Dioxin-like compounds in human milk – A time-trend analysis

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1 Introduction

The Stockholm Convention on Persistent Organic Pollutants (POPs) was adopted on 22 May 2001 and entered into force on 17 May 2004 with twelve POPs listed in either Annexes A, B, or C (UNEP, 2001). Since 2007, a global monitoring plan (GMP) of POPs was established to provide comparable monitoring information on the presence of POPs listed in Annexes A, B, and C of the Convention and to follow changes over time (UNEP, 2007). A regional approach based on the five regions of the United Nations was proposed and implemented (UN regions). Human milk was chosen as the preferred matrix to assess human exposure and the biomonitoring component of the GMP has been put in place through the joint implementation by the United Nations Environment Programme (UNEP) and the World Health Organization (WHO) (UNEP/POPS/COP.6/28). The results of the first phase of the human milk survey and an analysis of the human health implications of such concentrations have been published in a joint report by UNEP and WHO (UNEP, 2013) and in the scientific literature (van den Berg, Kypke, Kotz, Tritscher, Lee, Magulova, Fiedler and Malisch, 2017).
Polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans (PCDD/PCDF), and polychlorinated biphenyls (PCB) are three of the initial POPs listed in the Convention and have been monitored by WHO and others since the mid-1980s. Here we assess data from various sources for the dioxin-like POPs (dl-POPs) in national pools of human milk over time and across geographies.

Materials and Methods

Quantitative results from measurements of PCDD PDF, and dl-PCB have been retrieved from the following sources:

- Data from 1980s and 1990s: Two rounds of WHO surveys (Rounds 1 and 2) published as (Yrjanheikki, 1989) and WHO European Centre for Human Health (1996). The reports were screened for results of the 29 dl-POPs; datasets were manually extracted and for each country weighted by the number of samples to generate values for one "national pool" (UNEP, Fiedler and Baruffol, 2014).
- Data generated in support of the Stockholm Convention: Results from WHO surveys (2000-2008) contained in reporting to UNEP (UNEP, Malisch and Fiedler, 2012) and projects coordinated by UNEP (2008-2014) (Fiedler, Abad, van Bavel, de Boer, Bogdal and Malisch, 2013; UNEP, 2013; van den Berg, Kypke, Kotz, Tritscher, Lee, Magulova, Fiedler and Malisch, 2017).
- Data from the UNEP/GMP2 projects (Fiedler and UNEP, 2022).
- Data from China: National Institute of Nutrition and Food Safety (today; Chinese Food and Safety Authority), Beijing, P.R. China (Li, Zhang, Wu, Liu, Zhou, Wen, Liu, Zhao and Li, 2009).

All results were transferred and maintained in MsExcel. Since the time covers more than 30 years, five-year periods have been grouped together, indicated by the first and the last year of the period. In summary, 181 national pools were available for assessment with the number of samples per period and UN region as shown in Table 1. For the first two periods, no data were available for Africa and GRULAC.

Table 1: Availability of national pools according to 5-year period, UN region (n=181) CEE=Central and Eastern European countries; GRULAC=Group of Latin America and the Caribbean; WEOG=Western Europe and other groups

Region	1985-1989	1990-1994	2000-2004	2005-2009	2010-2014	2015-2019	Overall
# of pools	15	15	27	33	41	50	181
Regions							
Africa			1	9	5	17	32 (17.7%)
Asia	2		3	8	13	12	38 (21.0%)
CEE	2	8	8	6	5	4	33 (18.2%)
GRULAC			2	3	11	10	26 (14.4%)
WEOG	11	7	13	7	7	7	52 (28.7%)

