maximum levels. This goal is achieved by confirmatory methods enabling the PCDDs, PCDFs and DL-PCBs to be identified and quantified unequivocally at the level of interest. These methods can be used for confirmation of results obtained by screening methods and for determination of low background levels in food monitoring. They are also important for establishing congener patterns in order to identify the source of a possible contamination. At present such methods utilize HRGC/HRMS.

On the other hand, the applicable detection methods for official control of the levels of NDL-PCBs in foodstuffs are GC/ECD, GC/MSMS, GC/Low Resolution Mass Spectrometry (LRMS), GC/High Resolution Mass Spectrometry (HRMS) or equivalent methods. Regarding identification and confirmation of analytes of interest, several requirements are specified in Annex IV to Commission Regulation (EU) No. 252/2012, such as relative retention time in relation to internal standards or reference standards and gas chromatographic separation of all six indicator PCBs from interfering substances, especially co-eluting PCBs, in particular if levels of samples are in the range of legal limits and non-compliance is to be confirmed. Besides, for GC/MS techniques is required monitoring of at least two specific ions for HRMS, two specific ions of m/z > 200 or three specific ions of m/z > 100 for LRMS, 1 precursor and 2 product ions for MS-MS, and specific maximum permitted tolerances for abundance ratios for selected mass fragments; while for GC/ECD techniques is required confirmation of results exceeding the tolerance with two GC columns with stationary phases of different polarity. Finally, other requirements are established in this Anex

IV about demonstration of performance of method, limit of quantification, quality control, control of recoveries, requirements for laboratories, criteria for the sum of the six indicator PCBs at the level of interest, and reporting of results.

The European strategy for dioxin monitoring of the food chain has defined HRGC/HRMS as the confirmatory method that can provide reliable and comparable results at sub-parts per trillion (ppt) levels (Eppe et al., 2004). Reiner et al. (2006) affirmed that many detection techniques have been investigated, but none of them have had the selectivity and sensitivity of HRMS. MS/MS uses to be more selective but less sensitive than HRMS for PCDD and PCDF analysis. However, this enhanced selectivity observed with MS/MS analysis for PCDDs and PCDFs was not achieved for PCBs. These authors also highlighted that interfering peaks could be detected in the MS/MS chromatograms of PCBs because the loss of Cl_2 from the parent molecule is not unique to polychlorinated compounds. On the other hand, EI with reduced electron energy (~35 eV) was marked by these researchers as the typical method of ionization used in PCDD, PCDF and PCB analysis because enhances sensitivity. Negative ion chemical ionization (NICI) is also a low-energy ionization technique, which has been investigated for PCDD, PCDF and PCB analysis. In this sense, detection limits achieved for these POPs by NICI were similar to those obtained by EI, but NCI has not been used for this type of analysis because other co-extractives also fragmented to the chloride anion, reducing selectivity.

Muir et al. (2006) commented in their review that access to modern capillary GC equipment with either electron capture or mass spectrometry detection (ECD or MS, respectively) to separate and quantify PCBs with other compounds with Cl, such as organochlorine pesticides (OCPs), is required in order to conduct the analysis and to take part in regional and international inter-comparisons. In this sense, spiking surrogate recovery standards into each routine sample provides useful information on losses of analyte

from the extraction step. However, no single PCB or OCP can be representative of all the organochlorines being determined, so recovery correction should be performed with caution. Moreover, isotopically labeled surrogates are ideal for the quantification of PCBs and many OCPs via HRMS, and the application of isotope dilution techniques can correct for the recoveries of these surrogates. With regard to detection limits, they depend on the analytical method used, the sample size and quality assurance (QA) considerations, although these detection limits should be calculated as described by USEPA or by IUPAC/ISO methodology.

Certified reference materials (CRMs)

An effective analytical quality control should have appropriate certified reference materials (CRMs). The lack of especially CRMs for the DL-PCBs was considered by Eljarrat and Barceló (2002). In this way, different materials have been certified for PCDD and PCDF determinations, such as incineration fly ash, industrial soils, sewage sludge and milk powder, although these materials were not certified for the DL-PCB determination.

The number of certified values for PCB/OCP congeners in certified reference materials is limited (approximately 23 PCB congeners and 15 OCPs in cod liver). At least, the PCB/OCPs for which there are certified values in readily available CRMs should be determined (approximately 38). With this number of analytes, the information would be useful for both regulatory actions and source identification by using multivariate analysis or other “fingerprinting” methods (Muir et al., 2006).

National Institute of Standards and Technology (NIST) has developed over 40 natural-matrix standard reference materials (SRMs) and 40 solution SRMs for determination of environmental organic pollutants in

USA. The certification approach based on the use of multiple analytical methods has been established for a variety of POPs. In this way, natural-matrix SRMs are typically certified for several POPs, including 25-35 PCBs and 10-15 OCPs. The uncertainties associated with the certified values for these POPs in the natural-matrix SRMs are typically in the range 5 to 10%. The NIST natural-matrix SRMs are the most extensively characterized matrix CRMs available worldwide, including air and diesel particulate matter, coal tar, marine and river sediment, mussel tissue, fish oil and tissue, and human serum (Wise et al., 2006).

1.4. Legislation

The Scientific Committee on Food (SCF) adopted on 30 May 2001 an opinion on PCDDs, PCDFs and DL-PCBs in food (EC SCF 2001), updating its opinion of 22 November 2000 (EC SCF 2000) fixing a tolerable weekly intake (TWI) of 14 pg World Health Organization toxic equivalent (WHO-TEQ)/kg of body weight (bw) for PCDDs, PCDFs and DL-PCBs. In this way, exposure estimates taking into account the SCOOP-task 'Assessment of dietary intake of dioxins and related PCBs by the population of EU Member States' finalized in June 2000 (EC DG HCP 2000) indicated that a considerable proportion of the Community population had a dietary intake in excess of the TWI.

Each congener of PCDDs, PCDFs and DL-PCBs exhibits a different level of toxicity. In order to be able to sum up the toxicity of these different congeners, the concept of toxic equivalency factors (TEFs) has been introduced to facilitate risk assessment and regulatory control. This means that the analytical results relating to all the individual PCDD, PCDF and DL-PCB congeners of toxicological concern are expressed in terms of a quantifiable unit, namely the TCDD toxic equivalent quantity (TEQ).

From a toxicological point of view, any level set should apply to both PCDDs, PCDFs and DL-PCBs but, in

2001, maximum levels were set on Community level only for PCDDs, PCDFs and not for DL-PCBs, due to the very limited data available at that time on the prevalence of DL-PCBs. However, since then, more data on the presence of DL-PCBs have become available and maximum levels (MLs) for the sum of PCDDs, PCDFs and DL-PCBs have been set in 2006 by Commission Regulation (EC) No 1881/2006. In order to ensure a smooth transition, the levels for PCDDs and PCDFs should continue to apply for a transitional period in addition to the levels for the sum of PCDDs, PCDFs and DL-PCBs. In particular, foodstuffs must comply during that transitional period with the MLs for PCDDs and PCDFs, and with the MLs for the sum of PCDDs, PCDFs and DL-PCBs.

In order to encourage a reduction of PCDDs, PCDFs and DL-PCBs in food and feed, action levels were set by Commission Recommendation 2006/88/EC of 6 February 2006 on the reduction of the presence of dioxins, furans and PCBs in feedingstuffs and foodstuffs. These action levels were a tool for competent authorities and operators to highlight those cases where it is appropriate to identify a source of contamination and to take measures to reduce or eliminate it. Since the sources of PCDDs, PCDFs and DL-PCBs are different, separate action levels were determined for both types of POPs. More recently, the MLs applicable for sum of PCDDs, PCDFs, for sum of PCDDs, PCDFs and DL-PCBs, and for sum of indicator PCBs in food and feed were reviewed with the objective to set lower levels. As a result, the European Commission reported Commission Regulation (EU) No. 1259/2011 of 2 December 2011 amending Commission Regulation (EC) No 1881/2006 as regards maximum levels for dioxins, dioxin-like PCBs and non dioxin-like PCBs in foodstuffs. In this current regulation, the MLs for the sum of the six marker or indicator PCBs was included because comprises about half of the amount of total NDL-PCBs present in feed and food and, therefore, such sum is considered as an appropriate marker for occurrence and human exposure to NDL-PCBs. Furthermore, all these MLs have been established taking into account

recent occurrence data compiled in the EFSA scientific report 'Results of the monitoring of non dioxin-like PCBs in food and feed' (EFSA 2010b), as well as using the EFSA scientific report 'Results of the monitoring of dioxin levels in food and feed' (EFSA 2010a).

2. Toxicity

The most toxic PCDD and PCDF congener is TCDD and the toxicity of other PCDDs, PCDFs and chemicals like PCBs that act like dioxin are measured in relation to TCDD. TCDD toxicity is mostly caused by the parent compounds since some authors observed that these former compounds are several orders of magnitude more active than their metabolites (Mason and Safe 1986).

2.1. Toxicokinetics

Reviews about the toxicokinetics and metabolism of PCDDs, PCDFs are available in the literature in which is stated that the absorption, body distribution, and metabolism of these POPs can vary greatly between species and also may depend on the congener and dose. In biota, the 2,3,7,8-substituted PCDDs and PCDFs are almost exclusively retained in all tissue types, preferably liver and fat. This selective tissue retention and bioaccumulation are caused by a reduced rate of biotransformation and subsequent elimination of congeners with chlorine substitution at the 2,3,7, and 8 positions. 2,3,7,8-substituted PCDDs and PCDFs have the greatest toxic and biological activity and affinity for the cytosolic arylhydrocarbon (Ah)-receptor protein (Van den Berg, 1994).

The parent compound is the causal agent for Ah-receptor-mediated toxic and biological effects, with metabolism and subsequent elimination of 2,3,7,8- substituted congeners representing a detoxification process. The main factors, which contribute to the relative in vivo potency of an individual PCDDs and

PCDFs in a given species, are congener-specific affinity of PCDDs and PCDFs for the Ah-receptor, genetic events following receptor binding, and toxicokinetics. Moreover, limited human data have indicated that marked species differences exist in the toxicokinetics of these compounds. Thus, human risk assessment for PCDDs and PCDFs needs to consider species-, congener-, and dose-specific toxicokinetic data. In addition, exposure to complex mixtures, including PCBs, has the potential to alter the toxicokinetics of individual compounds, and these alterations may be involved in some of the non-additive toxic or biological effects that are observed after exposure to mixtures of PCDDs and PCDFs with PCBs (Van den Berg, 1994).

Iwata et al. (2004) concluded that toxicokinetics of individual PCDD, PCDF and coplanar PCB congeners in Baikal seals is dependent on factors including sex, tissue concentration, binding to cytochrome P450 (CYP), and rates of absorption and metabolism/excretion. Besides, these authors suggested the necessity for the determination of sex-, tissue-, and growth stage-specific TEQs to assess the risk of a complex mixture of PCDDs, PCDFs and coplanar PCBs in wild population, more precisely. This conclusion is in agreement with the results obtained by Kubota el al. (2004; 2006) for PCDDs, PCDFs and coplanar PCBs in common cormorants and black-eared kites, respectively.

Correia-Carreira et al. (2011) highlighted that are poorly characterized, and affirmed that transplacental kinetics of NDL-PCBs can be studied in a variety of models, but careful validation of each model is crucial. In this way, these authors developed a standard operating procedure for establishing an in vitro model of the human placental barrier, which was useful to investigate placental transport kinetics of two NDL-PCB congeners (PCB52 and PCB180) and observed that both NDL-PCBs crossed the placental barrier within 2.5 h. Moreover, they also found PCB180 to transfer more rapidly and PCB52 to associate more with placental tissue. Finally, these researchers hypothesized that the observed differences in transport and

association patterns of NDL-PCBs may indicate that toxic effects of PCB52 have a more important role regarding placental function, whereas PCB180 may be of greater importance for fetal toxicity.

