WHO- and UNEP-Coordinated Exposure Studies 2000–2019: Findings of Polychlorinated Biphenyls, Polychlorinated Dibenzo-*p*-Dioxins, and Polychlorinated Dibenzofurans

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Abstract

The concentrations of polychlorinated biphenyls (PCB), polychlorinated dibenzo-*p*-dioxins (PCDD), and polychlorinated dibenzofurans (PCDF) were determined in 232 pooled human milk samples from 82 countries from all United Nations regions participating in five exposure studies coordinated by the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) between 2000 and 2019.

The highest concentrations of **PCB** were found in European countries. Countries of all other regions had considerably lower concentrations.

The highest median concentrations of **toxic equivalents (TEQ) of PCDD/PCDF and dioxin-like PCB** (expressed as **WHO_{2005}-TEQ**) were found in Eastern and Western European countries, the widest variation in Africa. The median concentrations and maximum levels in the Pacific region and countries from Latin America and the Caribbean were at the lower end of the distribution.

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R. Malisch et al. (eds.), *Persistent Organic Pollutants in Human Milk*,
https://doi.org/10.1007/978-3-031-34087-1_7

However, also time trends have to be considered for this overall picture for a period of 20 years.

Keywords

Human milk biomonitoring · Stockholm Convention on Persistent Organic Pollutants · PCB · PCDD/PCDF ("dioxins") · Global WHO/UNEP studies · UN regions · Time trends

1 Introduction

Polychlorinated biphenyls (PCB) are industrial chemicals that were manufactured for decades before their production and use was banned by many countries around 1985. Polychlorinated dibenzo-*p*-dioxins (PCDD) and polychlorinated dibenzofurans (PCDF) are unintentional by-products formed in (1) a number of chemical processes and, therefore, found as contaminants in certain chemicals; (2) many combustion processes; and, (3) certain geological processes and are, therefore, present in certain clays. PCB and PCDD/PCDF are especially chemically and physiologically stable, and thus persist in the environmental and biological systems. They are also highly lipophilic, which results in their biomagnification in the food chain and bioaccumulation in fatty tissues of animals and humans. Therefore, PCB and PCDD/PCDF are classified as persistent organic pollutants (POPs) and were included in the initial 12 POPs listed by Stockholm Convention on Persistent Organic Pollutants (UNEP 2001). The objective of this Convention is to protect human health and the environment from POPs by reducing or eliminating releases to the environment.

In the late 1980s and early 1990s, the World Health Organization (WHO) initiated two global human exposure studies for certain congeners of PCB and PCDD/PCDF in human milk. The third round of the WHO-coordinated exposure studies was performed from 2000 to 2003. After a sufficient number of countries ratified the Stockholm Convention in 2004, the WHO and the United Nations Environment Programme (UNEP) agreed to collaborate in joint studies to support the implementation of the convention. In particular, the Article 16 requires the periodic evaluation of the effectiveness of the convention in reducing emissions of POPs, which includes the three groups of POPs in this paper. One of the pillars of this evaluation is to be based on comparable and consistent monitoring data on the presence of POPs in the environment and in humans (UNEP 2007, 2019). Therefore, four more rounds were organized by WHO and UNEP between 2005 and 2019. Note that the number of POPs initially covered by the convention was expanded considerably since its adoption (UNEP 2020).

Results of certain studies or periods were presented in individual publications, e.g. on the 2000–2003 round (Malisch and van Leeuwen 2003), the 2000–2008 period (Malisch et al. 2008), and the 2008–2009 round (Malisch et al. 2010). The worldwide presence of POPs in air and in humans was demonstrated by UNEP

projects in 32 developing countries with human milk data of the period 2008–2010 (Fiedler et al. 2013). A comprehensive report for the 6th Conference of the Parties to the Stockholm Convention on POPs in 2013 provided an overview on all samples of the third, fourth, and fifth round, spanning the period 2000–2012. It revealed large global differences among various POPs and a decreasing trend in PCDD and PCDF levels in a number of countries (UNEP 2013a). Also, aspects of a risk–benefit assessment of breastfeeding were addressed that were published later in more detail (Van den Berg et al. 2017). It indicated that human milk levels of PCDD, PCDF, and PCB were still significantly above those considered toxicologically safe, in some countries an order of magnitude. These observations provided a strong argument for a plea to further global source-directed measures to reduce human exposure to dioxin-like compounds.

All substance-specific data are contained at the POPs Global Monitoring Plan Data Warehouse (GMP DWH) and can be publicly retrieved. This serves as the source of information for the regional and global reports of the GMP and effectiveness evaluation (Global Monitoring Plan Data Warehouse 2020).

In this compendium, human milk surveys are reviewed. In five parts, specific papers address various aspects. Part I gives a review of human milk surveys on POPs (Fürst 2023), an overview of the WHO/UNEP-coordinated exposure studies performed between 1987 and 2019 (Malisch et al. 2023a), and a review on the Stockholm Convention and its implementation by regional and global monitoring reports (Šebková 2023). Part II presents the analytical aspects of these studies, including methods for PCB and PCDD/PCDF and their validation (Malisch and Schächtele 2023). In Part III, the findings between 2000 and 2019 are presented in various publications, in this paper in relation to PCB and PCDD/PCDF. Countries are assigned to one of the five United Nations (UN) regions (see Sect. 2.1). It should, therefore, be noted that these results are not intended to be used for the ranking of countries. Part IV presents assessments of time trends derived from countries with repeated participation in the WHO- and UNEP-coordinated studies, among them for PCDD/PCDF and PCB (Malisch et al. 2023b) and a review of possible health risks for the breastfed infant from dioxin-like compounds (Van den Berg et al. 2023). Part V presents conclusions and key messages.

In addition to the above-mentioned compilation (Fürst 2023), a review of scientific publications between 1995 and 2011 on the spatial and temporal trends of Stockholm Convention on POPs in breast milk can be used to compare results of PCB and PCDD/PCDF levels (Fång et al. 2015). Furthermore, the regional and global monitoring reports for the Global Monitoring Plan assess datasets in the core media—ambient air, human tissues (human breast milk or blood), and water for hydrophilic POPs, but also other media such as soil, biota, plants are used to support interpretation of observed levels and their trends (Šebková 2023). These reports are available at the homepage of the Stockholm Convention (>Implementation>Global Monitoring Plan>Monitoring Reports).

This article compiles the results of a total of 82 countries participating in one or more of the five WHO/UNEP-coordinated exposure studies conducted between 2000 and 2019 with submission of a total of 232 pooled human milk samples. As

relevant congeners, 17 PCDD/PCDF, 12 dioxin-like PCB, and 6 Indicator PCB were determined. Toxic Equivalent (TEQ) concentrations were calculated based on Toxic Equivalency Factors recommended by WHO in 2005 (see Sect. 2.4). Four main summarizing parameters are given for: (1) PCDD and PCDF as WHO-PCDD/PCDF-TEQ; (2) dioxin-like PCB as WHO-PCB-TEQ; (3) the sum of PCDD, PCDF, and dioxin-like PCB ("total TEQ") as WHO_{2005}-TEQ; and (4) the sum of 6 Indicator PCB (ΣPCB_6) as the total concentration of the 6 selected non-dioxin-like PCB (see Sect. 2.6). Note that all concentrations in this paper are expressed on a lipid basis.

These TEQ and ΣPCB_6 results give a complex but comprehensive picture of the global exposure to these POPs over the past 20 years. The results for all samples and parameters are given and discussed from various perspectives in the following sections, namely: General aspects (Sect. 2); overall comparison of concentrations of TEQ and non-dioxin-like PCB among UN regions (Sect. 3); the five WHO- and UNEP-coordinated studies from 2000 to 2019 (Sect. 4); detailed comparison of concentrations on a Regional Group scale (Sect. 5), correlation between indicator PCB and dioxin-like PCB and between dioxin-like PCB and PCDF (Sect. 6) and summary (Sect. 7).

2 General Aspects

2.1 Link to the General Introduction (Countries, UN Regions, Protocol)

An overview of the scope, protocols for collection of samples and participation of countries with classification in UN regions and temporal differentiation is given in the general introduction (Malisch et al. 2023a). Shortly, in all rounds the design was based on collection of a number of individual samples and preparation of pooled samples following a standardized protocol that was supervised by national coordinators. Equal aliquots of individual samples were combined to give composite samples, which are considered representative of the average levels of the analytes of interest in human milk for a certain country or subgroup/region of a country at the time of sampling. The pooled samples were sent to WHO/UNEP Reference Laboratories for analysis.

In accordance with the implementation of the Global Monitoring Plan (GMP), parties report flexibly through one of the five United Nations Regional Groups. Therefore, countries are classified according to one of these five UN geopolitical groups (United Nations 2019): the African Group, the Asia-Pacific Group, the Group of Latin American and Caribbean Countries (GRULAC), the Eastern European Group, and the Western European and Others Group (WEOG). Note that Australia, Israel, New Zealand, and USA (being informally a member) are included as "Others" in the WEOG category, whereas Cyprus belongs to the Asia-Pacific Group.

2.2 Number of Samples, Aggregation of Data and Analysis

During the five studies conducted from 2000 to 2019, a total of 232 pooled samples were submitted for analysis by 82 countries and analysed for PCB and PCDD/PCDF at CVUA Freiburg, Germany. The detailed data for all 232 pooled samples is contained at the POPs Global Monitoring Plan Data Warehouse and can be publicly retrieved (Global Monitoring Plan Data Warehouse 2020).

In the 2000–2003 study, countries were particularly encouraged to submit at least two pooled samples, whereas in the following rounds in most cases one pooled sample was submitted by a country. To allow a quick and easy comparison, if a country had sent two or more samples in a certain round, the median has been used for aggregation. 113 results were from a single pooled sample submitted by countries in a certain round, whereas 31 results from the following countries were aggregated from two or more samples using the median:

- Australia, 2002 and 2013
- Belgium, 2002
- Brazil, 2001 and 2012
- Bulgaria, 2001
- Croatia, 2001
- Czech Republic, 2001
- Egypt, 2001
- Fiji, 2002 and 2006
- Finland, 2001 and 2007
- Germany, 2002 and 2019
- Hong Kong, 2002 and 2009
- Hungary, 2001
- Ireland, 2001
- Italy, 2001
- Luxembourg, 2002
- Netherlands, 2001
- New Zealand, 2000
- Norway, 2001
- Philippines, 2002
- Romania, 2001
- Russia, 2001
- Slovak Republic, 2001
- Spain, 2001
- Ukraine, 2001
- USA, 2003

With the approach of "one country – one result" for a certain round, altogether 144 country results are available for 82 countries. In this article, both the country results (from 113 single pooled samples and from aggregation of data as median in the above listed 31 cases) and the ranges found without aggregation are given.

The analytical methods for determination of PCB and PCDD/PCDF and their validation are presented in Part II (Malisch and Schächtele 2023).

2.3 Cost-Effectiveness and Possible Range of Individual Samples Using Pooled Samples

An important advantage of the WHO- and UNEP-coordinated exposure studies is the cost-effectiveness of the concept (Malisch et al. 2023a). Shortly, the analysis of the 232 pooled samples obtained from between 10 and 50 individual samples and considered to be representative for countries or subgroups/regions provides the same information as would be received by calculation of the mean of more than 2000 individual samples (assuming 10 individual samples per pool) or more than 11,000 individual samples (assuming 50 individual samples per pool). Thus, the analysis of pooled samples is an extremely cost-efficient way to get information on the average levels of the relevant POPs in humans in these countries at specific times. It also saves considerable time with respect to chemical analysis and is environmentally friendly, because less extraction solvents could be used.

On the other hand, the analysis of individual samples (from specific donors) can provide information on exposure distribution in a population and on factors possibly contributing to exposure. A follow-up might be of interest in case of considerably elevated levels. As an example of the range of concentrations in individual samples, the frequency distribution derived from 271 individual human milk samples collected in Germany during the period 1995–1998 can be used as illustration of this distribution: It shows a log-normal distribution with a maximum of the curve around 16 ng I-TEQ/kg lipids (based on International Toxic Equivalency Factors) and a range of roughly between 4 and 40 ng I-TEQ/kg lipids (Fig. 1) (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit 2002).

2.4 Toxic Equivalency Factors (TEF) and Toxic Equivalents (TEQ)

Of the theoretically possible congeners of PCDD and PCDF (75 PCDD and 135 PCDF, respectively), only the 17 congeners with at least four chlorine atoms with substitution in the 2,3,7,8-positions were considered to be relevant for human health. Similarly, from the 209 theoretically possible PCB congeners, only 12 congeners (8 mono-ortho substituted and 4 non-ortho substituted) have dioxin-like properties. These congeners show different toxic potencies that are expressed as toxic equivalency factors (TEF) compared to the most toxic congener, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD). With the TEF, the toxicity of a mixture of PCDD/PCDF and dioxin-like PCB can be expressed in a single number—the toxic equivalents (TEQ). This is defined by the sum of the products of the concentration of each compound (17 PCDD/PCDF congeners with 2,3,7,8-substitution and 12 dioxin-like PCB congeners) multiplied by their corresponding TEF value. This is an estimate of the total 2,3,7,8-TCDD-like toxicity of the mixture.

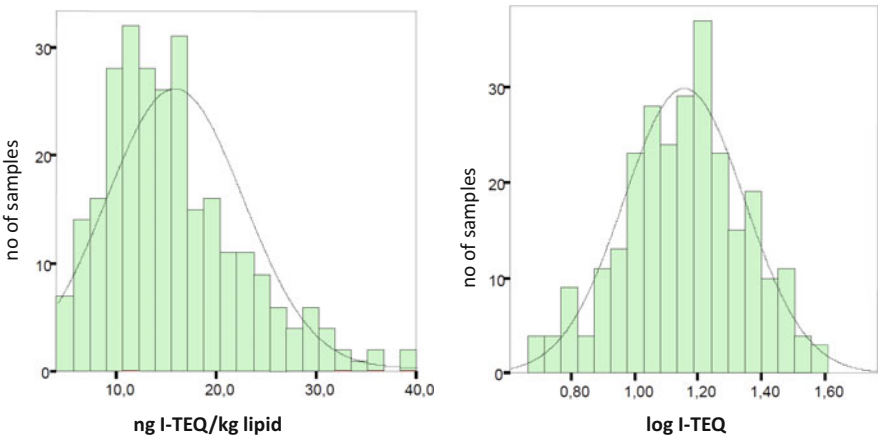

Fig. 1 Frequency distribution of 271 individual human milk samples collected in Germany from 1995 to 1998 (reprint from Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit [BMU] 2002, with permission from BMU)

Several institutions have derived different TEF schemes. When the first WHO-coordinated exposure study on levels of dioxins and dioxin-like PCB in human milk was performed (1987–1988), TEQ levels were calculated on the basis of TEF from US EPA and Nordic models (WHO 1989). Subsequently, TEQ levels for the second study (1992–1993) were calculated on the basis of International Toxic Equivalency Factors (I-TEF) and TEF proposed by WHO in 1994 (WHO 1996).

At an expert meeting held by the European Centre of Environmental Health of WHO (ECEH-WHO) and the International Programme on Chemical Safety (ICPS) in 1997, TEF values were re-evaluated. This resulted in a consensus on the WHO_{1998}-TEF (Van den Berg et al. 1998), which were widely used for many years, including the two WHO-coordinated studies covering the sampling periods from 2000 to 2003 and from 2004 to 2007.

Changes in WHO_{1998}-TEF values were proposed at another WHO expert meeting held in 2005 and resulted in WHO_{2005}-TEF (Van den Berg et al. 2006). The values of these WHO_{2005}-TEF have been validated since then and have been used for subsequent reports. Since 2011, EU regulations setting maximum limits for PCDD/PCDF and dioxin-like PCB in food and animal feed were amended to use WHO_{2005}-TEF for calculating maximum levels (European Commission 2011; European Commission 2012). The 2019 version of the "Guidance on the Global Monitoring Plan for persistent organic pollutants" mentions that according to the text of the Stockholm Convention (Annex C), the TEF as established by a WHO Expert Group and published in 1998, i.e., WHO_{1998}-TEF, should be used. However, state-of-the-art presentation of results would use the WHO_{2005}-TEFs and, therefore, it was recommended to report these as well in order to allow comparison with data from the literature and other reports (UNEP 2019).

Table 1 Changes of concentrations expressed as WHO-PCDD/PCDF-TEQ, WHO-PCB-TEQ, and WHO-PCDD/PCDF-PCB-TEQ, when WHO_{1998}-TEF are used instead of WHO_{2005}-TEF (as 100%: concentrations calculated as WHO_{2005}-TEQ) (232 samples)

	TEQ (WHO_{1998}-TEF) as % of TEQ (WHO_{2005}-TEF)					
	Minimum	25th percentile	Median	75th percentile	95th percentile	Maximum
WHO-PCDD/PCDF-TEQ	103%	112%	116%	120%	125%	132%
WHO-PCB-TEQ	92.2%	128%	145%	162%	195%	248%
WHO-PCDD/PCDF-PCB-TEQ	106%	118%	123%	134%	155%	191%

Table 1 presents the changes of WHO-TEQ-based results for all 232 samples if the former WHO_{1998}-TEF were applied instead of the current WHO_{2005}-TEF. The evaluation of the 232 data sets from all samples shows that concentrations calculated with WHO_{1998}-TEF as toxic equivalents of PCDD/PCDF (WHO_{1998}-PCDD/PCDF-TEQ) are on average about 16% higher (range about 3–32%) than for WHO_{2005}-PCDD/PCDF-TEQ. In particular, TEQ of dioxin-like PCB (WHO_{1998}-PCB-TEQ) were on average about 45% higher compared to the WHO_{2005}-PCB-TEQ results (range between about 10% lower and 150% higher). The total TEQ (WHO_{1998}-PCDD/PCDF-PCB-TEQ) were on average about 23% higher (range between 6 and 91%) than the corresponding WHO_{2005}-PCDD/PCDF-TEQ results. In general, this is in line with studies on human milk reporting a 20–25% decrease when WHO_{2005}-TEF are used instead of WHO_{1998}-TEF (Van den Berg et al. 2006; Wittsiepe et al. 2007).

In its recent assessment on the risk for human and animal health related to the presence of PCDD/PCDF and dioxin-like PCB in food and feed, the European Food Safety Authority (EFSA) re-evaluated its previous tolerable weekly intake for humans. As part of this re-evaluation, it was concluded that the current WHO_{2005}-TEF for the dioxin-like PCB 126 might be too high and a further discussion on all WHO_{2005}-TEF was proposed (EFSA, 2018). Therefore, the European Commission formally requested WHO to review the values for the WHO_{2005}-TEF. As conclusion, it is of general importance to always clarify which TEF values were applied for a reported TEQ value, e.g. as WHO_{1998}-TEQ or WHO_{2005}-TEQ. If data on the actual concentrations of the relevant congeners are available, re-calculation of the TEQ using modified TEF values is possible.

2.5 Lower and Upper Bounds TEQ Concentrations

Details on the calculation of toxic equivalents (TEQ) of mixtures of PCDD/PCDF and dioxin-like PCB using toxic equivalency factors (TEF) and on analytical criteria are given in the analytical chapter in Part II (Malisch and Schächtele 2023). An important criterion for assessment of the reliability of results is the difference between the lower-bound TEQ result (where non-detects = 0) and the upper-bound TEQ result (where non-detects = limit of quantification), as proposed as part of harmonized quality criteria for analyses of PCDD and PCDF (Malisch et al. 2001).

The 2019 version of the document 'Guidance on the Global Monitoring Plan for persistent organic pollutants' recommends that this difference between the lower-bound and upper-bound concentrations should be reported. As a measure of analytical quality assurance and quality control (QA/QC), this difference should be less than 20% (UNEP 2019).

The acceptable difference between lower- and upper-bound values is of particular importance for the analysis of samples intended to be used as a control of time trends for the effectiveness evaluation of the Stockholm Convention. If the difference is too high, changes of WHO-TEQ levels might be actually caused by changes of the analytical sensitivity and not by changes of the real levels of POPs in samples. In particular, samples with limited amounts or samples with low fat levels are at considerable risk of having a high difference between lower- and upper-bound WHO-TEQ levels. Therefore, regardless of whether human milk, human blood, air, or other matrices are analysed, all studies intended to be used for the effectiveness evaluation of the Stockholm Convention should report lower- and upper-bound WHO-TEQ levels that are within the acceptable range.

One of the features of the WHO/UNEP protocol is the collection of 50 ml individual human milk samples, which is relatively easy and non-invasive. With a lipid content of about 4% and preparation of a pooled sample of 50 individuals, a sufficient amount of sample is available to apply different analytical methods for determination of all 30 POPs presently listed in the Stockholm Convention and to assure that QA/QC criteria are met, including acceptable differences between lower- and upper-bound values for PCDD/PCDF analysis.

In contrast, human blood has a number of sampling difficulties as well as considerably lower lipid content. Therefore, meeting the requirement of an acceptable difference between lower- and upper-bound WHO_{2005}-TEQ levels takes considerably more effort for blood samples.

Table 2 summarizes the differences (in %) between lower and upper bounds for total TEQ concentrations of PCDD/PCDF and dioxin-like PCB (WHO_{2005}-TEQ) in all 232 samples. In particular, all samples fulfilled the QA/QC criterion with 98% of all samples having differences below 1%, which is considered negligible. Therefore, only the upper-bound WHO_{2005}-TEQ levels are used for discussion of the results.