The data assessed here were from donor mothers that fulfilled the criteria of an initial WHO protocol and an updated guidance document by UNEP (UNEP, 2017; WHO, 2007). Briefly, *primiparae* were selected on national basis for donation of 50 mL of breast milk. 25 mL were compiled into one national pool and analyzed for POPs. It was recommended that one national pool be prepared for each 50 million inhabitants. The identity of the donor mother was not disclosed to UNEP, WHO nor the analytical laboratories.
For dl-POPs, all values of the 29 compounds were calculated as toxic equivalents (TEQ) using the 2005 WHO TEF scheme (van den Berg, Birnbaum, Denison, De Vito, Farland, Feeley, Fiedler, Hakansson, Hanberg, Haws, Rose, Safe, Schrenk, Tohyama, Tritscher, Tuomisto, Tysklind, Walker and Peterson, 2006). According to the listing in the Annex C of the Stockholm Convention, Seven PCDD were recorded as TEQ_PCDD, 10 2,3,7,8-substituted PCDF as TEQ_PCDF, and 12 dl-PCB as TEQ_PCB. All concentrations are given in pg TEQ/g lipid.
Mathematical operations, time trends and visualization were performed using R packages (R version 4.0.3) with R Studio. Grouping of samples was done according to UN regions with Africa, Asia, Central and Eastern Europe (CEE), Group of Latin American and Caribbean counties (GRULAC) and Western European and other groups (WEOG). Country names are shown by their ISO-3 alpha codes.

Results

The descriptive statistics are shown in Table 2. For the 1980s, there was no information available for dl-PCB. The first two periods also had the smallest number of national pools, 15 each (Table 1. On scale, the mean and median values across all samples showed that the values for TEQ_PCDD were greater than for TEQ_PCB and TEQ_PCDF. For all three dl-POPs, the highest values were observed in the earliest samples and overall decreases in concentrations were found. For most regions, especially for PCDD and PCDF, it can be seen that older samples have higher median values than the more recent pools. It is also noticed that the samples from the 1980s and 1990s have wider ranges.

Table 2: Descriptive statistics for three dl-POPs according to period (concentrations in pg TEQ/g lipid)

Period (# samples)	1985-1989 (N=15)	1990-1994 (N=15)	2000-2004 (N=27)	2005-2009 (N=33)	2010-2014 (N=41)	2015-2019 (N=50)	Overall (N=181)
TEQ_PCDD							
Mean (SD)	16.0 (7.58)	8.61 (3.97)	5.18 (2.37)	3.62 (3.09)	2.45 (1.36)	2.08 (1.74)	4.60 (4.97)
Median [Min, Max]	14.7 [6.79, 33.2]	7.08 [2.34, 16.1]	4.94 [2.40, 12.0]	2.84 [0.90, 17.4]	2.23 [0.58, 9.50]	1.57 [0.57, 9.16]	2.75 [0.57, 33.2]
TEQ_PCDF							
Mean (SD)	6.45 (3.07)	4.66 (1.94)	2.72 (1.84)	1.75 (1.07)	1.15 (0.579)	1.00 (0.478)	2.18 (2.14)
Median [Min, Max]	5.71 [2.03, 13.5]	4.18 [1.69, 8.69]	2.60 [0.54, 9.48]	1.55 [0.41, 4.74]	0.87 [0.45, 2.86]	0.927 [0.33, 2.26]	1.38 [0.33, 13.5]
TEQ_PCB							
Mean (SD)	NA	7.17 (4.46)	5.06 (2.76)	3.01 (1.82)	1.87 (0.917)	1.42 (1.00)	2.97 (2.72)
Median [Min, Max]	NA	6.64 [1.29, 16.2]	4.91 [1.34, 10.6]	2.61 [0.703, 7.47]	1.66 [0.530, 3.92]	1.05 [0.271, 4.72]	1.96 [0.27, 16.2]
Missing	15 (100%)	0 (0%)	0 (0%)	0 (0%)	1 (2.4%)	0 (0%)	16 (8.8%)

The global (linear) trends for PCDD, PCDF, and dl-PCB by year is shown in Figure 1; note that the standard deviations were also decreasing with increasing years.