Absorption

PCDDs and PCDFs can be absorbed by routes of exposure such as inhalation, ingestion, transcutaneous and transplacental via and/or through breast milk, while PCB absorption can be by adsorption on particles due to their low volatility, heavy skin exposure, transplacental via and also through breast milk.

Birnbaum and Couture (1988) concluded that uptake of higher chlorinated PCDD congeners in rats is much lower because of lower solubility and larger molecular size. So, gastrointestinal absorption of OCDD in rats was low, demonstrating 2-15% absorption of the administered dose following oral exposure (Kubota et al., 2004). With regard to breast-fed infants, almost complete PCDD, PCDF and PCB absorption (> 90%) has been demonstrated by McLachlan et al. (1993).

Iwata et al. (2004) observed that highly chlorinated PCDD and PCDF congeners (hepta-(Hp) and OCDD/Fs) showed low absorption efficiency from the intestinal tract and rapid metabolism, and highlighted that the absorption of PCDDs from the gastrointestinal tract in several species including rat and mouse indicated congener-specific absorption after oral exposure. In rodents, absorption of highly insoluble congeners, such as Hp- and OCDDs, is not highly effective across the intestinal wall. Furthermore, highly chlorinated congeners may be more efficiently absorbed in rat treated with subcutaneous administration.

Regarding the congener-specific accumulation related to life stages of cormorant, life-stage-related compositional differences were observed for PCDD and PCDF congeners. The predominant congener in the liver of adult cormorants was 2,3,4,7,8-PeCDF, followed by 1,2,3,6,7,8-HxCDD and 1,2,3,7,8-PeCDD,

whereas OCDD contribution was as high as 2,3,4,7,8-PeCDF in juvenile birds, followed by 1,2,3,4,6,7,8-HpCDD/1,2,3,7,8-PeCDD. For several PCDD and PCDF congeners, there were significant compositional differences between adult and juvenile birds. In the adult, contributions of 1,2,3,7,8-PeCDD and 1,2,3,6,7,8-HxCDD/F to total PCDD and PCDF levels were significantly higher than those in the juvenile. On the other hand, the contribution of OCDD, 2,3,7,8-TCDF, and 1,2,3,4,6,7,8-HpCDF were significantly higher in juvenile than in adult birds. Underdeveloped gastrointestinal tract in juvenile may lead to enhancement of absorption of congeners with large molecules such as OCDD and HpCDD/Fs. With respect to PCBs, adult cormorants retained non-ortho coplanar PCBs in the order of PCB126 > PCB169/PCB81 > PCB77, and the juvenile birds in the order of PCB126 > PCB77 >PCB81 > PCB169 (Kubota et al., 2004).

Distribution

There are clear differences in the kinetic behavior of PCDDs and PCDFs in different species. Pirkle et al. (1989) estimated that the plasma half-life of TCDD in humans was approximately 7 years, which was much longer than the half-life of TCDD reported in animals. Besides, USEPA (1994) reviewed physiologically based pharmacokinetic (PBPK) modeling of TCDD, and Carrier et al. (1995a; 1995b) developed a physiologically based model which described the absorption and disposition kinetics of PCDDs and PCDFs accumulated in human organism after uptake from food, since it was considered important to develop toxicokinetic models capable of predicting PCDD and PCDF distribution in human tissues as a result of their long residence time in the body and their potential adverse health effects for humans.

Iwata et al. (2004) analyzed seven blubber tissues from male seals and the data were used for understanding the age trend and tissue distribution in combination with data from livers. As in previous

findings in rats and mice, similar results were observed by these authors as the tissue distribution of PCDD, PCDF and PCB congeners is dose dependent. On the other hand, tissue distribution patterns of PCDD, PCDF and PCB congeners appeared to be different between Baikal seals and rodents. The liver/adipose tissue concentration ratios increased with the degree of chlorination in Wistar rats following the repeated subcutaneous administration of PCDD and PCDF mixture. Detected differences in the tissue distribution patterns between Baikal seals and rats may be attributed to the difference in exposure routes since the wild seal population absorbs PCDDs, PCDFs and PCBs from the gastrointestinal tract, but the rat was subcutaneously treated. Another possibility of explaining the different distribution may be due to the difference in the metabolic capability of congeners: lower chlorinated congeners may be more readily metabolized in rats than in Baikal seals.

The tissue distribution of PCDDs, PCDFs and PCBs had been extensively investigated by acute or subchronic studies using experimental animals, but still needed to be verified in wildlife, which is chronically exposed to PCDDs, PCDFs and PCBs. Tissue distribution following chronic exposure to environmental pollutants in wildlife could be in steady state. Assuming the steady-state tissue distribution of PCDDs, PCDFs and PCBs in common cormorants, concentration ratios of liver to pectoral muscle on a lipid weight basis were examined for individual congeners. For most PCDDs and PCDFs, liver/muscle ratios were greater than 1.0 in all specimens. OCDD had the highest liver/muscle ratios, reaching a maximum value of 30. Liver/muscle ratios for PCB77 and all mono-ortho coplanar PCB congeners were less than or nearly equal to 1.0 in all specimens. The liver/muscle ratios progressively increased with degree of chlorination of PCDDs. Although molecular size and limited solubility may reduce the uptake of highly chlorinated congeners including from the gastrointestinal tract, OCDD had the highest hepatic affinity. The liver/muscle ratios of PCDF congeners showed no increase with degree of chlorination. Increase in liver deposition

depending upon the number of chlorination was also observed for non-ortho coplanar PCBs. For mono-ortho coplanar PCBs, there was less variance of the liver/muscle ratios between each congener (Kubota et al., 2004).

Metabolism

The aim of the metabolization is to increase their polarity to obtain hydrophilic substances in order expedite their excretion. Metabolism of xenobiotics is divided into two phases: phase I generally involves alteration of the structure of the compound to increase polarity and formation of a functional group that can undergo further conjugation (hydroxy- (OH-) and/or methylsulfonyl- ($MeSO_2$-)) or in some cases react with macromolecules such as DNA; and phase II, addition of polar groups. PCBs are metabolized to a complex mixture of quinines, phenols, dihydrols, triols and tetrols in the biological system.

TCDD pretreatment in rats increased the hepatic concentrations as well as the metabolism of [^{14}C]-TCDF. Iwata et al. (2004) deduced that induction of TCDF metabolism occurred in the rat pretreated with TCDD at a dose that also elicited enhanced hepatic uptake. Besides, these authors concluded that more 2,3,7,8-TCDF uptake than metabolism by coexistence of other congeners including TCDD might result in an increasing concentration with age in Baikal seal liver. Less metabolism of 2,3,7,8-TCDF in muscle, and efficient redistribution from muscle back to the liver due to poor retention of OCDD, 1,2,3,6,7,8-HxCDF, and 1,2,3,4,6,7,8-HpCDF in muscle could lead to no significant compositional difference between adult and juvenile in pectoral muscle of common cormorants. For TCDD, adult specimens exhibited significantly higher contribution than juveniles in pectoral muscle, but did not exhibit a similar trend in the liver. This result could reflect the hepatic metabolism and/or efficient distribution of TCDD from liver to pectoral

muscle (Kubota et al., 2004). Tulp and Hutzinger (1978) and Wacker et al. (1986) studied the metabolism of OCDD in the rat, in which no metabolite of OCDD was detected in tissues, bile, or excreta, which may be due to the lack of metabolism. Birnbaum and Couture (1988) argued that this is because of the complete chlorination of the OCDD molecule and hence the absence of C-H bonds, which are needed for enzymatic oxidization.

Studies about in vitro metabolism of [^{14}C]-PCB77 by hepatic microsomes from rats pretreated with Ah-receptor agonists (McKinley et al., 1993; Morse et al., 1995) identified three hydroxylated metabolites (4-OH-3,3´,4,5´-, 5-OH-3,3´,4,4´-, and 6-OH-3,3´,4,4´-tetrachlorobiphenyl) after incubations in the microsomes, indicating that the formation of phenolic metabolites of [^{14}C]-PCB77 depend on CYP1A induction. Murk et al. (1994) performed a qualitative study on the capacity of seal hepatic microsomes to metabolize PCB77 by incubating the microsomes of harbor seal environmentally exposed to PCBs with [^{14}C]-PCB77. The study showed that the metabolic rate of PCB77 was correlated with the EROD activity, and the presence of 4-OH-, 5-OH-, and 6-OH-tetrachlorobiphenyl metabolites were identified. No comprehensive data on the metabolism and elimination of PCB123 are available. Efficient degradation of PCB77 and PCB123 may be due to the presence of two unsubstituted adjacent carbon atoms.

OH-PCBs have been quantified in the blood of relatively few species, such as humans, seals, polar bears and fish. The introduction of the OH group into the aromatic ring of the parent PCB congener can occur either by direct insertion in the position *meta* or by arene epoxide formation and subsequent epoxide hydrolase-mediated ring opening with or without an intermolecular 1,2-shift of H and Cl atoms (Hoekstra et al., 2003). OH-PCBs have emerged as important classes of environmental contaminants in wildlife and humans because of their ability to bind with the thyroxin transport protein, transthyretin (TTR), and their interaction with thyroid hormone receptors. However, data on their occurrence in wildlife and their behavior

in the matrices of environment are limited (Kawano et al., 2005). Several studies have assessed the effects of OH-PCBs and $MeSO_2$-PCBs, mostly following systemic administration. The OH-PCBs are commonly detected at low concentrations in pregnant women and their infants within the first year of life (Dallaire et al., 2009). The chemical structures of OH-PCBs resemble natural hormones and, in this way, Otake et al. (2007) concluded that certain OH-PCBs have the capability to interact with thyroid hormone status in newborn humans.

With regard to $MeSO_2$-PCBs, they have been found in the fat and liver tissues of several biota, and formation is conditional on the capacity of an organism to form 3,4- and/or 2,3-arene epoxide PCB intermediates, which are intermediates of cytochrome P450 (CYP) isozyme products that are subsequently transformed to $MeSO_2$-containing analogues of the parent congeners, mainly by CYP2B-like mediated enzymatic processes. The $MeSO_2$-PCBs are sufficiently lipophilic to accumulate in biota and have been linked to endocrine-related effects, including disruption of thyroid hormone homeostasis, cytotoxicity, and competitive binding with the glucocorticoid receptor (Hoekstra et al., 2003). Metabolites of tetra-, penta- and hexachlorinated biphenyls are the major $MeSO_2$-PCBs detected in human milk, liver and adipose tissue.

Excretion

PCDDs, and PCDFs are excreted by biliary via, subject to enterohepatic circulation. Specifically, TCDD is excreted into bile and enters in feces, while TCDD metabolites are excreted in urine and bile. Other significant route of excretion for these POPs in lactating women is mobilizing into breast milk. Regarding PCBs, the main routes of excretion are bile, feces and breast milk.

Moser and McLachlan (2001) examined dietary intakes, faecal excretion and blood concentrations of

PCDDs, PCDFs and PCBs in 5 male volunteers. These authors demonstrated by examining the differing impacts of 3 diets containing high, ‘‘typical’’ and low PCDD, PCDF and PCB levels that while net absorption efficiency of PCDDs, PCDFs and PCBs was dependent on intake levels; excretion rates were independent of the intake level, and were instead linearly dependent on body burden. This implies that for those PCDDs, PCDFs and PCBs with long human residence times and for which intake exceeded contemporary exposure, older subjects would be expected to carry higher body burdens and display greater faecal elimination. On the other hand, absorption of PCDDs, PCDFs and PCBs from the diet is very efficient, as their presence in faeces arises as a result of endogenous excretion.