Table 2 Differences (in %) between lower- and upper-bound total TEQ concentrations of PCDD/PCDF and dioxin-like PCB (WHO_{2005}-TEQ)

	No of samples	Min	25th percentile	Median	Mean	90th percentile	95th percentile	98th percentile	Max
Differences (in %) between lower- and upper-bound WHO_{2005}-TEQ levels	232	0	0	0.03	0.15	0.14	0.20	0.46	15.3

2.6 Non-dioxin-like PCB

Concentrations of non-dioxin-like PCB are expressed as the sum of six Indicator PCB (ΣPCB_6) including the congeners number 28, 52, 101, 138, 153, and 180. These are major marker congeners of the technical PCB mixtures (Schulte and Malisch 1983; Takasuga et al. 2006). Their sum usually comprises about half of the amount of total non-dioxin-like PCB present in feed, food, and humans and is considered to be an appropriate marker for occurrence in food and for human exposure to non-dioxin-like PCB. Therefore, this sum has been used in EU legislation since 2011 for setting maximum levels for non-dioxin-like PCB in food (European Commission 2011) and feed (European Commission 2012). Through biomagnification in the food chain, certain PCB, including PCB 28, PCB 52, and PCB 101, can be metabolized, e.g., by cows and finally by humans. As a result, PCB 138, PCB 153, and PCB 180 contribute on average about 50% in butter fat or in lipids in raw milk and about 60% to the sum of the individual concentrations of PCB in human milk (Schulte and Malisch 1984; Malisch and Schulte 1985; Kypke-Hutter and Malisch 1989).

Initially, the sum of these six congeners plus PCB 118 (ΣPCB_7) was used by UNEP (UNEP 2007). However, the mono-ortho PCB 118 also has dioxin-like properties and is included in the TEQ calculations as well (Van den Berg et al. 2006). As no chemical should be reported or regulated twice, since 2013 the revised "Guidance document on the Global Monitoring Plan for persistent organic pollutants" uses also the sum of six Indicator PCB (ΣPCB_6) (UNEP 2013b, 2019). As guidance for the differences between ΣPCB_6 and ΣPCB_7, the concentrations of PCB 118 contribute about 10% (calculated as median; range 2–30%) to the sum of 7 Indicator PCB based on the evaluation of all 232 samples received.

2.7 Use of Terms for TEQ

A complete and unambiguous system for concentrations expressed in terms of TEQ is needed to indicate which specific TEF is used (WHO_{1998}-TEF, or WHO_{2005}-TEF) and whether the calculation is the lower bound (LB) or upper bound (UB). European Union legislation uses the notation "WHO-PCDD/F-TEQ" for PCDD and PCDF, "WHO-PCB-TEQ" for dioxin-like PCB, and "WHO-PCDD/F-PCB-TEQ" for total TEQ to specify maximum levels of these contaminants in feed and food, with the definition that WHO_{2005}-TEFs are applied and upper-bound results are used. Without this separate definition, an unambiguous term for total TEQ would be, e.g., "WHO-PCDD/PCDF-PCB-TEQ (2005, UB)" or "WHO-PCDD/PCDF-PCB-TEQ (WHO_{2005}-TEF, UB)".

However, this system considerably reduces the readability. Though inaccurately, PCDD are sometimes shortly called "dioxins", and PCDF "furans". Moreover, the term 'dioxins' is commonly used also to refer to both PCDD and PCDF and is therefore quite ambiguous. For the sake of clarity in the following sections, the term PCDD/PCDF will be used consistently to refer to this group of compounds. In the text, "Total TEQ of PCDD/PCDF and dioxin-like PCB" or "WHO_{2005}-TEQ" is used comprising PCDD/PCDF and dioxin-like PCB. "TEQ of PCDD/PCDF" is used for "WHO-PCDD/PCDF-TEQ" and "TEQ of dioxin-like PCB" for "WHO-PCB-TEQ".

Tables and figures will employ the explicit EU terminology to avoid confusion if the tables and figures are taken out of context. Unless otherwise stated, all TEQ concentrations are based on calculations applying the WHO_{2005}-TEF and are calculated as upper-bound (UB) concentrations.

All concentrations for PCDD/PCDF and PCB are reported on lipid basis.

2.8 Human Exposure and Congener Patterns

While accidental and occupational dioxin exposure is normally limited to more or less small subgroups of the population, environmental exposure due to diffuse sources affects all humans. In comparison to other exposure routes (inhalation of air; ingestion of soil; dermal absorption), more than 90% of human dioxin exposure derives from food. Of this, about 90% normally comes from food of animal origin. Contamination of food is primarily caused by release of dioxins from various sources (e.g. waste incineration, production of chemicals, metal industry), and their subsequent accumulation in the food chain where they are particularly associated with fat (Fürst et al. 1992; European Commission—Scientific Committee on Food 2001a). The total global PCDD/PCDF release from 196 countries/regions was estimated to be 100.4 kg TEQ/year. Reference years were between 1998 and 2011, with the period 2000–2005 for about 90% of the countries (Wang et al. 2016).

Congener patterns of PCDD/PCDF and PCB differ between sources and are important tools for source identification. The review of congener patterns of PCDD/PCDF and PCB as useful aid to source identification during a contamination incident in the food chain (Hoogenboom et al. 2020), the review of the relevance of dioxin and PCB sources for food from animal origin (Weber et al. 2018), and the review of the investigative work necessary to find the source of contamination in incidents with dioxins and PCB in feed and food (Malisch 2017) might be helpful to find sources and to reduce exposure.

3 Overall Comparison of Concentrations of TEQ and Non-dioxin-like PCB Among UN Regions

A suitable starting point for the discussion of the complex picture is the comparison of the results for the most important sum parameters among UN regions, namely: (1) total TEQ of PCDD/PCDF and dioxin-like PCB, with further differentiation between TEQ of PCDD/PCDF and TEQ of dioxin-like PCB, and (2) Indicator PCB, calculated as ΣPCB_6.

3.1 TEQ

The range of concentrations of total TEQ in 232 samples from 82 countries collected between 2000 and 2019 varies between 1.29 and 49 pg WHO_{2005}-TEQ/g, with a median of 7.24 pg/g (Table 3; Fig. 2). The highest median WHO_{2005}-TEQ

Table 3 Range of concentrations of total TEQ (WHO_{2005}-TEQ), WHO-PCDD/PCDF-TEQ, and WHO-PCB-TEQ among UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands; pg/g lipid; $N = 232$)

UN Regional Group	No of countries	No of samples	WHO_{2005}-TEQ			WHO-PCDD/PCDF-TEQ			WHO-PCB-TEQ		
			Min	Median	Max	Min	Median	Max	Min	Median	Max
African	19	40	1.29	5.79	49.0	1.01	3.14	41.2	0.27	1.95	7.79
Asia-Pacific/Asia[a]	12	29	2.38	8.55	26.7	1.80	6.06	22.2	0.58	3.05	4.51
Asia-Pacific/Pacific	10	24	1.76	4.06	11.6	1.29	2.63	9.32	0.47	1.23	2.62
Latin American and Caribbean	14	36	1.81	4.68	10.4	1.26	3.41	8.44	0.55	1.16	4.95
Eastern European	11	43	4.10	12.0	24.3	2.40	6.04	10.7	1.53	5.71	13.6
Western European and "Others"[b]	16	60	3.85	10.3	26.9	2.68	6.72	18.6	1.09	3.60	11.3
All Regional Groups	82	232	1.29	7.24	49.0	1.01	4.65	41.2	0.27	2.57	13.6
Non-European countries (Asia, Pacific, Latin American and Caribbean, "Others"[b]	58	140	1.29	5.38	49.0	1.01	3.48	41.2	0.27	1.62	7.79
European countries[a] (Eastern and Western except "Others"[b])	24	92	4.10	12.0	26.9	2.40	6.50	18.6	1.39	5.00	13.6

[a]Including Cyprus
[b]"Others": Australia, Israel, New Zealand, USA (see Sect. 2.1)

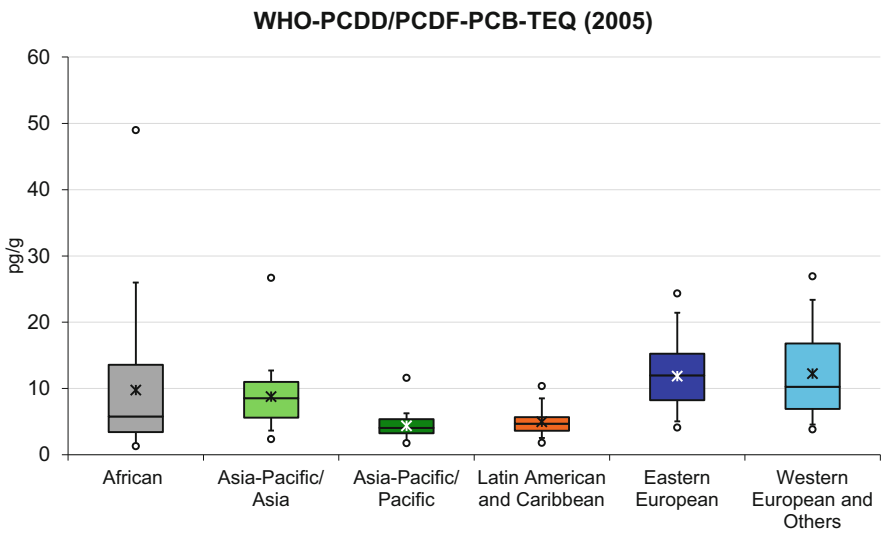

Fig. 2 Range of concentrations of total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) among UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands; pg/g lipid, upper bound; $N = 232$) [box plot; minimum and maximum: as circles; 5th and 95th percentile: as whiskers; lower (25–50%) and upper (50–75%) quartiles, separated by the line for the median: as box; mean: as asterisk]

concentrations were found in countries of the Eastern European Group and the Western European and Others Group with 12.0 pg/g and 10.3 pg/g, respectively. The widest variation was in Africa (range 1.29–49 pg/g). With median concentrations between 4 and 5 pg/g and maximum levels between 10 and 12 pg/g, the Pacific region in the Asia-Pacific Group and countries from the Latin American and Caribbean Group were at the lower end of the distribution.

A closer look reveals that countries of the Eastern European Group and the Western European and Others Group have a higher contribution of dioxin-like PCB to the total TEQ than countries from other regions. As the Western European and Others Group comprises also Australia, Israel, New Zealand, and USA and the Asian Group also Cyprus, Table 3 includes also a differentiation between the 24 European countries and the 58 Non-European countries. Whereas in European countries the contribution of the median of dioxin-like PCB to the total TEQ is about 42%, this is in Non-European countries about 30%.

3.2 Non-dioxin-like PCB

The range of concentrations of the sum of 6 indicator PCB (ΣPCB_6) varies between approximately 1 and 1000 ng/g lipid, with a median of about 30 ng/g lipid (Table 4, Fig. 3). The highest concentrations were found in the Eastern European Group (median of about 120 ng/g lipid and maximum of about 1000 ng/g lipid), followed

Table 4 Median and range of concentrations of the sum of 6 Indicator PCB (ΣPCB_6) among UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands; ng/g lipid; $N = 232$)

Regional Group	No of countries	No of samples	Sum 6 indicator PCB (ΣPCB_6)		
			Minimum	Median	Maximum
African	19	40	0.90	22.3	90.3
Asia-Pacific/Asia[a]	12	29	3.25	22.2	79.8
Asia-Pacific/Pacific	10	24	2.55	8.3	23.4
Latin American and Caribbean	14	36	3.01	15.8	96.5
Eastern European	11	43	14.6	121	1009
Western European and "Others"[b]	16	60	12.0	74.6	467
All Regional Groups	82	232	0.90	31.7	1009
Non-European countries (Asia, Pacific, Latin American and Caribbean, "Others"[b]	58	140	0.90	16.4	96.5
European countries[a] (Eastern and Western except "Others"[b])	24	92	14.6	118	1009

[a]Including Cyprus
[b]"Others": Australia, Israel, New Zealand, USA (see Sect. 2.1)

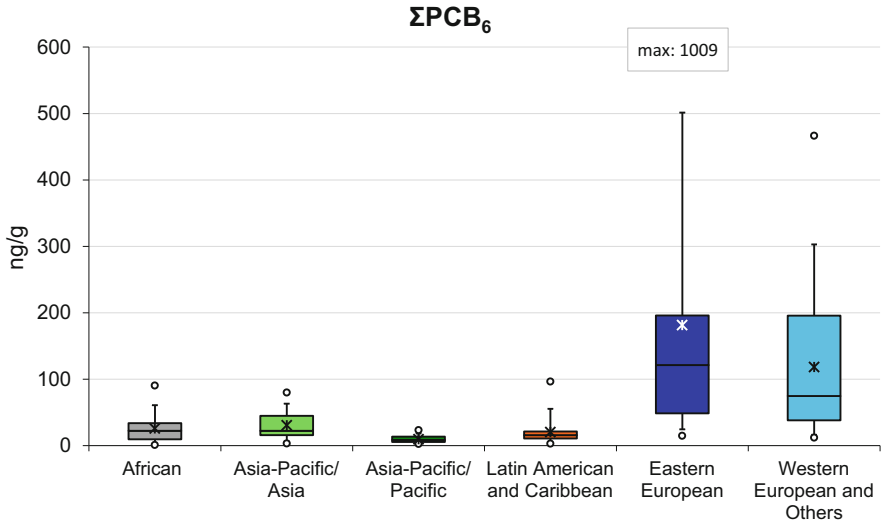

Fig. 3 Median and range and of levels of 6 Indicator PCB (ΣPCB_6) among UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands; ng/g lipid, upper bound; $N = 232$) [Box plot; minimum and maximum: as circles; 5th and 95th percentile: as whiskers; lower (25–50%) and upper (50–75%) quartiles, separated by the line for the median: as box; mean: as asterisk]

by the group of Western European and Other States (median about 75 ng/g lipid, maximum 467 ng/g lipid). In all other groups, considerably lower PCB levels were found (maximum lower than 100 ng/g lipid, median approximately between 8 and 22 ng/g).

With regard to the above-mentioned inclusion of Australia, Israel, New Zealand, and USA in the Western European and Others Group and of Cyprus in the Asian Group, Table 4 includes the differentiation between the 24 European countries (median 118 ng/g lipid, range about 15–1000 ng/g) and the 58 Non-European countries (median 16 ng/g lipid, range about 1–100 ng/g). This clearly supports the conclusion that PCB concentrations are considerably higher in Europe than in the other geographic regions.

4 The Five WHO- and UNEP-Coordinated Studies from 2000 to 2019

As a first step in differentiation, results of the five studies are compared "round by round" in chronological order. As the five studies performed over 20 years had different time lengths, it is considered more appropriate to present the participation of countries in five equal rounds of 4 year each, namely: 2000–2003, 2004–2007, 2008–2011, 2012–2015, and 2016–2019 (Malisch et al. 2023a).

Following the protocol that was in effect, most countries of the 2000–2003 round submitted two or more pooled samples, with the option to add pooled samples from exposure groups expected to be high compared to the exposure group considered to be representative for the country. In subsequent rounds, most countries submitted only one pooled sample, which was considered as representative of the country, and the option to include pooled samples from expected high exposure groups was discontinued. In order to represent one country in each period by one result as "country results" in some summarizing figures, aggregated data based on the median levels were derived if a country submitted two or more pooled samples in a certain period (see Sect. 2.2).

For each of these rounds, the most important statistical data (minimum, median, and maximum) for the most important sum parameters, namely the toxic equivalents of PCDD and PCDF (WHO-PCDD/PCDF-TEQ), dioxin-like PCB (WHO-PCB-TEQ) and the total TEQ (WHO_{2005}-TEQ) and the sum of 6 Indicator PCB (ΣPCB_6), are compiled in Table 5 with regard to (1) the country results (1 result/country) and (2) the individual 232 pooled samples. The results in this table show that for all rounds, the median of the country results with aggregated data and that of single pooled samples for TEQ-based results are rather comparable: The country results with aggregated data for **TEQ of PCDD and PCDF** range from 1.01 to 22.2 pg/g with a median of 3.81 pg/g, for **TEQ of dioxin-like PCB** from 0.27 to 10.7 pg/g with a median of 1.86 pg/g, and for **total TEQ** from 1.29 to 26.7 pg/g with a median of 5.69 pg/g. The highest concentrations in the single pooled samples were 41.2 pg/g for TEQ from PCDD and PCDF, 13.6 pg/g for TEQ from dioxin-like PCB, and 49.0 pg/g for total TEQ, all found in the 2000–2003 round.

The country results with aggregated data for **ΣPCB_6** range from 0.90 to 502 ng/g with a median of 23.6 ng/g. At the 2000–2003 round, the optional inclusion of samples from expected high exposure groups might have caused the observed differences between the median of 123 ng/g for aggregated data (with aggregation

Table 5 Median and range of concentrations of (1) TEQ of PCDD and PCDF (WHO_{2005}-PCDD/PCDF-TEQ), dioxin-like PCB (WHO_{2005}-PCB-TEQ), and total TEQ (WHO_{2005}-PCDD/PCDF-PCB-TEQ) and (2) ΣPCB_6 in the five rounds performed between 2000 and 2019 with differentiation between country results with aggregated data (1 result/country with use of median or if 2 or more samples were submitted by a country, the median) and all single pooled samples

			WHO-PCDD/F-TEQ (2005/UB)	WHO-PCDD/F-TEQ (2005/UB)	WHO-PCB-TEQ (2005/UB)	WHO-PCB-TEQ (2005/UB)	WHO-PCDD/F-PCB-TEQ (2005/UB)	WHO-PCDD/F-PCB-TEQ (2005/UB)	Sum 6 Indicator PCB	Sum 6 Indicator PCB
			1 result/country (median, if 2 or more samples)	Single pooled samples	1 result/country (median, if 2 or more samples)	Single pooled samples	1 result/country (median, if 2 or more samples)	Single pooled samples	1 result/country (median, if 2 or more samples)	Single pooled samples
			pg/g lipid	pg/g lipid	pg/g lipid	pg/g lipid	pg/g lipid	pg/g lipid	ng/g lipid	ng/g lipid
Period	2000–2003	Min	3.08	2.46	1.16	0.96	4.42	3.53	16.4	9.94
No of countries	26	Median	7.34	7.58	4.93	4.70	12.4	12.5	123	72.2
No of samples	102	Max	18.03	41.18	10.7	13.6	23.0	49.0	502	1009
Period	2004–2007	Min	2.94	2.94	1.22	1.07	5.06	4.75	10.1	8.61
No of countries	13	Median	4.83	4.73	2.62	2.59	6.93	6.87	49.2	42.7
No of samples	16	Max	8.93	8.93	6.96	6.96	15.7	15.7	376	376
Period	2008–2011	Min	1.31	1.31	0.70	0.70	2.01	2.01	4.05	4.05
No of countries	45	Median	3.81	3.91	1.86	1.93	5.62	5.67	18.1	17.2
No of samples	50	Max	22.2	22.2	7.47	7.47	26.7	26.7	78.9	78.9

Period	2012–2015	Min	1.01	1.01	0.53	0.53	1.54	1.54	2.15	2.15
No of countries	17	Median	3.81	3.27	2.47	2.19	6.30	5.70	24.1	22.5
No of samples	20	Max	8.61	8.61	4.72	4.72	11.1	11.1	158	158
Period	2016–2019	Min	1.02	1.02	0.27	0.27	1.29	1.29	0.90	0.90
No of countries	43	Median	2.62	2.63	1.00	1.00	3.88	3.90	12.7	13.2
No of samples	44	Max	9.97	9.97	3.70	3.70	11.6	11.6	109	109
Period	2000–2019	Min	1.01	1.01	0.27	0.27	1.29	1.29	0.90	0.90
No of countries	144	Median	3.81	4.64	1.86	2.62	5.69	7.32	23.6	31.7
No of samples	232	Max	22.2	41.2	10.7	13.6	26.7	49.0	502	1009

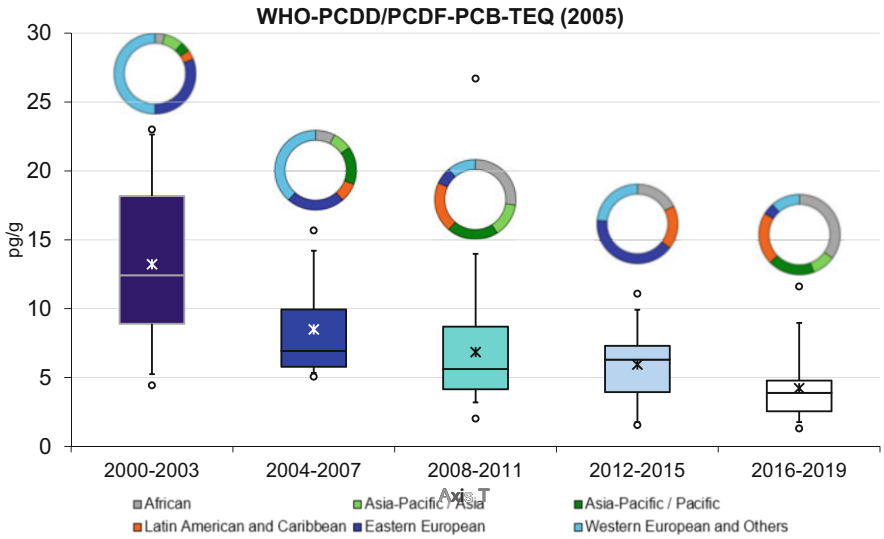

Fig. 4 Median and range of concentrations of total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) in the five rounds performed between 2000 and 2019 and fraction of results among UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands; country results with aggregated data; pg/g lipid) [Box plot; minimum and maximum: as circles; 5th and 95th percentile: as whiskers; lower (25–50%) and upper (50–75%) quartiles, separated by the line for the median: as box; mean: as asterisk]

for 25 of 26 countries) and the median of 72.2 for 102 single pooled samples. The highest concentration in the single pooled samples was 1009 ng/g for the sum of 6 Indicator PCB in the 2000–2003 period.

