EVALUATION OF WHO-COORDINATED EXPOSURE STUDIES ON LEVELS OF PERSISTENT ORGANIC POLLUTANTS (POPs) IN HUMAN MILK WITH REGARD TO THE GLOBAL MONITORING PLAN

Rainer Malisch [1], Karin Kypke [1], FX Rolaf van Leeuwen [2], Gerald Moy [3] and Seongsoo Park [3]

[1] State Institute for Chemical and Veterinary Analysis of Food, Bissierstrasse 5, D-79114 Freiburg, Germany (WHO Reference Laboratory of the 3rd and 4th round of the WHO studies)
[2] National Institute of Public Health and the Environment, P.O.Box 1, NL-3720 BA Bilthoven, The Netherlands (Coordinator of the 3rd round on behalf of WHO)
[3] WHO GEMS / Food Programme, Food Safety, Zoonoses and Foodborne Diseases Department, WHO, 1211 Geneva 27, Switzerland (Coordinators of the 4th round on behalf of WHO)

Introduction

Since the mid-eighties, the World Health Organization (WHO) has coordinated a comprehensive programme on possible health risks of polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). This programme was carried out in collaboration with other international organisations and national institutions, and concentrated particularly on the health risk of infants, due to exposure through contaminated human milk, and aiming to prevent and control environmental exposure to these chemicals. Because human milk contains many lipid soluble compounds that are also present in mother's adipose tissue, it can also be assumed that the levels of PCDDs, PCDFs and PCBs in human milk are representative for those in plasma, serum lipid and adipose tissue. Therefore levels of these contaminants in human milk do reflect the body burden and can thus be used as an indicator for the overall exposure of the general population. The collection of human milk is a non-invasive sampling method, offering several advantages over the collection of other biological samples to assess overall human exposure. In addition, the high content of fat makes the extraction method easier and the precision of the measurements higher.

WHO has carried out a series of international exposure studies on levels of these contaminants in human milk. The first WHO-coordinated exposure study took place in 1987-1988 (1), the second round in 1992-1993 (2), the third round in 2000 - 2003 (3), and the fourth round has been initiated in 2005. In order to collect data on more countries, the fourth study was organised in collaboration with the WHO Global Environment Monitoring System / Food Contamination Monitoring and Assessment (GEMS / Food) Programme.

The third round of exposure studies had the following aims: a) produce reliable and comparable data on levels of PCBs, PCDDs and PCDFs in human milk for further improvement of the health risk assessment in infants; b) determine time trends in exposure levels in the countries and areas already studied in the first and second round of the study in the period 1987-88 and 1992-1993, respectively; c) provide a better overview of exposure levels in various countries and geographical areas; d) identify highly exposed local populations in relation to their daily intake for guidance on risk management actions, including epidemiological follow-up studies; e) promote, if necessary, additional national studies to be closely linked with the present study through the use of the same protocol.

The Stockholm Convention on Persistent Organic Pollutants (POPs) (4) entered into force 17 May, 2004. The objective is the protection of human health and the environment from POPs by reducing or eliminating releases into the environment. Parties have agreed that they need a mechanism to measure whether this objective is achieved. According to Article 16 of the Convention, its effectiveness shall be evaluated starting four years after the date of entry into force of the Convention and periodically thereafter at intervals to be decided by the Convention of Parties (COP). For this, a guidance document on the Global Monitoring Plan (GMP) was prepared by UNEP (5). In May 2008, the Convention had 152 Signatories and 154 Parties.

With the signing of the Stockholm Convention on POPs, a pilot study was conducted with remaining fat of the human milk samples collected for the third round. The aim of the study was expanded to include other POPs, as

well. The feasibility of measuring the relevant POPs in human milk was checked using basically the same procedures as used in the earlier studies on dioxins.

Participants in a series of meetings convened by UNEP Chemicals on this issue have consistently recommended that human milk should be one of the media to be monitored (6, 7; see also 5). Therefore, a close collaboration between WHO and UNEP was agreed to perform the ongoing 4th round as joint study for implementation of the Stockholm Convention. This necessitated a significant modification of the existing WHO protocol for the collection, handling and analysis of human milk samples. This report presents summarized results of a global survey of the third and fourth round of the WHO-coordinated exposure studies on human milk.