Iwata et al. (2004) affirmed that hepta- and octachlorinated PCDD congeners presented low excretion through lactation, which is consistent with observations from previous studies using rodents and monkeys, in which excretion via milk decreased with increasing chlorine content (Van den berg et al., 1994).

2.2. Toxicological database for PCDDs, PCDFs and PCBs

Initially, the International Toxicity Equivalency Factor (I-TEF) method of risk assessment was a revised interim procedure for assessing the risks associated with exposures to complex mixtures of PCDDs and PCDFs. This method was developed by a working group of the North Atlantic Treaty Organization's Committee on the Challenges of Modern Society (NATO/CCMS 1988) and since then was officially adopted by several countries. Prior to the development of this I-TEF method, at least ten slightly different schemes had been used throughout the world, which complicated communication among scientists and regulatory agencies concerning the toxicological significance of complex mixtures of PCDDs and PCDFs. The I-TEF approach facilitated risk communication internationally by reducing large volumes of analytical data into a

single number-International Toxicity Equivalents (I-TEQ) (Kutz et al., 1990). Each congener of PCDDs, PCDFs and DL-PCBs shows different toxicity levels. In order to synthesize the toxicity of all these different substances, the concept of TEF was re-evaluated in 1997 by World Health Organization (WHO) for both human (**Table 2**), fish, and wildlife risk assessment, which facilitated regulatory controls. As a result of this, analytical results related to each PCDD, PCDF and DL-PCB congeners were expressed in a quantifiable unit, TEQ of TCDD. With respect to this item, uncertainties that could compromise the TEF concept were reviewed by Van der Berg et al. (1998), including non-additive interactions, differences in shape of the dose-response curve, and species responsiveness. In spite of these uncertainties, these authors concluded that the TEF concept was still the most plausible and feasible approach for risk assessment of PCDDs, PCDFs and PCBs.

However, a new WHO expert meeting was held in Geneva (June 2005) during which the TEFs for PCDDs, PCDFs and DL-PCBs were again re-evaluated (**Table 2**). Several values were modified, especially DL-PCB values, octachlorinated congeners and pentachlorinated furans. Consequently, Van den Berg et al. (2006) published an article in which summarized the process followed by WHO experts in each decision about modifying TEF values for PCDDs, PCDFs and DL-PCBs during their 2005 meeting, with the objective to harmonize these TEFs on the international level, thereby giving recommendations to national regulatory authorities. In this sense, these authors explained several subjects about the mode of action of this WHO expert panel, such as the criteria for inclusion of a compound in the TEF concept and the process used to determine TEF values (point estimates, expert judgement and probabilistic distribution) for PCDDs, PCDFs and DL-PCBs, as well as the discussion about possible inclusion of other compounds in the TEF scheme.

Finally, data about the effect of these new TEF values and their recent appearances were compiled in scientific reports drafted by European Food Safety Authority (EFSA 2010a; 2010b), which were recently

used by the European Commission to report the current regulation about maximum levels for dioxins, dioxin-like PCBs and non dioxin-like PCBs in foodstuffs (Commission Regulation (EU) No. 1259/2011).

3. Contamination of food for PCDDs, PCDFs and PCBs

3.1. Routes of exposure

As a consequence that major environmental sources of dioxins are emissions from industrial chlorination processes and combustion of materials containing chlorine, inhalation and water have been regarded as significant PCDD and PCDF exposure pathways so food (**Table 3**) could be considered as primary source, especially fatty animal products and seafood (Fernández-González et al., 2012a,b; Yebra-Pimentel et al., 2012). In this sense, Schecter et al. (1994) checked that food, especially meat, milk, and fish, is the immediate source of almost all PCDDs, PCDFs and DL-PCBs in the general population. The main pathways of PCDDs and PCDFs entry into food chains are atmospheric transport of emissions and their subsequent deposition on plants, soils, and water. However, PCDDs and PCDFs use to be not taken up and translocated by plants, so residues in foods and feeds derived from seeds should be negligible. Specifically, animals in which accumulate more PCDD and PCDF residues from the environment are often those fed with high-roughage diets or those that ingest contaminated soil (Fries 1995). This fact is in agreement with the study accomplished by Svensson et al. (1995) in which these authors observed that Swedish fishermen from the east coast, who used to eat more fatty fish than Swedish fishermen from the west coast, had higher blood levels of PCDDs, PCDFs and PCBs than Swedish west coast fishermen.

3.2. Occurrence of PCDDs, PCDFs and PCBs in foods

PCDDs, PCDFs and PCBs are a group of POPs, which are highly resistant to chemical and biological

degradation, can enter the food chain and eventually bio-accumulate in the human body (Vosniakos et al., 2011). Consequently, food intake is the major pathway for human exposure to PCBs, PCDDs and PCDFs, especially high-surface vegetables and animal fatty foods. Xing et al. (2008) analyzed the bioaccessibility of PCBs in different food items (fish and vegetables) using an in vitro digestion method. The results of this research showed average bioaccessibilities of PCBs in bighead carp, oriental weather fish, spinach and cabbage of 2, 3, 25 and 27%, respectively. So, differences between vegetables and freshwater fish bioaccessibilities of PCBs were found which were related to food sequestration, biomagnification, and relative accumulation of different congeners. In conclusion, bioaccessibility should be included in the risk assessment process because provide a practical estimation of human exposure and health effect assessment for PCBs.

Animal fatty foods

The current concern about PCDD, PCDF and PCB presence in the food chain has been mainly determined by the use of contaminated feeds because small sources of contamination at farm level could have a major impact (Brambilla et al., 2004). The occurrence of these POPs in animal fatty foods has been accounted to estimate the human exposure of most Europeans and North Americans (Birmingham et al., 1989; Fürst et al., 1990a; MAFF 1992; Theelen et al., 1993). As a consequence, the regulatory authorities of the EU have defined different PCDD, PCDF and PCB contamination threshold levels for the compliance of both marketed feeds and foods. Specifically, maximum levels for PCDDs and PCDFs have been established for foods of animal origin, and such thresholds were identified based on the European Commission (EC) Scientific Committees' knowledge of the pollution levels of the food chain in the EU (**Figure 2**). In this sense, the main objective of the current regulatory framework for dioxins and furans is to devise an

appropriate risk management to prevent high human exposures in the case of production/distribution of unacceptably polluted foodstuffs (Brambilla et al., 2004).

In the last decade, several studies have studied the occurrence of PCDDs, PCDFs and PCBs in animal fatty foods. Corsolini et al. (2002) reported accumulation patterns of PCDDs, PCDFs and PCBs for Arctic and Antarctic marine food webs. These authors found PCDD and PCDF levels <90 pg/g wet weight (wet wt) in polar animals and observed that PCDD congeners showed peculiar accumulation patterns in different organism, as well as that higher PCB levels were found in skua liver (11150 ng/g wet wt). Moreover, in this research was concluded that the high levels of dioxin-like chemicals founded in skua suggest the importance of intake via diet and migration habits, thus POP detection can be useful to trace migration behavior. Finally, the POP transfer from the mother to eggs was proved due to the POP levels detected both penguin and skua eggs.

Sasamoto et al. (2006) suggested that more detailed PCDD, PCDF and DL-PCB dietary intake studies should be carried out based on the anticipated changes of fish and shellfish consumption because Japan is one of the world's leading consumers of these animal fatty foods. In this sense, Japanese retail fish contain an average dioxin level of 1.6 pg TEQ/g and about 60% of the dietary intake of dioxins is likely to come from the intake of fish and shellfish. Besides, these authors noted that an appropriate disposal of PCB containing materials should be promoted with methods such as base catalyzed decomposition and supercritical water oxidation.

Fernandes et al. (2010) reported a study in which PCDD, PCDF and PCB levels were investigated in commonly consumed offals (lamb, ox, deer and pig's liver, kidneys, tongue and heart) and offal products (pâté, haggis, tripe and black pudding). The results obtained in this research generally confirmed the fact of that the highest PCDD, PCDF levels were observed in liver samples, particularly deer and lamb liver.

Regarding lamb liver, nine samples were found to show PCDD, PCDF levels above the EU maximum limit of 6 ng·kg^{-1} fat weight. These authors found out for most of analyzed samples that the dioxin-like toxicity derived mainly from PCDD/Fs and the contribution to ∑WHO-TEQ from PCBs and ortho-PCBs in particular was relatively low.

Bruns-Weller et al. (2010) also investigated the occurrence of several PCDDs, PCDFs and DL-PCBs in livers of sheep from Lower Saxony (Germany) and found that 93 % of the investigated sheep liver samples exceeded the EU maximum tolerance level for PCDD/Fs of 6.0 pg WHO-PCDD/F-TEQ·g^{-1} fat, with a measured average value of 24 pg WHO-PCDD-PCDF-TEQ·g^{-1} fat. Furthermore, these researchers observed that 92 % of analyzed samples also exceeded the cumulative maximum tolerance level of 12 pg WHO-PCDD-PCDF-PCB-TEQ·g^{-1} fat set in the EU for the sum of PCDDs, PCDFs and DL-PCBs in livers of sheep and derived products, with an average value of 43 pg WHO- PCDD-PCDF-PCB-TEQ·g^{-1} fat. Low PCDD, PCDF and DL-PCB levels were detected in the meat of the sheep, which never exceeded the respective maximum tolerance levels. No significant differences in the burden of pollution of sheep liver samples were appreciated between male and female sheep and between rural and municipal areas. No correlation was found between the age of the sheep and the PCDD, PCDF or DL-PCB burden in their liver. These authors concluded that the high level of pollution with PCDD, PCDF and DL-PCB in sheep livers may be caused by physiological differences with respect to other animal species and by the environmental pollution related to historic PCDD, PCDF and PCB sources.

In other study, Suominen et al. (2011) researched the occurrence of PCDDs, PCDFs and PCBs in several samples of fishmeal, fish oil and fish feed. These authors observed that all measured TEQ levels of PCDDs, PCDFs and PCBs were below the maximum levels established by Directive 2002/32/EC. Besides, no correlation between levels of WHO-PCDD-PCDF-TEQ and indicator PCBs was observed in analyzed

samples. This research highlighted the need to take into account the origin and purity of feed raw material of marine origin. In this sense, these researchers concluded that possibilities for cleaning raw materials from POPs should be used in order to reduce levels of these pollutants in feed and food. Additionally, they showed that indicator PCBs alone are not suitable for predicting total TEQ levels in processed marine products because PCDDs and PCDFs have a significant contribution to the total TEQ level in the sample.

Marin et al. (2011) conducted a monitoring program about the occurrence of PCDDs, PCDFs and DL-PCBs in several food samples marketed in the Region of Valencia (Spain), and observed that the food groups which presented higher contamination were fish oil (6.4 pg WHO-TEQ·g^{-1} fat), fish (1.2 pg WHO-TEQ·g^{-1} wet wt) and milk and dairy products (0.90 pg WHO-TEQ·g^{-1} fat). As a consequence of the results, these authors concluded that the main contributors to total PCDD, PCDF and DL-PCB intake for adults were fish (59 %), milk and dairy products (19 %), and fat and oils (9.0 %).