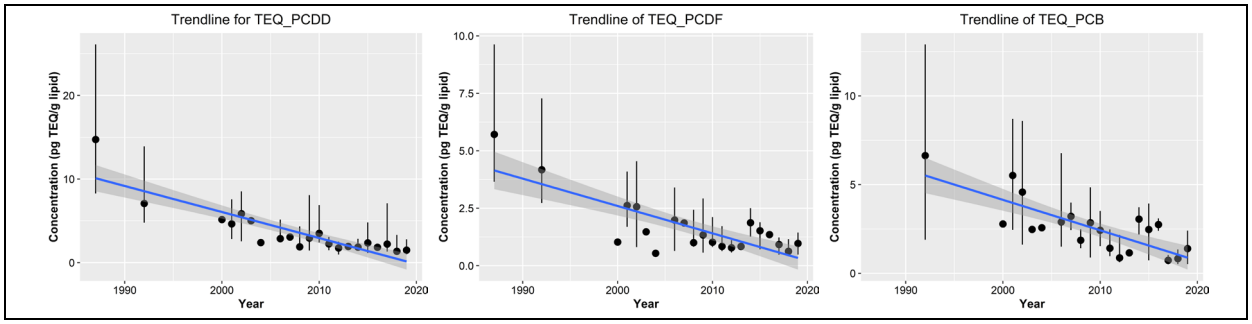

Figure 1: Global trends for PCDD, PCDF and dl-PCB as TEQs with linear trendline

The following figures show the time trends for PCDD (Figure 2), PCDF (Figure 3), and dl-PCB (Figure 4) in each region. As already shown in Table 1, data for Africa and GRULAC became available only after the year 2000. From Figure 4 it is evident that data for dl-PCB were not available for the first round of the WHO surveys, *i.e.,* 1987 but trendlines for PCDD and PCDF go back to the 1980s for Asia, CEE, and WEOG (Figure 2, Figure 3). From Figure 3 it can be seen that the linear trendline is not adequate for PCDF in Africa. For GRULAC and PCDF, no decline could be identified

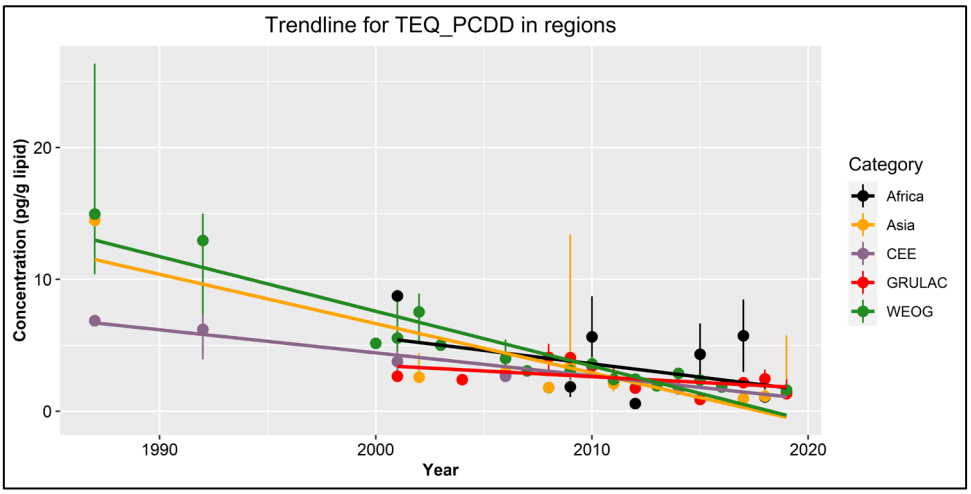

Figure 2: Time trends of PCDD for each region (concentrations in pg TEQ/g lipid)