This compilation of data can be used for a general estimation of time trends. In Fig. 4, box plots illustrate the time trends over the five rounds: Over these 20 years, the median and range of **total TEQ** concentrations of the country results with aggregated data found in these five rounds went gradually down from initially 12.4 pg/g as median (range from 4.4 to 23.0) in the period 2000–2003 to 3.9 pg/g (range 1.3–11.6) in the period 2016–2019—a reduction of the median concentrations by 69%. However, changes in the fraction of regional groups over these periods have to be taken into consideration indicated by coloured circles above the box plots. Whereas in the 2000–2003 period, the majority of participants came from countries of the Eastern European Group and Western European and Others Group, in the 2016–2019 round, the majority came from the African Group, followed by the Group of Latin American and Caribbean Countries and then the Asia-Pacific Group.

For each of the five rounds, the country-specific results for the total TEQ are depicted in Figs. 28, 29, 30, 31, and 32 (in the appendix) and differ between (1) period of these studies and (2) UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands) (Fig. 28: period 2000–2003, Fig. 29: 2004–2007, Fig. 30: 2008–2011, Fig. 31: 2012–2015, and Fig. 32: 2016–2019). These figures are normalized to 30 pg/g as maximum value allowing

a direct visual comparison of the TEQ concentrations among the different collection periods as an indication of time trends. If two or more pooled samples were submitted, error bars indicate the range of the single pooled samples (minimum and maximum) around the median.

In the third round (2000–2003), 21 of the 26 countries participating were from the Eastern European or Western European and Others Groups. In comparison to other regions, countries from these groups had quite high total TEQ concentrations, e.g. (as aggregated data) Netherlands 22.8 pg/g (2001), Belgium 22.1 pg/g (2002), Luxembourg 21.7 pg/g (2002), Italy 20.3 pg/g (2001), Ukraine 19.2 pg/g (2002), and Germany 18.9 pg/g (2002). These countries were not all represented in the following rounds. However, if European countries participated, they were likely to be in the upper third or middle of the frequency distribution.

In the 2000–2003 round, Egypt had total TEQ concentrations comparable to European countries (23.0 pg/g in 2001; as aggregated data). In two African countries that were later found to be in the upper range of concentrations, i.e., Democratic Republic of Congo with 14.1 pg/g in 2009 and Côte d'Ivoire with 13.4 pg/g in 2010, a non-industrial source of contamination is assumed to have caused the elevated levels (see Sect. 5.1). The lower range of the frequency distribution curve for total TEQ in the period 2000–2008 was in the range of 5 pg/g and found in Fiji (4.42 pg/g in 2002; 5.06 pg/g in 2006), Brazil (5.24 pg/g in 2001–2002), Philippines (5.27 pg/g in 2002), Haiti (5.51 pg/g in 2004), Cyprus (5.70 pg/g in 2006), and Hungary (5.77 pg/g in 2006).

In the period 2012–2019, the low end of the frequency distribution of total TEQ (below 2 pg/g) were Ethiopia (1.29 pg/g in 2019; 1.54 in 2012), Uganda (1.59 pg/g in 2018), Niue (1.76 pg/g in 2017), Haiti (1.81 pg/g in 2015), Zambia (1.83 pg/g in 2019), and Vanuatu (1.95 pg/g in 2018). With concentrations between 6.7 and 11.6 pg/g, four countries from the African Group (Morocco, Senegal, Egypt, and Democratic Republic of Congo) and the Marshall Islands are found at the upper end of the frequency distribution curve of the 2016–2019 round.

For the sum of the 6 Indicator PCB ($\mathbf{\Sigma PCB_6}$), the country results with aggregated data are illustrated in Fig. 5. The highest concentrations by far were found in the period 2000–2003 with a median 123 ng/g (range 16–502), followed by the period 2004–2007 with a median 49 ng/g (range from 10 to 376 ng/g). In comparison, the other three rounds had considerably lower concentrations: The 2008–2011 round had a median of 18 ng/g (range from 4 to 79 ng/g); the 2012–2015 round had a median of 24 ng/g (range 2–158 ng/g); the 2016–2019 round had a median of 13 ng/g (range 1–109 ng/g). Thus, a considerable downward trend from the 2000–2003 round is observed to the period 2008–2011, obviously with a reduction by about 85% in the first decade of the 2000–2019 period, but the subsequent rounds seem to show a levelling out. However again, changes in the fraction of regional groups over these periods have to be taken into consideration. Whereas in the 2000–2003 period, the majority of participants came from European countries, which had higher PCB concentrations than other countries, in the 2016–2019 round, the majority came from Non-European countries. Therefore, this first indication of overall time trends needs to consider country-specific aspects, as well.

For each of the five rounds, the country results for the $\sum$ 6 Indicator PCB are depicted in Figs. 33, 34, 35, 36, and 37 (in the appendix) differentiating between:

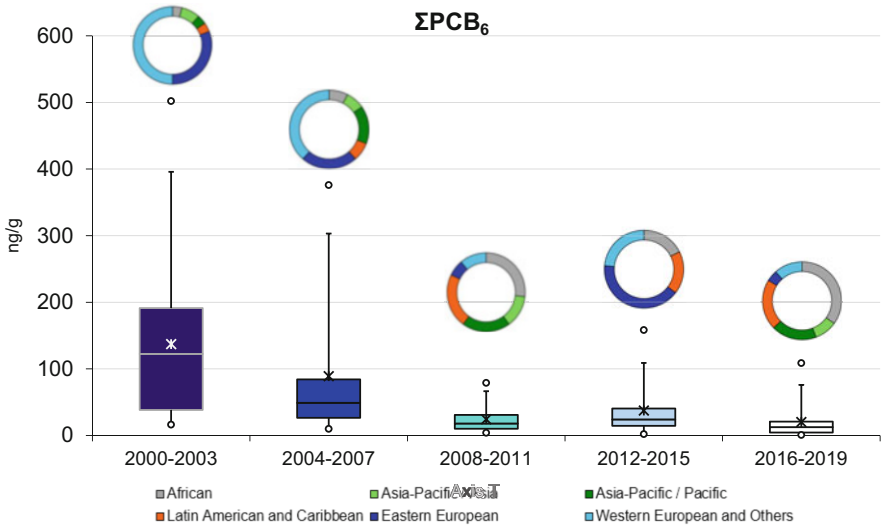

Fig. 5 Median and range of concentrations of the sum of 6 Indicator PCBs (ΣPCB_6) in the five rounds performed between 2000 and 2019 and fraction of results among UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands; country results with aggregated data; ng/g lipid) [box plot; minimum and maximum: as circles; 5th and 95th percentile: as whiskers; lower (25–50%) and upper (50–75%) quartiles, separated by the median: as box; mean: as asterisk]

(1) period of these rounds performed between 2000 and 2019 and (2) UN regions (with split of the Asia-Pacific Group into the subgroups Asia and Pacific Islands). Figure 33 for the 2000–2003 round is normalized to 600 ng/g due to high levels, but the other results are normalized to lower levels. Note that the bold red line at the 100 ng/g level in all figures allows the downward trend over time to be easily observed. Following the principle of "one country – one result per round", the median is shown with error bars indicating the range of these samples (minimum and maximum), if a country submitted two or more pooled samples.

Between 2000 and 2003, the majority of participants were European countries. Later, WHO and UNEP encouraged countries of other groups to participate through special programmes. As shown in Sect. 3.2, European countries had by far the highest ΣPCB_6 concentrations. This is supported by the results of the 2000–2003 round, when only Eastern European and Western European and Others Regional Group countries were found in the upper third and middle part of the frequency distribution (Fig. 33). The 2004–2007 round also had considerably higher non-dioxin-like PCB concentrations in European countries (Fig. 34).

In these rounds, the highest ΣPCB_6 concentrations were found in samples from the Czech and the Slovak Republics. In one of the three pooled samples submitted by the Czech Republic in 2001, the highest concentration of 1009 ng/g was found. The median of the three submitted samples was 502 ng/g. However, the PCB concentrations in samples of these two countries decreased considerably to

109 ng/g in the Czech Republic and 78 ng/g in the Slovak Republic in the samples from 2019.

In the 2000–2003 round, other countries with elevated aggregated levels higher than 150 ng/g for ΣPCB_6 were Romania (173 ng/g in 2001), Belgium (191 ng/g in 2002), Netherlands (191 ng/g in 2001), Luxembourg (217 ng/g in 2002), Germany (220 ng/g in 2002), Spain (241 ng/g in 2002), and Italy (253 ng/g in 2001).

This estimation of time trends based on comparison of median concentrations in the five periods provides a first orientation. However, as the number of countries participating from a certain UN region in a certain period varies considerably, it can be influenced by the fraction of regions in a certain round or single results of a country submitted at a certain time. Thus, it is more precise to only use results of countries with repeated participation in these studies: This allows drawing conclusions on temporal trends, which are not potentially influenced by these possible factors. This assessment of time trends based only on the results of countries with repeated participation is published separately in Part IV (Malisch et al. 2023b).

5 Detailed Comparison of Concentrations on a Regional Group Scale

The Stockholm Convention's Global Monitoring Plan (GMP) for POPs is implemented in the five geopolitical United Nations regions, namely Africa, Asia and the Pacific, Eastern Europe, Latin America and the Caribbean, and Western Europe and Others. Countries that are party of the Convention are to report flexibly using one of these five UN Regional Groups. As the studies were performed since 2004 with the aim to contribute to the effectiveness evaluation of the Stockholm Convention, countries participating in WHO- and UNEP-coordinated studies have been classified by these five UN regions (Malisch et al. 2023a). The detailed results for all congeners and sum parameters are available at the GMP Data Warehouse (Global Monitoring Plan Data Warehouse 2020). In this section, the following figures illustrating the results of the 2000–2019 surveys for total TEQ and NDL-PCB in the regions were prepared by use of country results with aggregated data, if two or more samples were submitted (see Sect. 2.2).

5.1 African Group

Africa had the widest variation in contamination of human milk with **total TEQ** that was observed in any group. Figure 6 illustrates these results (with the five 4-year studies between 2000 and 2019 shown in different colours).

On one side was Ethiopia with the lowest levels of total TEQ of all countries in the 2000–2019 studies (1.54 pg WHO_{2005}-TEQ/g in 2012 and 1.29 pg/g in 2019). On the other side was Egypt with a median of 23.0 pg WHO_{2005}-TEQ/g for 9 pooled samples collected in 2001 and 2002, which are comparable to levels found in Europe at that time. With 49.0 pg WHO_{2005}-TEQ/g, one of the pooled samples from Egypt

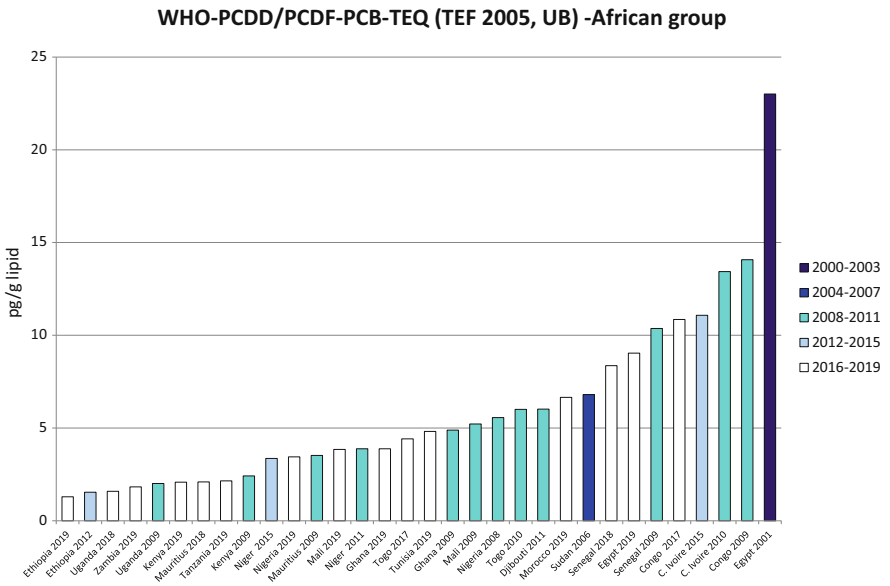

Fig. 6 Results of the 2000–2019 surveys for total TEQ in human milk in countries from Africa with indication of the period and year of sample submission (pg WHO-PCDD/PCDF-PCB-TEQ [TEF 2005, UB])/g lipid)

submitted in 2001 had a very high level of total TEQ and was probably from a contaminated area. However, the pooled sample from Egypt of 2019 (9.0 pg WHO_{2005}-TEQ/g) had considerably lower concentrations.

Uganda (2009 and 2018), Zambia (2019), Kenya (2009 and 2019), Mauritius (2018), and Tanzania (2019) were at the lower end of the frequency distribution among African countries (below 3 pg WHO_{2005}-TEQ/g). Niger (2011, 2015), Nigeria (2008, 2019), Mauritius (2009), Mali (2009, 2019), Ghana (2009, 2019), Togo (2010, 2017), Tunisia (2019), Djibouti (2011), Morocco (2019), and Sudan (2006) were in the middle (range 3–7 pg WHO_{2005}-TEQ/g). Senegal (2009, 2018), Côte d'Ivoire (2010 and 2015), Democratic Republic of Congo (2009, 2017) and, as mentioned, Egypt (2001, 2019) were in the upper third of the frequency distribution in the African Group (range 8–23 pg WHO_{2005}-TEQ/g).

Figure 38 (in the appendix) illustrates the relative contributions of toxic equivalency resulting from PCDD (WHO-PCDD-TEQ), PCDF (WHO-PCDF-TEQ), and dioxin-like PCB (WHO-PCB-TEQ) to total TEQ (WHO-PCDD/PCDF-PCB-TEQ) in human milk in countries from Africa. Interestingly, the three countries with the highest levels of the total TEQ (Côte d'Ivoire [2010], Democratic Republic of Congo [2009], and Egypt [samples of 2001–2002]) were among the countries with low contributions from dioxin-like PCB (range 8–22%). Consistent with NDL-PCB concentrations between 10 and 50 ng/g lipid, this observation indicates that the elevated TEQ levels are not caused by a PCB contamination. However, whereas Egypt (2001) had the highest contribution to total TEQ from PCDF (41% from

WHO-PCDF-TEQ), Côte d'Ivoire (2010 and 2015) and Democratic Republic of Congo (2009 and 2017) had the highest contribution to total TEQ from PCDD (range 65–85% from WHO-PCDD-TEQ).

The PCDD-dominated patterns in human milk in the Democratic Republic of Congo and Côte d'Ivoire mirror with the patterns found in certain clays with high concentrations of PCDD/PCDF collected on the Dutch market originating from African countries and in trading centres in various African countries (Reeuwijk et al. 2013). Such patterns were found before, e.g. in the 1990s in clay from a mine in Mississippi causing a contamination of poultry and fish (Hayward et al. 1999) and later at contamination incidents in Germany and the Netherlands (reviewed by Malisch 2017). These congener patterns would be expected after bioaccumulation and hint at consumption of such clays ("geophagy") by pregnant women in these African countries as the likely source for these remarkably high levels in human milk (Hoogenboom et al. 2011, 2020; Reeuwijk et al. 2013; Malisch et al. 2011). It should be noted that with regard to the contribution to toxic equivalency, 1,2,3,7,8-PeCDD *(pentachlorodibenzo-p-dioxin)* is predominant in both samples from Côte d'Ivoire (2010, 2015), whereas in the Democratic Republic of Congo, 1,2,3,7,8,9-HxCDD *(hexachlorodibenzo-p-dioxin)* is by far the dominant congener in both samples (2009, 2017) (Fig. 7).

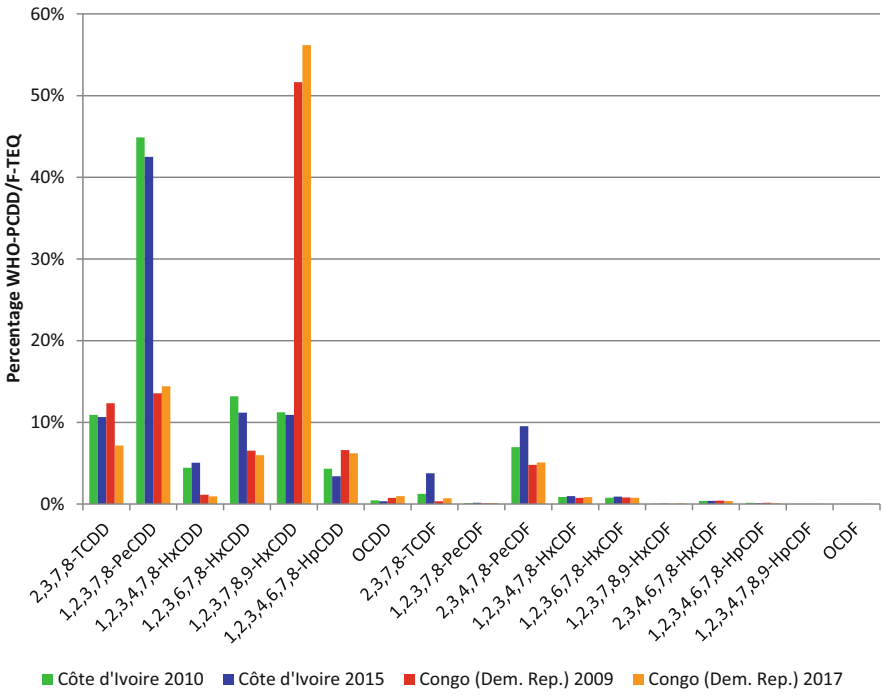

Fig. 7 PCDD/PCDF congener patterns in human milk in Côte d'Ivoire (2010, 2015) and Democratic Republic of Congo (2009, 2017)

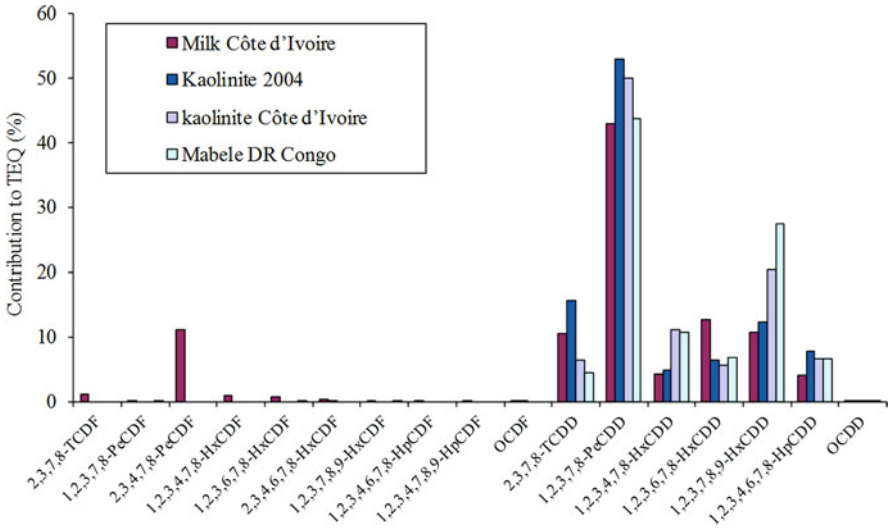

Fig. 8 Comparison of the congener patterns in human milk from Côte d'Ivoire (sample from 2010 for the WHO- and UNEP-coordinated exposure studies) with patterns observed in two Kaolinite and one Mabele clay samples (reprinted from Reeuwijk et al. 2013, with permission from Elsevier)

The pattern found in a kaolinic clay sample from Côte d'Ivoire was highly comparable with the kaolinic clay causing the 2004 contamination incident in the Netherlands. Also the pattern in the Mabele clay sample collected in the Netherlands and labelled "Democratic Republic of Congo" showed a similar pattern of congeners (Fig. 8, from Reeuwijk et al. 2013).

Figure 9 (from Reeuwijk et al. 2013) shows the congener pattern in samples of human milk from the Democratic Republic of Congo (sample from 2009) compared with three different clays that were all characterized by an usually high contribution of 1,2,3,7,8,9-HxCDD. In some clay samples, this congener showed the highest contribution to the TEQ-level (>60%). These clay patterns are remarkably similar to the patterns seen in human milk from the Democratic Republic of Congo and suggest that consumption of such contaminated clay is the reason for high PCDD/PCDF levels in human milk in this country.

Both the relatively high levels of PCDD in the human milk from Congo and Côte d'Ivoire collected for the fifth round (2008–2012) of the WHO- and UNEP-coordinated exposure studies and the similarity of the congener patterns with those from the clays, strongly suggest that the consumption of clays during pregnancy contributes to these high levels in human milk. Considering the susceptibility of the developing foetus and young children to PCDD/PCDF, the consumption of contaminated clays should be discouraged.