High-surface vegetables

Soils and vegetation is the major sink for airborne POPs. The measurement of PCDD, PCDF and PCB levels in these media is useful to establish trends in their abundance and their consequences as result of natural and anthropogenic changes. Furthermore, the levels of POPs in soils provide information about environmental contamination of an area for long periods of time, while vegetation gives more information about pollution for short periods of time. In this way, the lowest chlorinated POP congeners use to have a relative higher abundance in vegetation samples than in soil samples (Schuhmacher et al., 2004).

A study performed by Hülster et al. (1994) showed that the high PCDD and PCDF levels in above-ground parts of some plant species from the family *Cucurbitaceae* (zucchini and pumpkin). It could be due to the

uptake of these pollutants through the roots and subsequent translocation to the shoots, although these vegetables, as well as cucumber, are mainly polluted *via* atmospheric deposition of PCDDs and PCDFs. The mechanism responsible for the transfer of PCDDs and PCDFs into these vegetables could be the release of root exudates with PCDDs and PCDFs, because certain compounds in these exudates may desorb PCDDs and PCDFs from organic matter particles in the rhizosphere, and thus possibly enhance their availability for root uptake.

Nakagawa et al. (2002) conducted an investigation to understand the PCDD and PCDF pollution of leafy vegetables (spinach), in which PCDD and PCDF levels were higher in the leaves than in the stem and red collar, but considerably lower than in the primary and secondary roots, and such roots are significantly affected by the soil, which is recognized as a drain of airborne PCDDs and PCDFs. Furthermore, several lower-chlorinated PCDDs, PCDFs and *non-ortho* PCBs were much more presents in the leaves than in the secondary roots. So, as a consequence of this fact, these authors suggest that the deposition of moderately volatile PCDDs and PCDFs in the wax from the leaves of leafy vegetables is another way of exposure to consider.

On the other hand, Tsutsumi et al. (2002) found a strong correlation (r= 0.957) between 2,3,4,7,8-PeCDF TEQ levels and total TEQ levels in the analyzed leafy vegetables samples. So, this congener could be applicable as an indicator for dioxin contamination in the analysis of leafy vegetables. These authors also demonstrated that the dioxin levels in spinach samples were decreased by effect of washing and washing followed by boiling processes. Thereby, the average levels of PCDDs, PCDFs and *non-ortho* PCBs were respectively decreased to 38%, 73% and 88% with respect to initial levels by washing and to 21%, 35% and 61% with respect to initial levels by washing followed by boiling. Thus, cooking processes could reduce the risk of dioxin intake from the leafy vegetables, and this fact seems to be due to the exclusion of particle-

bound dioxins from the spinach surface by washing and boiling.

As result of the studies previously cited (Nakagawa et al., 2002; Tsutsumi et al., 2002), the extent of human PCDD and PCDF exposure due to the consumption of colored leafy vegetables (such as spinach) could be considerably decreased. So, vegetable itself does not have a substantial role as a PCDD and PCDF source for exposure to humans. In fact, in the 1998 and 1999 national Japanese investigations, the dioxin intake from colored vegetables were corresponded to 1.5% and 1.1% with respect to the total dietary intake of dioxins per person, respectively. Therefore, Nakagawa et al. (2002) considered reasonable to conclude that the PCDD and PCDF pollution of commercial leafy vegetables is actually a minor problem, and that leafy vegetables should be recommended as part of a healthy diet.

Fiedler et al. (2002) determined PCDD and PCDF levels in Chinese tea samples, as well as in the infusions prepared from these teas, and concluded that dioxin levels in green tea leaves were due to uptake of atmospheric PCDDs and PCDFs. Besides, these authors considered that the higher concentrations in brick tea leaves were caused by the longer exposure time, the use of old leaves, branches and roots for making tea, and additional components such as soil particulates. Finally, these researchers indicated that certain Chinese populations consume more tea (>31 per day) than Europeans or North Americans, and this fact results in a comparably higher intake of PCDDs and PCDFs.

Amakura et al. (2003) evaluated dioxin contamination (PCDDs, PCDFs and *non-ortho* PCBs) in fresh vegetables obtained from Japanese supermarkets in 2002. Among the samples, dioxins were generally detected in green leafy vegetables and the highest TEQ value was for mulukhiya (0.089 pg-TEQ·g^{-1}), followed by spinach and komatsuna (Japanese mustard spinach) (0.077 and 0.074 pg-TEQ·g^{-1}, respectively). However, as can be seen, these values are relatively low.

4. Bioaccumulation of PCDDs, PCDFs and PCBs

Bioaccumulation can be defined as the process by which chemicals are absorbed and removed from the water directly by organisms or through the ingestion of food, and use to be assessed by analyzing certain characteristics of POPs, such as K_{ow}, bioconcentration factor from water (BCF), bioaccumulation factor (BAF), the biota-sediment accumulation factor (BSAF) and biomagnification factor (BMF). As a consequence of the need to understand POP movement within food webs, various food web models have been developed and applied to supplement our understanding of field and laboratory studies about their behavior within organisms and through the food web (Yebra-Pimentel et al., 2012).

In particular, PCDDs, PCDFs and PCBs are removed from the atmosphere by physical processes, such as wet and dry deposition and vapor uptake, and are deposited on soils, surface waters, and plant surfaces. Most of these POPs that are deposited on surface waters sorb onto suspended sediments and once bound to soil and sediment these chemicals generally remain fixed, except for bulk transport due to soil erosion, flooding, and dredging (USEPA 2006). So, the ingestion of these compounds by animals results in their preferential bioaccumulation and biomagnifications in higher trophic levels of the food chain (Weisbrod et al., 2009).

Van der Oost et al. (1996) determined BSAFs for PCDDs, PCDFs and PCBs in sediments and eel from six Amsterdam freshwater sites, and discussed bioaccumulation of these POPs in eel considering partitioning, uptake from contaminated water (bioconcentration) and food (biomagnification), clearance, and bioavailability. In this way, the high BSAF values obtained for PCBs indicated that biomagnification contributed significantly to the total bioaccumulation process. Higher chlorinated PCBs presented the higher BSAF values, which may be due to a more efficient biomagnification of these congeners and to a selective metabolism of the lower chlorinated congeners. On the other hand, these authors observed that

bioaccumulation of PCDD and PCDF congeners were considerably low in eel and that their BSAF values decreased with increasing chlorine substitution. Moreover, BSAF values amply varied for most of these pollutants, which suggests that bioaccumulation depends on type of organism and analyte, but also on site-specific factors. This fact could be due to differences in bioavailability of the chemicals or to differences in the diet of the fish when biomagnifications is involved.

McLachlan (1996) examined the bioaccumulation of PCDDs, PCDFs and PCBs in an air-plant/soil-cow-human food chain using data collected in Germany. In this study, it was observed that the fugacity of these pollutants was similar in air, soil, and plants, suggesting near-equilibrium partitioning with somewhat higher fugacities in cows' milk indicative of moderate biomagnification. However, the fugacities of the more non volatile POPs decreased from air to plants to cows' milk. This phenomenon was named biodilution and can be explained by the kinetically limited uptake of less volatile compounds in plants and the reduced absorption of very hydrophobic compounds in cows. Furthermore, human milk presented fugacities 20-50 times higher than cows´milk, and this is indicative of strong biomagnifications in humans.

There are several ways by which animals can be and have been exposed to PCDDs, PCDFs and PCBs such as ingestion of low POP concentrations through consumption of environmentally contaminated feeds or feed components, and accidental incorporation of the POP into the feed, resulting in exposure to relatively high POP levels. Usually, food animal exposures to PCBs, PCDD and PCDFs occur below levels which result in acute toxicity. Thereby, clinical signs are not evident and there is not often a remarkable economic impact on animal health, although there may be detectable contamination of some food products such as milk, meat, and eggs (IPCS 1989; 1992). An example that has showed this fact is seen in **Figure 3,** in which the real distribution of PCDD and PCDF levels in food products is illustrated by the French data set for milk and milk products (EC DG HCP 2000)**.** Besides, the lognormal shape of the frequency

distribution is also observed for other food groups, such as meat and fish, as well as their related products.

Historically, biomarkers of in vivo chemical exposure retrospectively led to the identification of POPs. Several in vivo measurement approaches can be used to assess the bioaccumulation of POPs in aquatic or terrestrial species using laboratory-exposed, field-deployed, or collected organisms. In this way, important issues associated with laboratory measurements of bioaccumulation include appropriate test species selection, test chemical dosing methods, exposure duration, and chemical and statistical analyses. Both laboratory and field methods also require reliable determination of POP levels in exposure media of interest (water, sediment, food, etc.), accumulated body residues, or both of them (Weisbrod et al., 2009).

On the other hand, the advantages and disadvantages of various bioindicator species (mussels, squids, fish, birds, marine mammals, human tissues and organs) for POP monitoring were reviewed and discussed in detail by Tanabe and Subramanian (2005). Regarding this subject, a remarkable type of bioindicator for body burden of PCDDs, PCDFs and PCBs is human milk. In this way, Fürst et al. (1990b) determined PCDDs, PCDFs and PCBs in human milk samples from nursing mothers in Germany, although only PCDD and PCDF congeners with 2,3,7,8-chlorine substitution were found. With regard to the pattern observed for PCDDs, OCDD normally showed the highest level, while the levels of the other PCDD congeners decreased with decreasing number of chlorine atoms. However, a different pattern was found for PCDFs in which 2,3,4,7,8-PCDF was the most abundant congener, followed by the hexachlorodibenzofurans. The mean level of TCDD in human milk samples was of 3.2 pg/g fat, while for total PCDDs and PCDFs, calculated as I-TEQ, of 29 pg/g fat. Subsequent investigations revealed lower levels compared to former years, which could be an indication that the efforts undertaken to minimize PCDD and PCDF emissions and to shut down known sources had a positive effect on the body burden of humans. With respect to PCBs, these researchers observed a similar trend.

With regard to the accumulation of PCBs in fruits and vegetables, Grassi et al. (2010) affirmed that a specific subject of particular interest were the high values for total PCB and TEQ-DL-PCB levels in rosemary plants, which could be related to the characteristics of the leaves. PCB accumulation in these plants may come from re-suspension in air from the soil with subsequent deposition on their leaves, which are particularly rich in vegetable waxes. Consequently, rosemary leaves seemed to have the potential to accumulate lipophilic compounds such as PCBs, as suggested by the PCB profiles in their leaves, with relative enrichment in the highly volatile PCBs, low-chlorination congeners (PCB118, PCB105, PCB77, PCB99 and PCB126), as well as lower levels of the less volatile PCBs, high-chlorination congeners (PCB156, PCB170, and PCB180).

Furthermore, Grassi et al. (2010) also highlighted the possibility of using conifer needles as passive bio-monitors of PCBs, and suggested rosemary as an indicator of this kind of environmental pollution. In this sense, these authors indicated that rosemary is an evergreen plant with a lifespan of several years, which could increase its potential to accumulate POPs for longer than seasonal vegetables. Besides, these researchers declared that the marked difference in PCB levels between rosemary and all the other vegetables supported the idea of continuous accumulation in the leaves, and, therefore, concluded that levels in rosemary might grossly indicate the global PCB pollution in a specific area. Finally, Grassi et al. (2010) also observed that PCDD and PCDF levels were higher in rosemary samples, confirming that this plant also accumulated these POPs.

