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Item 5 (i) of the provisional agenda*

Matters related to the implementation of the Convention: effectiveness evaluation

Results of the global survey on concentrations in human milk of persistent organic pollutants by the United Nations Environment Programme and the World Health Organization

Note by the Secretariat

1. By its decision SC-5/18 on the global monitoring plan for effectiveness evaluation, the Conference of the Parties to the Stockholm Convention on Persistent Organic Pollutants encouraged parties to engage actively in the implementation of the global monitoring plan and the effectiveness evaluation, in particular to continue to monitor the core media of air and human breast milk or human blood.

2. As referred to in document UNEP/POPS/COP.6/28 on the global monitoring plan for effectiveness evaluation, sustainable, harmonized and comparable human biomonitoring activities have been put in place through the joint implementation by the United Nations Environment Programme (UNEP) and the World Health Organization (WHO) of a global survey to generate consistent data from the five United Nations regions on concentrations in human milk of the 22 persistent organic pollutants listed in the Stockholm Convention.

3. The results of the first phase of the survey and an analysis of the human health implications of such concentrations have been published in a joint report by UNEP and WHO. The results were reviewed by the global coordination group for the global monitoring plan at its meeting held in Geneva from 10 to 12 October 2012. The report is set out in the annex to the present note and has not been formally edited.

* UNEP/POPS/COP.6/1.

Annex

HUMAN EXPOSURE TO POPS ACROSS THE GLOBE: POPS LEVELS AND HUMAN HEALTH IMPLICATIONS

RESULTS OF THE WHO/UNEP HUMAN MILK SURVEY

ACKNOWLEDGEMENTS

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The implementation of the human milk survey was made possible thanks to the generous contributions to the Stockholm Convention Voluntary Trust Fund from the Governments of Australia, Japan, Sweden and the United States of America, as well as through the European Commission Thematic Programme for Environment and Sustainable Management of Natural Resources, including Energy (ENRTP). The contribution of the GEF and SAICM projects to support POPs monitoring activities in regions is greatly acknowledged. Thanks are also extended to the UNEP Chemicals Branch for the work in support of the implementation of the GEF projects. Further thanks are expressed to the national coordinators of the joint WHO/UNEP exposure study for all the work done to collect and process the human milk samples.

CONTENTS

INTRODUCTION

Persistent organic pollutants (POPs) are chemicals of global concern due to their potential for long-range transport, persistence in the environment, ability to bio- magnify and bio-accumulate in ecosystems, as well as their significant negative effects on human health and the environment. Humans are exposed to these chemicals in a variety of ways: mainly through the food they eat, but also through the air they breathe, in the outdoors, indoors and at their workplaces. Many products used in our daily lives may contain POPs, which have been added to improve product characteristics, for example as flame retardants or surfactants. As a result, POPs can be found virtually everywhere on our planet in measurable concentrations.

POPs characteristics

POPs bio-magnify throughout the food chain and bio-accumulate in organisms. The highest concentrations of POPs are thus found in organisms at the top of the food chain, including humans. The most commonly encountered POPs are organochlorine pesticides, such as DDT, industrial chemicals, most notably polychlorinated biphenyls (PCB), as well as unintentional by-products, especially polychlorinated dibenzo-p-dioxins (PCDD) and dibenzofurans (PCDF).

Health effects

Scientific evidence shows that long-term exposure - for some compounds and scenarios, even to low levels of POPs - can lead, among others, to increased cancer risk, reproductive disorders, alteration of the immune system, neurobehavioral impairment, endocrine disruption, genotoxicity and increased birth defects.

Stockholm Convention

In 2001, an international legally binding agreement, the Stockholm Convention on Persistent Organic Pollutants, was adopted by a large majority of the world’s countries to protect human health and the environment from POPs by reducing or eliminating their releases. The agreement entered into force on 17 May 2004 and includes 178 parties as of January 2013. Through Article 16, the Stockholm Convention mandates a process for evaluating its effectiveness, in particular the progress towards POPs reduction and elimination globally. The effectiveness of the Convention is periodically evaluated on the basis of available scientific, environmental, technical and socio-economic information. This evaluation includes monitoring reports on levels of POPs measured in the environment, national reports submitted pursuant to Article 15, as well as compliance information provided pursuant to Article 17. An overview of the global monitoring plan under the Stockholm Convention is included in Box 1.

At the time the Stockholm Convention was adopted, only limited measurement data were available on the actual human exposure to POPs, focusing mainly on developed countries and certain POPs, mainly PCB and PCDD/PCDF. There was virtually no reliable biomonitoring information available from developing countries.

In 2005, at the second meeting of the Conference of the Parties to the Stockholm Convention, it was recognized that human biomonitoring is essential to evaluate whether human exposure to POPs is indeed decreasing over time. Monitoring of human milk allows thus countries and regions to identify contamination problems and formulate measures to reduce and prevent human and environmental exposure to these chemicals. Building on the previous WHO human milk monitoring studies, the United Nations Environment Programme (UNEP) and the World Health Organisation (WHO) jointly implement a global study to monitor changes in human exposure over time. The survey measures POPs levels in human milk and is implemented in a wide range of countries with large differences in food consumption patterns and environmental levels of POPs. This long-term programme is part of a comprehensive Global Monitoring Plan for POPs established under the Stockholm Convention.

Human breast milk

Concentrations of POPs in human milk are considered good indicators of the actual body burden. In addition, human milk is considered as one of the best sampling matrices for biomonitoring due to its availability and non-invasive approach when collecting individual samples. Its high lipid content makes the extraction method for POPs easier and the precision of the measurements higher. Over the last decades, human milk has generally been used as a medium to measure contamination in humans, and analytical techniques have been well established for most POPs included in the Stockholm Convention.

Furthermore, the uptake of these chemicals by the infant via human milk is of high toxicological relevance. The risk-benefit assessment of breastfed infants represents one of the most challenging aspects of human toxicology, as possible adverse health effects associated with exposure to POPs concur with significant health benefits of breastfeeding.

In this perspective, the results of the human milk survey are not meant to derive a "ranking" of countries with respect to risks for the breastfed infant. The surveys are primarily aimed at identifying worldwide quantitative differences of human milk contamination with these POPs, and provide a baseline for those countries for which such information was previously not available. This will allow in the future evaluating the effectiveness of measures taken to reduce POPs exposure. The quantitative differences observed in these surveys may provide a suitable basis for possible source-directed measures to further reduce levels of specific POPs on a country-by-country basis. Therefore it is useful to interpret the results in a national/regional context, and introduce targeted measures to further decrease human exposure.

BOX 1 Global Monitoring Plan for POPs

Mandate

The Stockholm Convention on persistent organic pollutants (POPs) calls for reduction or elimination of releases of POPs globally, which would translate into reduced environmental levels over time. Through Article 16, the Convention mandates a process for evaluating the progress towards POPs reduction and elimination globally. The effectiveness of the Convention is evaluated on the basis of available scientific, environmental, technical and economic information, including monitoring reports on levels of POPs measured in the environment, national reports submitted pursuant to Article 15, as well as non-compliance information provided pursuant to Article 17.

Purpose

An important component of the effectiveness evaluation is thus the development of a global monitoring plan providing a harmonized framework for the collection of comparable monitoring data or information on the presence of POPs in all regions, in order to identify changes in levels over time and provide information on their regional and global environmental transport. Determining the effectiveness of control measures on POPs requires detailed information on background environmental concentrations of priority POPs from monitoring programs that are statistically robust and can detect changes in contaminants over time.

Core matrices

A number of environmental media have been used to monitor environmental levels of POPs and trends over time. The parties to the Stockholm Convention have recognized the role that many of these media could play in a global monitoring program. National programmes reporting the concentration of priority chemicals in mussels, fish tissue, bird eggs and sediments have all been used to establish trends over time, but these programs are often regional in nature and may not be widely applicable across the globe. Each of these media has specific advantages and disadvantages for trend detection and difficulties in terms of sample collection, storage and analysis.

Considering the global dimension of the monitoring plan under the Stockholm Convention, the Conference of the Parties has chosen as core matrices - air, and human milk and/or blood - as they provide information on the sources and transport of priority POPs and the levels of exposure in human populations. Data from regional programmes using other media can be used to complement data from the core matrices and help to establish trends using a weight of evidence approach.

Regional and global structure

The implementation of the global monitoring plan is at the regional level, through regional organization groups in each of the five UN regions. The groups' role is to define and implement a regional strategy for information gathering, including capacity building and establishment of strategic partnerships in order to fill the identified data gaps, and prepare the regional monitoring reports as a contribution to the effectiveness evaluation process. A global coordination group has also been established to harmonize and coordinate activities and cooperation among the regions, evaluate the implementation of the global monitoring plan and develop recommendations for the Conference of Parties to the Stockholm Convention.

Scope and implementation

Timelines and participating countries

Early WHO surveys performed mainly in Europe and North America in 1987-1989 and 1992-1993 exclusively focused on PCB, PCDD and PCDF. In 2001-2003, a larger global survey was implemented, covering the twelve POP compounds initially listed in the Stockholm Convention[1]. Following the ratification of the Stockholm Convention, WHO and UNEP started their collaboration, and two additional global surveys were completed in 2005-2007 and 2008-2012. These significantly enlarged the geographical scope of the study to provide representative results for all regions of the globe.

The table below provides an overview of the participating countries according to the rounds of the exposure study.

Countries	Round 1	Round 2	Round 3	Round 4	Round 5
	1987-1989	1992-1993	2000-2003	2004-2007	2008-2012
Antigua and Barbuda					x
Australia			x		x
Austria	x	x			
Barbados					x
Belgium	x	x	x	x	x
Brazil			x		
Bulgaria			x		
Canada	x	x			
Chile					x
Croatia			x		
Congo					x
Cote d'Ivoire					x
Cyprus				x	
Cuba					x
Czech Republic			x	x	
Djibouti					x
Denmark	x	x			
Egypt			x		
Ethiopia					x
Fiji			x	x	x
Finland	x	x	x	x	
Germany	x	x	x		
Georgia					x
Ghana					x
Haiti				x	x
Hong Kong			x		x
Hungary			x	x	
India					x
Indonesia					x
Ireland			x		x
Italy			x		
Israel					x
Jamaica					x
Kenya					x
Countries	Round 1	Round 2	Round 3	Round 4	Round 5

[1] These include: aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, toxaphene, polychlorinated biphenyls (PCB), polychlorinated dibenzo-p-dioxins (PCDD), polychlorinated dibenzofurans (PCDF).

	1987-1989	1992-1993	2000-2003	2004-2007	2008-2012
Kiribati				x	x
Korea, Rep.					x
Lithuania					x
Luxembourg			x	x	
Mali					x
Marshall Islands					x
Mauritius					x
Mexico					x
Moldova					x
Netherlands	x	x	x		
New Zealand	x		x		x
Niue					x
Niger					x
Nigeria					x
Norway	x	x	x	x	
Palau					x
Peru					x
Philippines			x		
Romania			x		
Russian Fed.			x		
Samoa					x
Senegal					x
Solomon Islands					x
Slovak Republic			x	x	
Spain		x	x		
Syria					x
Sudan				x	
Sweden	x		x	x	
Switzerland					x
Tajikistan					x
Togo					x
Tonga					x
Tuvalu					x
Uganda				x	
Ukraine			x		
United Kingdom	x	x			
Uruguay					x
USA	x		x		

Method

In order to promote reliability and comparability of results, samples were collected by the participating countries following a comprehensive protocol and guidelines developed by WHO. Participating countries were encouraged to adhere as closely as possible to the protocol, which provides guidance on the number and type of samples, selection of donors, collection, storage and pooling of samples, and shipping of samples to the reference laboratory. For all studies, the following criteria for selection of donating mothers 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 five years.

Individual milk samples were mixed to form a standardized pooled sample, which was analyzed for the 12 POP compounds and their transformation products. In particular, PCDD, PCDF and dioxin-like PCB are reported on the basis of toxic equivalents (TEQ) using the WHO toxic equivalency factors published in 1998. As for the sum of the six indicator PCB, this includes PCB congeners 28, 52, 101, 138, 153 and 180. Finally, the sum DDT includes o,p'-DDT, p,p'-DDT, p,p'-DDE and p,p'-DDD. Archived milk samples were also analyzed for the ten POPs newly added to the Stockholm Convention in 2009 and 2010.

It should be noted that the sampling concept for the mothers' milk exposure studies changed between 2000 and 2012. Whereas in the third round (2000-2003) countries were encouraged to prepare two or more pooled samples to address differences within a country, the guidance document for the Global Monitoring Plan under the Stockholm Convention asks for one representative sample for up to 50 million citizens. In order to obtain comparable results, for this overview the median concentration from all national pools that were submitted for the respective rounds was used.

Reference Laboratory

To further ensure consistency in measurements, all samples were analyzed by the WHO reference laboratory, the State Institute for Chemical and Veterinary Analysis of Food, Freiburg, Germany, using validated methods. Perfluorinated chemicals were likewise analyzed in a single laboratory at the MTM Research Centre, Örebro University, Sweden.

Presentation of results

The results from the third, foruth and fifth rounds of the survey, spanning over the period 2000-2012, are presented in this report based on the findings by Malisch et al. 2013a. Figures 1-4 capture some of the most interesting highlights of the survey results and are introduced in the main report. The annex includes further detailed results as follows: Figure 5 through Figure 7 show the results for the dioxin-like POPs using the WHO_{1998}-TEFs, Figure 8 presents the results for the sum of the six indicator PCB, and Figures 9-14 present the results of the national pools for the POPs pesticides that were included in the initial twelve POPs. The results for the newly listed POPs are shown in Figures 15-22.

When comparing the graphs, the scale of the concentrations and the units (y-axis) should be carefully observed. Whereas for dioxin-like POPs and the sum of the six indicator PCB, the difference between upper-bound and lower-bound values is less than 1%, POPs pesticides could not be quantified in many countries. Countries that had POPs pesticide concentrations below the limit of quantification are either displayed in grey-colored bars or listed in the figures' legends.

RESULTS

THE TWELVE LEGACY POPS LISTED IN THE STOCKHOLM CONVENTION

The human exposure data published by Malisch et al. 2013a for a total of 68 countries world-wide show that elevated levels of industrial contaminants or by-products of burning processes like PCDDs, PCDFs, PCBs and HCB are mostly found in Europe, India and some African countries, whereas (sub)tropical countries have a tendency to elevated DDT levels.

Dioxin-like compounds

In particular, measurable levels of dioxins and furans are observed worldwide in both industrialized and less industrialized regions. While it is well-known that combustion and industrial processes are major sources of PCDDs and PCDFs, equal attention should be given to relevant sources in less-industrialized areas – such as open burning processes - and promote measures to reduce releases from such sources.

The results confirm that the islands of the Southern Hemisphere have comparably low levels of PCDDs, PCDFs as well as dioxin-like PCBs. In Africa, the widest variation in contamination of human milk was observed with distinct differences between PCDD/PCDFs and PCBs. Kenya and Uganda clearly have the lowest levels observed in this study for both groups of compounds. In contrast, West and Central African countries like Côte d'Ivoire, the Democratic Republic of Congo, Ghana, Mali, Nigeria, Sudan and Senegal have much higher levels of PCCDs and PCDFs in human milk, which can be more than four times higher as those observed in the East African region. These results indicate that exposure levels to dioxin-like compounds are significant and among the highest observed worldwide. Regional-specific exposure pathways, such as geophagy illustrated in box 2, may explain these high levels, and indicate the potential to reduce human exposure through targeted measures and awareness-raising.