The mixture of a PCDF-dominated pattern with particularly high contribution of 2,3,4,7,8-PeCDF *(pentachlorodibenzofuran)* and PCDD to the TEQ levels as found in the nine human milk samples from Egypt (2000–2002) (Fig. 10) could indicate

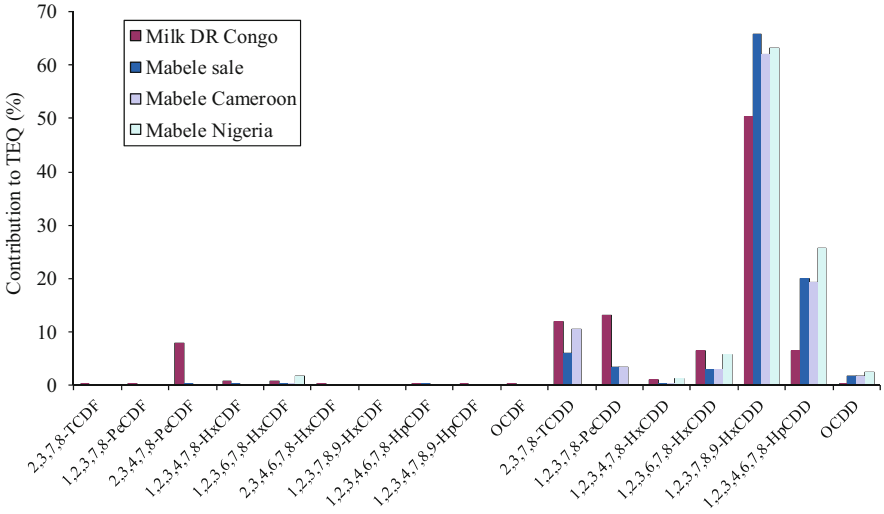

Fig. 9 Comparison of the congener pattern in human milk from the Democratic Republic of Congo (sample from 2009 for the WHO- and UNEP-coordinated exposure studies) with the patterns observed in three different Mabele clay samples with unusually high contribution of 1,2,3,7,8,9-HxCDD (reprinted from Reeuwijk et al. 2013, with permission from Elsevier)

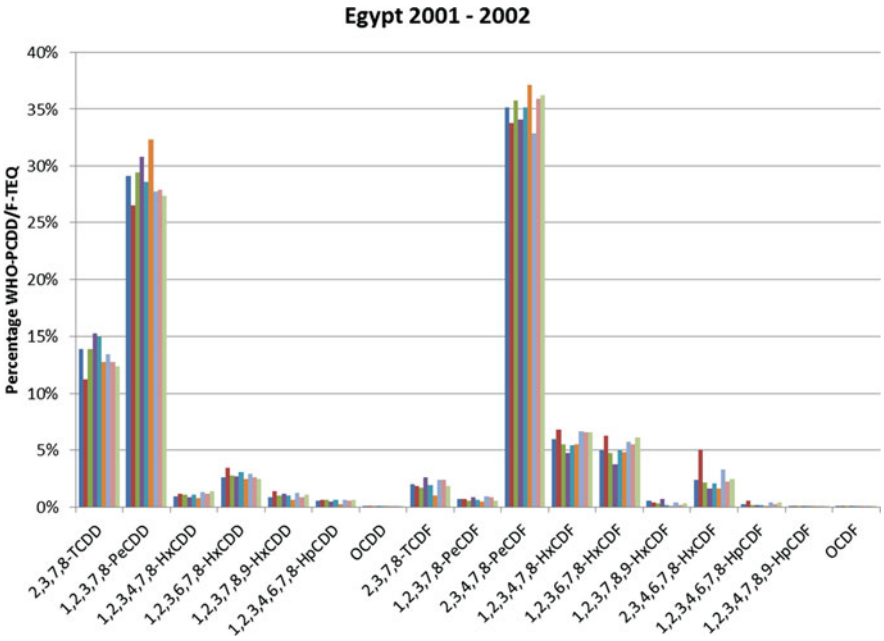

Fig. 10 Congener contributions (%) to toxic equivalency from PCDD and PCDF (WHO-PCDD/PCDF-TEQ) in human milk from Egypt (2001–2002)

combustion and drying processes as a source for this contamination (Hoogenboom et al. 2020). While Egypt covers an area of about 1,000,000 square kilometers, the great majority of its nearly 100 million people live along the banks of the Nile River with about half of the population living in urban areas. In this relatively small area, possible emission from industrial production as well as open burning of waste is in close proximity to agricultural production areas. This might explain the findings of high concentrations of PCDD and PCDF in foods in the 1990s, particularly in butter (Malisch and Saad 1994; Malisch and Saad 1996), and elevated levels of these contaminants in human milk collected in 1997 (Malisch et al. 2000).

The seven pooled samples collected in 2001 had a wide range (between 17.6 and 49.0 pg total TEQ/g). Note that these seven samples of 2001 were freeze-dried before shipment, and were apparently contaminated with lower chlorinated PCB during freeze-drying (Malisch et al. 2023b). Therefore, results for some PCB congeners are not useable. Hence, two additional pooled samples were submitted by Egypt in 2002, which were shipped frozen and not freeze-dried. These two samples had concentrations of 16.9 and 19.0 pg total TEQ/g lipid. In 2019, these levels decreased to 9.04 pg total TEQ/g lipid.

Figure 11 illustrates the results of the **sum of 6 Indicator PCB (ΣPCB_6)** with the period of participation between 2000 and 2019 indicated. Ethiopia also had the lowest levels of all countries in the 2000–2019 studies for this parameter: 2.15 ng ΣPCB_6/g lipid in 2012 and 0.90 ng/g in 2019. The highest level in Africa was found in Senegal where the sample of 2018 (90.3 ng/g lipid) showed an increasing trend in comparison to the sample of 2009 (65.8 ng/g lipid). This is at the upper end of the frequency distribution of all samples collected after 2010.

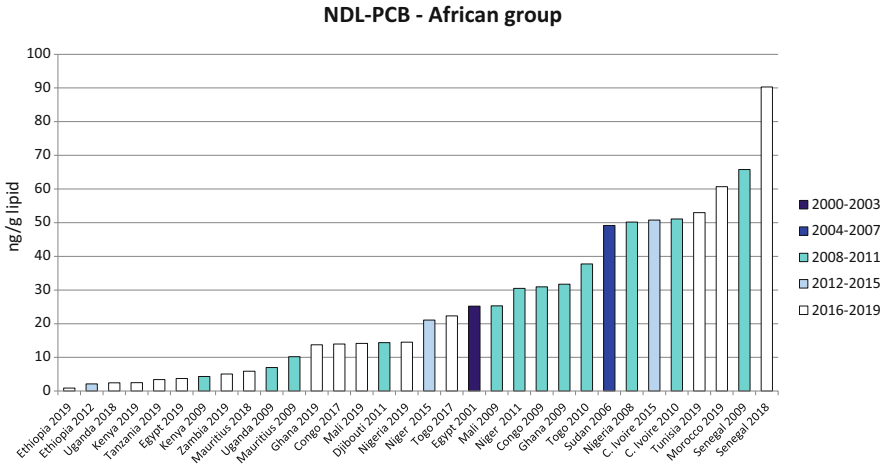

Fig. 11 Results of the 2000–2019 surveys for ΣPCB_6 (ng/g lipid) in human milk in countries from Africa with indication of the period and year of sample submission

5.2 Asia-Pacific Group

5.2.1 Asia Subgroup

Figure 12 illustrates the results of total TEQ with the period of participation between 2000 and 2019 indicated for the Asian countries of the Asia-Pacific Group. Concentrations below 5 pg WHO_{2005}-TEQ/g lipid were found in all samples of the 2016–2019 round (Thailand [2018], Mongolia [2018], Vietnam [2019], and Cambodia [2019]). Samples from previous rounds, with the exception of Syria (2009), had higher levels (UNEP 2013a). Hong Kong SAR of China participated twice, with a slight downward trend from the 2002 level of 10.8 pg total TEQ/g (median of 13 samples from different population subgroups [Hedley et al. 2006]) to the 2009 level of 9.4 pg/g total TEQ (median of 4 samples from different subgroups). Tajikistan (2009), Indonesia (2011), Cyprus (2006), Philippines (2002), and the Republic of Korea (2008) had concentrations between 5.2 and 7.3 pg/g lipid.

The lowest contribution of dioxin-like PCB to the total TEQ (14%) is found in Cambodia, the highest with 46% in Tajikistan. In Hong Kong SAR of China, the dioxin-like PCB contribution to TEQ was about 31 and 33% in 2002 and 2009, respectively (Fig. 39, in the appendix). The highest concentration of 46 ng ∑ 6 Indicator PCB/g found in Hong Kong SAR of China in 2002 was quite low in comparison to European countries at that time (see Fig. 33) and decreased to 22 ng/g in 2009 (Fig. 13).

5.2.2 Pacific Islands Subgroup

Figure 14 illustrates the results of total TEQ for samples from the Pacific Islands subgroup of the Asia-Pacific Group submitted between 2000 and 2019. All samples

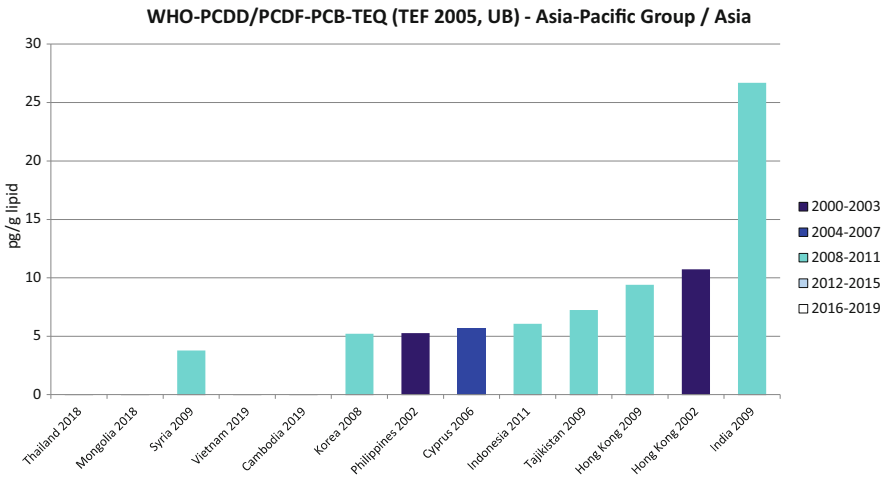

Fig. 12 Results of the 2000–2019 surveys for total TEQ in human milk from Asian countries of the Asia-Pacific Group with indication of the period and year of sample submission (pg WHO-PCDD/PCDF-PCB-TEQ [TEF 2005, UB])/g lipid)

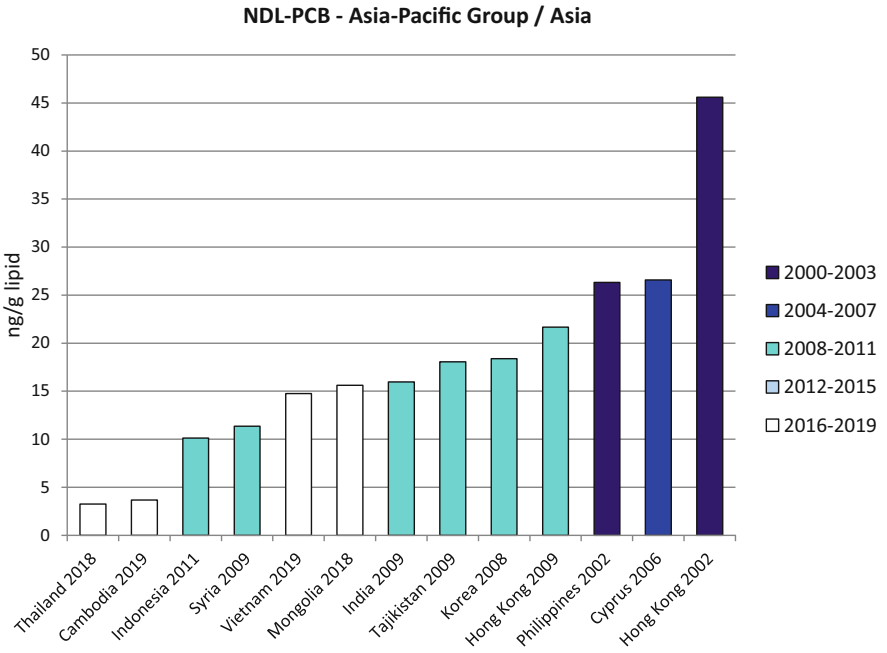

Fig. 13 Results of the 2000–2019 surveys for $\sum$ PCB_6 (ng/g lipid) in human milk from Asian countries of the Asia-Pacific Group with indication of the period and year of sample submission

submitted between 2000 and 2015 were approximately in the range 3–6 pg WHO_{2005}-TEQ/g lipid and included those from Tuvalu (2011), Fiji (2002, 2006, 2011), Solomon Islands (2011), Tonga (2008), Samoa (2011), Kiribati (2006, 2011), Niue (2011), and Palau (2011). In nearly all samples from the 2016 to 2019 period, concentrations were below 4 pg/g suggesting a downward trend, including samples from Niue (2017), Vanuatu (2018), Solomon Islands (2019), Fiji (2019), Kiribati (2018), Samoa (2019), and Palau (2018). Only one sample from the Marshall Islands (2019) had a substantially higher concentration of 11.6 pg/g, which was nearly double the 6.32 pg total TEQ/g lipid found in the sample from the Marshall Islands of 2011 and the highest concentration found in the Pacific Islands subgroup in the period 2000–2019.

With regard to the from 2011 to 2019 increasing concentration on Marshall Islands and the overall elevated concentration range of its two samples in the Pacific Islands subgroup, the changes of the relative contribution (%) of PCDD, PCDF, and dioxin-like PCB to the total toxic equivalents are of interest (Fig. 40, in the appendix). 73% contribution of PCDD to total TEQ in the sample from 2019 is the highest found in the Asia-Pacific Group. In this sample, 7% came from PCDF and 20% from dioxin-like PCB. This is a considerable change in comparison to its 2011 sample, when 40% of the total TEQ came from PCDD, 23% from PCDF, and 37% from dioxin-like PCB.

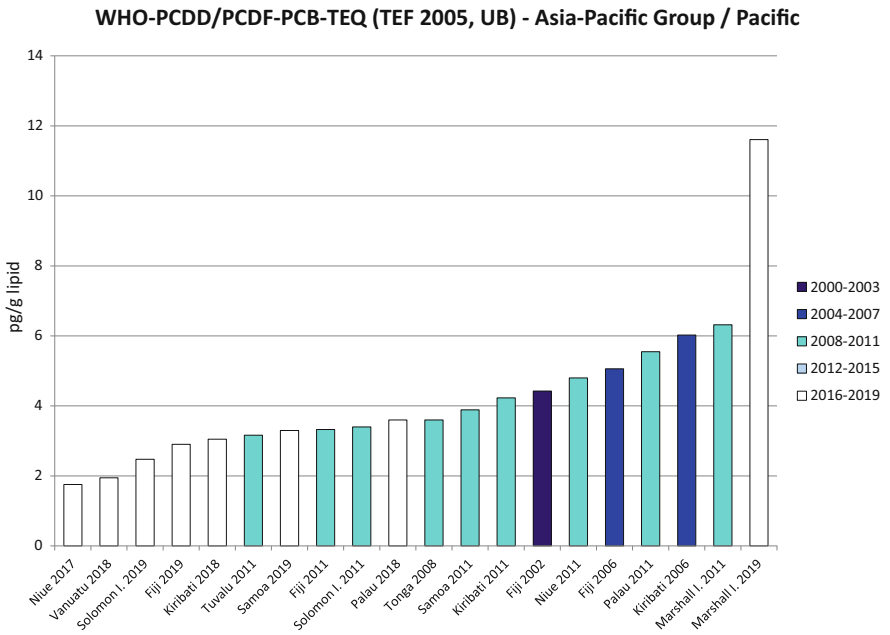

Fig. 14 Results of the 2000–2019 surveys for total TEQ in human milk from countries of the Pacific Islands subgroup in the Asia-Pacific Group with indication of the period and year of sample submission (pg WHO-PCDD/PCDF-PCB-TEQ [TEF-2005, UB])/g lipid)

A look into the PCDD/PCDF pattern of the 2019 sample from the Marshall Islands reveals that 1,2,3,7,8-PeCDD contributed 53% to the TEQ of PCDD and PCDF, 2,3,7,8-TCDD 13% and 2,3,4,7,8-PeCDF 5%, whereas these were 33%, 14%, and 24%, respectively, for the 2011 sample (Fig. 15). The 2019 pattern is less influenced by a thermal source than by chlorophenol-related substances. As example, a technical product of the pesticide 2,4-D (dichlorophenoxy acetic acid) was found to have 1,2,3,7,8-PeCDD as by far dominant TEQ contributor; within the 2,3,7,8-substituted HexaCDD, 1,2,3,6,7,8-HexaCDD contributed more than the other congeners (Holt et al. 2010). However, with regard to the huge variety of chlorophenol-related substances and their different and over time changing production processes, the PCDD/PCDF patterns can vary not only between different substances, but might vary also for the same chemical depending on the production process.

Regarding concentrations for NDL-PCB, most samples collected between 2000 and 2015 were in the range of approximately 4–17 ng/g for $\sum PCB_6$, whereas most samples for the period 2016–2019 were in the range of approximately 3–9 ng/g $\sum PCB_6$. Only the Marshall Islands showed an increase from 16 to 23 ng/g $\sum PCB_6$ from 2011 to 2019 (Fig. 16).

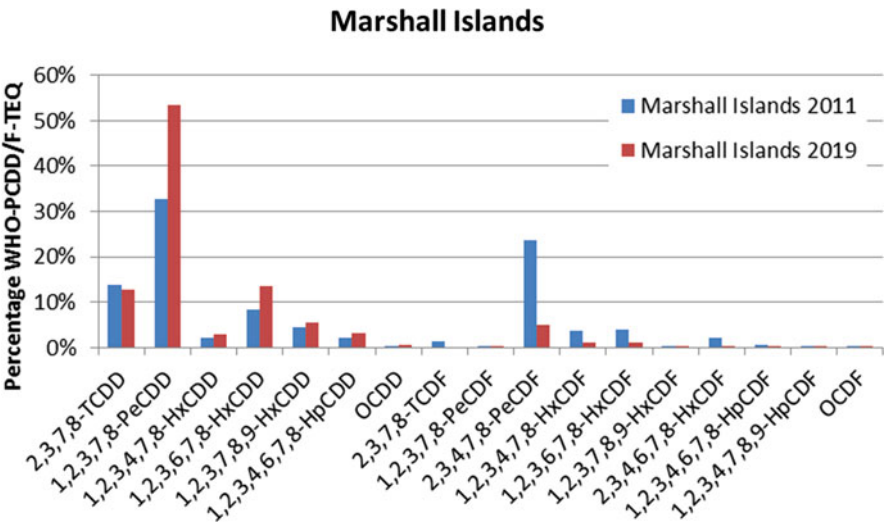

Fig. 15 Congeners contributions (%) from PCDD and PCDF to toxic equivalency (WHO-PCDD/PCDF-TEQ [2005]) in human milk from Marshall Islands in 2011 and 2019

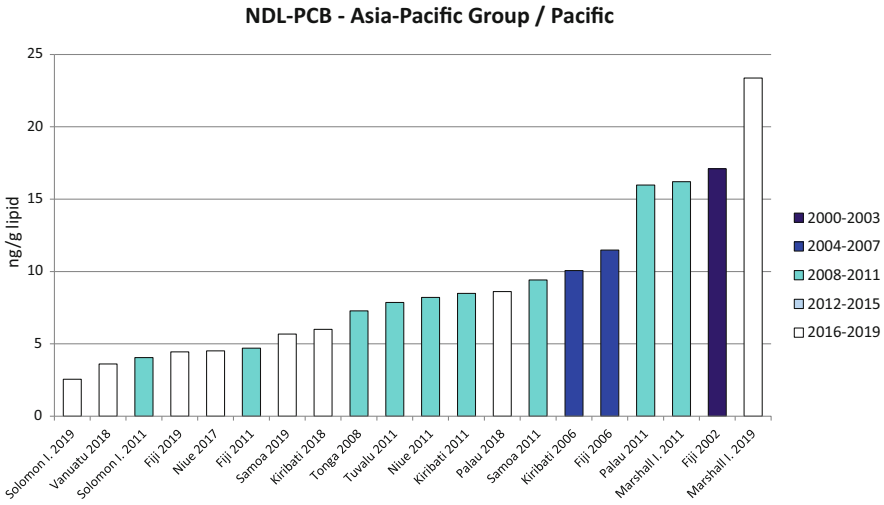

Fig. 16 Results of the 2000–2019 surveys for $\sum PCB_6$ (ng/g lipid) in human milk from countries of the Pacific Islands subgroup in the Asia-Pacific Group with indication of the period and year of sample submission

5.3 Group of Latin American and Caribbean Countries (GRULAC)

Figure 17 illustrates the results of total TEQ for the period 2000 and 2019 for countries from the Group of Latin American and Caribbean Countries. Note that for the period 2008–2011, Chile participated both in 2008 and in 2011. Also note

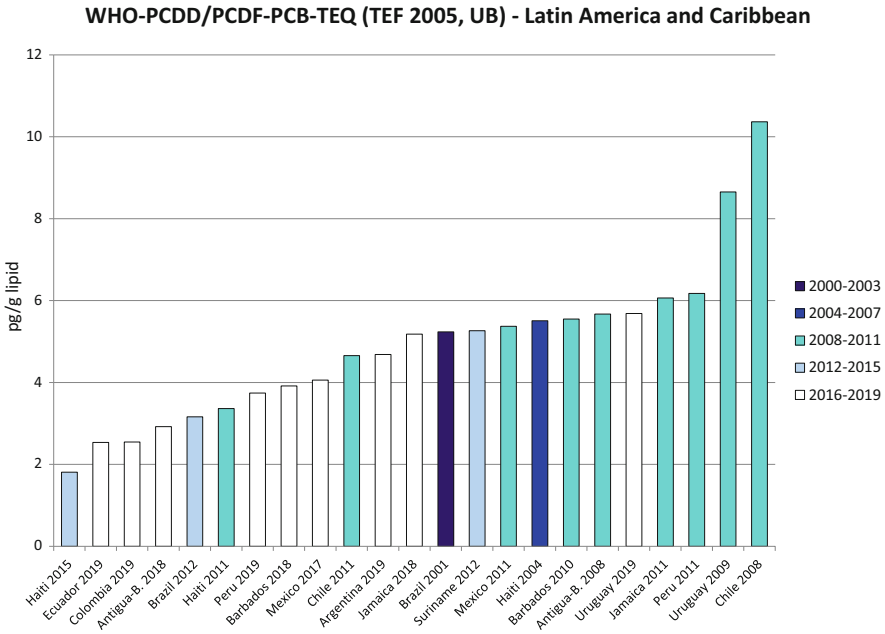

Fig. 17 Results of the 2000–2019 surveys for total TEQ in human milk samples from countries of the Group of Latin American and Caribbean Countries with indication of the period and year of sample submission (pg WHO-PCDD/PCDF-PCB-TEQ [TEF 2005, UB])/g lipid)

that the sample from Cuba (2011) was freeze-dried before shipment. As observed with freeze-dried samples from Egypt, a contamination with lower chlorinated PCB occurred during freeze-drying and resulted in an unusual PCB pattern (Malisch et al. 2023b). Therefore, results for dioxin-like PCB were not used in the calculation of WHO-PCB-TEQ and total TEQ in the Cuban sample.