5. Dietary exposure assessment to PCDDs, PCDFs and PCBs

Food consumption clearly represents the main route of exposure of PCDDs, PCDFs and DL-PCBs for the

general population. Specifically, 17 PCDDs, PCDFs and 12 DL-PCBs tend to accumulate through the food chain, such as in animal fats and products. Since these POPs act through the same toxicological pathway and due to cumulative observed effects, the exposure to these 17 PCDDs, PCDFs and 12 DL-PCBs is generally assessed using their corresponding TEFs, allowing the toxicity of a complex mixture to be expressed in TEQ unit. In 2001, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable monthly intake (PTMI) for the 17 PCDD and PCDFs and 12 DL-PCBs of 70 pg TEQ-WHO (kg bw)$^{-1}$ month^{-1} (Sirot et al., 2012). Regarding iPCBs, a tolerable daily intake (TDI) of 10 ng (kg bw)$^{-1}$ day^{-1} has been proposed for Sirot et al. (2012) based on neurological effects observed in Rhesus monkeys.

The Total Diet Studies (TDS) are standardized methods recommended by the WHO (WHO 2005; 2006) which aim at providing contamination data for food prepared as consumed by the population, and exposure data, in order to help risk managers make public health decisions. These TDS are also used for dietary exposure assessments of PCDDs, PCDFs and PCBs, consisting of three major steps: (i) food sampling, (ii) analysis of the samples, and (iii) evaluation of exposure by combining the contamination data with the national consumption data (Sirot et al., 2012).

In 2000, the Scientific Cooperation of the European Union achieved an assessment of dietary daily intakes in several European countries which resulted in an average estimation of 0.40 – 1.5 pg international (I)-TEQ per kg-bw for dioxins and 0.80 – 1.8 pg PCB-TEQ/kg-bw for DL-PCBs (HCPD-G 2000). Later, the Scientific Committee on Food of the European Commission adopted a tolerable weekly intake (TWI) for dioxins and DL-PCBs together (total TEQ) of 14 pg WHO-TEQ/kg-bw per week, corresponding to a tolerable daily intake (TDI) of 2.0 pg WHO-TEQ/kg-bw per day (SCF 2000; 2001).

According to the EU Scientific Cooperation results, TDI for PCDDs, PCDFs and DL-PCBs was exceeded by

a considerable part of the European population. As a result, several researches in different European countries were performed since then to quantify the daily intake of these persistent organic pollutants (**Table 4**). The average daily intakes estimated were slightly above the TDI adopted by SCF (2000; 2001) for almost all cited countries.

Tsutsumi et al. (2001) found in their study that the main source of PCDDs, PCDFs and DL-PCBs in Japanese population was the fish and shellfish group. Likewise, Focant et al. (2002) performed a similar research in which horsemeat and fishes presented the highest values, and whose results could serve as a set of reference data for general exposure of general population in Belgium.

Following this research line, Baars et al. (2004) noticed that the contribution of different food groups to the total intake of both PCDDs, PCDFs + DL-PCBs and NDL-PCBs is uniformly distributed over the foods consumed by Dutch population: meat products (23% and 27%, respectively), dairy products (27% and 17%, respectively), fish (16% and 26%, respectively), eggs (4% and 5%, respectively), vegetable products (13% and 7%, respectively), and industrial oils and fats (17% and 18%, respectively).

Later, Bocio and Domingo (2005) found that fish and seafood (33.7%), oils and fats (15.3%), cereals (14.4%), and dairy products (13.7%) were the most important contributors to the dietary intake of PCDDs and PCDFs in Tarragona (Spain). Similarly, Fattore et al. (2006) obtained results for the Italian population which indicate that the main contributions to total PCDDs, PCDFs and DL-PCB intake are due to fish and fish products (44%) and to milk and dairy products (27%).

Further works were carried out by Domingo and Bocio (2007) in which these authors reviewed PCDD, PCDF and PCB levels in marine species and human intake through fish and seafood consumption, and concluded that some groups of population frequently consuming high quantities of certain marine species

could be significantly increasing health risks due to PCDD, PCDF and PCB exposure. However, a significant decreasing trend in human dietary exposure to PCDDs, PCDFs and PCBs has been detected in the last years, which could be due to the decrease in the concentration of these pollutants in the majority of foodstuffs (Baars et al., 2004; Llobet et al., 2008).

6. Challenges of scientific research in PCDDs, PCDFs and PCBs

A large volume of epidemiologic and mechanistic data about PCDDs, PCDFs and PCBs has been published in the last years, so identifying research gaps for these pollutants is quite difficult.

6.1. Methods of removal

Nowadays, the main sources of exposure of PCDDs, PCDFs and PCBs in humans are considered feed and food. In this way, both fishmeal and fish oils are used as food and feed ingredients as one of the main sources of ω-3 fatty acids (EPA and DHA) in animal and human diet, but they can contain high levels of PCDDs, PCDFs and PCBs due to their lipophilic properties. As a consequence of this fact, several studies were performed in the last years about removal methods for dioxins and PCBs from fishmeal and fish oil.

Maes et al. (2005) pointed out that during fish oil refining process is important to remove these POPs without changing its nutritional quality, and treatments with non-polar adsorbent material (activated carbon) could be the most efficient process for such objective. These authors evaluated the efficiency in removing PCDDs, PCDFs and PCBs after using four grades of activated carbon, as well as the effects of this type of treatments in the nutritional quality of the oil. The results of this study showed that PCDD, PCDF and PCB removal efficiencies after treatment of contaminated cod liver oil with 0.5 % of activated carbon were below

30 % for *mono-ortho* PCBs, up to 80 % for DL-PCBs, and almost 100 % for PCDDs and PCDFs. Besides, this treatment caused no important changes on fatty acid composition.

Baron et al. (2007) performed a comparison study about extraction with organic solvents (ethanol, isopropanol and isohexane) and enzymatic treatments as methods to reduce PCDD, PCDF and PCB levels in fishmeal. The results showed that treatments with organic solvents lowered the oil content of the fishmeal by 80 % but this one may content traces of solvent and had lower fat content. Besides, PCDD, PCDF and PCB extraction with olive or fish oil was very effective with rates of 60-75 % after a single extraction step. This simple and quick treatment could be applied at an industrial scale in a cheap way for the producer. With regard to enzymatic treatments, protease alcalase and oxidoreductases were efficient neither for removing oil from fishmeal (30 %) nor for PCDD, PCDF and PCB degradation (10-15 %). Further studies in pilot scale were accomplished by Oterhals et al. (2008) who established that most of the dry matter and lipid content in the fishmeal is attached to the press cake intermediate product. Besides, dioxin and DL-PCBs process partitioning is reflected by the fat partitioning data in which quantification of fat content based on chloroform/methanol extraction was selected. The best reduction in dioxin and DL-PCB content was achieved by soybean oil extraction of the press cake (97 %) and when this process conditions were combined with fat separation of the stickwater concentrate, higher decontamination rates were got with respect to hexane and isopropanol extraction of the fishmeal.

Kawashima et al. (2009) carried out new studies about this subject in which the PCDD, PCDF and DL-PCB removal from fish oil by countercurrent supercritical CO_2 extraction (CC-SCE) and activated carbon treatments were investigated. When fish oil was treated by CC-SCE (70 ºC / 30 MPa / CO_2-oil ratio = 72), the obtained reduction rate in the sum of PCDD, PCDF and DL-PCB concentration was 93 % (85 % in TEQ), while in subsequent treatment by activated carbon this elimination rate was 94 % (93 % in TEQ).

Moreover, these authors concluded that CC-SCE and activated carbon treatment were effective for DL-PCB and dioxin removal, respectively. So, CC-SCE combined with activated carbon treatment seems to be applicable to PCDD/Fs and PCB removal from fish oil.

More recently, Ortiz et al. (2011) accomplished a screening study with several commercially available silicon-based and carbon-based solid adsorbents in order to determine their dioxin and PCB removal capacity from refined salmon oil, after evaluation and optimization of adsorption conditions (2.5 % of adsorbent amount, 37.5 min of adsorption time, 100 hPa and 80 ºC, using activated carbon obtained from coconut shell). According to the results, these authors observed that silicon-based adsorbents showed low dioxin and PCB removal efficiencies, while carbon-based adsorbents showed high removal rates for PCDD and PCDF and slightly lower ones for DL-PCBs. Besides, obtained removals in this study were 99 % for PCDDs and PCDFs, 36 % for DL-PCBs (81 % in pg WHO-TEQ·g^{-1} concentrations) and 11 % for marker PCBs.

On the other hand, the barrier common to all in situ PCDD, PCDF and PCB remediation technologies is their limited availability in soils and sediments because their hydrophobic nature allows them to tightly adsorb to organic matrices within soils and sediments, making them resistant to microbial attack and chemical reduction (Mondello 2002). Besides, these authors concluded that the degree of sorption is dependent on the organic content of the sediment/soil and demonstrated that at most 60 % of PCBs at any sediment depth are available to biological or chemical processes. In this same way, Gardner et al. (2004) affirmed that there is generally a fraction of sediment-bound PCBs that readily desorbs, as well as a “slow” fraction of strongly adsorbed particles. Results obtained by Dr. Gardner showed the impairment of PCB dechlorination in the clayey, organic-rich sediments of New Bedford Harbor.

Nowadays, addition of surfactants is the most common way to increase PCDD, PCDF and PCB desorption.

Surfactants are surface acting agents that increase solubility by lowering the interfacial surface tension between aqueous and non-aqueous phase fluids (Abraham et al., 2002). In respect to this subject, while past experiments conducted by Mondello (2002) using surfactant amendments to increase PCB degradation have had mixed results, Fava and Piccolo (2002) found that humic substances and most other surfactants increased PCB degradation and dechlorination yields. However, Abraham et al. (2002) concluded in another study that some surfactants adversely affect bioremediation by decreasing microbial populations.

An efficient and environmentally friendly method of PCDD, PCDF and PCB manipulation must be uncovered to allow in situ eradication of the contaminant due to despite years of research, an effective in situ remediation technique for PCDD, PCDF and PCB -contaminated soils and sediments does not exist. In this research line, a sequential anaerobic/aerobic bioremediation system has always exhibited enormous potential at the laboratory scale. Wu et al. (2002) identified dechlorinating cultures *o*-17 and DF-1, and this research has treated isolating PCB-respiring organisms. Besides, Bedard (2003) established the dechlorination pathways, and Shaodong et al. (2002) showed that doubly ortho-substituted congeners remain reluctant to the recombined strain. However, genetic engineering can avoid this problem by preventing 2,3-dihydroxybiphenyl-1,2-dioxygenase (DHBD) inhibition.

The main drawback about in situ remediation of PCDDs, PCDFs and PCBs is the general public phobia of genetically modified organisms (GMOs) and nanotechnology, so the use of GMOs and nanomaterials must be mindfully regulated because is maybe the most promising technology to work up new less destructive technologies for the remediation of PCB-contaminated soils and sediments. Besides, the use of engineered bacterias in the environment needs to be strictly controlled in order to prevent their dissemination and delivery of the modified genes in the environment. However, active and passive biological containment

(ABC) systems seem the most promising method for PCB remediation processes. These ABC systems are based on the use of a killing gene and a regulatory circuit that controls the expression of the killing gene in response to an environmental signal. Also mastery of these techniques might reduce the public fear about the use of GMOs (Sylvestre 2004). On the other hand, nanoparticles are feared in general population because these nanoscale materials can enter the food chain and be absorbed or transported by water and food. Moreover, other reasons of distrust in these nanoparticles use to be their self-replication capacity and the facility of dissemination for non-targeted pollutants (Masciangioli and Zhang 2003). As a consequence of all these subjects, a better understanding about the behavior of nanomaterials in sediments and soils is necessary.

Finally, control techniques for GMOs and nanomaterials are important, but public hysteria should not exclude the advancement of the most promising agents for the in situ remediation of PCDD, PCDF and PCB -contaminated soils and sediments.