For PCDD and PCDF, data from the last decade suggest that the levels of these POPs in human milk have fallen steadily from their earlier high levels, indicating the effectiveness of intervention measures to decrease environmental releases (Figure 1). For PCBs, the picture is less clear for some countries, but in general, declining levels are observed (Figure 2). The higher levels observed in early 2000 in a number of countries have been successfully mitigated. The measures implemented in these countries to address PCDD/PCDF release and contamination issues are thus shown to be successful in achieving their objectives and could be replicated in other parts of the world with similar positive outcomes.

BOX 2. Possible exposure pathways for dioxin-like compounds in Africa

Clay has been used medicinally for centuries in Africa, India, and China, and by Native American groups. Uses have included gastrointestinal disorders and as an antidote for poisoning.

The practice of eating dirt, clay, or other non-nutritious substances is usually referred to as "pica" or "geophagy". This practice is most common in early childhood, and in pregnant women. There is some evidence that mineral deficiencies, such as iron deficiency, may lead to pica, and prevalence is higher in developing countries and in poor communities. A review of potential health implications of this practice has been published in 2010 by Kutalek et al. and includes consideration of microbial infestation and exposure to heavy metals. High levels of lead were in particular detected.

Moreover, doxins have been detected in natural formations of clay in different parts of the world. A number of studies show that kaolin ball clays are contaminated with PCDD/PCDF worldwide (Horii et al. 2011). The potential for adverse effects with oral ingestion of clay may thus be high, in particular through significant exposure to heavy metals and toxic organic compounds such as PCDD/PCDF.

Malisch et al. 2011* have analyzed the possible consequences of clay contamination with dioxins for the food chain and bioaccumulation in humans. They conclude that the relatively high levels of PCDDs measured in human milk from some African countries and the similarity of the congener patterns with those from the clays strongly suggest that oral ingestion of clays during pregnancy contributes to these high levels measured in human milk.

*proceedings of the “1st Clays and Clay Minerals in Africa, and the 2nd Conference on Human and Enzootic Geophagia in Southern Africa” (19-21 October 2011, Central University of Technology, Bloemfontein, South Africa).

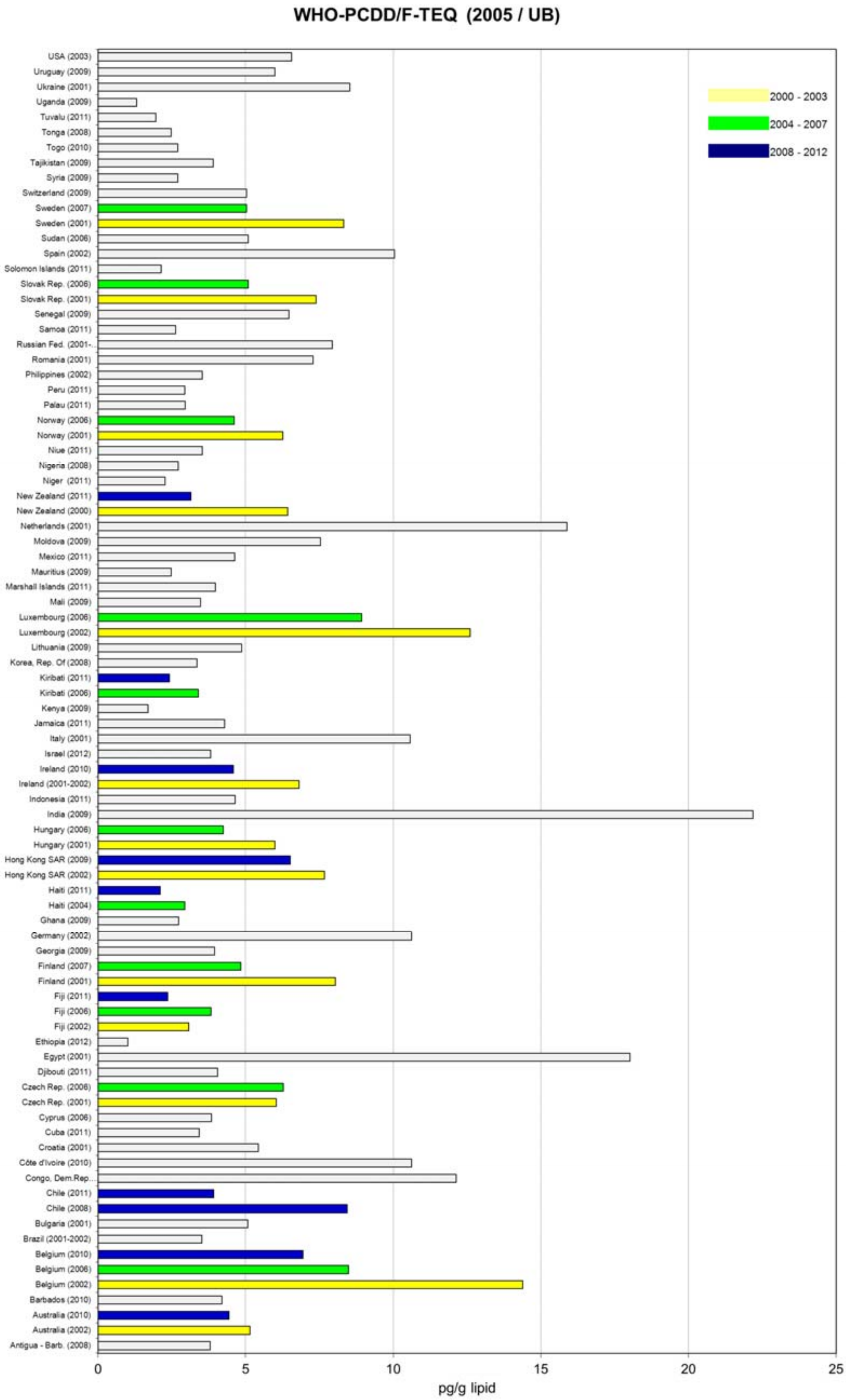


Fig.1: Levels of PCDD/PCDF in human milk: survey results over the period 2000-2012

The levels of indicator PCBs measured in human milk are illustrated in Figure 2, and, similarly to PCDD/PCDF levels, are shown to decrease over time, but still considered of human health concern.

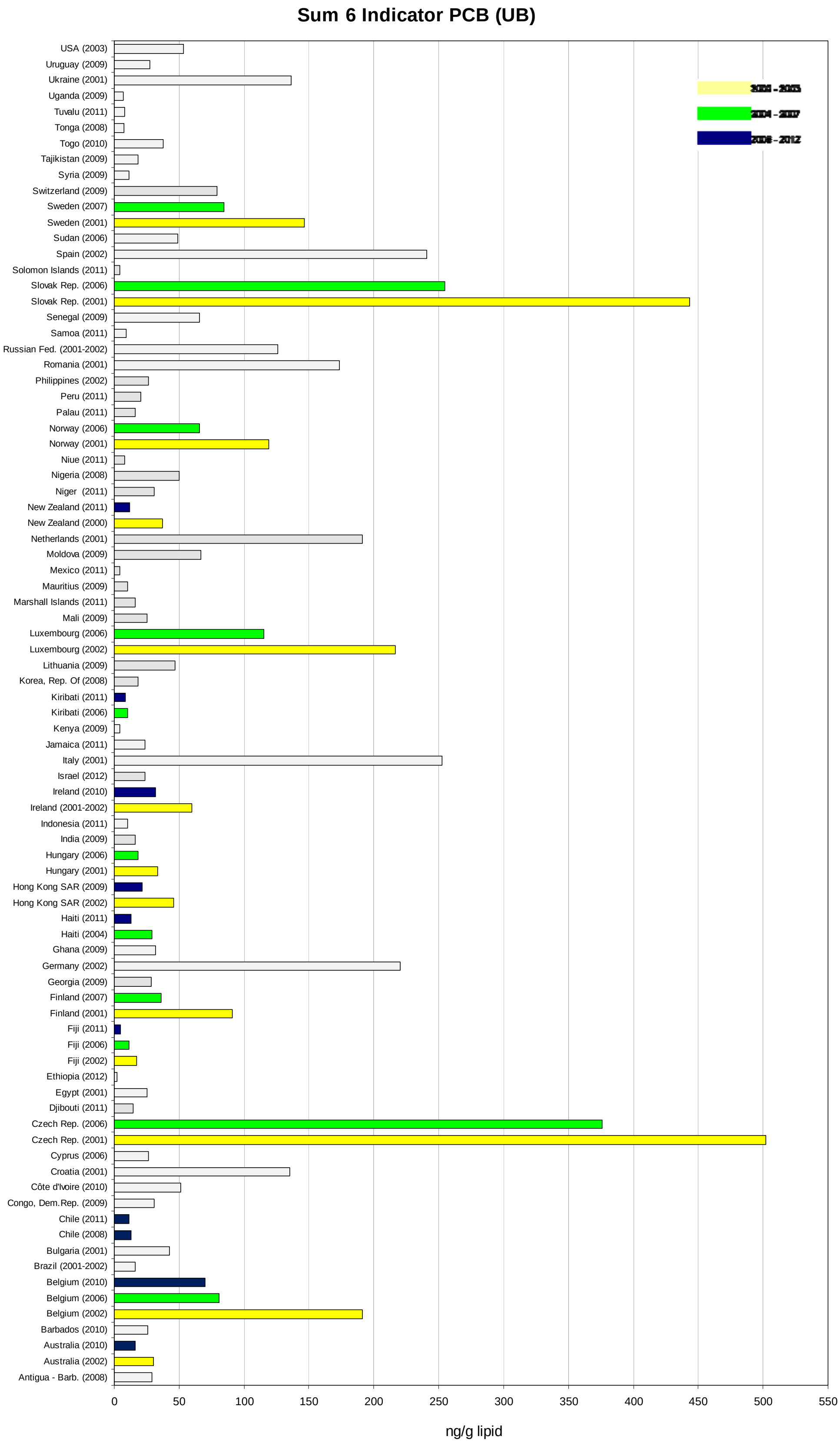
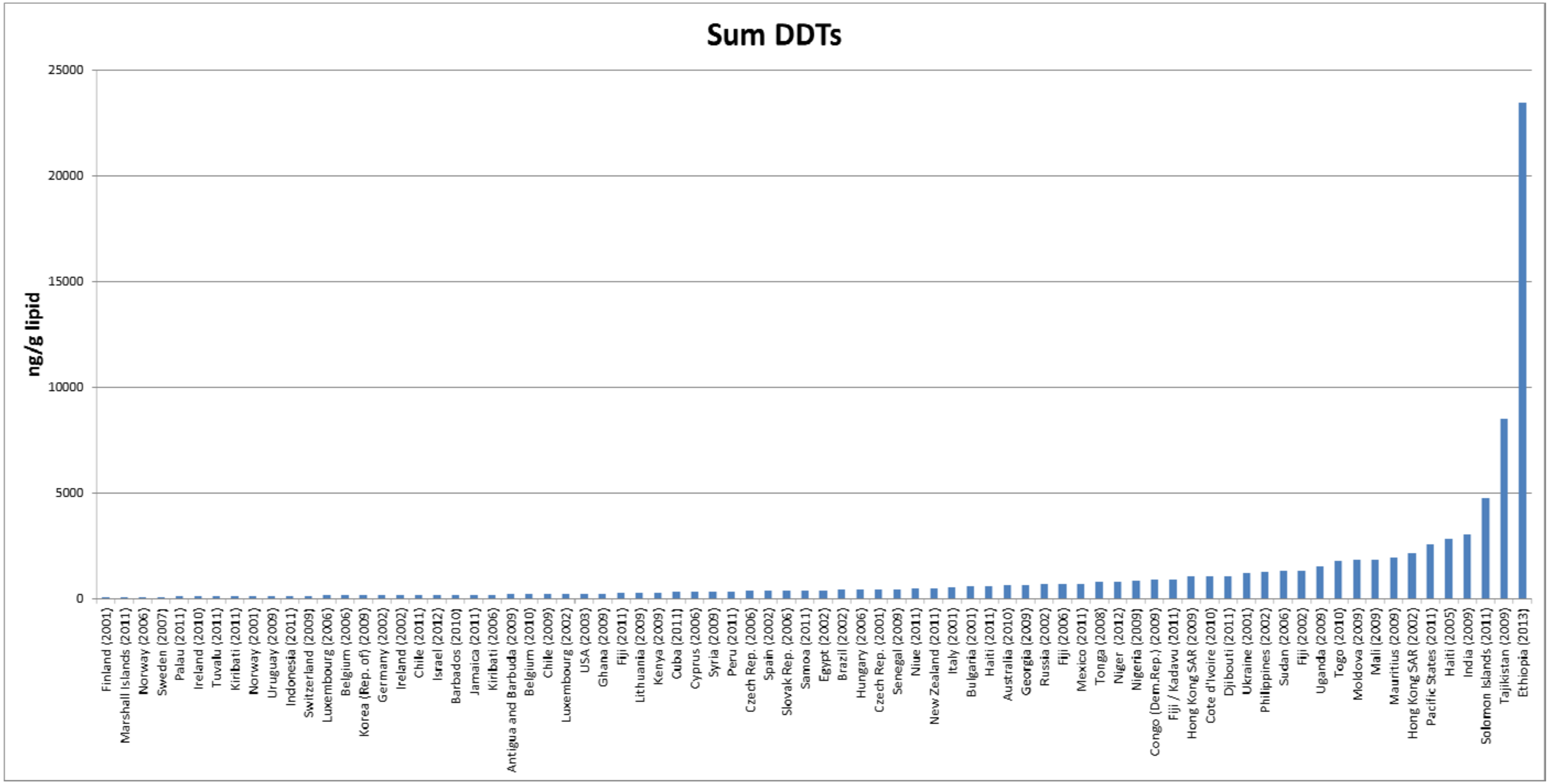


Fig. 2: Levels of indicator PCBs in human milk: survey results over the period 2000-2012

As for DDT, the highest levels were found in tropical and sub-tropical countries: Côte d'Ivoire, Ethiopia, Hong Kong SAR, Uganda, Mali, Mauritius, Haiti, India, Solomon Islands, Sudan and Tajikistan (Figure 3). This distribution reflects its use in relation to the occurrence and prevention of malaria in these regions.

Fig. 3: Levels of DDT in human milk: survey results over the period 2000-2012



It is important to note a significant contribution of the DDE metabolite to the sum DDT, which suggests legacy contamination through past exposure.

In comparison to DDT, the levels of other chlorinated pesticides are low. For example, aldrin and endrin (including endrin ketone) were not found in any human samples. Mirex was not detectable in the majority of cases, except in one region. Toxaphene was not detected in about half of the countries included in the surveys. The graphics showing the detailed results for the twelve legacy POPs are presented in Figures 7-14 in the Annex to this document.