Most samples of the period 2000–2011 were approximately in the range 3–6 pg total TEQ/g including samples from Antigua and Barbuda (2008), Barbados (2010), Brazil (2001), Chile (2011), Haiti (2004, 2011), Jamaica (2011), Mexico (2011), and Peru (2011). Uruguay (2009) and Chile (2008) were at the upper end with 8.65 and 10.4 pg total TEQ/g lipid, respectively. In the samples of the 2012–2019 period, total TEQ concentrations were found in the range from 1.8 to 5.7 pg/g suggesting a downward trend, which included samples from Antigua and Barbuda (2018), Argentina (2019), Barbados (2018), Brazil (2012), Colombia (2019), Ecuador (2019), Haiti (2015), Jamaica (2018), Mexico (2017), Peru (2019), Suriname (2012), and Uruguay (2019). With 3.44 pg WHO-PCDD/PCDF-TEQ/g lipid, Cuba (2011) was in the middle of the range of concentrations found for PCDD/PCDF in this group at that time, but, as noted above, this did not include a contribution of dioxin-like PCB.

Due to its huge size and population of over 200 million, Brazil submitted altogether 10 samples in 2001 and 2002 representing national and provincial areas

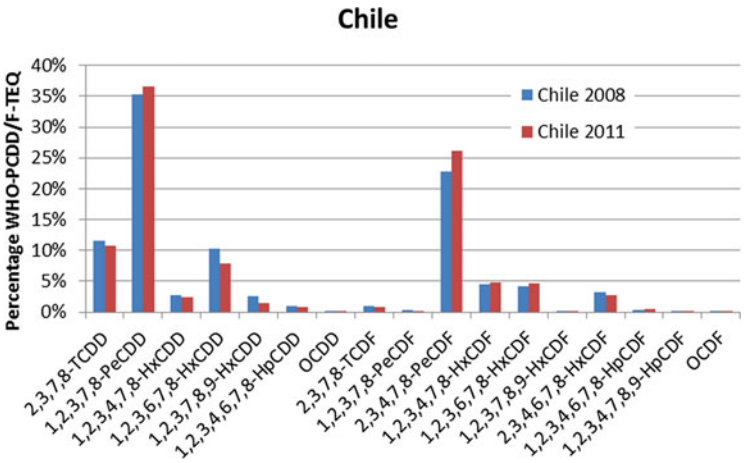

Fig. 18 Congener patterns (as contribution [%] of PCDD and PCDF to their toxic equivalency) in human milk samples from Chile in 2008 and 2011

(Braga et al. 2002). Total TEQ concentrations ranged between 3.53 and 8.47 pg/g with a median of 5.24 pg/g. Three national samples collected in 2012 had 3.00, 3.16, and 3.42 pg WHO_{2005}-TEQ/g lipid. Brazil is an example of the need for flexible criteria in collecting a representative sample for a country. According to the protocol, one pooled sample for countries with populations less than 50 million is requested. Countries with populations well over 50 million (or with sufficient resources) were encouraged to prepare a second pooled sample (or more) if feasible.

The relative contribution of PCDD, PCDF, and dioxin-like PCB to the total TEQ is depicted in Fig. 41 (in the appendix). The contribution of PCDD to the TEQ ranged from 30% (Peru [2011]) to 64% (Jamaica [2018]), for PCDF from 10% (Haiti [2004]) to 34% (Chile [2011]), and for dioxin-like PCB from 14% (Mexico [2011]) to 52% (Peru [2011]).

Figure 17 shows that the two samples from Chile were considerably different in total TEQ concentrations between 2008 (10.4 pg/g) and 2011 (4.7 pg/g). Neither the contribution of PCDD, PCDF, and dioxin-like PCB to the TEQ (Fig. 41) nor the PCDD/PCDF pattern (Fig. 18) changed during this relatively short time period of 3 years. Thus, differences in the regional origin of these two samples might explain these findings.

As the intake of PCDD/PCDF and PCB comes mainly from food (see Sect. 2.8), it might be of interest to understand the difficulties to find sources of contamination with the example of two incidents in the food chain in Chile. In 2008, the formation of PCDD/PCDF from a refinery process for zinc oxide used in feed additives was detected as source of a dioxin contamination in Chilean pork. PCDD/PCDF were formed at remarkably high concentrations in zinc oxide (17,147 pg TEQ/g) from a metal refinery process. 2,3,4,7,8-PeCDF contributed about 30% to TEQ concentrations. As follow-up of investigations of meat and associated supplies, in vegetal and animal fatty acid components more PCDD, especially 2,3,7,8-TCDD

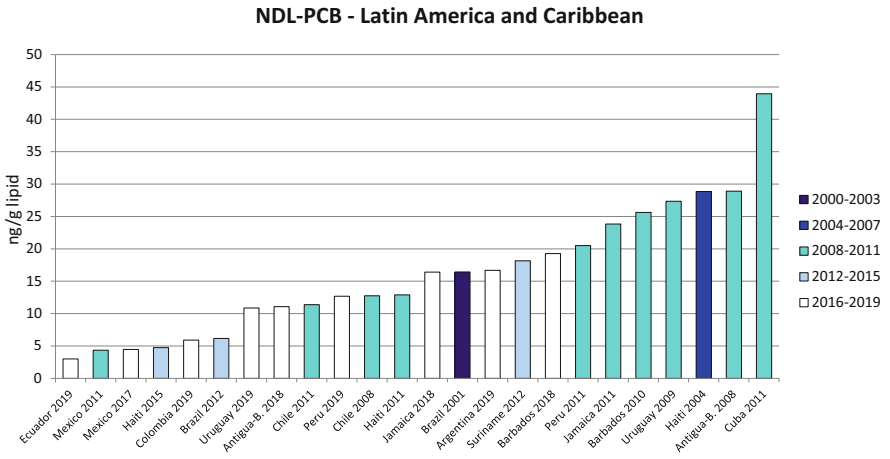

Fig. 19 Results of the 2000–2019 surveys for $\sum$ PCB_6 (ng/g) in human milk samples from countries of the Latin America and Caribbean Group with indication of the period and year of sample submission

and 1,2,3,7,8-PeCDD were found. This suggested that a secondary source of contamination may have existed in addition to zinc oxide, although the exact source could not be confirmed (Kim et al. 2011). As for the Marshall Islands, the kind of PCDD pattern in the secondary source is an indication for chlorophenol-related chemicals. Another incident occurred in Chile in 2013, when samples of chicken with elevated PCDD/PCDF concentrations showed a pattern not reported before. Certain non-2,3,7,8-PeCDD were present at much higher levels than 1,2,3,7,8-PeCDD. However, the actual source and site of the contamination was never discovered (Hoogenboom et al. 2020).

With regard to NDL-PCB in the Latin America and Caribbean Group, most samples collected between 2000 and 2011 were in the range of about 11–30 ng/g for $\sum PCB_6$ with a maximum of 44 ng/g in Cuba, whereas all samples of the period 2012–2019 were in the range of approximately 3–20 ng/g for $\sum$ PCB_6 (Fig. 19).

5.4 Eastern European Group

Figure 20 illustrates the results of total TEQ for the period between 2000 and 2019 for countries of the Eastern European Group. The eight countries submitting samples in the period 2000–2004 had concentrations that ranged between 8.18 pg WHO-PCDD/PCDF-PCB-TEQ/g for Hungary (2001) and 19.2 pg/g for Ukraine (2001). The samples collected between 2004 and 2011 were in the range between 5.8 pg/g (Hungary [2006]) and 15 pg/g (Modova [2009]). The trend to lower concentrations continued during the period 2012–2019, with the lowest concentrations being between 4 and 5 pg/g found in Croatia (2014), Czech Republic (2019), and Slovak Republic (2019). Samples from Bulgaria (2014), Czech Republic

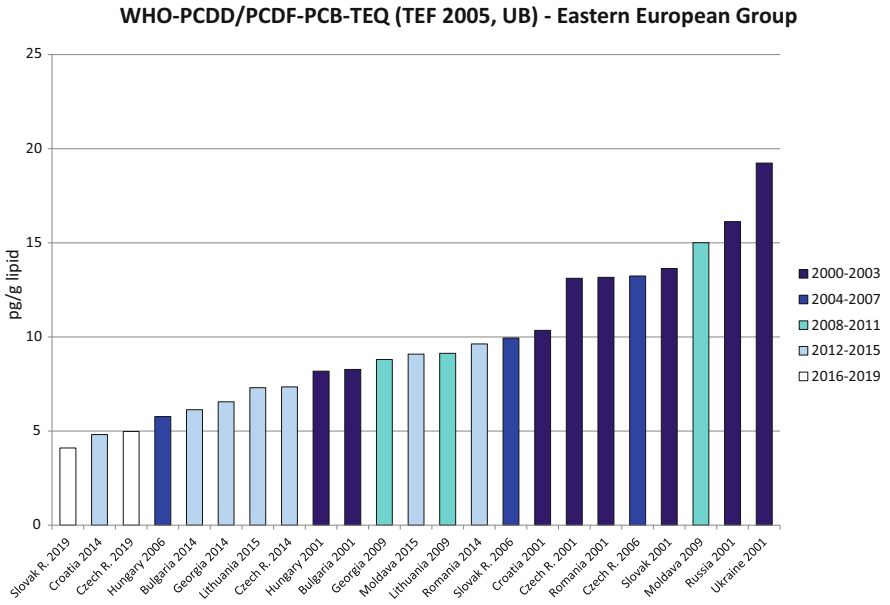

Fig. 20 Results of the 2000–2019 surveys for total TEQ in human milk samples from countries of the Eastern European Group with indication of the period and year of sample submission (pg WHO-PCDD/PCDF-PCB-TEQ [TEF 2005, UB])/g lipid)

(2014), Georgia (2014), Lithuania (2014), Moldova (2015), and Romania (2014) were in the range between 6 and 10 pg/g.

Most countries in the third round (2001–2002) submitted two or three pooled samples, however Russia submitted seven samples from various regions of this huge and populous country with concentrations ranging from 13.2 to 24.3 pg/g total TEQ with a median of 16.1 pg/g.

The contribution of PCDD to the total TEQ ranged from 18% for Czech Republic (2001) to 51% for Hungary (2001). The contribution of PCDF ranged from 17% for Russia (2001) to 35% for Bulgaria (2014) and the contribution for dioxin-like PCB was from 27% for Hungary (2001]) to 56% for the Czech Republic (2001) (Fig. 42, in the appendix).

Figure 21 illustrates the range of NDL-PCB concentrations. The highest concentrations were found in 2001 in samples from the Czech Republic (median 502 ng/g $\sum PCB_6$) and the Slovak Republic (median 443 ng/g $\sum PCB_6$). The highest concentration in single pooled sample was 1009 ng/g found in one of the three pooled samples submitted in 2001 from the Czech Republic. In 2006, however, a decrease in levels was apparent in samples from both these countries (Czech Republic: 376 ng/g; Slovak Republic: 255 ng/g). This substantial downward trend continued with samples submitted in 2019 (Czech Republic: 109 ng/g; Slovak Republic: 78 ng/g).

Of interest is the question how non-dioxin-like PCB correlate with TEQ of dioxin-like PCB. Figure 22 illustrates the range of WHO-PCB-TEQ concentrations.

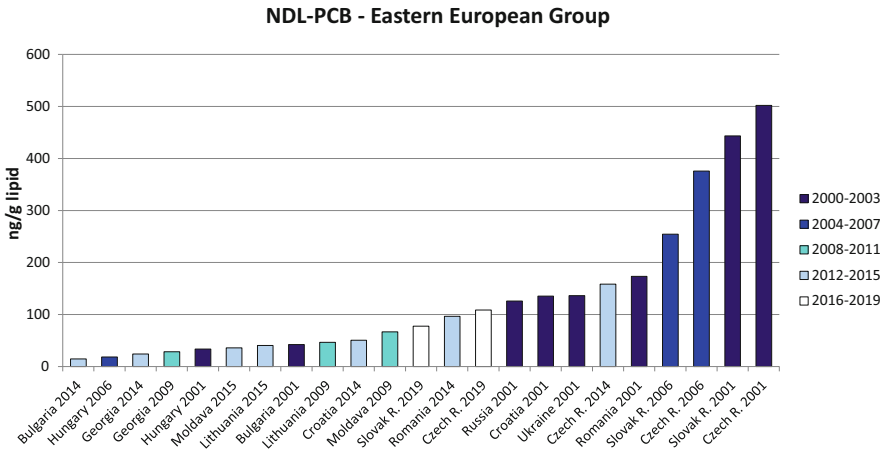

Fig. 21 Results of the 2000–2019 surveys for ∑ PCB6 (ng/g) in human milk samples from countries of the Eastern European Group with indication of the period and year of sample submission

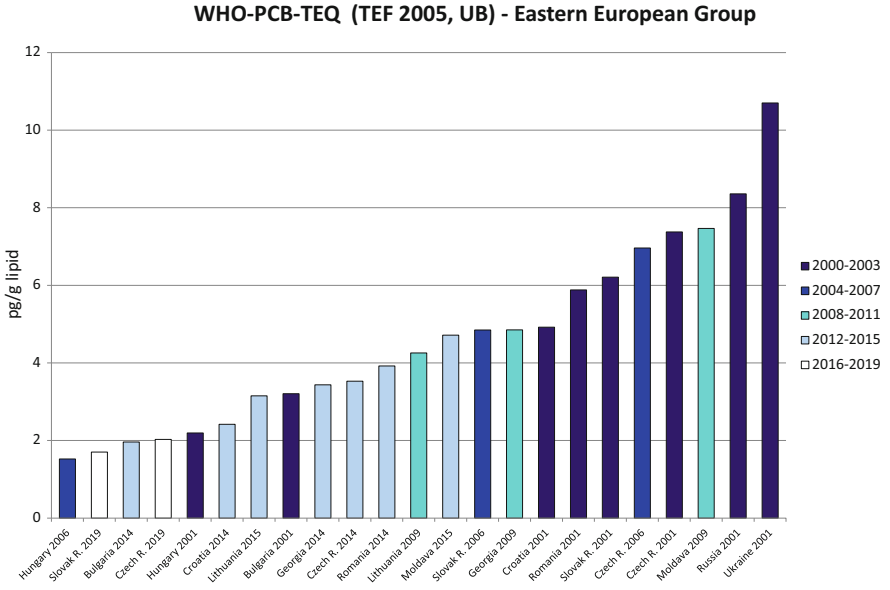

Fig. 22 Results of the 2000–2019 surveys for TEQ from dioxin-like PCB in human milk samples from countries of the Eastern European Group with indication of the period and year of sample submission (pg WHO-PCB-TEQ [TEF 2005, UB])/g lipid)

The highest concentration was found in a single pool sample from Russia (13.6 pg/g). As discussed in Sect. 6, concentrations of TEQ for dioxin-like PCB tend to increase with NDL-PCB concentrations, although with a wide range of variation. As example from the group of Eastern European countries, 13.5 pg/g of TEQ for dioxin-like PCB in the highest contaminated sample from the Czech Republic corresponds to 1009 ng/g $\sum PCB_6$, whereas 13.6 pg/g of TEQ for dioxin-like PCB in a sample from Russia corresponds to 311 ng/g $\sum PCB_6$. Because of this weak correlation between dioxin-like PCB and NDL-PCB in many countries, it can be concluded that the determination of NDL-PCB is no substitute for the determination of dioxin-like PCB.

The Czech Republic has participated in five periods (1992–1993; 200–2003; 2004–2007; 2012–2015; and 2016–2019). The frequent repeated participation over such a long period allows to derive statistically significant temporal trends for this country (Malisch et al. 2023b).

5.5 Western European and Others Group (WEOG)

Figure 23 illustrates the results of total TEQ for the period 2000 and 2019 for countries of the Western European and Others Group. As in the Eastern European Group, the countries from this group submitting samples in the period 2000–2003 also had high concentrations of total TEQ. However, as this UN Regional Group is comprised of industrialized countries from different continents (in addition to

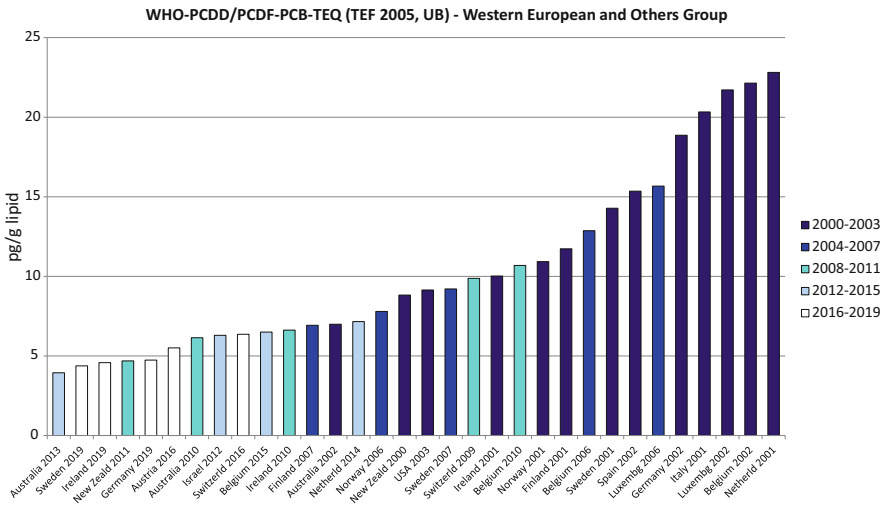

Fig. 23 Results of the 2000–2019 surveys for total TEQ in human milk samples from countries in the Western European and Others Group with indication of the period and year of sample submission (pg WHO-PCDD/PCDF-PCB-TEQ [TEF 2005, UB])/g lipid)

Western European countries, Australia, New Zealand, USA, and Israel are included), a differentiation within this group is possible between European and non-European countries. In the 2000–2003 period, the lowest concentrations of total TEQ were found in Australia (2002), New Zealand (2000), and USA (2003) with a range between 7 and 9 pg/g, whereas the Western European countries had concentrations between 10 pg/g (Ireland, 2001) and 23 pg/g (Netherlands, 2001).

Samples collected between 2004 and 2011 were in the range between 4.69 pg/g total TEQ for New Zealand (2011) and 15.7 pg/g for Luxembourg (2006). The trend to lower concentrations continued through 2019 with the lowest concentrations between 4 and 5 pg/g total TEQ found in Australia (2013), Germany (2019), Ireland (2019), and Sweden (2019). Samples from Austria (2016), Belgium (2015), Israel (2012), Netherlands (2014), and Switzerland (2016) were in the range between about 5 and 7 pg/g.

As shown in Fig. 43 (in the appendix), the contribution of PCDD to the total TEQ ranged from 29% for Switzerland (2016) to 61% for Australia (2002). The contribution of PCDF ranged from 11% for New Zealand (2000) to 29% for Ireland (2019) and of dioxin-like PCB from 26% for Australia (2002) to 50% for Switzerland (2016).