6.2. Transfer from feed ingredients to animal products

Animal feed can be simple forage or can be a complex matrix of many ingredients, with concerns about inherent toxic substances in some forage plants, added veterinary drugs and other contaminants such as mycotoxins, heavy metals or industrial chemical contaminants. Nowadays, it is well known that there are clear indications that the major source of human background exposure is food (> 90 %) with animal food being the predominant source. The SCF was recently asked to advise to European Commission on the scientific elements necessary for the establishment of limits and/or alternative measures aiming at reducing the dietary intake of PCBs and dioxins, because the recent cases of contamination of feedstuffs (citrus pulp

pellets, oils and fats and kaolinitic clay) highlighted the impact of contaminated feedstuffs as a source of contamination of food of animal origin with dioxins or PCBs (SCAN 2000).

In this sense, Malisch (2000) concluded that animal feed could contribute considerably to the contamination of food. This author found out PCDD and PCDF transfer processes from feed ingredients to food of animal origin (milk, butter and milk) as a consequence of use of citrus pulp in cow feed with PCDD and PCDF concentration of 5-10 ng I-TEQ/Kg. This feed component was about 20-100 times more highly contaminated than average feed with background contamination. So, it is important to pay attention to the dioxin contamination on food and feed by continuous control.

On the other hand, during the Belgian dioxin crisis, feed contaminated with dioxin and PCBs resulted in dioxin levels of eggs up to 713 pg I-TEQ/g fat, as well as even higher levels of DL-PCBs (Schoeters et al., 2006). In this way, Traag et al. (2006) established that the behavior of PCDDs, PCDFs and PCBs in laying hens, which were fed with feed from the Belgian dioxin incident, is comparable, and these authors highlighted the need of replacing the contaminated feed with clean feed to avoid PCDD, PCDF and PCB residues in eggs, fat and livers of laying hens. Therefore, Schmid et al. (2002) found elevated PCDD/F concentrations in eggs (13 pg I-TEQ/g fat), poultry (3.9 pg I-TEQ/g fat) and pork (7.5 pg I-TEQ/g fat) from Swiss farms, whose contamination could be attributed to PCDD, PCDF contaminated kaolin that was used as an anti-caking agent in feedstuffs.

Due to incidents like these, it is necessary a strict control of PCDD, PCDF and PCB levels in commercial feed and in particular feed ingredients. So, in order to complement the SCF evaluation of risks related to human dietary exposure, the European Commission requests an evaluation of the contribution of feedstuffs contaminated with dioxins, PCBs and dioxin-like PCBs to the contamination of food of animal origin (SCAN 2000). In this respect, fish meal and fish oil are the most heavily contaminated feed materials with products

of European fish stocks (1.2 and 4.8 ng WHO-TEQ/kg DM) more heavily contaminated than those from South Pacific stock (0.14 and 0.61 ng WHO-TEQ/kg DM). Animal fat is next in order of dioxins concentration (1 ng WHO-TEQ/kg DM), although values observed depend on the bioaccumulation of dioxins in fatty tissues along the feed/food chain (Ábalos et al., 2010; Easton et al., 2002).

Nowadays, consumers are increasingly aware of, and sensitive to, food safety issues and their linkage to animal production, including feeding practices. But at the same time, in many countries, people are chronically short of food and there is a need to improve the efficiency of animal production to provide better access to affordable protein. In this sense, global trade in food and feed continues to expand, with countries and sectors continually emerging as new participants. However, trade problems continue to arise as a result of countries establishing different national tolerances for residues, lack of harmonization with international standards, and sometimes from the lack of international standards. Therefore, differences among countries' capabilities to conduct analyses also contribute to trade problems. Finally, economics and technological advances are driving the development of new feed products, which may challenge established regulatory approaches to feed and food safety (FAO 2007).

6.3. Human health effects

Human exposure occurs by three main routes: inhalation, dermal absorption and ingestion of contaminated food and soil/sediments. However and it was previously commented, the most important source of PCDD, PCDF and PCB exposure of the general population is food of animal origin. NDL-PCB levels can be significantly correlated with DL-PCB levels (**Figure 4**), expressed either in analytical units or in toxicity equivalent units, this indicating that sources of contamination for both groups of PCBs were possibly the

same, such as in the work by De Felip et al. (2008).

Toxicity studies use to employ PCDD, PCDF and PCB (DL and NDL-PCB) technical mixtures. In general, these mixtures induce several toxicological effects such as effects on liver, thyroid, immune function, reproduction and behavior, as well as carcinogenicity. However, most of the epidemiological studies do not differentiate between DL-PCBs and NDL-PCBs, and when they do, congener exposures are highly correlated, thereby complicating causal inferences. Particularly, the adverse effects reported following exposure to individual NDL-PCBs in laboratory animal were effects on the thyroid, liver and brain biochemistry, as well as immunotoxicity, oestrogenicity, and reproductive and neurodevelopmental effects. Latter effects are particularly found in the offspring of rodents following in utero exposure. These effects are not all specific for NDL-PCBs but are also to be seen following exposure to PCDDs, PCDFs and DL-PCBs (EFSA 2005).

Human carcinogenicity

Sometimes, mortality studies have reported excess rates from cancers of the liver, gall bladder, biliary tract and gastrointestinal tract, and malignant melanoma in capacitor manufacturing workers and electrical utility workers exposed to various PCB technical mixtures (Brown 1987; Sinks et al., 1992; Tironi et al., 1996; Loomis et al., 1997; Gustavsson and Hogstedt 1997). Further studies included a large number of subjects, but relatively few of them were employed for periods longer than 10 years, so the duration of follow-up was limited. Besides, many studies have focused on breast cancer, although most of them did not reveal significant associations with PCB levels in blood (Moysich et al., 2002). Previously, Moysich et al. (1998) performed a study, which suggested that a PCB-associated breast cancer risk was limited to women with a

mutation in a metabolizing enzyme. Hardell et al. (1996) found a significant association between PCB levels in adipose tissue and non-Hodgkin's lymphoma in another assay.

Effects on reproductive system

Information is available about the effects of PCDD, PCDF and PCB mixtures on human reproduction from studies of people exposed via environmental: consumption of contaminated rice oil and fish, and occupational exposures. In this way, several studies were reported in which elevated PCB exposure was related with menstrual irregularities (Kusuda 1971), miscarriages (Gerhard et al., 1988), shorter length in menstrual cycle (Mendola et al., 1997) and spontaneous fetal death (Mendola et al., 1995). With respect to male reproductive functions, some studies reported a PCB-associated risk of infertility (Pines et al., 1987).

A study published by Mocarelli et al. (2000) concluded that male births decreased relative to all births couples exposed to TCDD in Seveso (Italy). Another study of subjects exposed to environmental PCBs from eating Great Lakes fish indicated that maternal exposure to PCBs decreased the ratio number of boys/number of girls of offspring, but that paternal exposure to PCBs could possibly have the opposite effect (Weisskopf et al., 2003).

Effects on nervous system function and development

A large variety of neurological symptoms were reported about workers exposed to technical PCDD, PCDF and PCB mixtures, however any dysfunction could be documented after routine medical examination of these workers. Schantz et al. (2001) found out limited evidence for deficits in learning and memory in Michigan residents who had eaten contaminated Great Lakes fish in the past as a result of dietary

exposure to environmental PCBs. On the other hand, Seegal (2004) suggested in a preliminary report that an excess occurrence of Parkinson's disease is present in former capacitor production workers.

Epidemiological studies on nervous system developmental adversity were carried out both in the US and Europe. Rogan et al. (1986) conducted this type of study in North Carolina where was observed that hyporeflexia, hypotonicity and delayed motor development up to 24 months postnatally were related to the prenatal PCB body burden of the mothers as indexed by total PCBs in early milk samples. Jacobson and Jacobson (1996) performed a similar study in Michigan where total PCB levels were measured in maternal and umbilical cord serum and in maternal milk from breastfeeding mothers. These authors concluded that Visual Recognition Memory at seven months was negatively related to total PCB levels, and at four years of age this was also true for memory performance. In New York, infants and children from birth to 54 months of age were studied by Darvill et al. (2000) and Stewart et al. (2000; 2003). In this sense, negative associations with perinatal PCBs were found at 6, 12 and 38 months of age for different neurodevelopmental outcomes.

With respect to this type of research in Europe, healthy mother-infant pairs were recruited by Huisman et al. (1995) both in Groningen and Rotterdam (Holland). Four PCB-congeners (118, 138, 153, and 180) were measured in maternal and cord plasma, as well as additional PCB congeners and a number of dioxins in early breast milk samples. However, negative associations were reported between milk levels of PCDDs, PCDFs and PCBs and neurological status and psychomotor development. A similar study was achieved by Walkowiak et al. (2001) with healthy mother-infant pairs from Düsseldorf (Germany), in which an association was found between PCB levels and mental development at 30 months. Besides, a re-examination of the Rotterdam part of the Dutch cohort at age of nine years revealed that prenatal PCB exposure was associated with longer response times, greater variability, and lower scores on an executive

function test. The latencies on event-related potentials of the brain were longer at higher PCB exposure levels, but breastfeeding was associated with a decrease (Vreugdenhil et al., 2004a; 2004b). So, these results suggest that the neurobehavioural manifestations reported to be associated with PCB exposure are likely to be permanent, but that the appearance may change during development.

Effects on thyroid gland

Langer et al. (1998; 2003; 2005) reported that exposure to technical PCB mixtures was associated with an increased thyroid gland volume which was checked in workers at a PCB production facility and nearby residents as compared to subjects from less polluted areas. Besides, these authors found that exposed workers and nearby residents had an elevated prevalence of antibodies against thyroid peroxidase, although serum concentrations of thyroid hormones were mostly within normal ranges. With regard to the infants, some studies demonstrated that PCB, PCDD and PCDF exposures were associated with reduced T3 and T4 in the infants at age two weeks and three months, while TSH was increased (Koopman-Esseboom et al., 1994).

Effects on cardiovascular system

Although the causative role of PCBs in injurious effects on cardiovascular system remains uncertain, Kreiss et al. (1981) observed that increased systolic and diastolic blood pressures in a general population showed significant associations with serum PCB levels. Besides, several studies concluded that PCBs may interfere with lipid metabolism (Tokunaga and Kataoka 2003; Grandjean and Weihe 2003), changing cardiovascular risk profile towards a higher one (Bell et al., 1994; Lind et al., 2004).

Effects on perinatal growth and early postnatal development

Decreased birth weight and early postnatal growth are regarded as possible indicators of adverse developmental effects of PCB mixtures. In this sense, several studies reported significant negative associations between anthropometric measures at birth and exposure to PCBs (Rylander et al., 1998; Hertz-Picciotto et al., 2005), but other studies found equivocal or no-significant results (Grandjean et al., 2001; Longnecker et al., 2005). Taylor et al. (1989) found a significant association between the increased PCB exposure and decreased birth weight and gestational age in women occupationally exposed to technical PCB mixtures through the manufacture of capacitors. In regard to postnatal growth, Patandin et al. (1998) found no significant association between PCB exposure and growth up to age 42 months. Finally, Grandjean et al. (2003) concluded that reduced body size was associated with the transfer of contaminants via human milk.

Effects on immune functions

The number of infectious illnesses (colds, earaches, and/or flu symptoms) found in children (0-4 months of age), whose mothers had consumed contaminated fish, was positively correlated with maternal serum PCB levels (Smith 1984). In this way, Dewailly et al. (2000) reported associations between risk of acute otitis media and increasing exposure to PCBs during the first year of life in infants.