THE TEN NEWLY LISTED POPS ADDED TO THE STOCKHOLM CONVENTION IN 2009 AND 2011

In 2009 and 2011, ten new chemicals[2] have been listed in the annexes to the Stockholm Convention, introducing further complexity in the monitoring activities under the global monitoring plan. Among the ten new POPs, perfluorooctane sulfonic acid (PFOS) and its salts do not follow the "classical" pattern of partitioning into fatty tissues, but instead bind preferentially to proteins in the plasma, which makes blood and liver the optimal medium for analyzing PFOS. The levels in human milk are generally much lower than those in blood, indicating that human milk is not a primary target for analyzing PFOS. A strong association between serum and milk concentrations of PFOS has nevertheless been reported, as shown in the figure below:

Correlation of PFOS levels measured in serum and breast milk

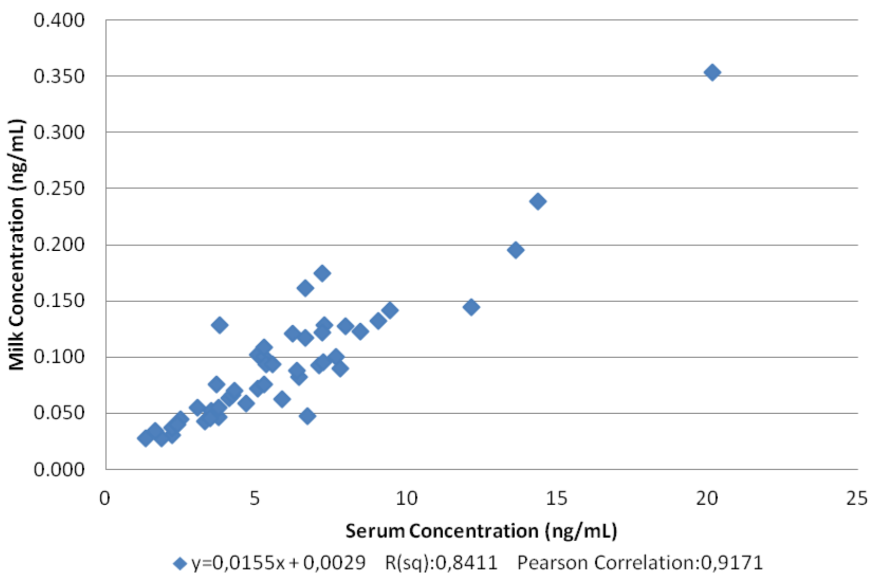


Fig. 4: PFOS concentrations (ng/mL) in serum and milk samples from Sweden, 2004-2011. The linear equation of the line, including R^2, is given together with Pearson's correlation coefficient (Kärrman and Davies 2013).

[2] These include: alpha-hexachlorocyclohexane, beta-hexachlorocyclohexane, chlordecone, hexabromobiphenyl, hexabromodiphenyl ether and heptabromodiphenyl ether (commercial octabromodiphenyl ether), lindane (gamma-hexachlorocyclohexane), pentachlorobenzene, perfluorooctane sulfonic acid, its salts and perfluorooctane sulfonyl fluoride, technical endosulfan and its related isomers, tetrabromodiphenyl ether and pentabromodiphenyl ether (commercial pentabromodiphenyl ether).

Samples that were collected during the 2008-2012 survey have been archived and used for the analysis of the ten newly listed POPs to establish a comprehensive baseline for these chemicals at the global level.

Results for newly listed POPs

Among the ten new POPs, measurable concentrations of perfluorinated chemicals have been detected in human milk. PFOS was quantified in 67% of the milk samples analyzed, with concentrations ranging from <4 to 65 ng/L (see Figure 22 in the Annex). The fact that PFOS could be detected at values above LOQ for a majority of samples shows that contamination and human exposure to PFOS in all regions where results are available is of significant concern. Other perfluorinated compounds have been quantified in limited number of samples, with relatively low levels compared to studies reported from other countries.

The results for polybrominated diphenyl ethers are shown in Figure 21 in the Annex. High concentrations have been measured in pooled samples from industrialized countries such as USA and Australia, but also in the Pacific Islands (Fiji, Tonga) and in the GRULAC region (Antigua and Barbuda, Haiti, Jamaica, Mexico).

Endosulfan has only been quantified in two samples, and hexabromobiphenyl in three samples. High levels of lindane have been measured in certain African countries, Central and Eastern Europe, and in Asia and the Pacific. The full range of results for the newly listed POPs is shown in Figures 15-20 in the Annex.

Benefits and Risks of Breastfeeding

Dioxin safety standards

Malisch et al. 2013b consider human health implications of POPs levels measured in human milk from a risk assessment perspective. Dioxin-like compounds have been studied extensively to assess the risk they pose to both human health and the environment. The WHO established a safety standard for chronic life time exposure to this class of compounds: the Tolerable Daily Intake (TDI) for dioxin-like equivalencies (TEQs), which is 1 to 4 pg TEQ/kg body weight (bw) and a Provisional Tolerable Monthly Intake (PTMI), which is 70 pg TEQs/kg bw per month. The only difference between these two values is that a daily variation above TDI on a monthly basis does not represent a health concern. In addition, US EPA proposed an oral reference dose (RfD) of 0.7 pg TCDD/kg bw per day, and ATSDR has set a minimum risk level (MRL) for acute and semichronic exposure of 20 and 1 pg TCDD/kg bw per day respectively.

The underlying data based on which the TDI and PTMI are derived show that the most sensitive adverse health endpoints for rodents are found in the offspring. These effects include immune suppression, sperm count, genital malformation and neurobehavioral effects, which have been frequently observed after exposure to these compounds in the period immediately before and after birth. In addition TDI derivation is based on relatively short-term experiments, albeit in the most sensitive life stage (often in utero or neonatal).

Thus, as the underlying experimental data used to derive the safety standards for life-time human exposure often involve pre- and/or postnatal experiments, the WHO derived TDI or PTMI can also be applied to the breastfed infant. Recent studies have estimated the uptake of TEQs via breastfeeding for several countries and reported a range between 30 to more than 200 pg TEQs/kg bw per day. The results of the human milk survey reported herein are in line with the data used for these TEQ calculations. The results show that the WHO TDI or PTMI is exceeded by one to two orders of magnitude during a period ranging from several months to more than a year.

PCB safety standards

Furthermore, a minimum risk level (MRL) has also been derived for PCBs. This is of 0.03µg/kg per day. When compared with the MRL, worldwide PCB levels as measured in the human milk survey exceed by one to two orders of magnitude those levels that are considered safe for the newborn. Consequently, the risk for possible adverse effects in the newborn via breastfeeding cannot be excluded, but the question remains whether experimental rodent data are applicable to the human situation.

Dioxin-related health risks

At present, several human epidemiological studies have been performed in relation to pre- and postnatal exposure to dioxin-like compounds. Subtle dose-dependent effects on thyroid hormones, psychomotoric development, immunology and physical development were observed in the breastfed infant. However, these effects were often transient and generally considered not to be clinically relevant. Nevertheless, these human studies indicate that at least in the 1990s the maternal body burden of dioxin-like compounds and/or PCBs in industrialized countries was sufficiently high to cause subtle effects in newborns.

DDT safety standards

DDT safety standards, such as a Tolerable Daily Intake (TDI), Reference Dose (RfD) or Minimum Risk Level (MRL) have also been derived, and WHO has set a provisional TDI of 10 µg/kg bw per day.

Based on these safety standards for dioxin-like compounds, PCBs and DDT, corresponding 'safe' levels of dioxin-like compounds and DDT in human milk were calculated and are presented in Table 1 below (Malisch et al. 2013b). These calculated 'safe' levels were compared with those measured in the two human milk surveys performed in 2005-2011. The results indicate that in all countries studied, the levels of dioxin-like compounds and PCbs are one to two orders of magnitude above those associated with a TDI, RfD or MRL value. However, in all countries except one, human milk levels of DDT are below or around those considered as safe based on the WHO TDI.

Organization	Safety Standard		Equivalent milk level	Endpoint
PCDD/PCDF/PCB (TEQs)				
WHO (2000)	TDI	1-4 pg/kg bw day	0.2 – 0.9 pg/g lipid	Perinatal effects rodents and monkeys
US EPA (2010)	RfD (proposed)	0.7 pg/kg bw day	0.2 pg/g lipid	Postnatal/childhood exposure humans
ATSDR (1998)	MRL subchronic	1 pg/kg bw day	0.2 pg/g lipid	Postnatal effect monkeys
Total PCBs				
ATSDR (2004)	MRL subchronic	0.03 µg/kg bw .d	7 ng/g lipid	Postnatal effect monkeys
DDT				
WHO (2001)	TDI	10 µg/kg bw day	2300 µg/kg lipid	Developmental toxicity in rats
<u>Information and formula used</u> (lipid set in human milk = 3.5% and consumption 125 g milk/kg bw day): [Acceptable concentration] = [Safety standard (pg or µg/kg bw day)] / 4,375 g lipid/ kg bw day				

Table 1: Different safety standards for dioxin like compounds (TEQs) and DDT with calculated equivalent human milk levels (Malisch et al. 2013b)

DDT health risks

Human health effects of DDT and its metabolites have also been extensively studied over the last decades. Two major problems arise when interpreting studies focusing on the development of the fetus and the infant. Firstly, a differentiation between effects due to fetal and/or neonatal exposure is often not possible. Secondly, DDT and its metabolites invariably occur with other POPs, for which similar effects on the neonate and infant have been described. This concurrence with other POPs in human milk makes it often difficult to identify the actual causal agent for an observed effect in the breastfed infant. Nevertheless, DDT or

DDE have been implicated in adverse health effects in the period immediately before and after birth or in early childhood. A number of these transient effects (for instance on thyroid hormones and body growth) are minor and possibly not clinically relevant. However, more significant effects have been observed on neuro-cognitive development, which can persist into childhood. From these studies, it also appears that prenatal exposure may be more toxicologically relevant than exposure through breastfeeding. In addition, it should be recognized that certain effects attributed to DDT and/or DDE cannot always be discerned from other POPs such as dioxins and PCBs.

Over the last decades the benefits of breastfeeding for the infant and mother have been promoted. In a recent review of the American Dietetic Association from 2009, it is concluded that breastfeeding is the preferred choice for the newborns. From a risk assessment point of view, the major question is whether positive health effects by breastfeeding outweigh the adverse effects of dioxin-like compounds and DDT that may be expected from the levels observed in the human milk survey. The underlying scientific evidence of positive health effects through breastfeeding has to be taken into consideration and balanced against possible adverse health effects. Recent studies reported that breastfeeding is associated with a 7 to 33 % decrease in overall postnatal survival. An examination of infant hospitalization in relation to the length of breastfeeding concluded that for every month of breastfeeding, 30% of the hospital admissions could have been avoided. These studies provide evidence that breastfeeding significantly reduces overall mortality in the first year of life. Furthermore, the US Department of Health and Human Services reviewed approximately 400 studies up to 2006 and concluded that breastfeeding reduced the risk of acute otitis, non-specific gastroenteritis, severe lower respiratory tract infections, atopic dermatitis, asthma, obesity, diabetes, childhood leukemia, sudden infant death syndrome (SIDS) and enterocolitis.

When these positive effects are compared with the reported negative effects associated with POPs in human milk, a conclusion can be drawn that beneficial effects may persist into later life, while most POP-related negative effects are mostly transient in nature and less clinically relevant.

Risk-benefit assessment

More worrisome adverse health effects have nevertheless been observed, of the association between dioxin-like compounds and DDT, after exposure in the pre- and postnatal period, coupled with a reduction of cognitive performance which may persist in later life. This observed reduced cognitive or neurobehavioral development in the first years of infancy and childhood is further supported by experimental evidence from animal studies that provides biological plausibility for such a mode of action of POPs. An important point of debate is whether or not these observed behavioral effects are the results of *in utero* or lactational exposure, or a combination of both. Considering the published human studies on dioxin-like compounds, PCBs and DDT, it has become clear during the last decade that *in utero* exposure to these compounds is more related to cognitive and behavioral changes. This is in spite of the fact that from a quantitative point of view the uptake by the infant during the breastfeeding period is much higher. These results from human studies clearly point towards the *in utero* life phase as the most sensitive life stage. This observation is in line with results from many experimental animal studies with these compounds. Thus, from a risk-benefit point of view, the amount of *in utero* exposure, caused by the maternal body burden, should be given priority above the exposure to these POPs via human milk, as the latter situation very likely presents a toxicologically less relevant situation. Since maternal body burden and placental transfer of POPs should be considered as the exposure situation that is very likely the most toxicologically relevant, it is of uttermost importance to monitor the body burden of women in the reproductive age. It is well established that levels of the dioxin-like compounds, PCBs and DDT in human milk are a good reflection of the actual maternal body burden. Levels of these POPs in human milk, therefore, provide an excellent and easy-to-obtain source of information for global studies on temporal and regional changes of overall human exposure. Recent studies indicate that maternal levels of these compounds are still able to cause possibly adverse health effects in the infant. In view of this important role of prenatal exposure, future risk-benefit assessments should be more focused on the *in utero* situation, rather than on the lactation period. Several human studies indicate that effects arising from exposure to POPs via lactation appear to be minor, if at all, when compared with the *in utero* situation. In view of the higher toxicological importance of the *in utero* exposure the debate on the risks and benefits of breast feeding becomes increasingly redundant.

The latter observations regarding the risks of prenatal exposure to these POPs provide strong arguments to call for further reductions in human exposure to these hazardous chemicals. The situation becomes more complex when taking into account the multiple interactions among all POPs measured in human milk and their coupled effects from which we have very limited knowledge but have clear indication these can exist.

Therefore, all efforts should be directed to further reduce human dietary and environmental exposure to these POPs, rather than reducing the breastfeeding period. The results of the human milk survey show that such remedial actions are still necessary everywhere.

CONCLUSIONS

The global monitoring plan for POPs provides a harmonized framework for the collection of comparable and consistent monitoring data or information on the presence of POPs in all regions of the world, in order to identify changes in POPs levels over time. Sustainability of monitoring activities under the Stockholm Convention is essential to provide the necessary information for the assessment of long-term trends in POPs levels in human populations.

As part of the global monitoring plan under the Stockholm Convention, the human milk surveys provide results that indicate success in eliminating certain POPs pesticides, such as aldrin, dieldrin, mirex, toxaphene, but also the ubiquitous presence of PCDD/PCDF. Besides the well-known sources of PCDD/PCDF such as combustion and industrial processes, equal attention should be given to relevant sources in less-industrialized areas – such as open burning - and promote measures to reduce releases from these sources.

Large global differences with respect to contamination of human milk with POPs are also apparent. Unexpectedly, contamination with dioxin-like compounds was among the highest in some African countries. Regional-specific exposure pathways, such as geophagy, may explain these high levels, and indicate the potential to reduce population exposure through targeted measures and awareness-raising activities.

A decreasing trend in PCDD/PCDF levels in human milk may be observed in a number of countries, indicating effectiveness of intervention measures to decrease environmental releases. Levels of dioxin-like PCBs and marker PCBs have also fallen steadily over time, although the picture is less clear for some countries and the distribution of PCB profiles observed among countries suggests that the sources of PCBs are different.