Figure 24 illustrates the range of non-dioxin-like PCB concentrations. As in the Eastern European Group, countries of the WEOG submitting samples in the period 2000–2003 also had substantially higher concentrations of $\sum$ PCB_6. As for total TEQ, also for PCB the geographical differences among countries become obvious in this UN region comprising countries from different continents. Starting with the

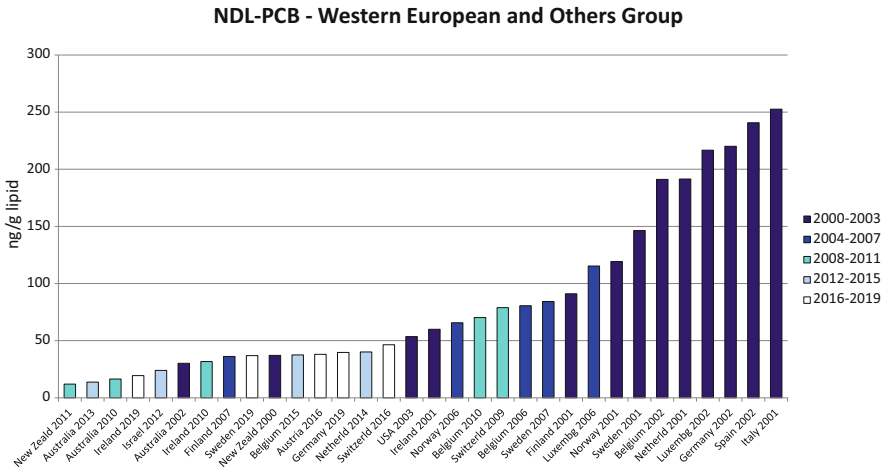

Fig. 24 Results of the 2000–2019 surveys for $\sum$ PCB_6 (ng/g lipid) in human milk samples from countries in the Western European and Others Group with indication of the period and year of sample submission

2000–2003 round, the lowest concentrations were found in Australia (2002), New Zealand (2000), and USA (2003) with a range between 30 and 55 ng/g $\sum PCB_6$, whereas the Western European countries had concentrations between 60 ng/g (Ireland, 2001) and 253 ng/g (Italy, 2001). A substantial decrease in the NDL-PCB concentrations was observed in samples collected between 2008 and 2011. The levels of non-dioxin-like PCB in New Zealand (2011) and Australia (2010) were 12 and 16 ng/g, respectively, whereas the levels in Western European countries ranged between 31 ng/g for Ireland (2010) and 79 ng/g for Switzerland (2009). This difference continued in the 2012–2015 round where Australia (2013) had 14 ng/g, and Israel (2012) had 24 ng/g and the two Western European countries had 38 ng/g (Belgium in 2015) and 40 ng/g (Netherlands in 2014). In comparison to previous rounds, in Germany, Ireland, Sweden, and Switzerland, the lowest concentrations were found in the 2016–2019 round.

Figure 25 illustrates the range of dioxin-like PCB concentrations. The maximum of 11.3 pg WHO-PCB-TEQ/g was found in 2001 in a sample from Italy.

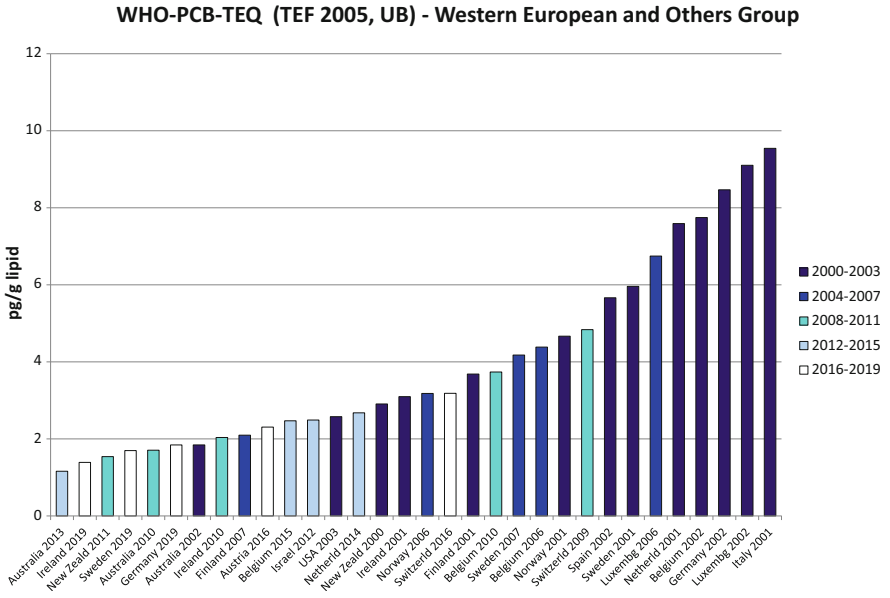

Fig. 25 Results of the 2000–2019 surveys for TEQ of dioxin-like PCB in human milk samples from countries in the Western European and Others Group with indication of the period and year of sample submission (pg WHO-PCB-TEQ [2005 UB]/g lipid)

6 Correlation Between Indicator PCB and Dioxin-like PCB and Between Dioxin-like PCB and PCDF

One question of interest is whether Indicator PCB (non-dioxin-like PCB expressed as ΣPCB_6) can be used to estimate TEQ of dioxin-like PCB (expressed as WHO_{2005}-PCB-TEQ) with PCB 126 being by far the most important congener contributing to toxic equivalency. As shown, European countries have clearly higher PCB concentrations in comparison with countries in the African, Latin American and Caribbean, and Asia-Pacific Groups; furthermore, the greatest variation in PCB concentrations is observed in European countries.

Figure 26 shows this correlation for countries of the Eastern European Group (EEG) and the Western European and Others Group (WEOG). It might be concluded that concentrations of non-dioxin-like PCB concentrations correlate with dioxin-like PCB increase, but with a wide range of variation.

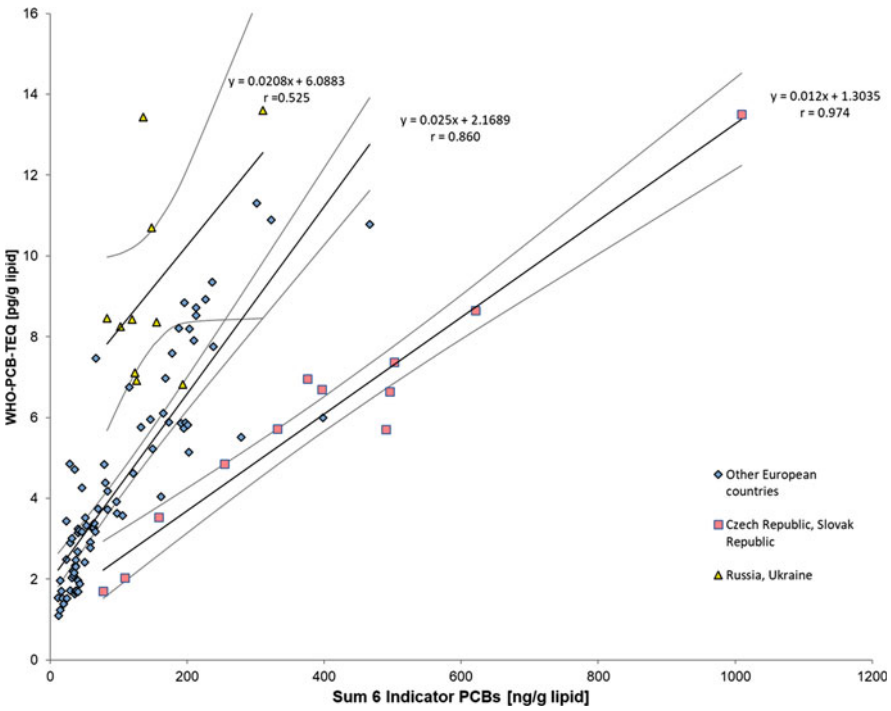

Fig. 26 Correlation between Indicator PCB as sum of the 6 non-dioxin-like PCB (ΣPCB_6) and dioxin-like PCB (WHO_{2005}-PCB-TEQ) in certain countries of the Eastern European Group and Western European and Others Group (linear regression and 95% confidence interval): Includes samples of the Czech Republic (3 in 2001, 1 in 2006, 1 in 2014, and 1 in 2019) and of the Slovak Republic (4 in 2001, 1 in 2006, and 1 in 2019); 10 samples submitted in 2001–2002 from Russia and the Ukraine

Samples from 2001 from the Czech and Slovak Republics had the highest non-dioxin-like PCB concentrations. PCB were produced in Slovakia during the period 1959–1984 in a total amount of about 21,500 tonnes causing elevated human exposure (Kocan et al. 1994, 2001, 2008; Petrik et al. 2001; Drobna et al. 2011). A national study on PCB in blood demonstrated the impact of this former PCB production on PCB blood levels of the population up to 70 km from the production site in the prevailing wind direction (Wimmerová et al. 2015). Assuming that these PCB products were largely used in the former Czechoslovakia and are the main PCB source in these countries, a differentiation is possible between the Czech and Slovak Republics (red squares in Fig. 26) and other European countries (blue diamonds in Fig. 26). Both for samples from the Czech and the Slovak Republics submitted between 2001 and 2019 ($r = 0.974$; $p < 0.001$) and for samples from other European countries ($r = 0.860$; $p < 0.001$), a positive linear correlation was found. However, the slope of the regression line for the samples from the Czech and the Slovak Republics is considerably smaller compared to the other European countries. Therefore, the concentrations of non-dioxin-like PCB in human milk from the Czech and Slovak Republics correlated with lower concentrations of dioxin-like PCB than in other European countries.

In contrast to the Czech and Slovak Republics, most samples collected in 2001–2002 in Russia and the Ukraine (marked as yellow triangles in Fig. 26) lie considerably above the trend line for other European countries. These data points are characterized by comparatively low concentrations of indicator PCB, but relatively high concentrations of dioxin-like PCB ($r = 0.525$; $p > 0.05$).

The congener-specific distributions of major non-dioxin-like and dioxin-like PCB showed a wide range of the TEQ concentrations in numerous commercial PCB formulations from Japan, Germany, USA, Russia, and Poland (Takasuga et al. 2006).

As conclusion, WHO-PCB-TEQ concentrations cannot be estimated exactly from non-dioxin-like PCB concentrations but depend on the correlation between dioxin-like and non-dioxin-like PCB in the various PCB products used in different countries.

Elevated levels of dioxin-like PCB contribute to elevated levels of PCDF as shown in Fig. 27. The correlation between TEQ resulting from dioxin-like PCB and TEQ resulting from PCDF (WHO_{2005}-PCDF-TEQ) for EEG and WEOG countries is observed in that PCDF-related TEQ concentrations increase along with dioxin-like PCB TEQ concentrations (positive correlation with $r = 0.835$, $p < 0.001$) indicating that a considerable share of the WHO-PCDF-TEQ burden stems from PCB. Here, the correlation of samples from Russia, the Ukraine, the Czech Republic, and Slovak Republic is comparable to samples from other European countries; therefore these countries are not separately identified in this figure.

With regard to the contribution of dioxin-like PCB to the total TEQ, attributed mostly by dioxin-like PCB 126, it is relevant to note that EFSA concluded that the current WHO_{2005}-TEF for the PCB 126 might be too high (Sect. 2.4). If this were

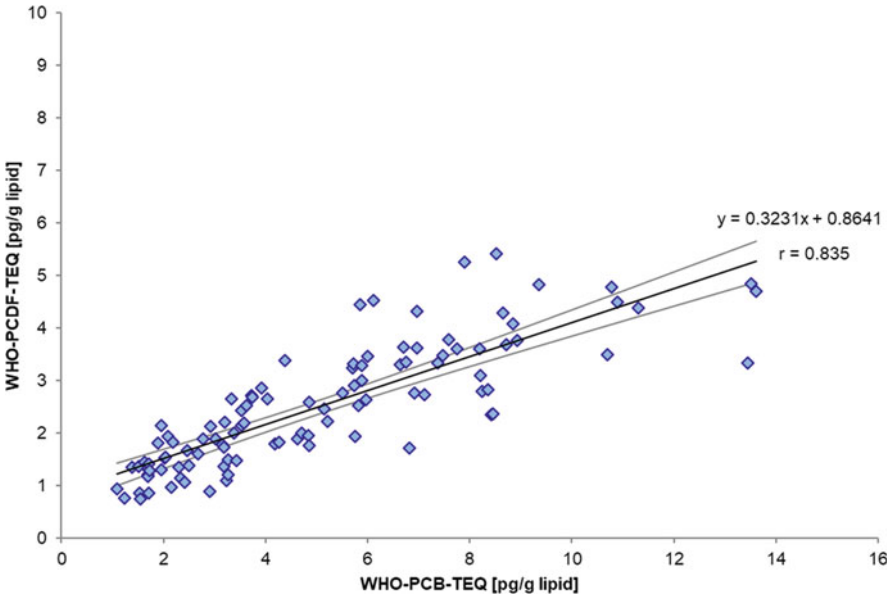

Fig. 27 Correlation between dioxin-like PCB (WHO_{2005}-PCB-TEQ]) and polychlorinated dibenzofurans (WHO_{2005}-PCDF-TEQ) in certain countries of the Eastern European Group and Western European and Others Group (linear regression and 95% confidence interval)

shown to be the case, the contribution of PCB 126 would overestimate the total TEQ and would especially affect European countries. As a result, a general discussion on TEF was proposed by EFSA (2018). Therefore, the TEF for PCB 126 as well as other congeners might be amended in the future.

Another aspect of this re-evaluation is a possible lowering of the Tolerable Weekly Intake (TWI) for the total TEQ for PCB, PCDD, and PCDF. In comparison to the current TWI of 14 pg total WHO_{2005}-TEQ/kg body weight/week (European Commission—Scientific Committee on Food 2001b), the new TWI of 2 pg total WHO_{2005}-TEQ/kg body weight/week proposed by EFSA (2018) is much lower. The requested review by WHO of the WHO_{2005}-TEF values is expected to also give an updated evaluation of the current Provisional Tolerably Monthly Intake (PTMI) of 70 pg total WHO_{2005}-TEQ/kg body weight/month as established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (WHO 2001). Lower tolerable intakes of PCDD/PCDF and PCB could raise public health concern as exposures could exceed these intake limits. Possible health risks for the breastfed infant from PCDD/PCDF and PCB as derived from the WHO- and UNEP-coordinated human milk studies are reviewed in Part IV (Van den Berg et al. 2023).

7 Summary

Between 2000 and 2019, the concentrations of specific congeners of polychlorinated biphenyls (PCB), polychlorinated dibenzo-*p*-dioxins (PCDD), and polychlorinated dibenzofurans (PCDF) were determined in a total of 232 pooled human milk samples submitted by 82 countries from all five United Nations regions. These composite samples were analysed over the years in human milk studies that were coordinated by the World Health Organization (WHO) and the United Nations Environment Programme (UNEP). They are considered to be representative of the national average of these analytes in human milk at the time of sampling. Some countries also submitted samples for specific population subgroups or regions.

Results presented here are based on United Nations regions and are not intended for ranking of countries. The highest concentrations of non-dioxin-like PCB were found in 24 European countries (median 118 ng/g (see footnote 1) for the sum of 6 Indicator PCB [PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, and PCB 180; ΣPCB_6], range 14.6–1009 ng/g). Results from 58 countries in other regional groups were generally lower (median 16.4 ng ΣPCB_6/g, range 0.90–96.5 ng/g). Total Toxic Equivalents (TEQ) concentrations of dioxin-like PCB and PCDD/PCDF varied between 1.29 and 49 pg WHO_{2005}-TEQ/g.[1,2] The median of concentrations found in the five UN Regional Groups was highest in countries of the Eastern European Group (12.0 pg WHO_{2005}-TEQ/g) and the Western European and Others Group (10.3 pg WHO_{2005}-TEQ/g). The widest variation in levels of submitted pooled samples was found in countries of the African Group, which ranged from 1.29 to 49 pg WHO_{2005}-TEQ/g. With median concentrations between 4 and 5 pg WHO_{2005}-TEQ/g and maximum levels between 10 and 12 pg WHO_{2005}-TEQ/g, the Pacific region in Asia and the Group of Latin American and Caribbean Countries were at the lower end of the distribution.

One of the objectives of these studies was to generate comparable and consistent monitoring data on the presence of these contaminants in order to identify trends in levels over time. The Guidance Document on the Global Monitoring Plans considers such data on the presence of POPs in the environment and in humans necessary for the evaluation of the effectiveness of the Stockholm Convention. For the sum of the 6 Indicator PCB, the highest country aggregated concentrations by far were found in the period 2000–2003 with a median 123 ng ΣPCB_6/g (range 16.4–502 ng/g) in 26 countries. A considerable downward trend was observed ending with the period 2016–2019 in which the median was 12.7 ng ΣPCB_6/g (range 0.9–109 ng/g) in 43 countries. The total TEQ concentrations for PCB and PCDD/PCDF gradually declined from an initial median of 12.4 pg WHO_{2005}-TEQ/g (range 4.42–23.0 pg WHO_{2005}-TEQ/g) for country aggregated data in the period 2000–2003 to a median

[1] All concentrations are expressed on a lipid basis.

[2] The total TEQ concentrations are expressed in Toxic Equivalents (TEQ) based on Toxic Equivalency Factors recommended by WHO in 2005 and calculated as upper bound values comprising the sum of the TEQ for dioxin-like PCB, PCDD, and PCDF.

of 3.88 pg WHO_{2005}-TEQ/g (range 1.29–11.6 pg WHO_{2005}-TEQ/g) in the period 2016–2019.

Acknowledgements This publication was developed in the framework of the projects titled "Implementation of the POPs Monitoring Plan in the Asian Region" and "Continuing regional Support for the POPs Global Monitoring Plan under the Stockholm Convention in the Africa, Pacific and Latin-American and Caribbean Region", funded by the Global Environment Facility and in close collaboration with and support of CVUA Freiburg.

The worldwide implementation of the Global Monitoring Plan for POPs, including that of the UNEP/WHO global human milk survey, is made possible thanks to the generous contributions to the Stockholm Convention Voluntary Trust Fund by the Governments of Japan, Norway, and Sweden and through the European Union's Global Public Goods and Challenges Programme (GPGC). Further, the substantial contributions made by the Global Environment Facility to support POPs monitoring activities in regions implemented by UNEP, in close collaboration with WHO, particularly for the global human milk surveys, is greatly appreciated.

The authors express their gratitude to the National Coordinators of the WHO- and UNEP-coordinated exposure surveys for their excellent work to collect the human milk samples and to prepare and send the pooled samples to the Reference Laboratory, which included great efforts to plan and implement the national studies with the assistance of the health, environment, laboratory, and administrative staff. The continuous exchange of information between the National Coordinators and WHO, UNEP and the Reference Laboratory was an important aspect for the successful organization of these studies on a global level.

Hae Jung Yoon, Seongsoo Park, and Philippe Verger (Department of Food Safety and Zoonoses) are acknowledged for their coordinating support during their time at WHO, and Lawrence Grant (WHO) for the statistical analysis of the sampling protocols.

The authors thank Katarina Magulova and Ana Witt (Secretariat of the Basel, Rotterdam and Stockholm Conventions) and Jacqueline Alvarez, Haosong Jiao, and Gamini Manuweera (United Nations Environment Programme, Economy Division, Chemicals and Health Branch) for their support and contributions to these surveys, furthermore Heidelore Fiedler for the conception and implementation of the GMP projects at her time at United Nations Environment Programme, Economy Division, Chemicals and Health Branch.

The authors also thank the team at CVUA Freiburg for their performance of the PCDD/PCDF and PCB analyses, in particular Renate Tritschler for her reliable analysis of samples and Helmut Winterhalter for his careful operation of the GC/HRMS systems since the inception of the dioxin laboratory in 1991. Furthermore, the authors thank Indra Peters and Lena Zeug for the analysis and Lukas Jänker, Stefan Leswal, and Jutta Schächtele for GC/HRMS measurements. Nicole Bitomsky, Katharina Djuchin, Annika Maixner, Karin Malisch, Sandra Schill, Biljana Trajkovska, Kerstin Wahl, and Christian Wambold are acknowledged for their scientific support and cooperation with the national coordinators.

Disclaimer The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the decisions, policy, or views of the World Health Organization and the United Nations Environment Programme.