Methods

Protocol. Samples were collected by the participating countries following a protocol which dealt primarily with number and type of samples, selection of donors, collection, storage and pooling of samples, and shipping of samples to the reference laboratory. Milk from well-defined groups of 10 mothers (3rd round) or 50 mothers (4th round) was collected and pooled. For selection of donating mothers the following criteria were applied: a) they should be primiparae, b) healthy, c) exclusively breastfeeding one child (i.e. no twins), and d) residing in the area for about 5 years. For further details of the study protocol of the third round the reader is referred to Van Leeuwen and Malisch (8), of the fourth round to the WHO homepage (9). Samples of the third round were collected mainly in 2001 - 2002, with one additional sample collected in 2000 and another one in 2003. Samples of the fourth round have been collected since 2005.

Analysis. To ensure reliability of exposure data and to improve comparability of analytical results from different laboratories, the WHO has co-ordinated a number of inter-laboratory quality assessment studies. The fourth round on levels of PCBs, PCDDs and PCDFs in human milk was conducted between February 1996 and April 1997, with the objective to identify laboratories, whose results could be accepted by WHO for exposure assessment studies (10). Only the State Institute for Chemical and Veterinary Analysis of Food in Freiburg, Germany, met all the pre-set criteria for analyses of PCDDs, PCDFs, dioxin-like PCBs, marker PCBs and fat in human milk, and was thus selected as reference laboratory for the 3rd round of the WHO exposure study. For determination of dioxins and PCBs in all samples of the WHO exposure studies the analysis and the rigid quality control programme was carried out as described (11, 12). Details of the method for determination of organochlorine pesticides and HCB will be published separately.

Results and Discussion

Substances to be monitored are initial twelve POPs. It is recommended not only to analyse the parent POPs but also "transformation products" which are metabolites (e.g. DDE and DDD as DDT metabolites) or by-products (e.g. nonachlor in chlordane). The analytical details were fixed in the UNEP Guidance document on the Global Monitoring Plan for POPs (5). However, it is recommendable to harmonize the following analytical details:

1. The sum of parent POPs and its metabolites can be calculated based on the reported levels or after correction for molecular weight. Following the principles for regulations for maximum levels in food, here the sum parameters are calculated after correction for molecular weight to give e.g "sum of o,p'-DDT, p,p'-DDT, p,p'-DDE and p,p'-DDD, calculated as DDT".
2. Dioxins, furans and dioxin-like PCBs are reported on the basis of a sum parameter "TEQ" (toxic equivalents) using the WHO-TEFs derived at an expert meeting in 1997 and published in 1998 (13).
3. For dioxins and dioxin-like PCBs, handling of non-detected analytes is of particular importance. There are different approaches, among them the calculation of the contribution of non-detects to the TEQ as zero (lower bound concentrations) or with the limit of quantification (upper bound concentrations) (14). Problems of differences between lower bound and upper bound levels or resulting from lack of knowledge about these differences were described elsewhere (15). It was recommended that for reliable determination in the range of the usual background contamination, the difference between upperbound limit of determination and lower bound limit of determination should not exceed the range of 10 to 20 % for food of animal origin with a dioxin contamination of about 1 pg WHO-TEQ/g fat (only PCDD/PCDF included). Such a criterion would be of particular importance for evaluation of time trends in the key matrices of the Global Monitoring Plan.

For the third round, one country (New Zealand) submitted samples in 2000. All other samples were received by the reference laboratory between the beginning of 2001 and the beginning of 2003. At last twenty six countries / regions (Australia, Belgium, Brazil, Bulgaria, Hong Kong SAR, Croatia, Czech Republic, Egypt, Fiji, Finland, Germany, Hungary, Ireland, Italy, Luxembourg, New Zealand, Norway, Philippines, Romania, Russia, Slovak Republic, Spain, Sweden, The Netherlands, Ukraine, United States) participated in this round of the WHO exposure study. For the fourth round, 14 countries sent samples between 2005 and 2007: Belgium, Cyprus, Czech Republic, Fiji, Finland, Haiti, Hungary, Kiribati, Luxembourg, Norway, Slovakia, Sudan, Sweden and Tonga.