The levels observed in human milk have been compared with the WHO safety standards with the conclusion that in many countries the levels of dioxin like compounds, PCB and in some cases DDT are still above those associated with these standards. However, based on the current state of knowledge, it can be concluded that the demonstrated benefits of breastfeeding outweigh the disadvantages. While the beneficiary effects of breastfeeding are likely to persist into later life, most POP related negative effects are mostly transient in nature and less clinically relevant. Nevertheless, some worrisome adverse health effects were observed, for instance the association between dioxin-like compounds in human milk and reduction of cognitive performance, which may persist in later life. Further complexities and uncertainties may arise when taking into account the effects of multiple interactions among all POPs measured in human milk.

Recent studies indicate that maternal levels of these compounds are still able to cause possibly adverse health effects in the infant. In view of this important role of prenatal exposure, future risk-benefit assessments should be more focused on the *in utero* situation, rather than on the lactation period. Several human studies indicate that effects arising from exposure to POPs via lactation appear to be minor, if at all, when compared with the *in utero* situation. In view of the higher toxicological importance of the *in utero* exposure the debate on the risks and benefits of breast feeding becomes increasingly redundant.

Among the newly listed POPs, measurable concentrations of perfluorinated chemicals have been detected in human milk. The fact that PFOS could be detected at values above LOQ for a majority of samples shows that contamination and human exposure to PFOS in all regions where results are available is of significant concern.

In view of the above considerations, all efforts should still be directed to further reducing human dietary and environmental exposure to these POPs. The results of the surveys show that further remedial actions are necessary in all regions of the world.

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ANNEX

POPs CONCENTRATIONS IN HUMAN MILK BY COUNTRY

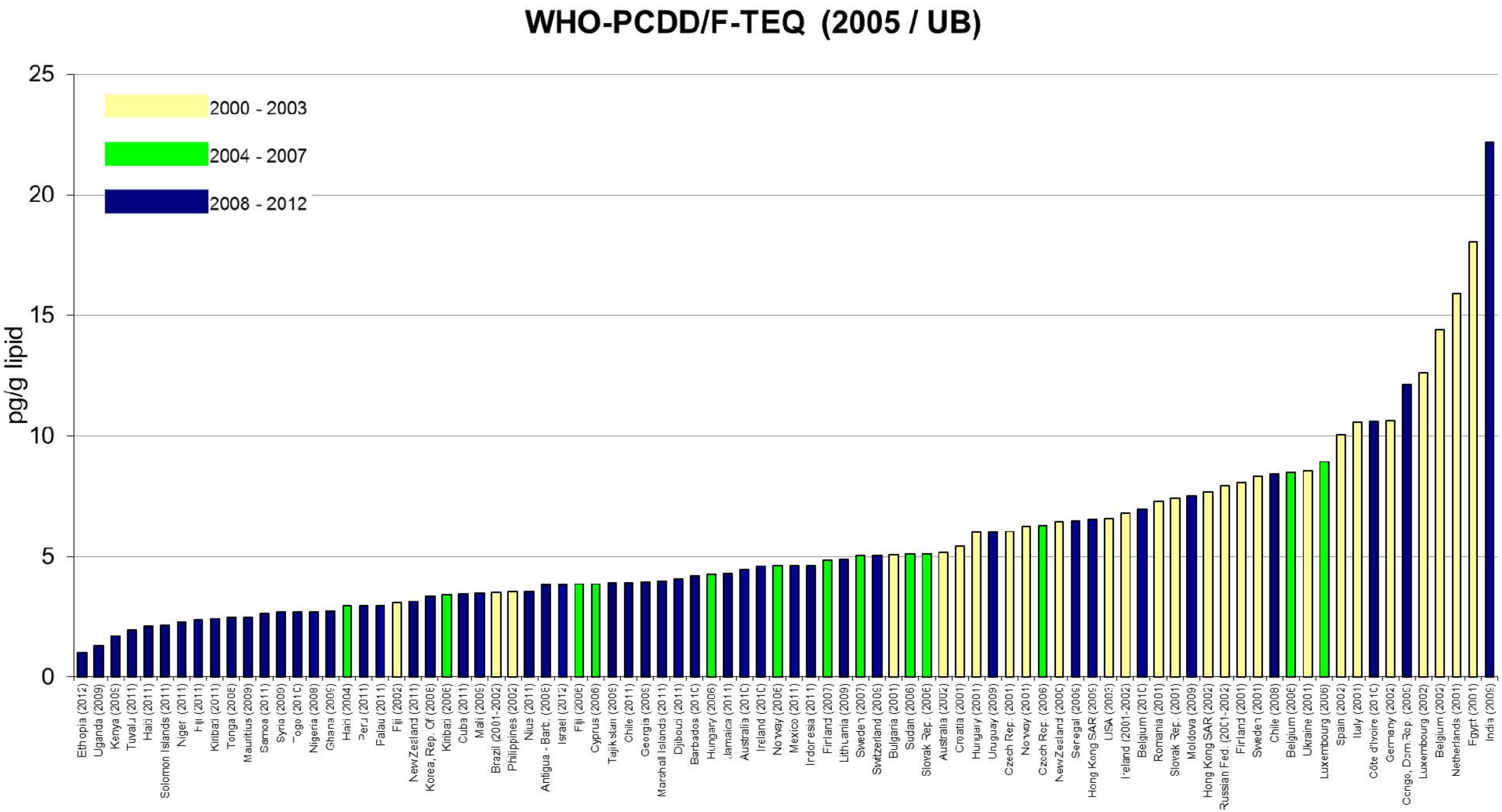

Figure 5: Levels of PCDD/PCDF in human milk: survey results over the period 2000-2012

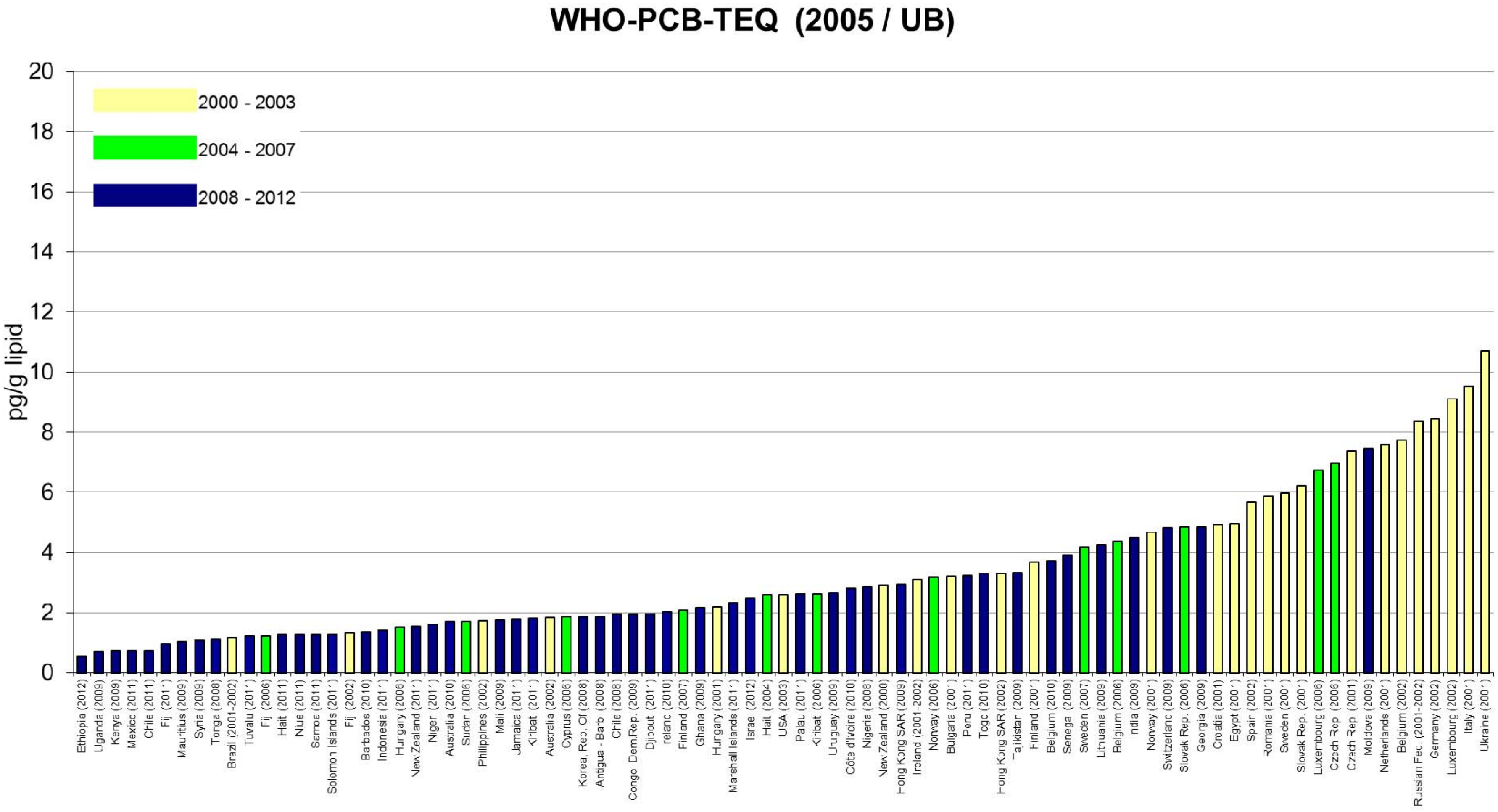

Figure 6: Levels of dioxin-like PCB in human milk: survey results over the period 2000-2012

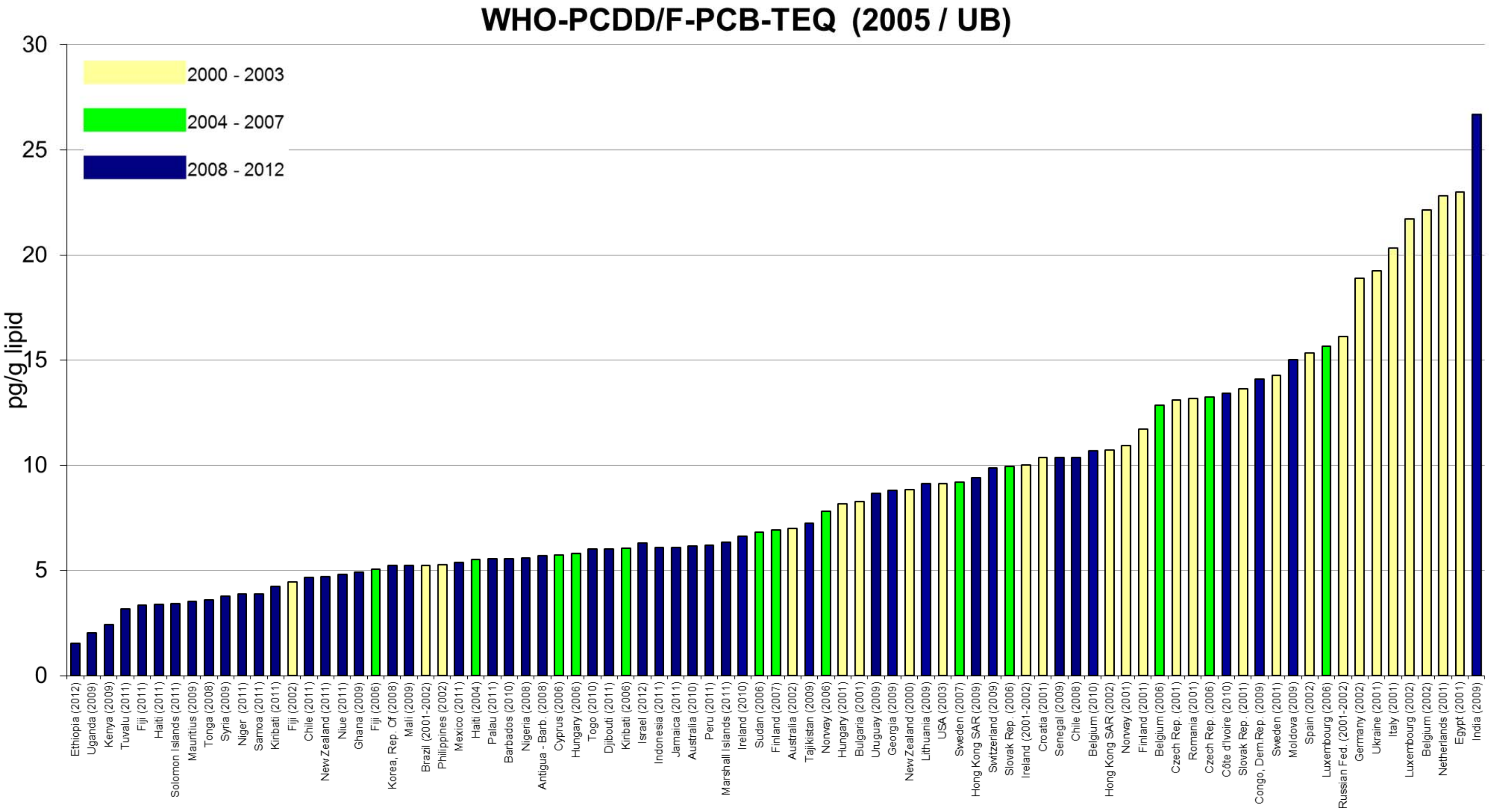

Figure 7: Total PCDD/PCDF and PCB TEQ levels in human milk: survey results over the period 2000-2012