Weisglas-Kuperus et al. (1995; 2000; 2004) performed several research studies about the PCB exposure effects on infant and children immune functions. Firstly, these authors found changes in lymphocyte T cell subpopulations in infants, but no increased incidence of infections or decreased concentrations of

antibodies to childhood vaccines during the first 18 months of life. However, the current PCB body burden was associated with higher prevalence of recurrent middle ear infections and of chicken pox, as well as lower prevalence of allergic reactions, when children were 42 months old. Finally, further studies were accomplished by these authors for children at school age, in which a higher postnatal PCB exposure through lactation was significantly associated with a greater prevalence of recurrent middle ear infections.

Heilman et al. (2003) performed a study in Faroe Islands (Denmark) where antibody responses to childhood vaccination were measured. In this sense, anti-diphtheria toxoid antibody showed a significant decrease at higher PCB exposure levels, whereas the correlation between PCB exposure and anti-tetanus toxoid antibody levels tended to be weaker. On the other hand, Chang et al. (1981) concluded that, after Yu-Cheng incident (China), in utero PCB exposure from heat-degraded transformer oil was associated with increased frequencies of childhood infections (middle ear and respiratory tract infections), and this fact was linked to reduced immune functions in exposed infants, such as decreased immunoglobulin levels and lymphocyte subset aberrations.

7. Conclusions

This study is a comprehensive worldwide review of literature on human exposure to PCDDs, PCDFs and PCBs through foods. These POPs exhibit chemical and physical analogies. There are 75 possible different positional congeners of PCDDs and 135 different congeners of PCDFs. Likewise, there are 209 possible different positional congeners of PCBs. They are ubiquitous in the environment, although the implementation of risk-reducing policies since the 1980s. Food, especially fatty animal products and seafood, could be as primary source of PCDDs, PCDFs and PCBs in the population. According to the EU Scientific Cooperation results, TDI for PCDDs, PCDFs and DL-PCBs was exceeded by a considerable part of the European population. The PCDD and PCDF congeners having 2,3,7,8-chlorination have received the

most research attention, with TCDD being the most intensely studied compound because of its toxicity, as well as DL-PCBs. The use of the TEF concept is the most plausible and feasible approach for risk assessment of PCDDs, PCDFs and PCBs. The findings on the adverse health affects of these compounds led regulatory bodies and the new guidelines mean that much more demanding detection, selectivity, and sensitivity levels are required during the testing process in order to confirm the presence of PCDDs, PCDFs and PCBs. HRGC/HRMS method, which is capable of increased levels of sensitivity, selectivity, and detection, has been cited as the most effective analytical technique for this application. A large volume of epidemiologic and mechanistic data about PCDDs, PCDFs and PCBs has been published in the last years, so identifying research gaps for these pollutants is quite difficult. Methods of their removal, transfer processes from feed ingredients and animal products, as well as, new studies of their health effects are the new challenges selected in this review.

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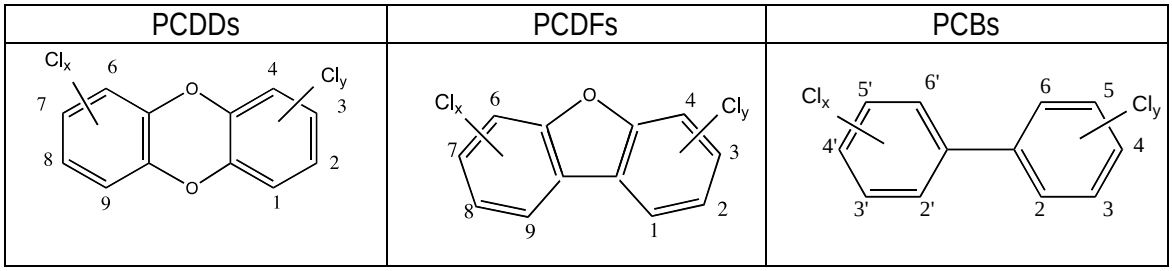

Figure 1. General chemical structure of PCDDs, PCDFs and PCBs.

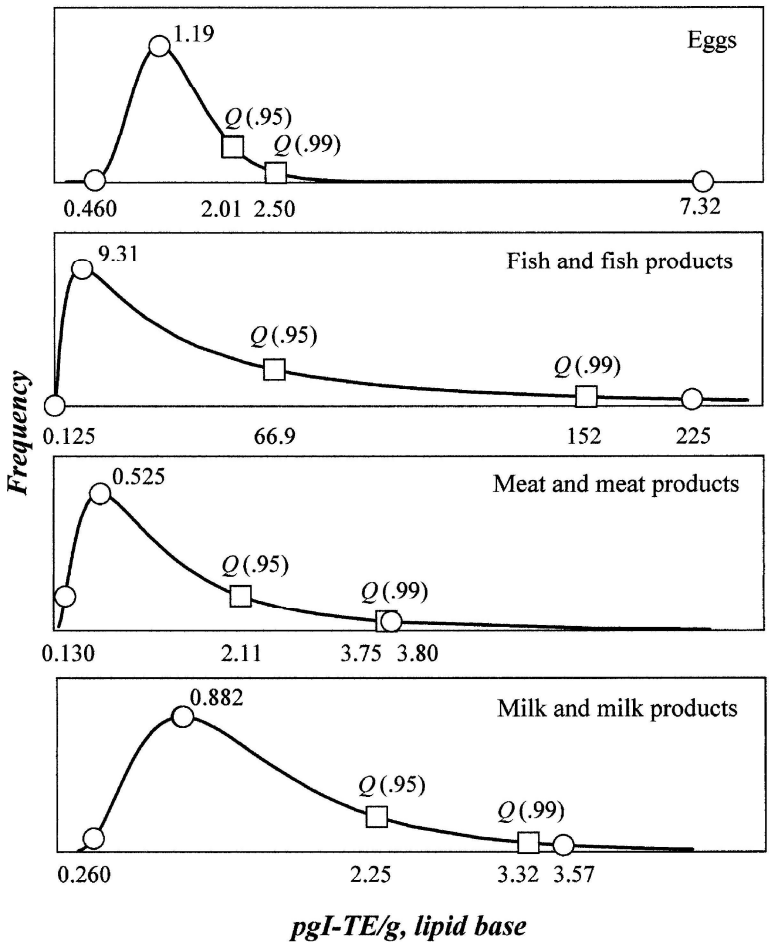

Figure 2. Frequency distribution curves of cumulative PCDD+PCDF I-TE levels in several foods of animal origin. The concentration figures identified by (o) are, from left to right, X_{min}, X_{mean}, and X_{max}. The 95th and 99th percentiles (Q) are identified from left to right by (□). Figure adapted from EC SCF (2000): Opinion on the Risk Assessment of Dioxins and Dioxin-like PCBs in Food.

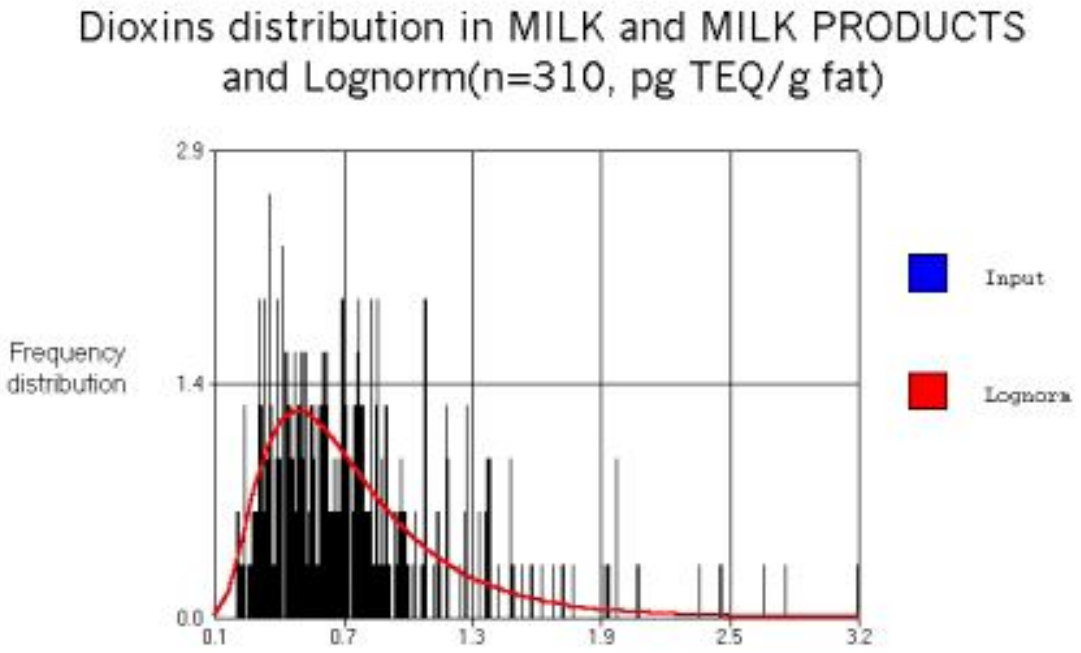

Figure 3. Frequency distribution of concentrations of dioxins in 310 individual samples of milk and milk products collected in France. The lognormal shape of the frequency distribution is also observed for the French datasets for meat and meat products, and for fish and fish products. Figure adapted from EC DG HCP (2000): Assessment of dietary intake of dioxins and related PCBs by the population of EU Member States.

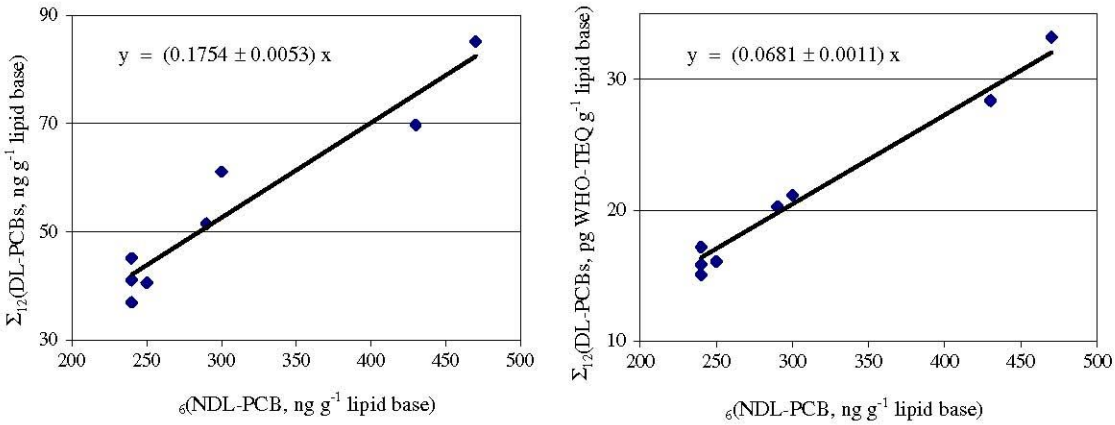

Figure 4. Correlation between DL-PCBs (Van den Berg et al., 1998) and NDL-PCBs, as sum of the six "indicators": PCBs 28, 52, 101, 138, 153, and 180. DL-PCBs are reported in analytical units (left box) and in toxicity equivalent units (right box); in both cases, correlation is high (R = 0.96, pR << 0.001, $F1,7$ = 81, pF = 0.0001, and R = 0.99, pR << 0.001, $F1,7$ = 320, pF << 0.0001, respectively) between DL-PCBs and NDL-PCBs, this likely indicating a common source of exposure. The correlation is still significant when the results relative to the two most contaminated pools (55+ age groups) are omitted (pF = 0.03 and pF = 0.005, respectively).