The draft implementation plan for the Global Monitoring Plan for the first effectiveness evaluation recommends to set up geographical entities in order to provide an adequate basis for generating, collecting, reporting and presenting the data (16): (a) Africa; (b) Australia, New Zealand and the Pacific Islands; (c) The Carribean, Central and South America; (d) Central, Eastern and Western Europe; (e) Eastern, Southern and Western Asia; (f) North America. Table 1 summarizes the regional distribution of the participating countries:

Africa	round	Australia, NZ, Pacific Islands	round	Carrabean, Centr/S America	round	Europe	round	Asia	round	North America	round
Egypt	3	Australia	3	Brazil	3	Belgium	3, 4	Hong Kong	3	USA	3
Sudan	4	Fiji	3, 4	Haiti	4	Bulgaria	3	Philippines	3		
		Kiribati	4			Croatia	3				
		New Zealand	3			Cyprus	4				
		Tonga	4			Czech Republic	3, 4				
						Finland	3, 4				
						Germany	3				
						Hungary	3, 4				
						Ireland	3				
						Italy	3				
						Luxembourg	3, 4				
						Netherlands	3				
						Norway	3, 4				
						Romania	3				
						Russia	3				
						Slovakia	3, 4				
						Spain	3				
						Sweden	3, 4				
						Ukraine	3				

In 2008, the study was expanded to include countries in so far little covered regions: As of 1 July 2008, Antigua and Barbuda, Azerbaijan, Chile, Costa Rica, Cote d'Ivoir, Democratic Republic of Congo, Georgia, Ghana, Guinea, India, Iran, Kenya, Lithuania, Mali, Mauritius, Moldova, Nigeria, Senegal, Syria and Uruguay agreed to participate.

The results are summarized with regional differentiation in table 2. Aldrin is metabolized to dieldrin and not found in human matrices; therefore it is not reported in Table 2. Endrin, endrin ketone and mirex were not detected in any sample and are therefore not reported in Table 2, as well. The levels of POPs in the regions were calculated using the median values of countries if two or more pooled samples were submitted.

The findings allow to set priorities in different regions and countries. In comparison to all participating countries, higher levels of dioxins are found in European and one African country. Elevated PCB levels are found in Europe, whereas (sub)tropical countries have a tendency to elevated DDT levels. In comparison to DDT, the levels of other chlorinated pesticides are low.

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Table 2. Levels of POPs in human milk of different regions

Region		No of countries	WHO-PCDDF-TEQ	WHO-PCB-TEQ	dieldrin	sum chlordane group	sum DDT	HCB	sum heptachlor	Sum Toxaphene
unit			pg/g fat	pg/g fat	ng/g fat	ng/g fat	ng/g fat	ng/g fat	ng/g fat	ng/g fat
Africa	Median	2	14,3	4,8	1,4	9,8	848	3,5		nn
Africa	Min	2	6,2	4,2	1,4	3,7	396	3,2	nn	nn
Africa	Max	2	22,3	5,5	1,4	15,9	1300	3,8	3,5	nn
Asia	Median	2	6,3	3,6	1,8	18,8	1713	13,9		nn
Asia	Min	2	3,9	2,4	1,5	12,3	1247	3,3	nn	nn
Asia	Max	2	8,7	4,7	2,0	25,3	2180	24,5	1,0	nn
Austr., NZ, Pacific	Median	5	3,9	2,3	2,2	3,2	740	3,4	nn	nn
Austr., NZ, Pacific	Min	5	2,8	1,3	1,6	2,3	189	3,1	nn	nn
Austr., NZ, Pacific	Max	5	6,9	3,9	3,8	3,7	1339	5,7	nn	1,4
Carrib., Central/S. America	Median	2	3,5	2,5	3,1	4,3	1629	3,7		nn
Carrib., Central/S. America	Min	2	3,2	1,8	1,1	3,5	428	3,0	nn	nn
Carrib., Central/S. America	Max	2	3,9	3,3	5,0	5,0	2830	4,4	1,1	nn
Europe	Median	19	8,9	9,4	3,6	9,3	324	17,8	1,9	3,7
Europe	Min	19	4,4	2,1	1,3	1,3	29	2,8	0,5	1,3
Europe	Max	19	18,3	20,0	8,0	26,4	1182	76,0	12,0	17,0
North America	1 country	1	7,2	4,6	5,3	30,1	217	6,6	4,4	nn

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