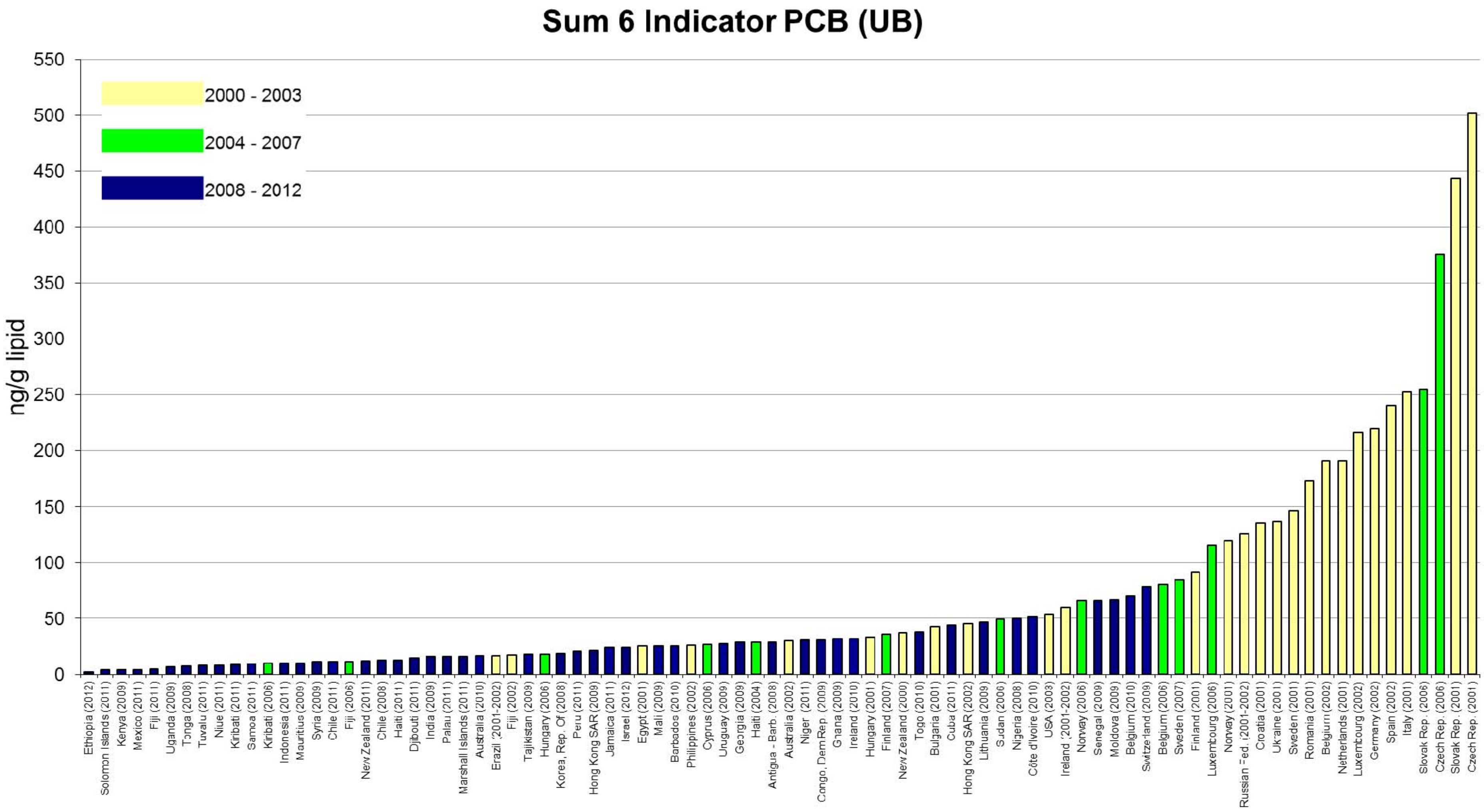

Figure 8: Concentrations of indicator PCB in human milk: survey results over the period 2000-2012

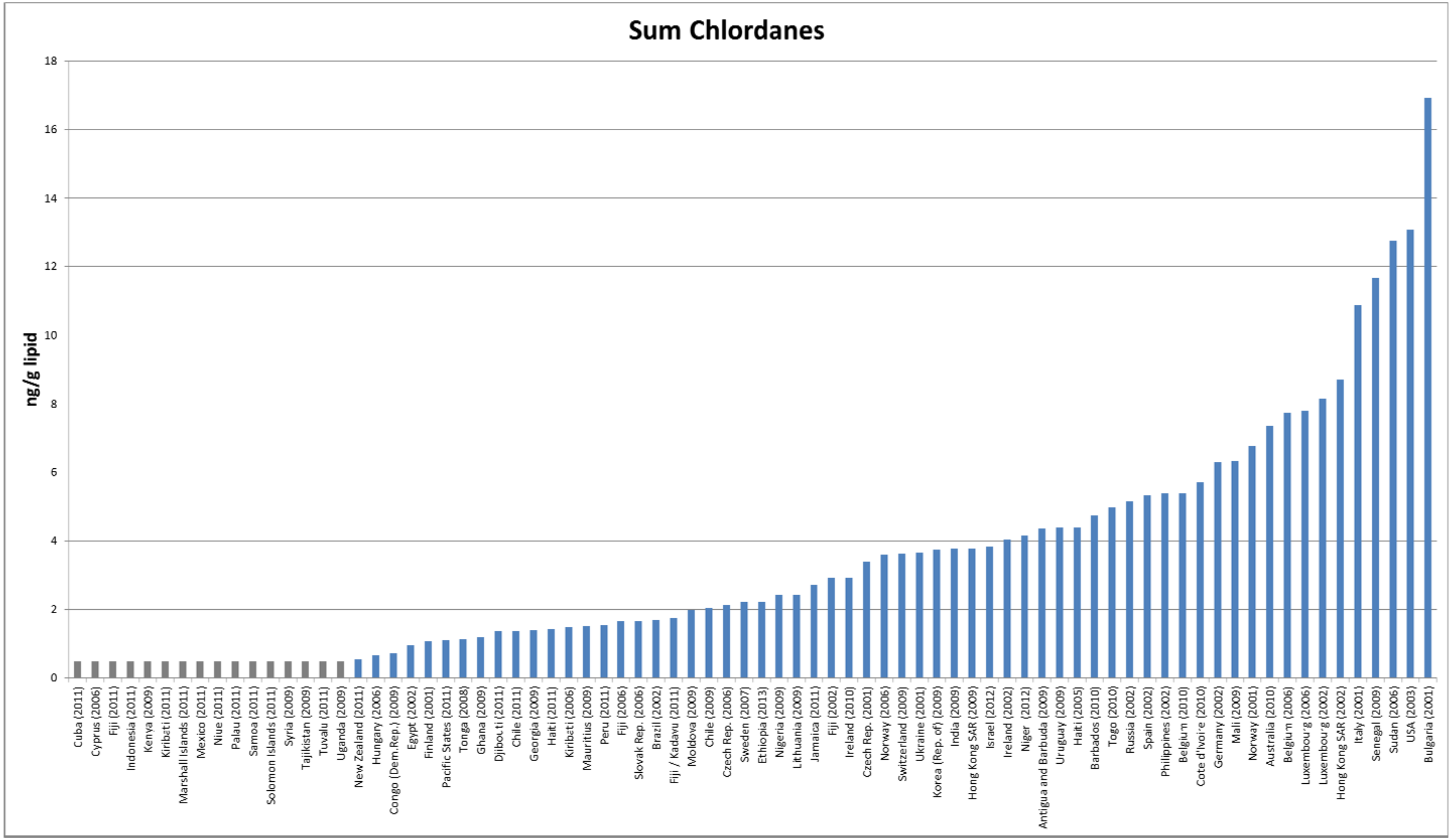

Figure 9: Concentrations of chlordane in human milk: survey results over the period 2000-2012

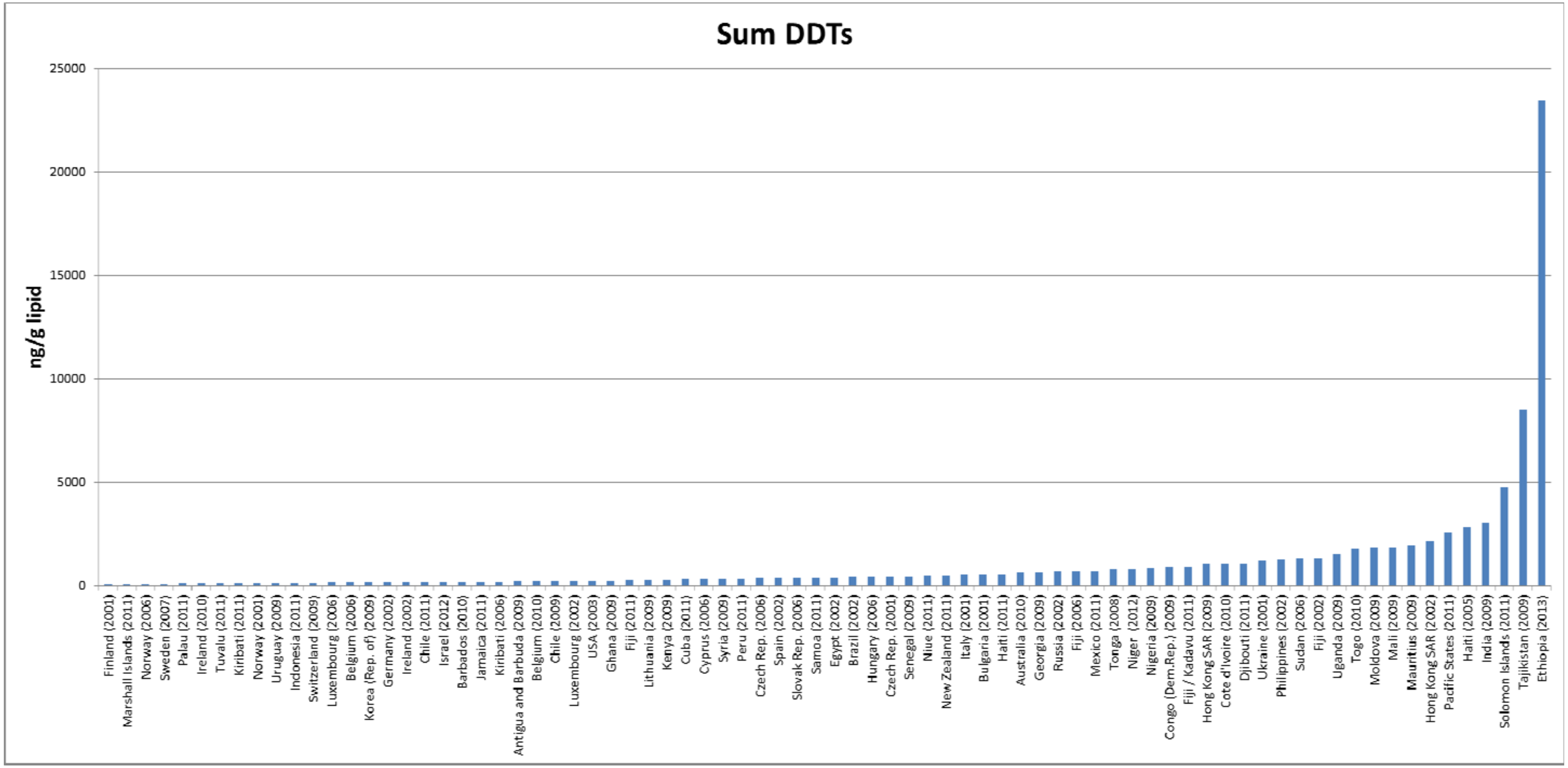

Figure 10: Concentrations of DDT in human milk: survey results over the period 2000-2012

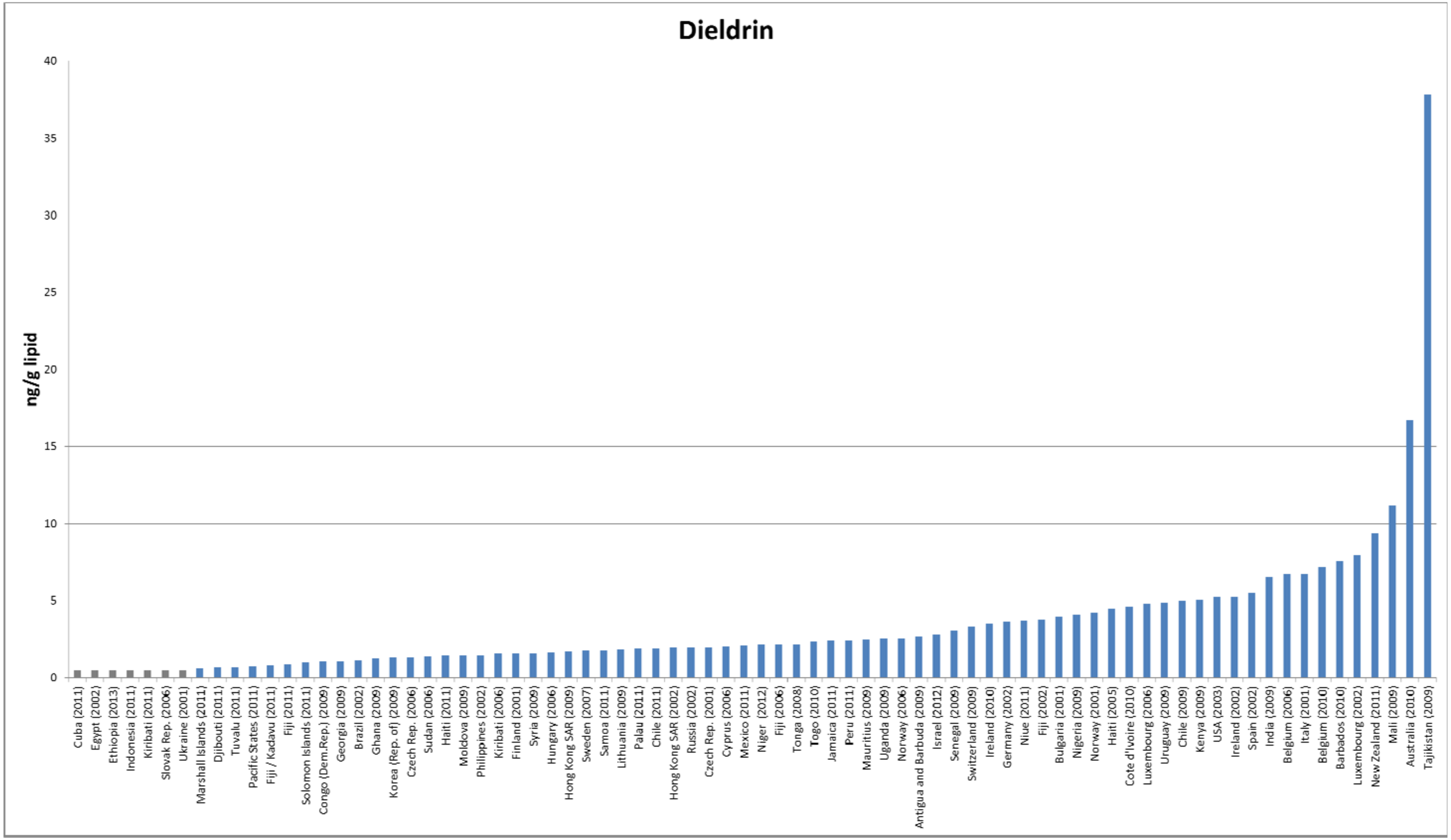

Figure 11: Concentrations of dieldrin in human milk: survey results over the period 2000-2012

