



**Final Results Workshop for the UNEP/GEF project
 “Establishing the Tools and Methods to Include the Nine New POPs into Global Monitoring Plan”
 and Inception Workshop for the UNEP/GEF project
 “Continuing Regional Support for the POPs Global Monitoring Plan
 under the Stockholm Convention in the Africa Region”
 Accra, Ghana, 6 – 8 July, 2016.**

Human milk surveys: the role of the UNEP/WHO reference laboratory

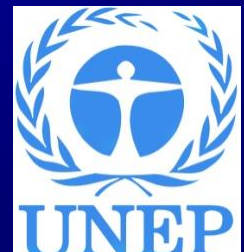
Ralf Lippold and Rainer Malisch

State Institute for Chemical and Veterinary Analysis of Food, Freiburg, Germany

WHO / UNEP Reference Laboratory

EU Reference Laboratory for Dioxins and PCBs in Feed and Food

EURL for Pesticides in Food of Animal Origin





Human milk

**Pillars for
reliability of
results**

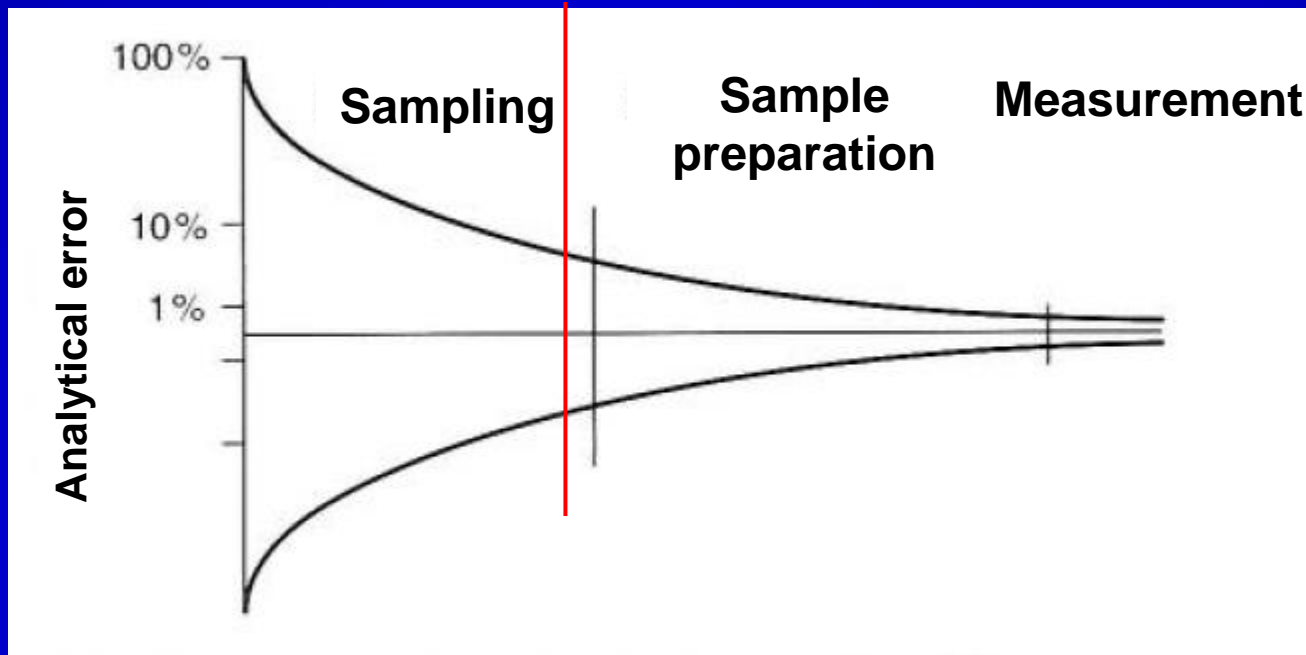
**Representative
sampling**

**Reliability of
analytical
results**

Sampling

Sampling very critical part of whole analytical procedure

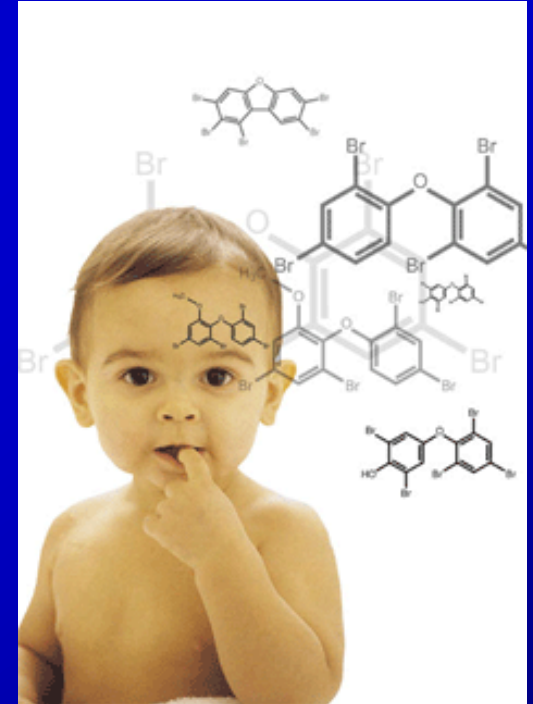
- Samples shall be representative (*examples: soil; eggs*)
- Prevention of **contamination** of sample or container during sampling
- Prevention of **change of concentrations**, change of matrix influencing the results