Appendix

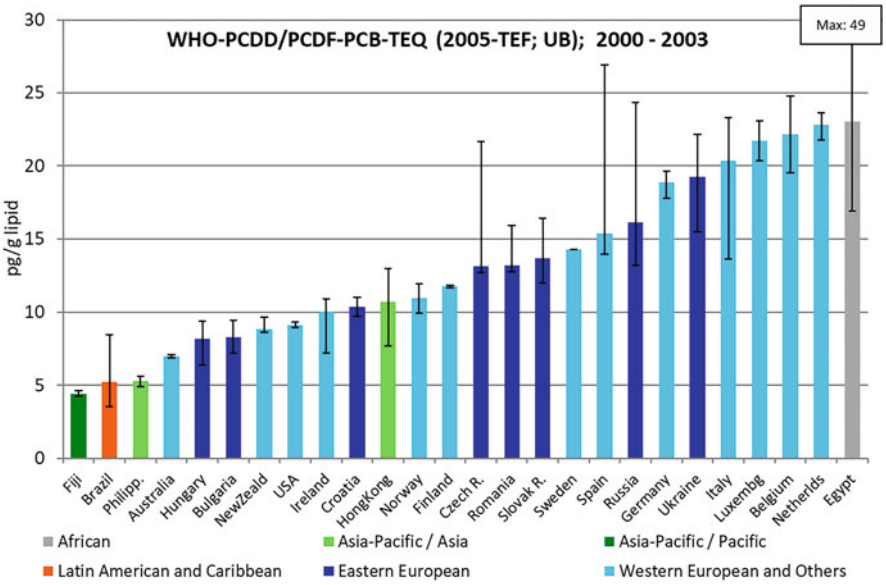

Fig. 28 Country results of the 2000–2003 round for total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) (pg/g lipid; median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

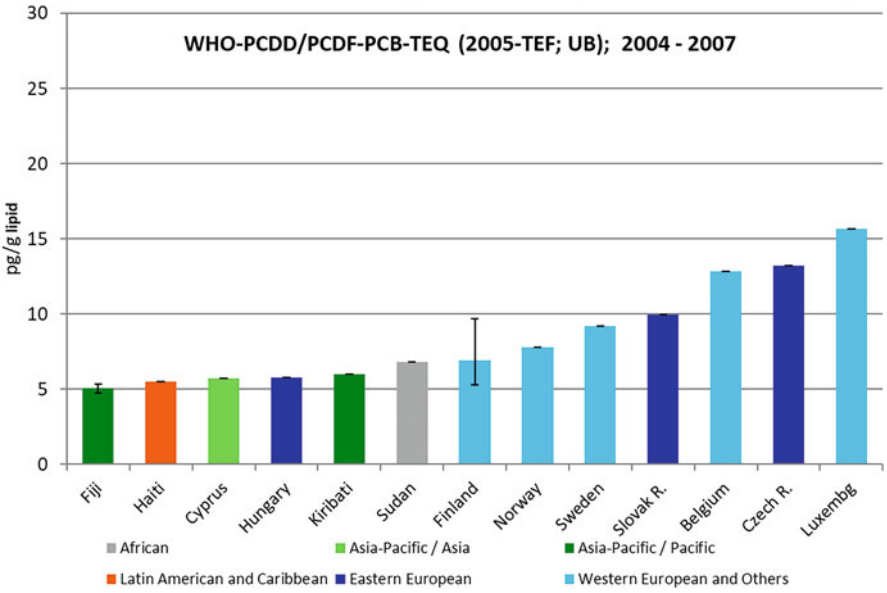

Fig. 29 Country results of the 2004–2007 round for total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) (pg/g lipid; median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

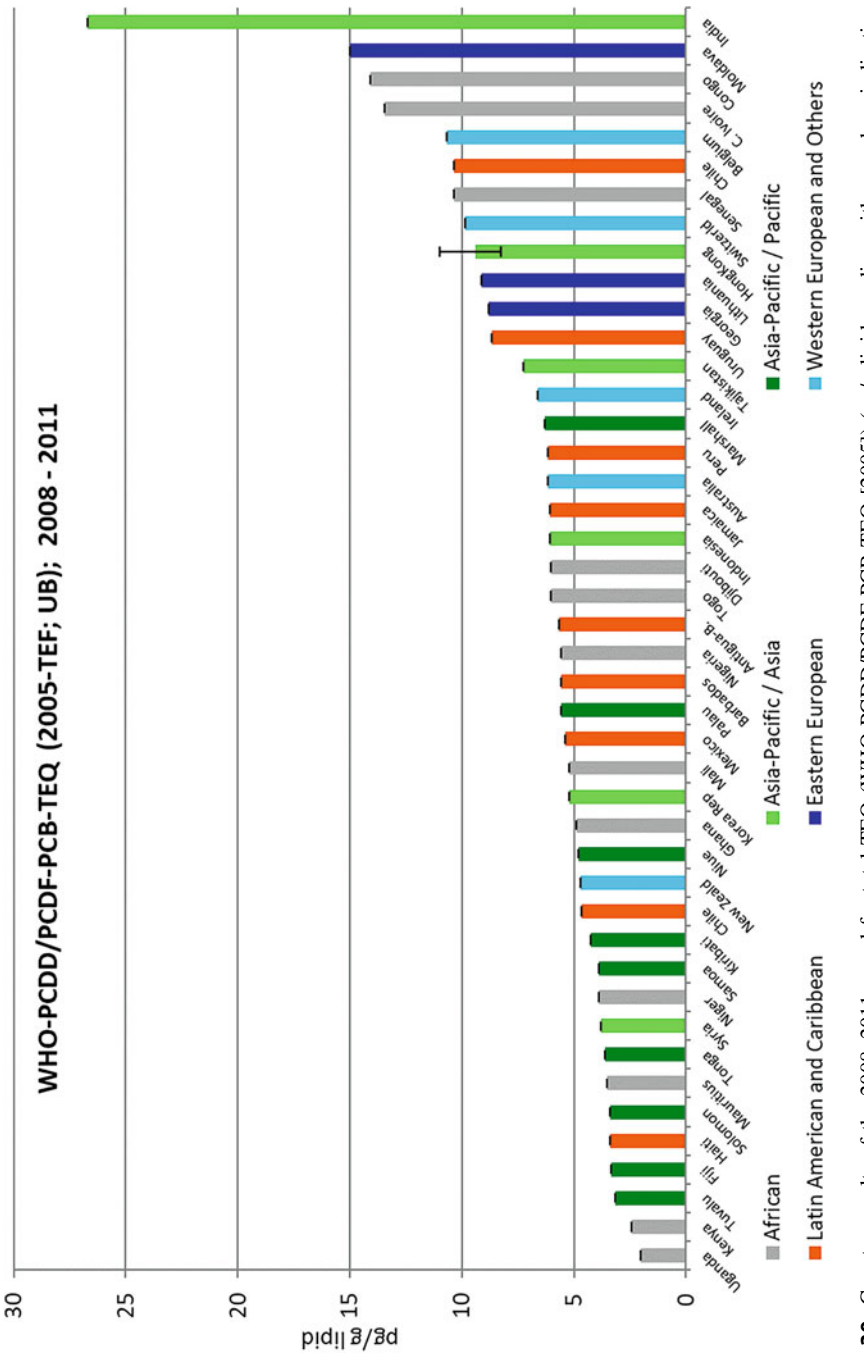

Fig. 30 Country results of the 2008–2011 round for total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) (pg/g lipid; median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

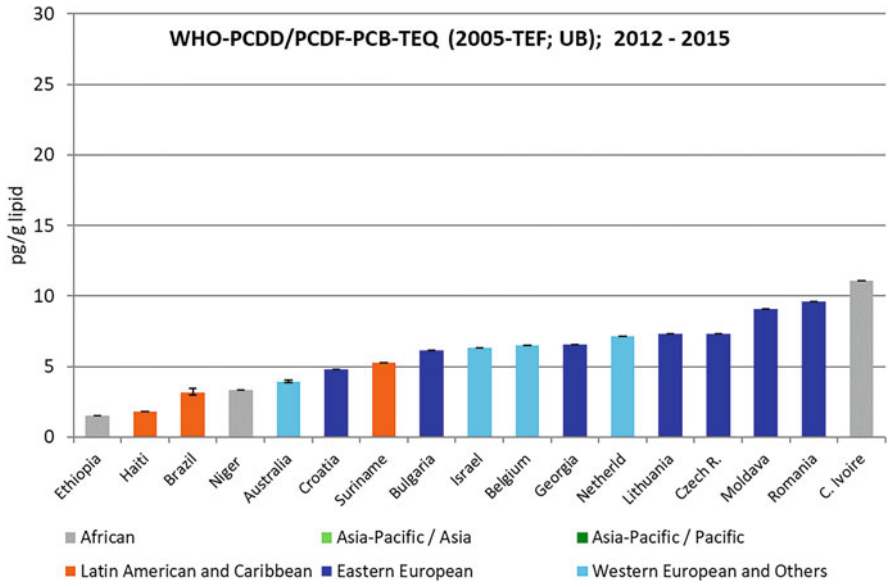

Fig. 31 Country results of the 2012–2015 round for total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) (pg/g lipid; median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

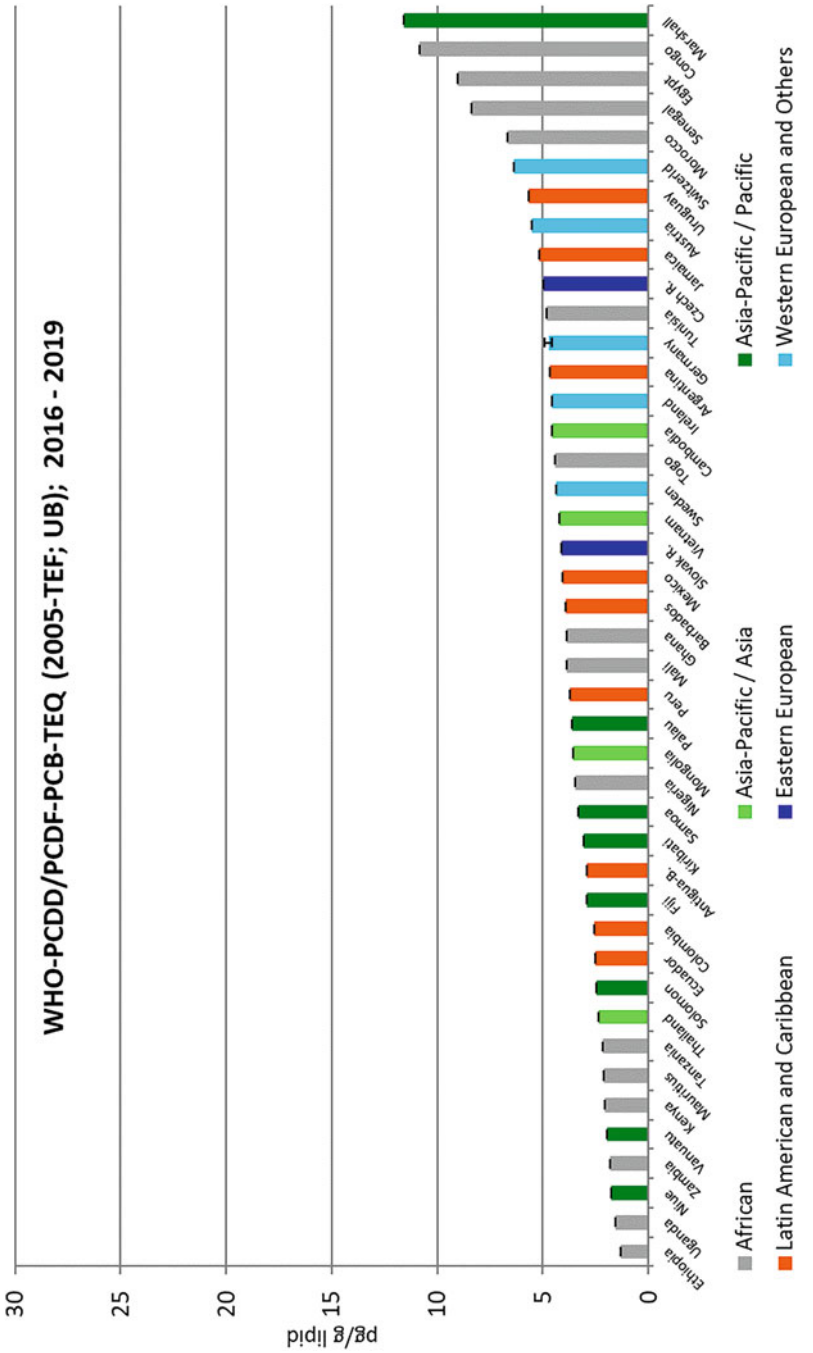

Fig. 32 Country results of the 2016–2019 round for total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) (pg/g lipid; median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

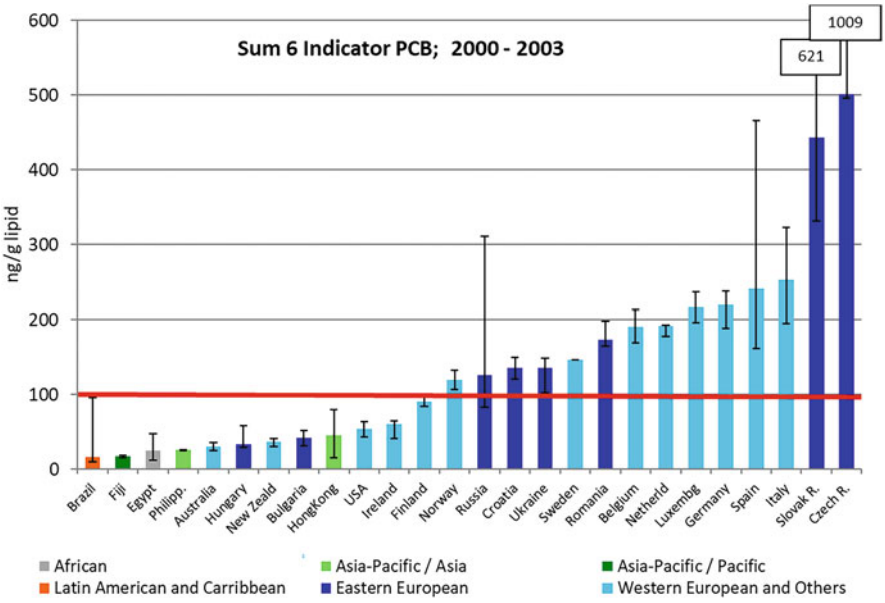

Fig. 33 Country results of the 2000–2003 round for ΣPCB_6 (ng/g lipid) (median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

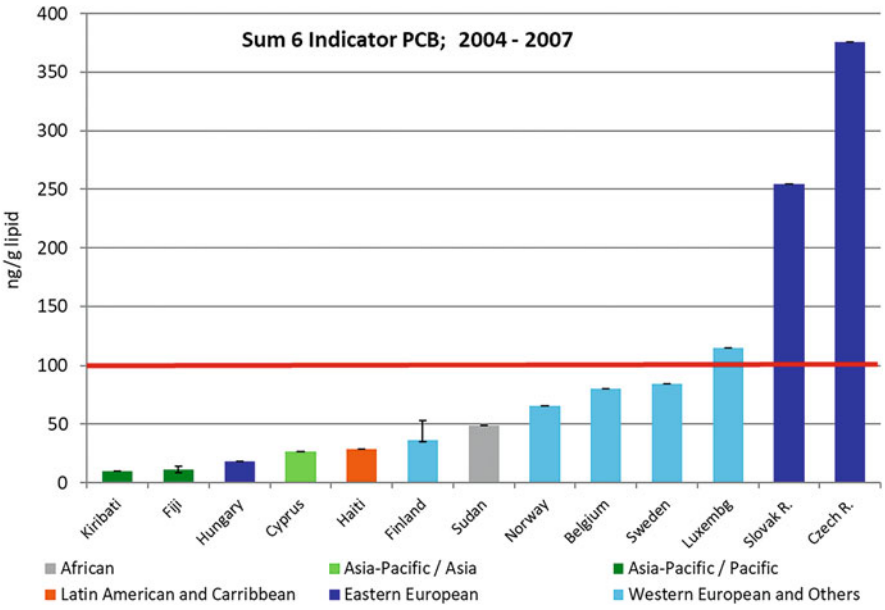

Fig. 34 Country results of the 2004–2007 round for ΣPCB_6 (ng/g lipid) (median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

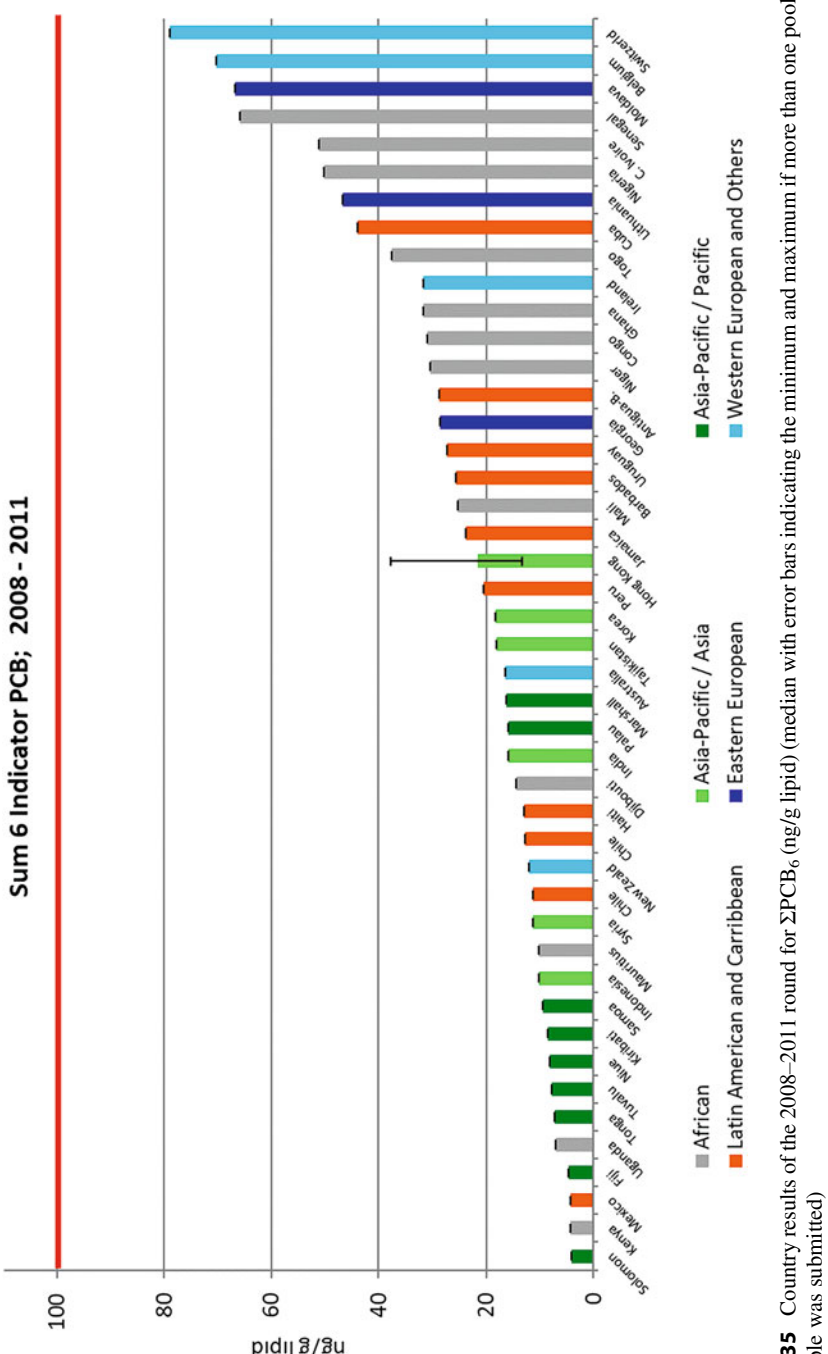

Fig. 35 Country results of the 2008–2011 round for ΣPCB_6 (ng/g lipid) (median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

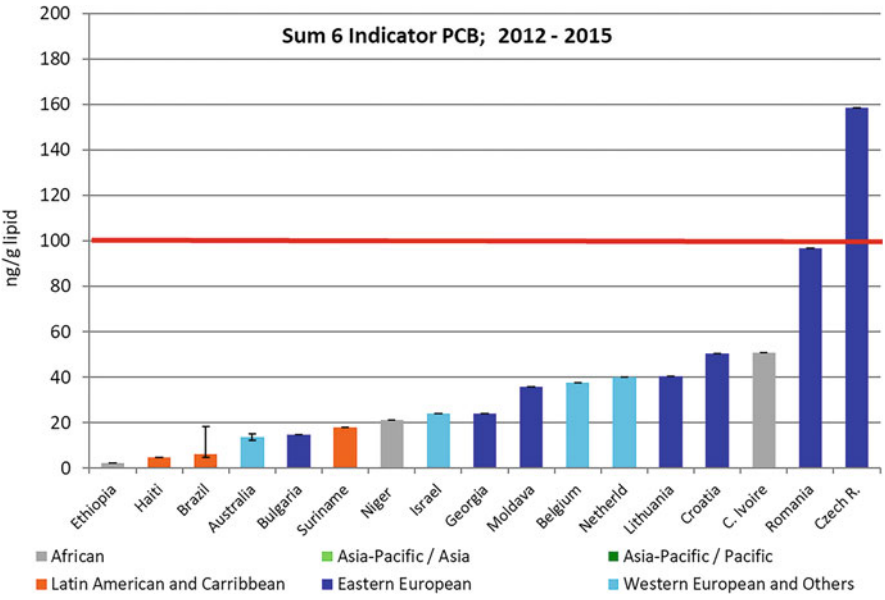

Fig. 36 Country results of the 2012–2015 round for ΣPCB_6 (ng/g lipid) (median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