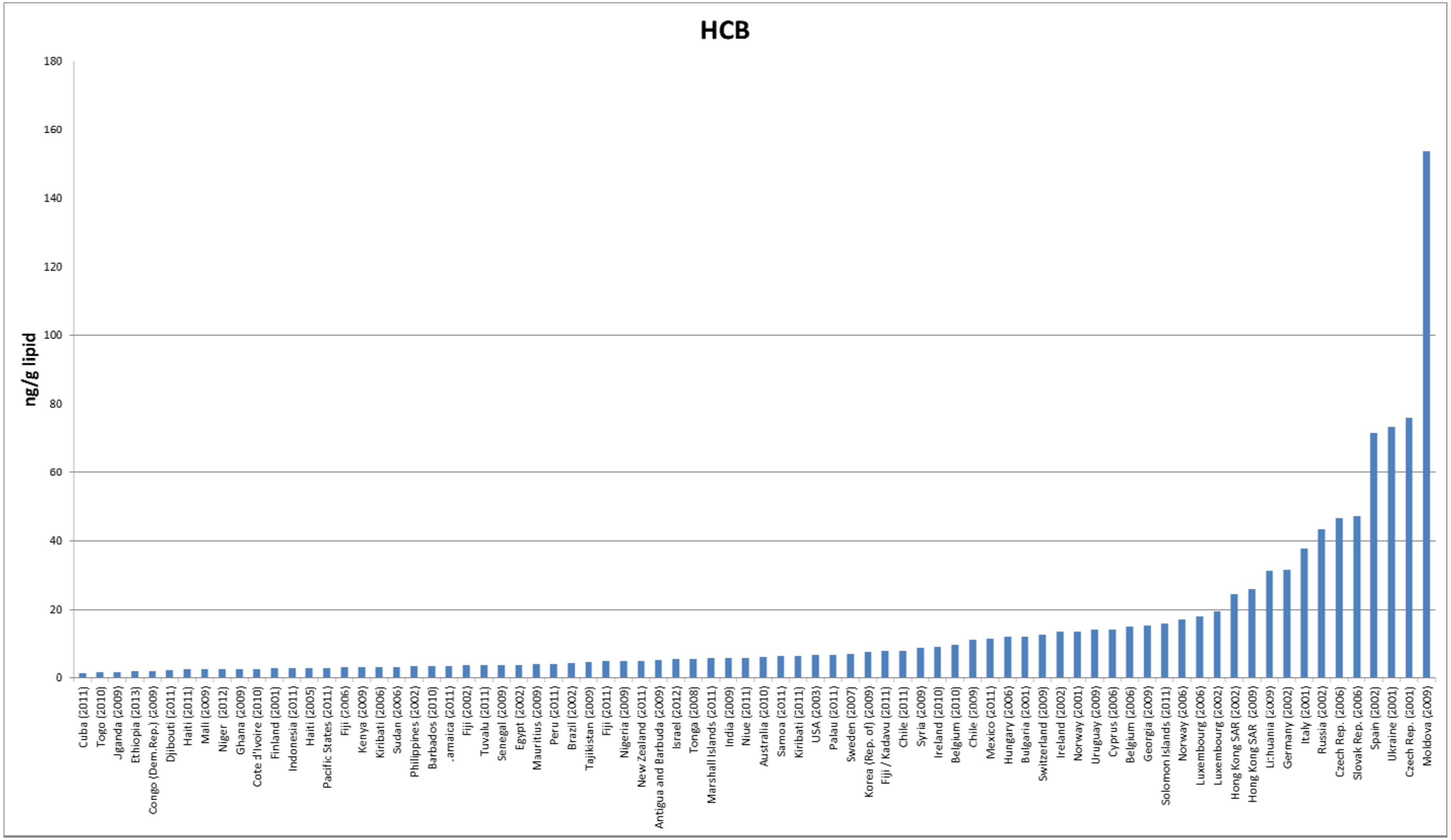

Figure 12: Concentrations of hexachlorobenzene in human milk: survey results over the period 2000-2012

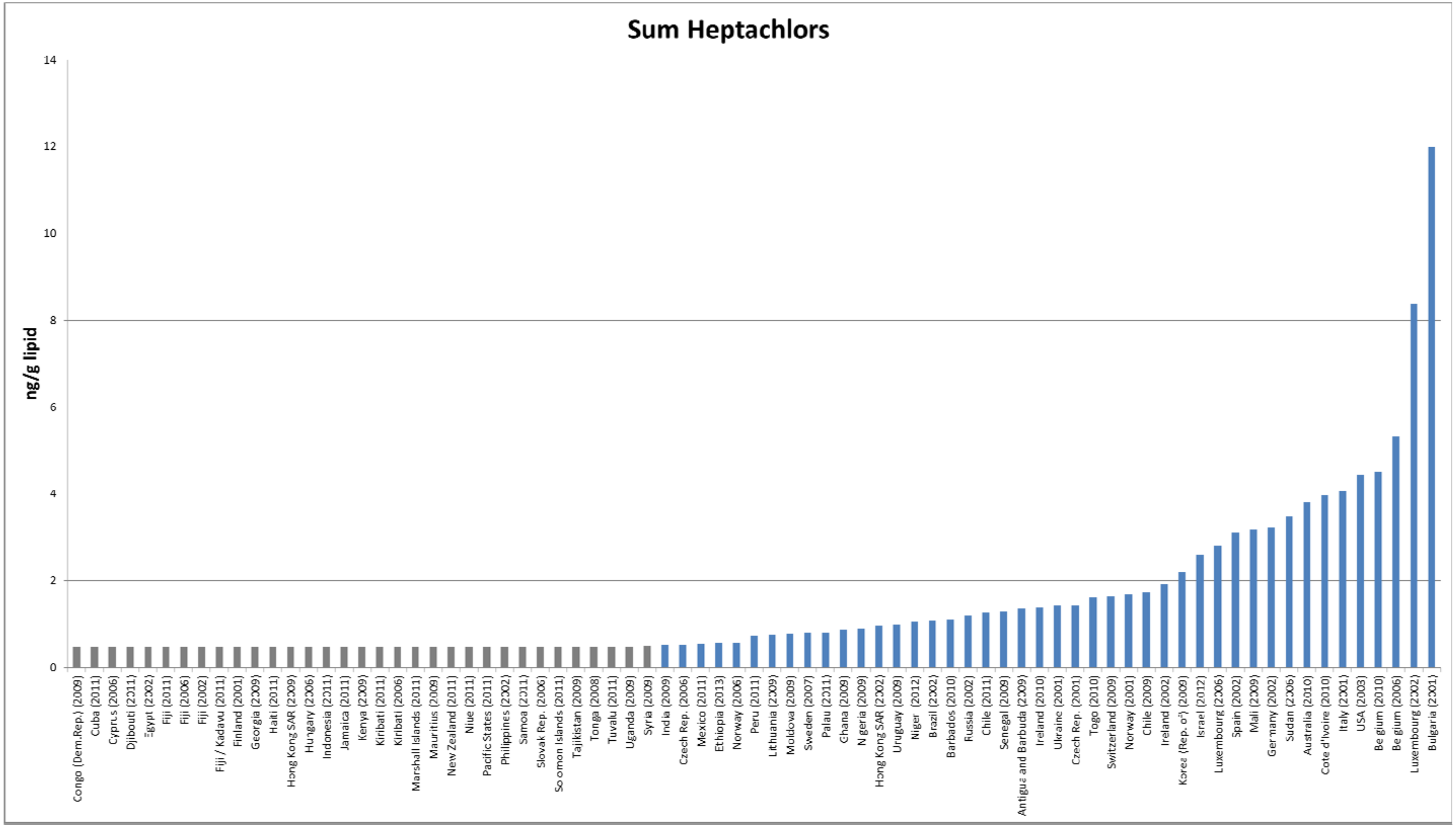

Figure 13: Concentrations of heptachlor in human milk: survey results over the period 2000-2012

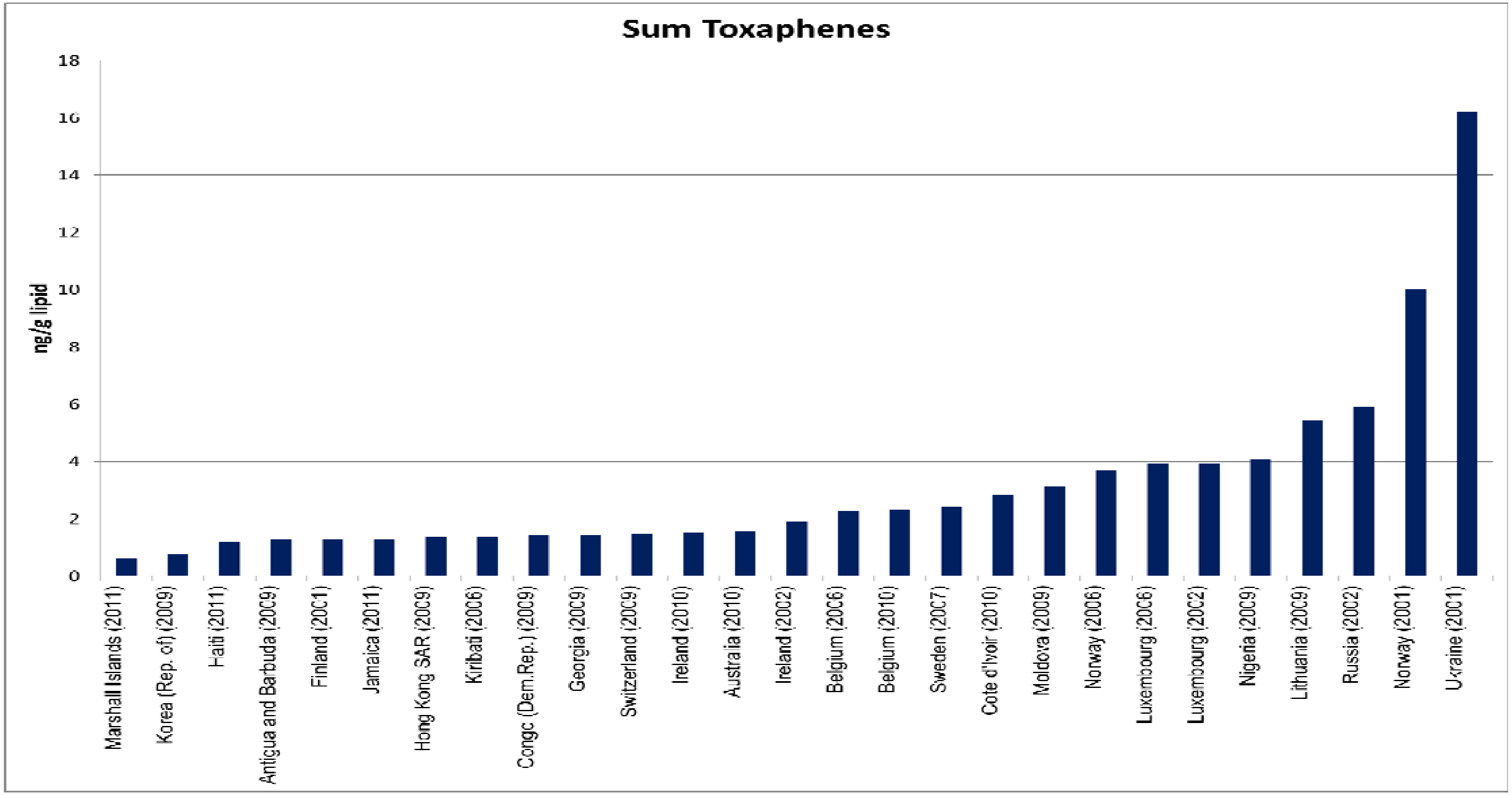

Figure 14: Concentrations of toxaphene in human milk: survey results over the period 2000-2012

Levels below LOQ (0,5 ng/g lipid) have been registered by: Barbados, Brazil, Bulgaria, Chile, Chile, Cuba, Cyprus, Czech Rep., Czech Rep., Djibouti, Egypt, Ethiopia, Fiji, Fiji, Fiji, Fiji / Kadavu, Germany, Ghana, Haiti, Hong Kong SAR, Hungary, India, Indonesia, Israel, Italy, Kenya, Kiribati, Mali, Mauritius, Mexico, New Zealand, Niger , Niue, Pacific States, Palau, Peru, Philippines, Samoa, Senegal, Slovak Rep., Solomon Islands, Spain, Sudan, Syria, Tajikistan, Togo, Tonga, Tuvalu, Uganda, Uruguay, USA

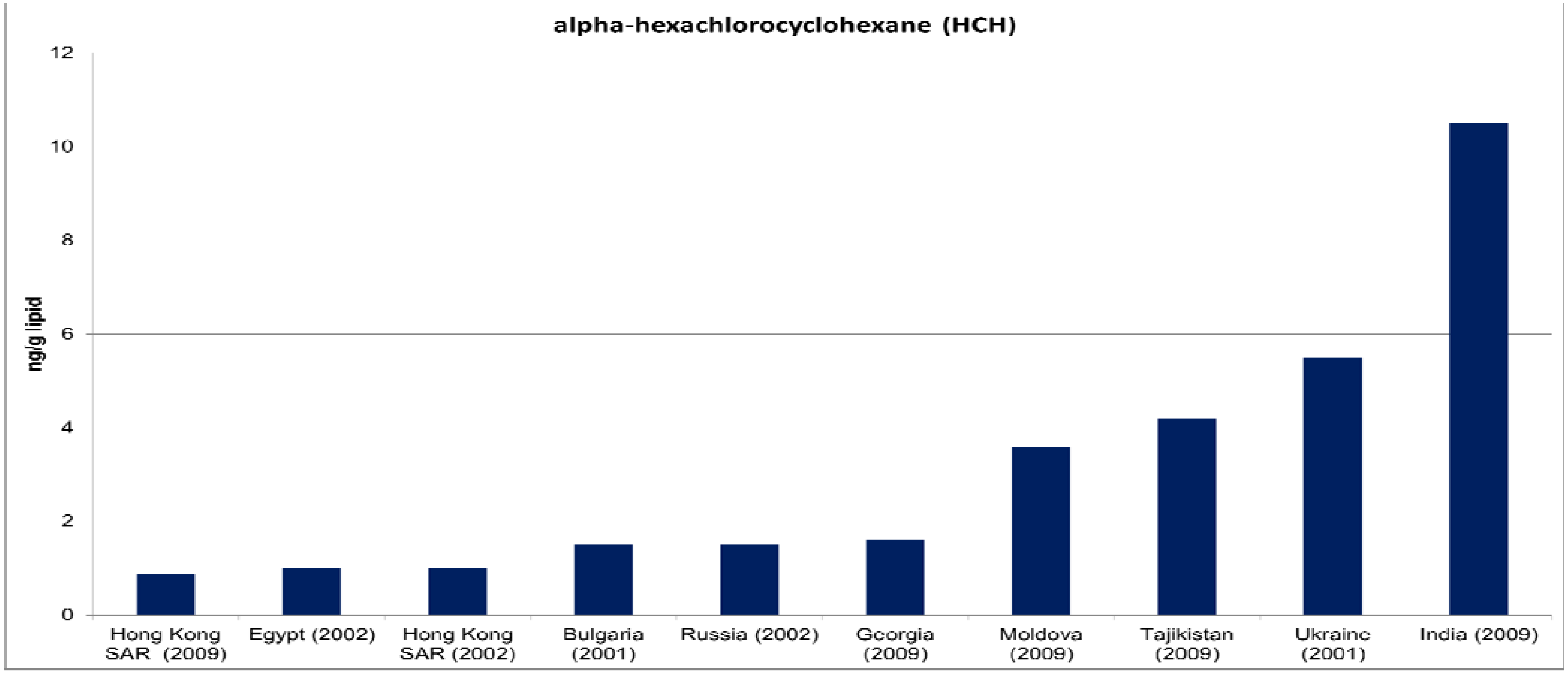

Figure 15: Concentrations of alpha-hexachlorocyclohexane in human milk: survey results over the period 2000-2012