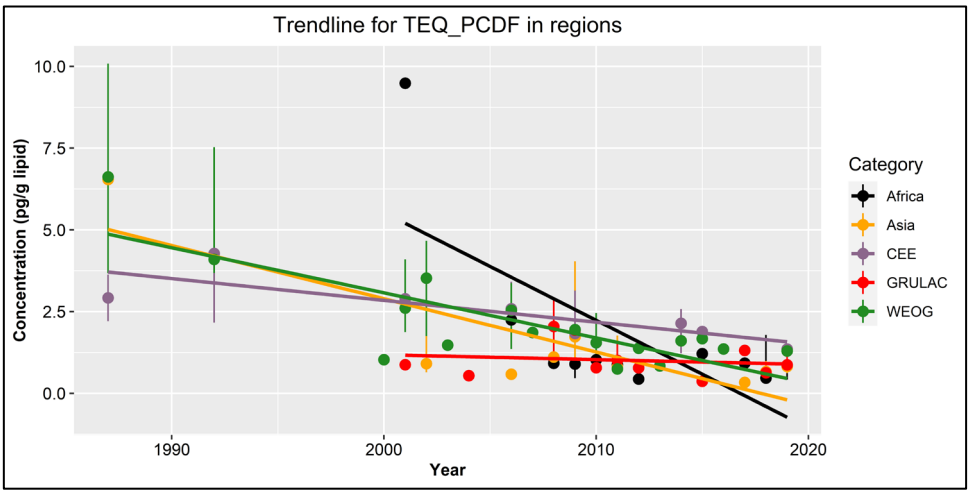

Figure 3: Time trends of PCDF for each region (concentrations in pg TEQ/g lipid)

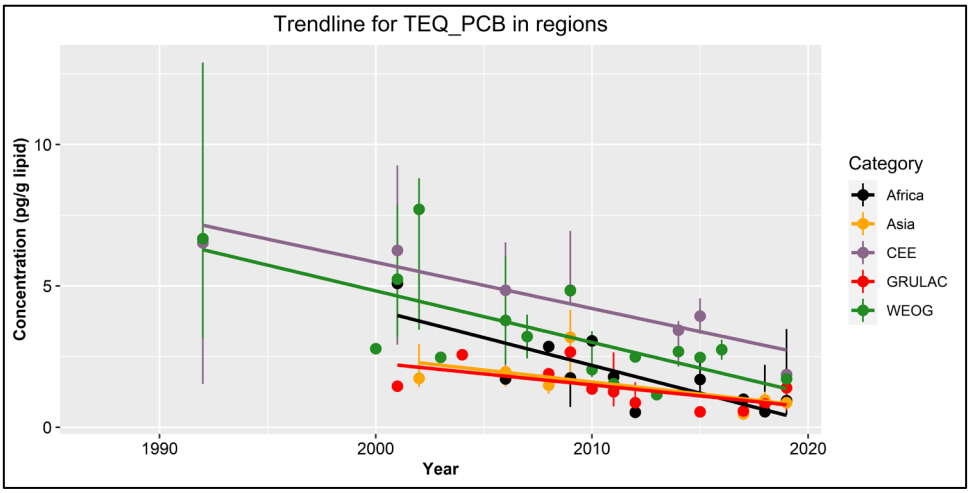

Figure 4: Time trend for dl-PCB for each region (concentrations in pg TEQ/g lipid)

Discussion

The assessment of dl-POPs in the national pools of human milk samples from available data aimed at identifying worldwide quantitative differences of human milk contamination to provide a baseline for countries for which such information is not available or that had initiated biomonitoring at a later stage or participated only once. This assessment of the human milk pools representing all UN regions and a timespan of 35 years for dioxin-like POPs showed that PCDD, PCDF, and dl-PCB were highly correlated with respect to TEQs (not shown here) and have declining trend overall. In the samples, the TEQs from PCDD dominated over the TEQ from PCDF and dl-PCB. Regional differences were seen with countries from WEOG having the highest TEQs for PCDD and PCDF (as mean and median value but also highest amounts). PCB (as TEQ) dominated in the CEE, followed by WEOG. The developing country regions – Africa, Asia, and GRULAC – had very similar median values for TEQ_PCDD, TEQ_PCDF, and TEQ_PCB.

Conclusions

Biomonitoring of human milk using national pools rather than individual samples is a powerful tool for trend analysis and spatial distribution. The method has shown to be efficient but so far, regular participation at defined intervals is not yet achieved. The downward slopes in Africa, Asia, and GRULAC for the three dl-POPs listed in the Stockholm Convention were flatter than for WEOG and CEE. More sophisticated assessment may show increasing trends especially for Africa and PCDF. For all three dl-POPs and all regions, the concentrations level off for the most recent years (period) except for dl-PCB in CEE and WEOG.

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