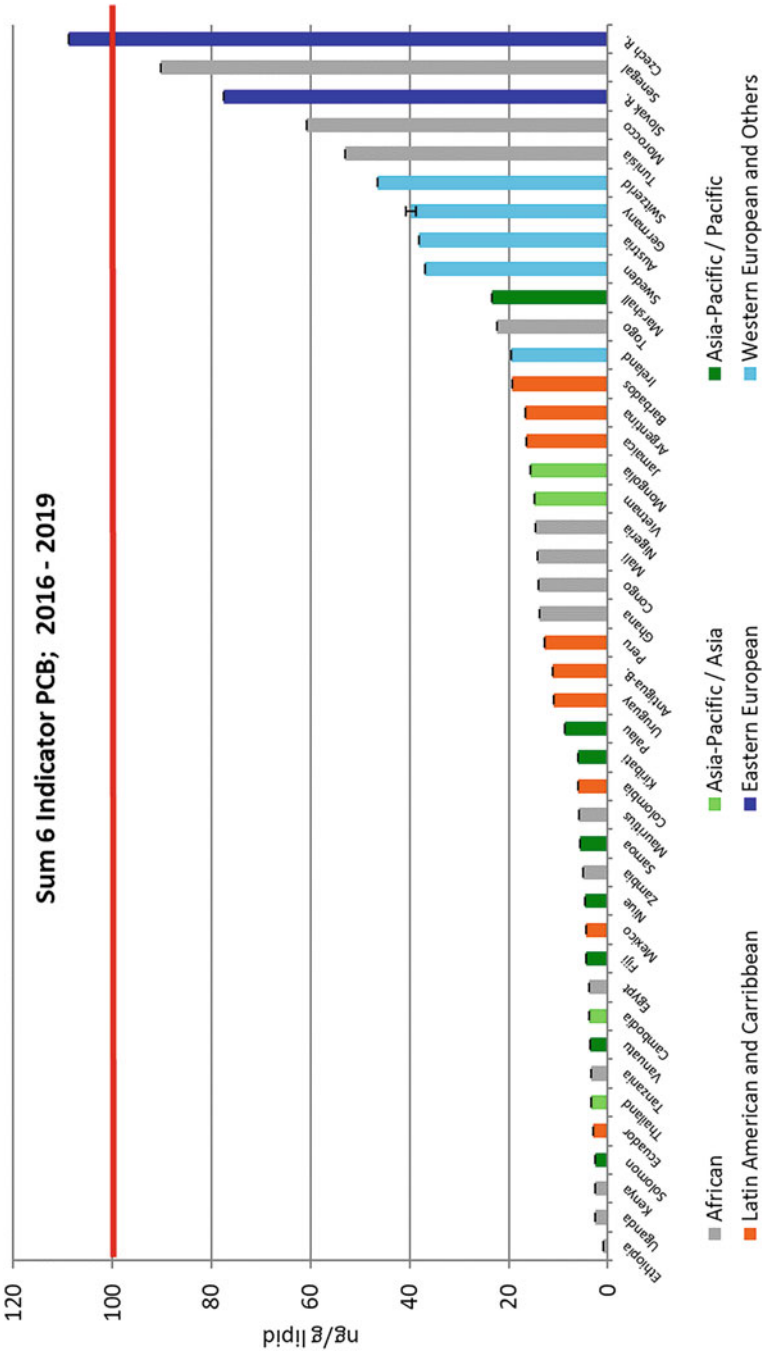

Fig. 37 Country results of the 2016–2019 round for ΣPCB_6 (ng/g lipid) (median with error bars indicating the minimum and maximum if more than one pooled sample was submitted)

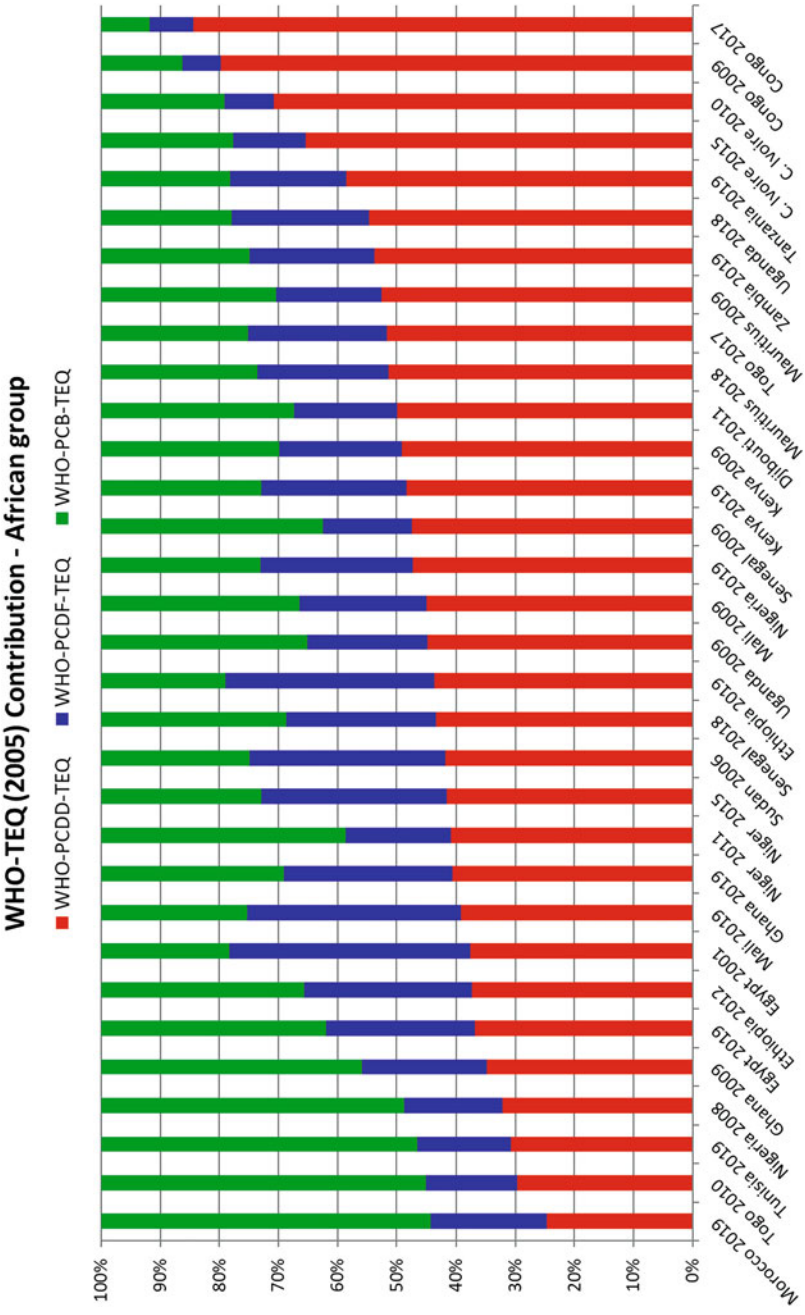

Fig. 38 Relative contribution (%) of toxic equivalents of PCDD (WHO-PCDD-TEQ [2005]), PCDF (WHO-PCDF-TEQ [2005]), and dioxin-like PCB (WHO-PCB-TEQ [2005]) to total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) in human milk samples from countries of the African Group and year of submission

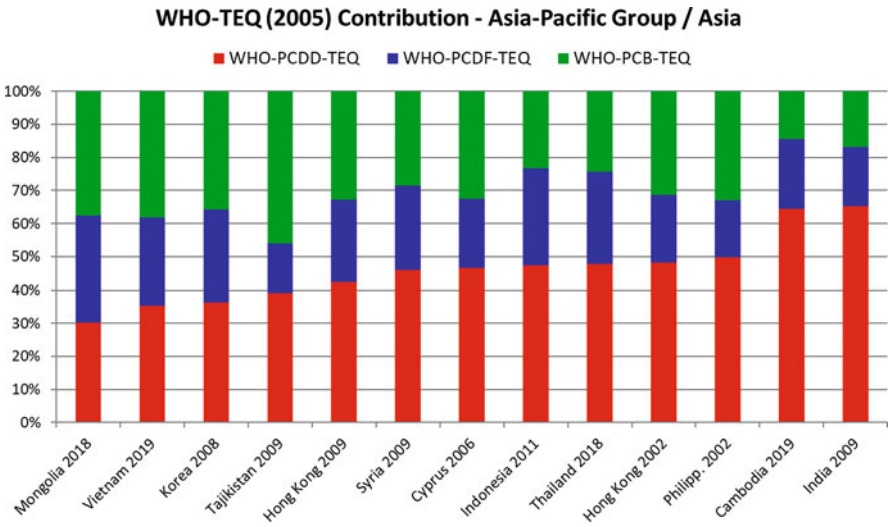

Fig. 39 Relative contribution (%) of toxic equivalents of PCDD (WHO-PCDD-TEQ [2005]), PCDF (WHO-PCDF-TEQ [2005]), and dioxin-like PCB (WHO-PCB-TEQ [2005]) to total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) in human milk from countries from the Asian Subregion of the Asia-Pacific Group and year of submission

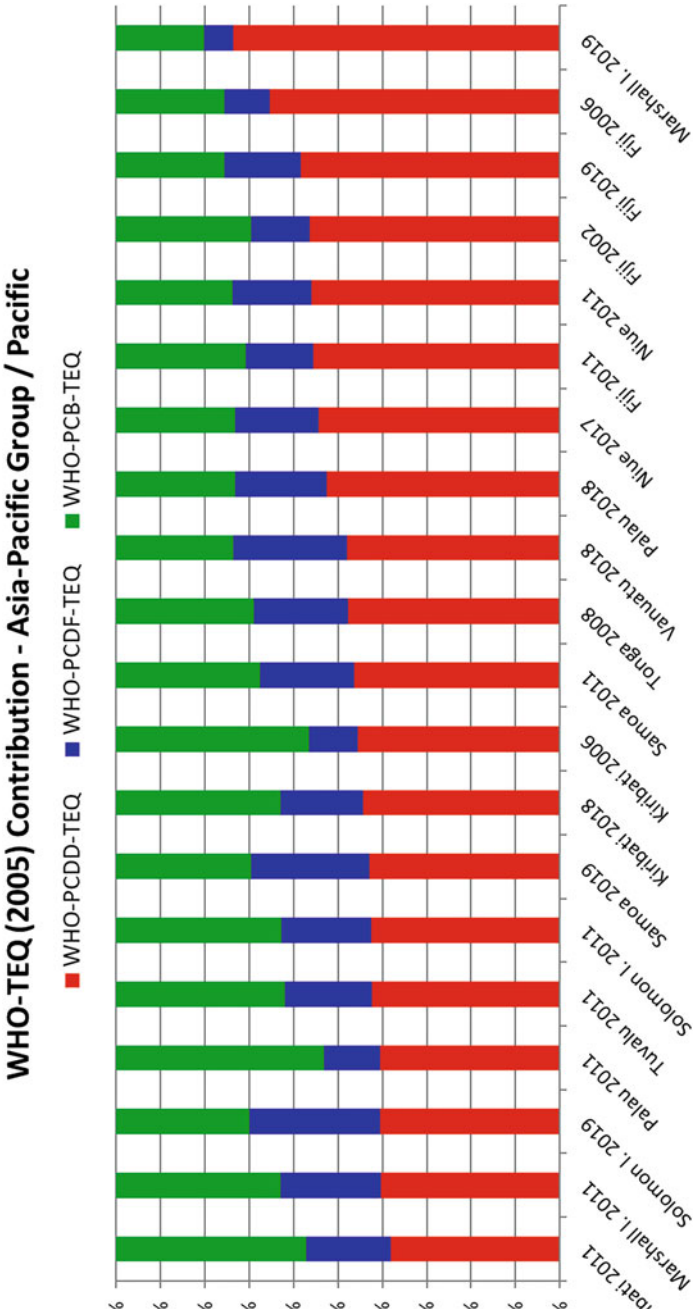

Fig. 40 Relative contribution (%) of toxic equivalents of PCDD (WHO-PCDD-TEQ [2005]), PCDF (WHO-PCDF-TEQ [2005]), and dioxin-like PCB (WHO-PCB-TEQ [2005]) to total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) in human milk from countries from the Pacific Islands Subregion of the Asia-Pacific Group and year of submission

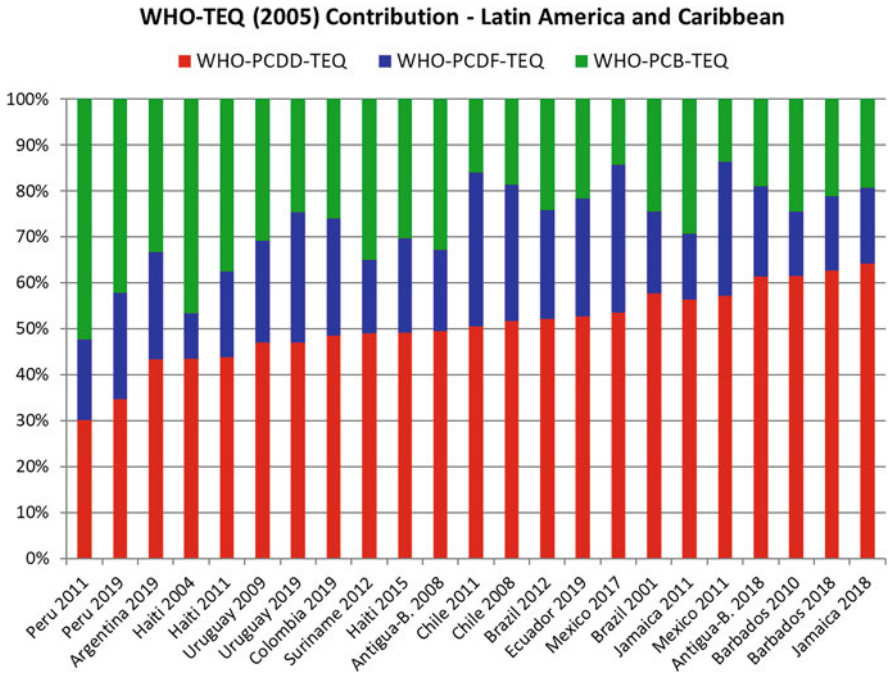

Fig. 41 Relative contribution (%) of toxic equivalents of PCDD (WHO-PCDD-TEQ [2005]), PCDF (WHO-PCDF-TEQ [2005]), and dioxin-like PCB (WHO-PCB-TEQ [2005]) to total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) in human milk from countries from Latin America and the Caribbean and year of submission

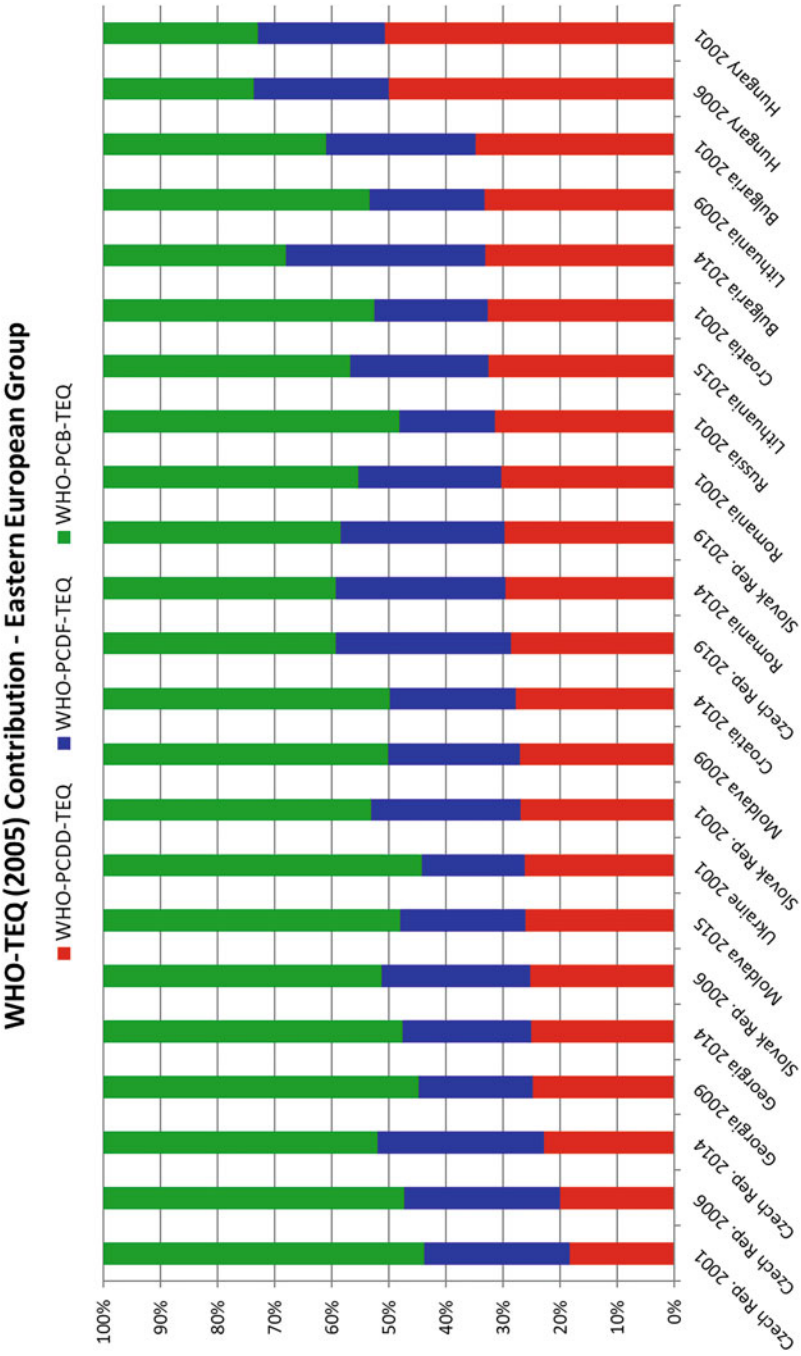

Fig. 42 Relative contribution (%) of toxic equivalents of PCDD (WHO-PCDD-TEQ [2005]), PCDF (WHO-PCDF-TEQ [2005]), and dioxin-like PCB (WHO-PCB-TEQ [2005]) to total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) in human milk from countries of the Eastern European Group and year of submission

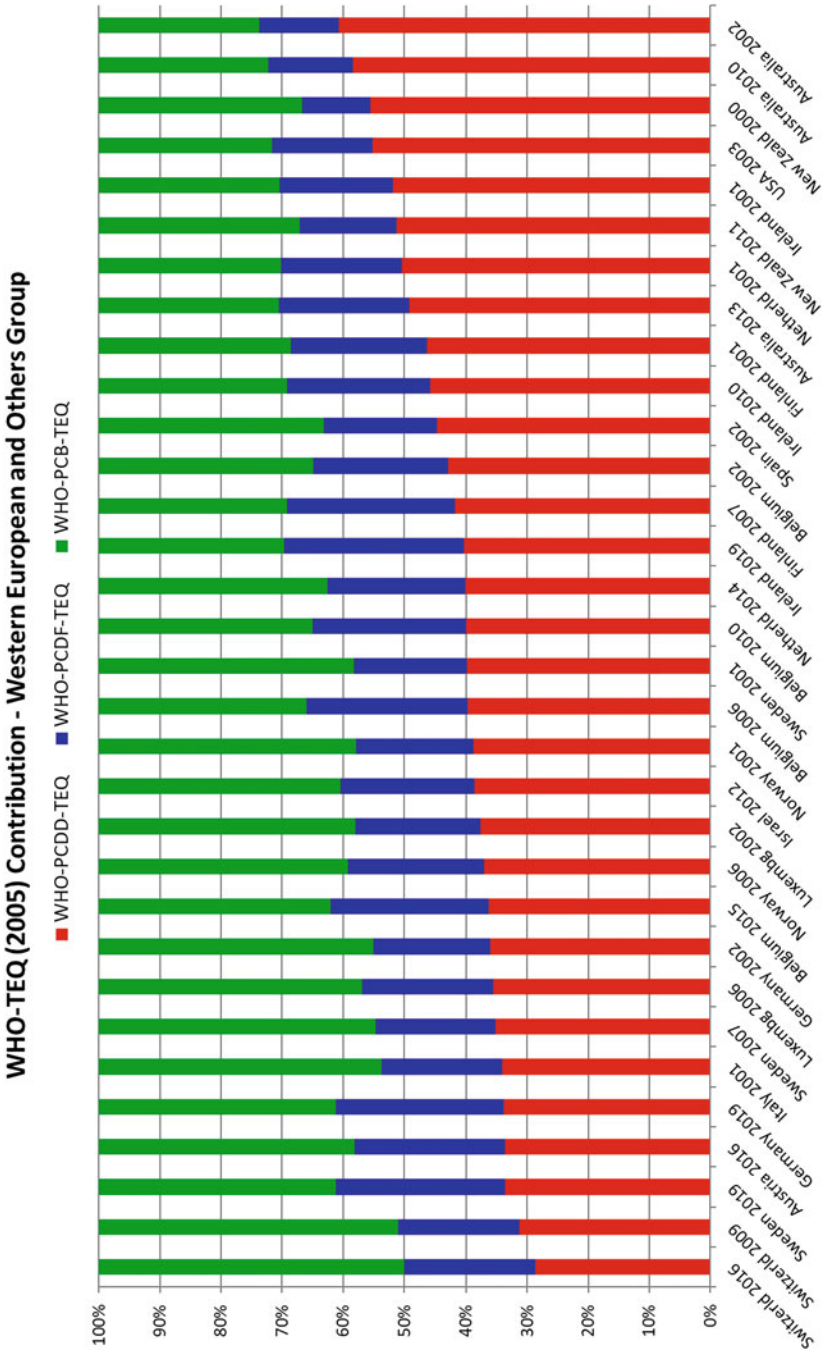

Fig. 43 Relative contribution (%) of toxic equivalents of PCDD (WHO-PCDD-TEQ [2005]), PCDF (WHO-PCDF-TEQ [2005]), and dioxin-like PCB (WHO-PCB-TEQ [2005]) to total TEQ (WHO-PCDD/PCDF-PCB-TEQ [2005]) in human milk from countries from the Western European and Others Group and year of submission

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