Levels below LOQ (0,5 ng/g lipid) have been registered by: Antigua and Barbuda, Australia, Barbados, Belgium, Belgium, Brazil, Chile, Chile, Congo (Dem.Rep.), Cote d'Ivoire, Cuba, Cyprus, Czech Rep., Czech Rep., Djibouti, Ethiopia, Fiji, Fiji, Fiji, Fiji / Kadavu, Finland, Germany, Ghana, Haiti, Haiti, Hungary, Indonesia, Ireland, Ireland, Israel, Italy, Jamaica, Kenya, Kiribati, Kiribati, Korea (Rep. of), Lithuania, Luxembourg, Luxembourg, Mali, Marshall Islands, Mauritius, Mexico, New Zealand, Niger , Nigeria, Niue, Norway, Norway, Pacific States, Palau, Peru, Philippines, Samoa, Senegal, Slovak Rep., Solomon Islands, Spain, Sudan, Sweden, Switzerland, Syria, Togo, Tonga, Tuvalu, Uganda, Uruguay, USA

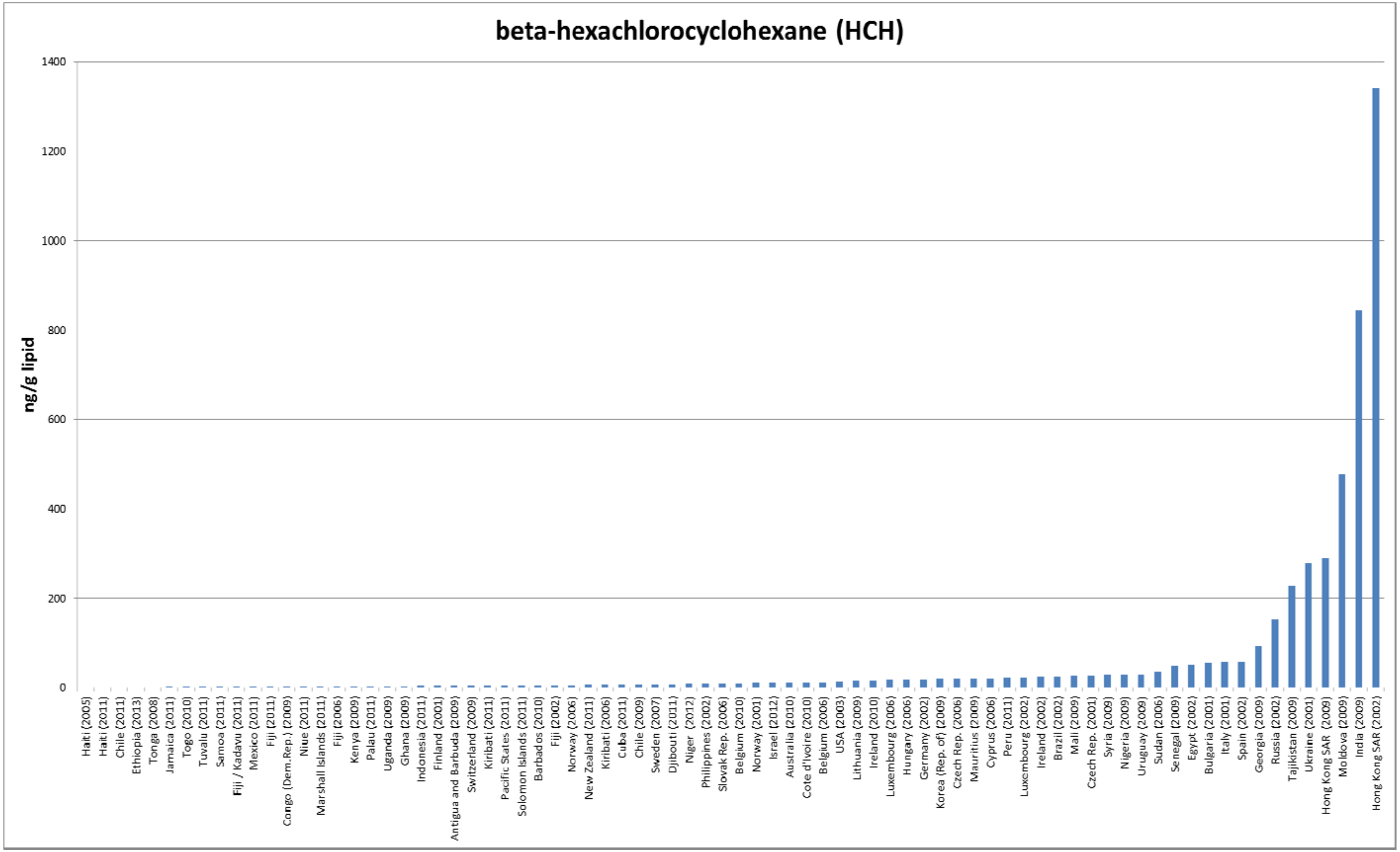

Figure 16: Concentrations of beta-hexachlorocyclohexane in human milk: survey results over the period 2000-2012

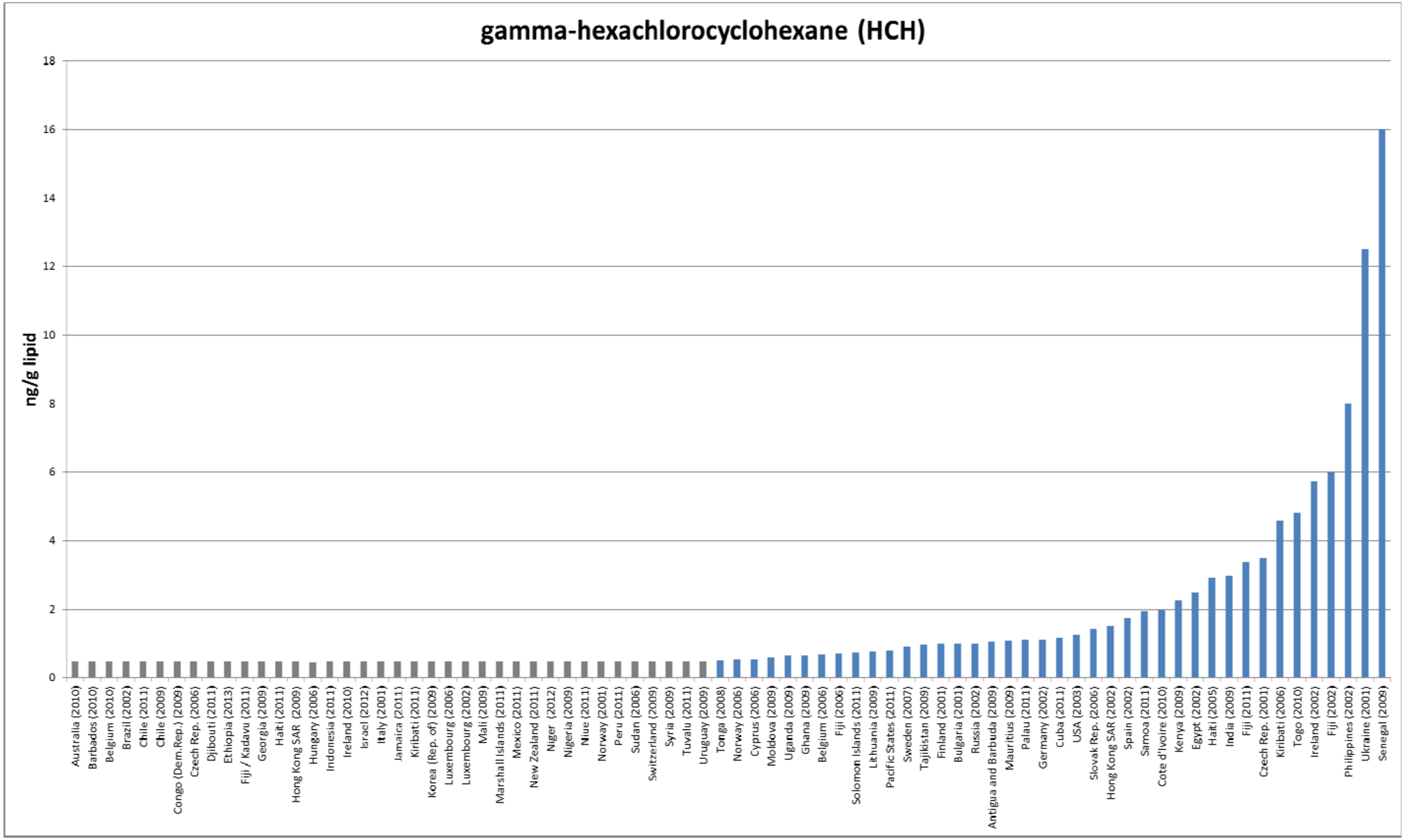

Figure 17: Concentrations of gamma-hexachlorocyclohexane in human milk: survey results over the period 2000-2012

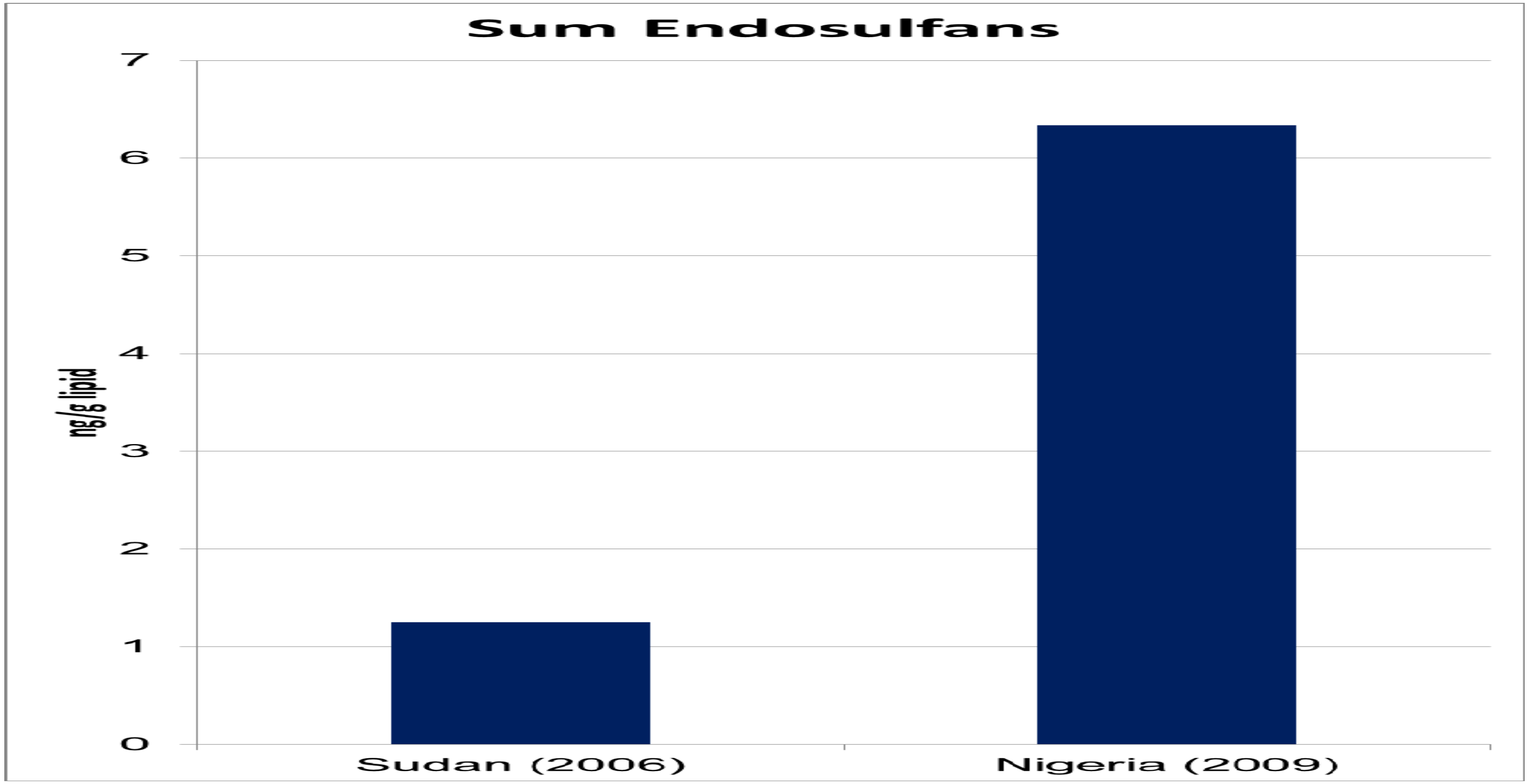

Figure 18: Concentrations of endosulfan in human milk (archived samples): survey results over the period 2008-2012

Levels below LOQ (0,5 ng/g lipid) have been registered by: Antigua and Barbuda, Australia, Barbados, Belgium, Belgium, Brazil, Bulgaria, Chile, Chile, Congo (Dem. Rep.), Cote d'Ivoire, Cuba, Cyprus, Czech Rep., Czech Rep., Djibouti, Egypt, Ethiopia, Fiji, Fiji, Fiji, Fiji / Kadavu, Finland, Georgia, Germany, Ghana, Haiti, Hong Kong SAR, Hong Kong SAR, Hungary, India, Indonesia, Ireland, Ireland, Israel, Italy, Jamaica, Kenya, Kiribati, Kiribati, Korea (Rep. of), Lithuania, Luxembourg, Luxembourg, Mali, Marshall Islands, Mauritius, Mexico, Moldova, New Zealand, Niger, Niue, Norway, Norway, Pacific States, Palau, Peru, Philippines, Russia, Samoa, Senegal, Slovak Rep., Solomon Islands, Spain, Sweden, Switzerland, Syria, Tajikistan, Togo, Tonga, Tuvalu, Uganda, Ukraine, Uruguay, USA