Table 1. Physical and chemical properties for PCDDs, PCDFs and PCBs

Physical and chemical properties												
POPs	**CAS**	**[1]MW (g/mol)**	**[1]log K_{ow}**	**[2]log K_{oa}**	**[1]s_w (mol/L)**	**[1]Pv (Torr)**	**[1]K_{oc}**	**[1]BF**	**[1]ρ (g/cm^3)**	**[1]H_{vap} (KJ/mol)**	**[2]MV (cm^3)**	**[2]Pol (cm^3)**
2,3,7,8-TCDD	1746-01-6	322	6.3	9.5	1.9E-09	8.3E-07	63000	35600	1.643	65	196	2.9E-23
1,2,3,7,8-PeCDD	40321-76-4	356	6.6	11	4.6E-10	8.1E-08	93100	61400	1.714	68	208	3.1E-23
1,2,3,4,7,8-HxCDD	39227-28-6	391	6.9	9.1	1.1E-10	1.0E-08	137000	105000	1.777	71	220	3.2E-23
1,2,3,6,7,8-HxCDD	57653-85-7	391	6.9	12	1.1E-10	7.7E-09	138000	106000	1.777	71	220	3.2E-23
1,2,3,7,8,9-HxCDD	19408-74-3	391	6.9	12	1.1E-10	7.7E-09	138000	106000	1.777	71	220	3.2E-23
1,2,3,4,6,7,8-HpCDD	35822-46-9	425	7.2	9.9	2.7E-11	9.2E-10	202000	181000	1.834	74	232	3.4E-23
OCDD	3268-87-9	460	7.5	11	6.7E-12	1.1E-10	296000	309000	1.886	77	244	3.6E-23
2,3,7,8-TCDF	51207-31-9	306	6.5	10	3.6E-09	6.5E-07	82900	52200	1.625	65	188	2.9E-23
2,3,4,7,8-PeCDF	57117-31-4	340	6.8	11	8.7E-10	6.9E-08	122000	90000	1.700	68	200	3.1E-23
1,2,3,7,8-PeCDF	57117-41-6	340	6.8	11	9.1E-10	6.9E-08	113000	80100	1.700	68	200	3.1E-23
2,3,4,6,7,8-HxCDF	60851-34-5	375	7.1	11	2.1E-10	7.3E-09	183000	158000	1.766	71	212	3.3E-23
1,2,3,7,8,9-HxCDF	72918-21-9	375	7.0	11	2.2E-10	7.3E-09	161000	161000	1.766	71	212	3.3E-23
1,2,3,6,7,8-HxCDF	57117-44-9	375	7.0	11	2.3E-10	7.3E-09	159000	159000	1.766	71	212	3.3E-23
1,2,3,4,7,8-HxCDF	70648-26-9	375	6.9	11	2.2E-10	9.5E-09	165000	165000	1.766	71	212	3.3E-23
1,2,3,4,7,8,9-HpCDF	55673-89-7	409	7.3	12	5.6E-11	9.7E-10	227000	227000	1.826	74	224	3.5E-23
1,2,3,4,6,7,8-HpCDF	67562-39-4	409	7.4	12	5.4E-11	9.7E-10	237000	237000	1.826	74	224	3.5E-23
OCDF	39001-02-0	444	7.6	13	1.4E-11	1.3E-10	323000	323000	1.879	77	236	3.7E-23
PCB 81	70362-50-4	292	6.5	8.6	5.0E-08	1.3E-05	81900	51300	1.441	60	203	2.8E-23
PCB 77	32598-13-3	292	6.5	10	4.9E-08	1.2E-05	82100	51500	1.441	60	203	2.8E-23
PCB 126	57465-28-8	326	7.0	9.4	1.1E-08	1.6E-06	159000	130000	1.522	64	214	2.9E-23
PCB 169	32774-16-6	361	7.6	10	2.7E-09	2.0E-07	309000	327000	1.593	67	226	3.2E-23
PCB 118	31508-00-6	326	6.8	9.4	1.9E-08	6.9E-06	115000	82700	1.522	61	214	2.9E-23
PCB 105	32598-14-4	326	6.7	9.0	2.0E-08	5.3E-06	107000	74400	1.522	62	214	2.9E-23
PCB 114	74472-37-0	326	6.7	8.3	2.0E-08	6.9E-06	106000	73400	1.522	61	214	2.9E-23
PCB 167	52663-72-6	361	7.3	10	4.4E-09	9.5E-07	223000	208000	1.593	64	226	3.2E-23
PCB 156	38380-08-4	361	7.2	9,8	4.8E-09	8.8E-07	206000	186000	1.593	64	226	3.2E-23

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PCB 157	69782-90-7	361	7.2	10	4.7E-09	7.1E-07	207000	188000	1.593	65	226	3.2E-23
PCB 189	39635-31-9	395	7.8	11	1.2E-09	1.2E-07	399000	468000	1.658	67	238	3.4E-23
PCB 17	37680-66-3	258	5.3	7.9	6.6E-07	7.6E-04	18700	6500	1.351	54	191	2.6E-23
PCB 20	38444-84-7	258	5.5	7.8	4.5E-07	1.9E-04	23300	8870	1.351	56	191	2.6E-23
PCB 28	7012-37-5	258	5.7	7.7	3.5E-07	3.2E-04	30700	13000	1.351	55	191	2.6E-23
PCB 44	41464-39-5	292	5.8	8.1	1.6E-07	9.9E-05	32800	14300	1.441	57	203	2.8E-23
PCB 52	35693-99-3	292	5.8	8.2	1.5E-07	1.3E-04	35400	15900	1.441	57	203	2.8E-23
PCB 101	37680-73-2	326	6.4	9.2	3.3E-08	2.3E-05	75700	46000	1.522	59	214	2.9E-23
PCB 138	35065-28-2	361	7.0	11	7.6E-09	3.0E-06	150000	119000	1.593	63	226	3.2E-23
PCB 149	38380-04-0	361	6.7	8.5	1.3E-08	9.6E-06	98400	66300	1.593	61	226	3.2E-23
PCB 153	35065-27-1	361	7.0	9.7	7.1E-09	3.9E-06	162000	133000	1.593	62	226	3.2E-23
PCB 170	35065-30-6	395	7.5	12	2.0E-09	3.9E-07	267000	268000	1.658	66	238	3.4E-23
PCB 180	35065-29-3	395	7.5	12	1.9E-09	5.2E-07	289000	298000	1.658	65	238	3.4E-23
PCB 194	35694-08-7	430	8.0	12	5.0E-10	6.4E-08	515000	670000	1.716	68	250	3.6E-23

CAS: CAS number, MW: molecular weight, log K_{ow}: octanol-water partitioning coefficient, log K_{oa}: octanol-air partitioning coefficient, s_w: solubility in water, Pv: vapor pressure, K_{oc}: organic carbon partition coefficient, BF: bioconcentration factor, ρ: density, H_{vap}: vaporization enthalpy, MV: molar volume, Pol: polarizability.

References:

[1]https://scifinder.cas.org

[2]http://www.chemspider.com

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Table 2. Re-evaluation of World Health Organization Toxic Equivalency Factors (WHO-TEFs) for dioxins (PCDD and PCDFs) and dioxin-like PCBs (DL-PCBs) in humans

Compounds	Congeners	WHO-TEFs (1997)[a]	WHO-TEFs (2005)[b]
Dibenzo-*p*-dioxins (PCDDs)	2,3,7,8-TCDD	1	1
	1,2,3,7,8-PeCDD	1	1
	1,2,3,4,7,8-HxCDD	0.1	0.1
	1,2,3,6,7,8-HxCDD	0.1	0.1
	1,2,3,7,8,9-HxCDD	0.1	0.1
	1,2,3,4,6,7,8-HpCDD	0.01	0.01
	OCDD	0.0001	0.0003
Dibenzofurans (PCDFs)	2,3,7,8-TCDF	0.1	0.1
	1,2,3,7,8-PeCDF	0.05	0.03
	2,3,4,7,8-PeCDF	0.5	0.3
	1,2,3,4,7,8-HxCDF	0.1	0.1
	1,2,3,6,7,8-HxCDF	0.1	0.1
	1,2,3,7,8,9-HxCDF	0.1	0.1
	2,3,4,6,7,8-HpCDF	0.1	0.1
	1,2,3,4,6,7,8-HpCDF	0.01	0.01
	1,2,3,4,7,8,9-HpCDF	0.01	0.01
	OCDF	0.0001	0.0003
Dioxin-like polychlorinated biphenyls (DL-PCBs)	*Non-ortho* PCBs		
	PCB77	0.0001	0.0001
	PCB81	0.0001	0.0003
	PCB126	0.1	0.1
	PCB169	0.01	0.03
	Mono-ortho PCBs		
	PCB105	0.0001	0.00003
	PCB114	0.0005	0.00003
	PCB118	0.0001	0.00003
	PCB123	0.0001	0.00003

	PCB156	0.0005	0.00003
	PCB157	0.0005	0.00003
	PCB167	0.00001	0.00003
	PCB189	0.0001	0.00003

[a]Van den Berg et al. (1998)

[b]Van den Berg et al. (2006) and Commission Regulation (EU) No. 1259/2011

Table 3. Food breakdown, lipid indicative levels, and mean TEQ concentrations based on European representative mean dioxin and dioxin-like PCB occurrence data (USEPA, 2002).

Food groups, subgroups, and specific items			Lipids Contents (%)	PCDDs + PCDFs	DL-PCBs
Groups	Subgroups	Items and notes		Concentrations (pg WHO-TE/g)[a]	
Cereals and cereal products				0.027 ww	0.0039 ww
Fruit and vegetables				0.028 ww	0.0039 ww
Eggs			8	0.63 fat	1.20 fat
Fats and oils (butter excluded)	Vegetable oil	Olive oil	100	0.21 fat	0.24 fat
		Seeds oil	100	same	same
		Margarine	90	same	same
Fish and fishery products				0.49 ww	1.30 ww
Meat and meat products	Poultry		6	0.65 fat	0.80 fat
	Ruminants	Beef	5	0.46 fat	1.22 fat
		Sheep	9	same	same
		Horse	3	same	same
		Rabbit[b]	4	same	same
	Pork	Fresh meat	7	0.21 fat	0.23 fat
		Ham, salami, sausages, etc.	23	same	same
	Liver	Offal[c]	5	5.33 fat	0.64 fat
Milk and dairy products		Milk	2.6	0.71 fat	2.42 fat
		Yogurt	3.0	same	same
		Cream	35	same	same
		Butter	83	same	same
		Cheese	23.5	same	same

a) ww: whole weight; rounding off to a maximum of three figures.

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b) And other “white” meat.

c) And miscellaneous meat.

Table 4. Average daily intake estimates (pg WHO-TEQ/kg b.w./day) for PCDD, PCDFs and DL-PCBs in adults from several countries

Country	PCDDs and PCDFs	DL-PCBs	Total TEQ	Adult weight assumed (kg)	References
Japan	0.89	1.36	2.25	50	Tsutsumi et al. (2001)
USA	1.67	0.65	2.32	-	Schecter et al. (2002)
Belgium	1.00	1.04	2.04	65	Focant et al. (2002)
Spain (Catalonia)	-	-	1.36	-	Llobet et al. (2003)
United Kingdom	-	-	1.09	-	Harrad et al. (2003)
The Netherlands	0.60	0.50	1.10	-	Baars et al. (2004)
Finland	0.79	0.74	1.53	-	Kiviranta et al. (2004)
Italy	0.96	1.30	2.28	-	Fattore et al. (2006)