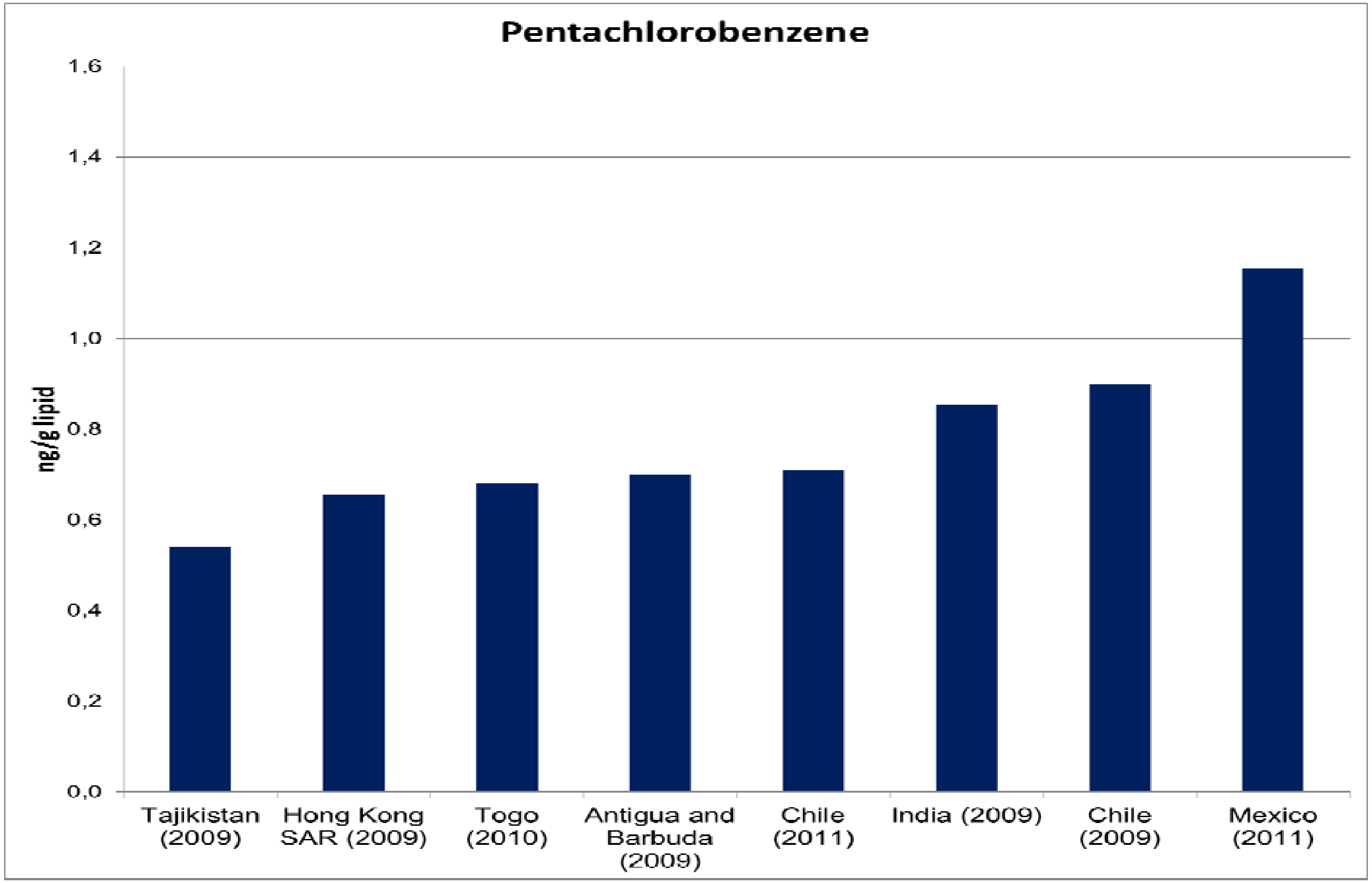

Figure 19: Concentrations of pentachlorobenzene in human milk (archived samples): survey results over the period 2008-2012

Levels below LOQ (0,5 ng/g lipid) have been registered by: Australia, Barbados, Belgium, Congo (Dem.Rep.) Cote d'Ivoire, Cuba, Djibouti, Ethiopia, Fiji, Fiji / Kadavu, Georgia, Ghana, Haiti, Indonesia, Ireland, Israel, Jamaica, Kenya, Kiribati, Lithuania, Mali, Marshall Islands, Mauritius, New Zealand, Niger, Nigeria, Pacific States, Peru, Samoa, Switzerland, Syria, Tuvalu, Uganda, Uruguay.

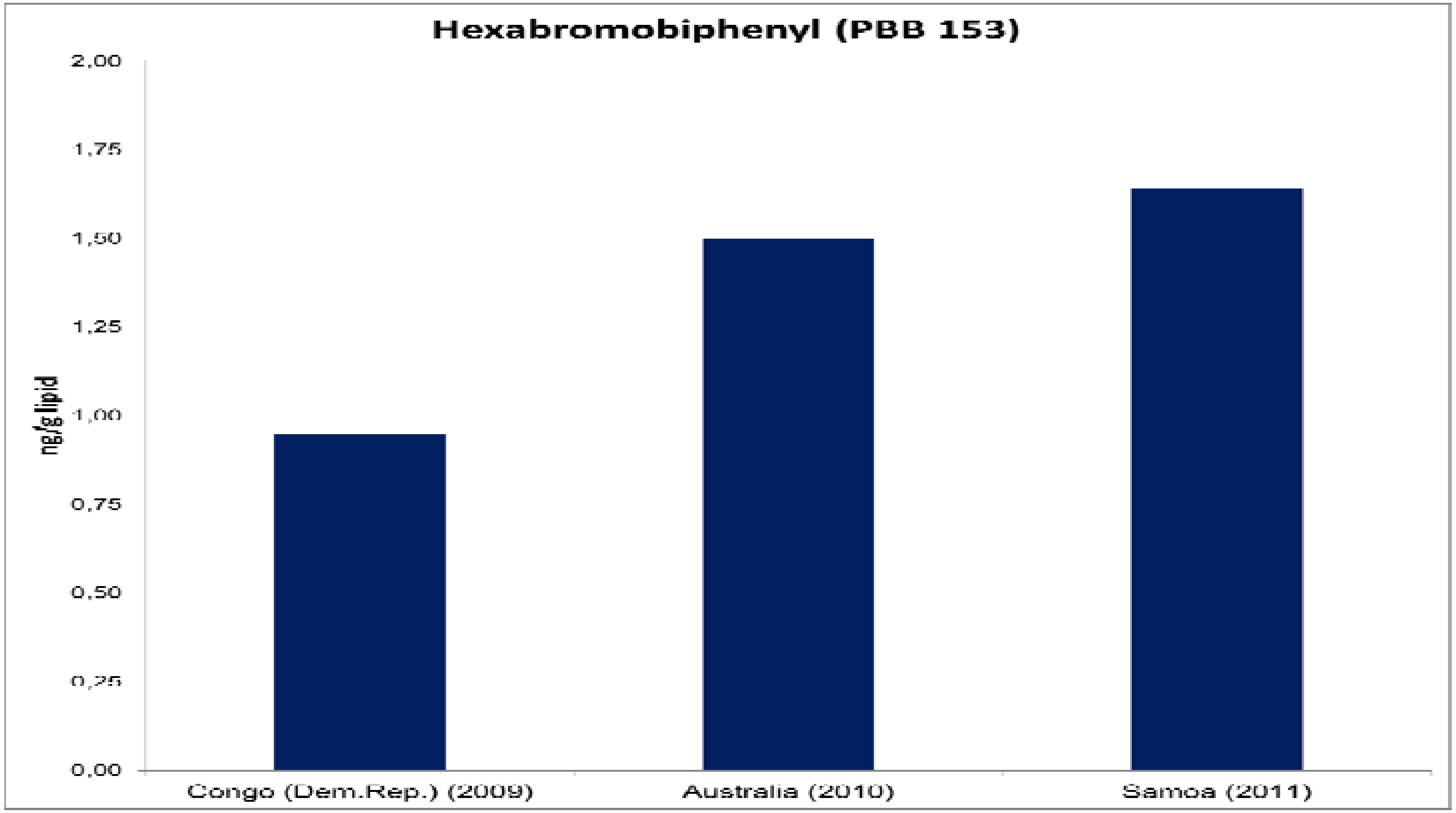

Figure 20: Concentrations of hexabromobiphenyl in human milk (archived samples): survey results over the period 2008-2012

Levels below LOQ (0,5 ng/g lipid) have been registered by: Barbados, Cuba, Djibouti, Ethiopia, Fiji, Fiji / Kadavu, Ghana, Indonesia, Israel, Kenya, Kiribati, Mali, Mauritius, New Zealand, Niger , Pacific States, Peru, Syria, Tuvalu, Uganda, Uruguay, Marshall Islands, Haiti, Jamaica, Georgia, Switzerland, Ireland, Belgium, Cote d'Ivoire, Nigeria, Lithuania, Tajikistan, Hong Kong SAR, Togo, Antigua and Barbuda, Chile, India, Chile, Mexico

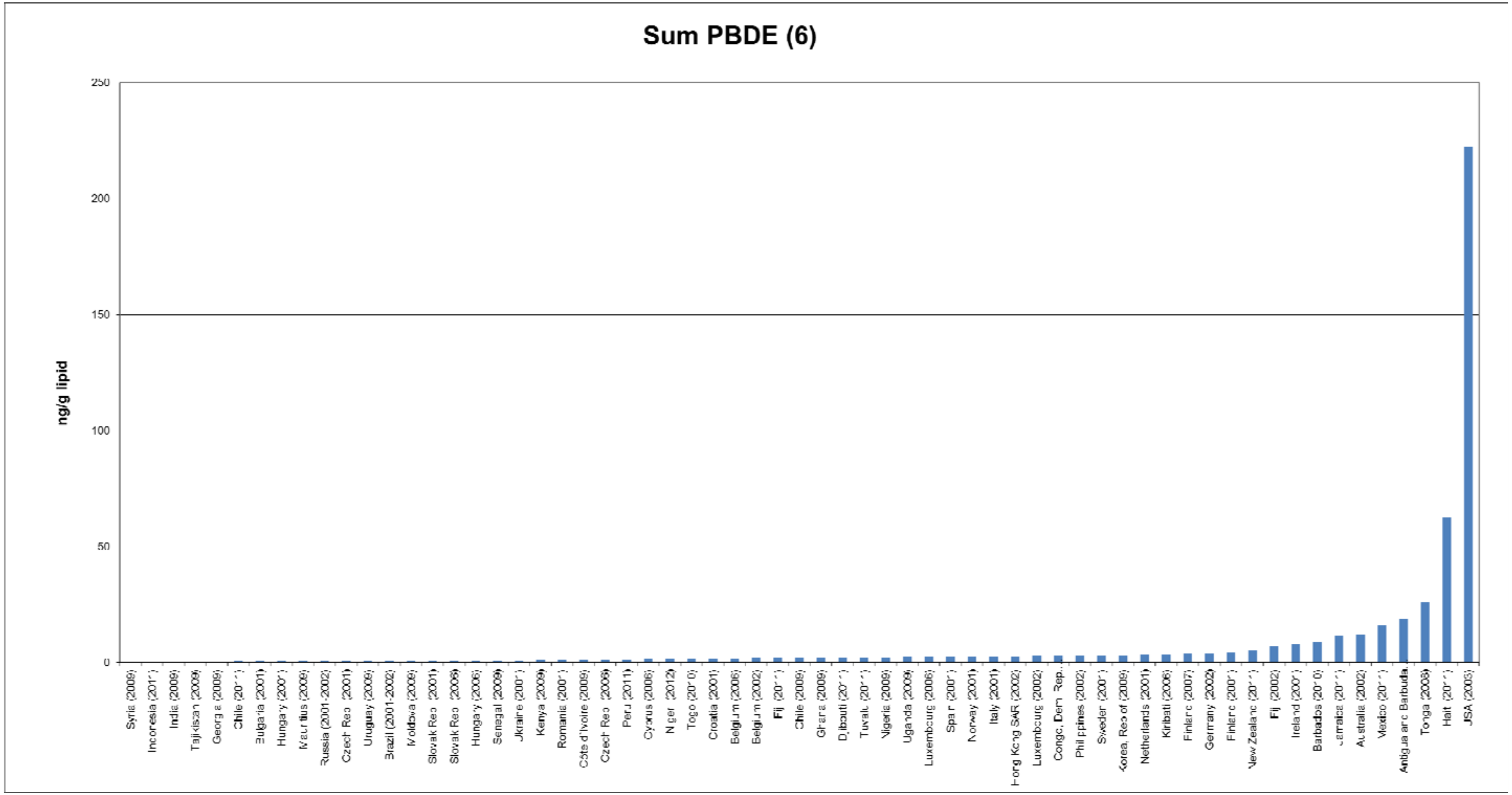

Figure 21: Concentrations of polybrominated diphenyl ethers in human milk: survey results over the period 2000-2012

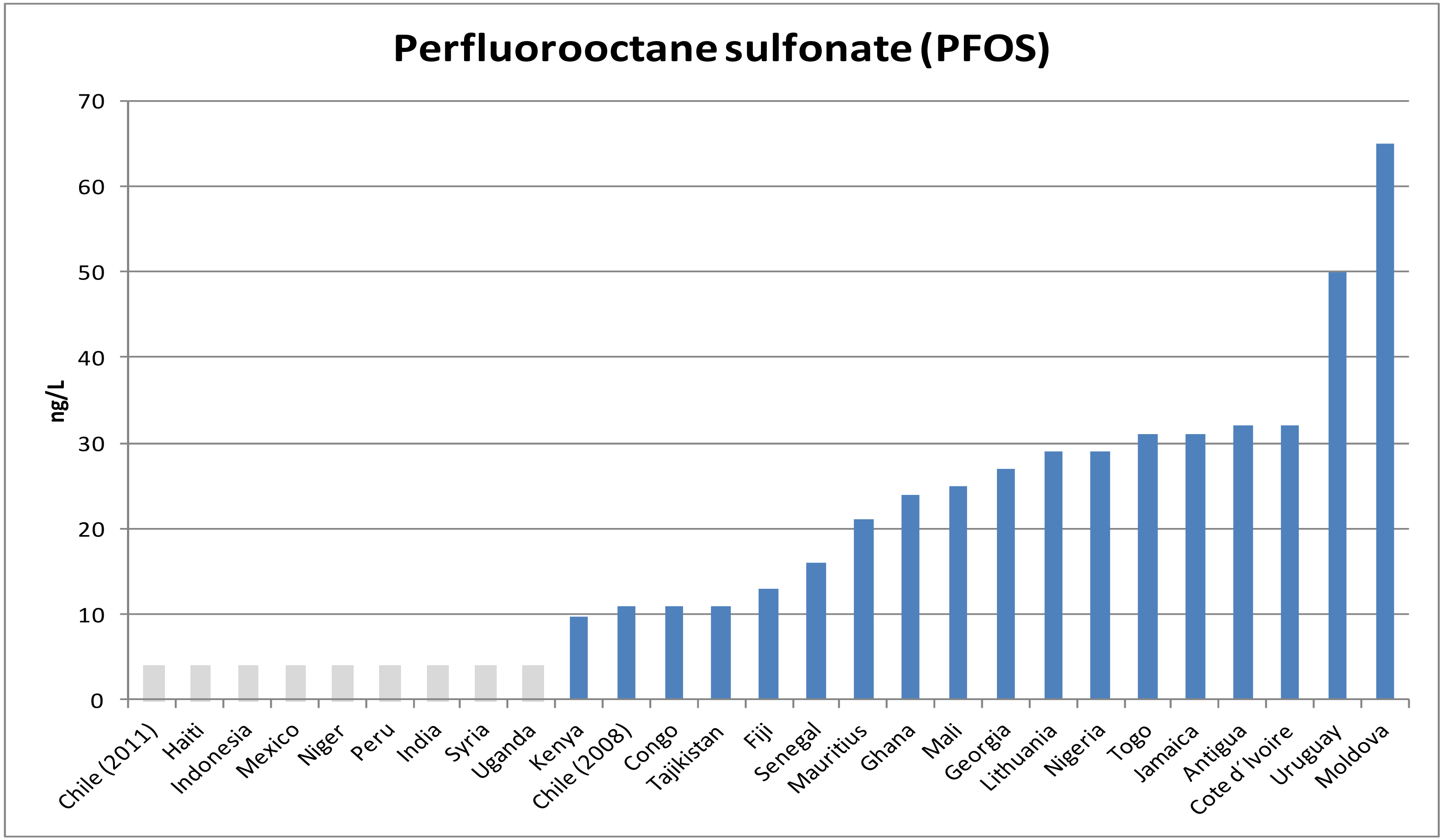

Figure 22: Concentrations of perfluorooctane sulfonic acid in human milk (archived samples): survey results over the period 2008-2012