Human tissues as indicators of human exposure to POPs

Human samples as suitable indicators for bioaccumulation of POPs :

- ✓ **Mother's milk**
- ✓ **Blood**
- ✓ **Adipose tissues**



Comparable results on fat basis –

Possible problem: correct determination of fat

Mother's milk as tissue for exposure monitoring

Advantage of mother's milk samples

- ✓ non-invasive mean to estimate the exposure
- ✓ Less toxicological concern (AIDS virus, hepatitis) than for human blood

Mother's milk for exposure monitoring

⇒ Individual samples

➤ for differentiation within a country

⇒ Representative pooled (mixed) samples

➤ to identify priority POPs and

➤ to follow time trends in countries

Mother's milk for exposure monitoring



**UNEP-coordinated Survey of Mothers'
Milk for Persistent Organic Pollutants**

**Guidelines for Organization, Sampling and
Analysis**

**Chemicals Branch
United Nations Environment Programme (UNEP)**

July 2012



**UNEP-coordinated Survey of Mothers'
Milk for Persistent Organic Pollutants**

**Annexes
Guidelines for Organization, Sampling and
Analysis**

**Chemicals Branch
United Nations Environment Programme (UNEP)**

July 2012

Prepared by: Dr. Karin Malisch and Dr. Heidelore Fiedler

Mother's milk for exposure monitoring

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- Mothers should have **first child** (*primiparae*)
- Be **under 30 years**
- Mother and child be apparently **healthy**
- Breastfeeding only **one child** (i.e. not twins)
- Have resided in the represented area (country) **> 10 years**
- **Exclusion of contaminated areas**
- **Sample collection within 3 to 8 weeks of delivery**

Advantage of pooled (mixed) mother's milk samples

- ✓ Possible to get a rough estimate on the exposure in different regions of the world with only very few samples
- (+) **Cost-effective** and useful non-invasive mean to estimate the overall exposure of a local population
- (-) Disadvantage: Lack of information about individuals

Basic Principles for Reliability and Comparability of Results (1)

Standardized protocol for sampling

- **Collection of human milk from representative individuals** (*since 2007: n = 50*)
- **Preparation of one** pooled (=mixed) sample representative for a country / region

Basic Principles for Reliability and Comparability of Results (2)

Analytical quality control:

Different concepts for

1. Individual samples:

analysed by laboratory selected by National Coordinator

2. pooled samples:

analysed by Reference Laboratory

WHO protocol (2008) /UNEP guidelines (2012) – 1a

- ✓ For statistically reliable data: appropriate minimum number of individual donors (50) is recommended for each country.
- ✓ Some flexibility may be necessary for countries with small populations and/or low birth rates.
- ✓ Power of the survey can be increased by the inclusion of more than 50 individual samples and is encouraged.

WHO protocol (2008) /UNEP guidelines (2012) – 1b

- ✓ In particular, countries with populations greater than 50 million should include at least one additional participant per one million population over 50 million.
- ✓ Countries with populations well over 50 million (or with sufficient resources) are encouraged to prepare a second pooled sample (or more) if feasible.

WHO protocol (2008) /UNEP guidelines (2012) - 2

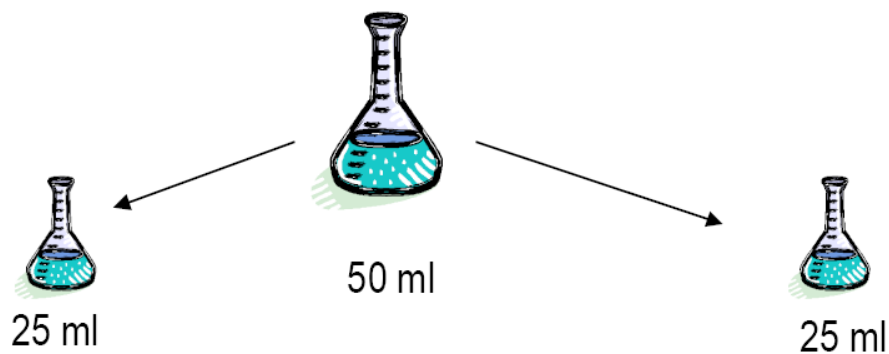
- ✓ **Responsibilities of the National Coordinator:**
number of samples can provide a sufficient statistical base to allow scientifically valid assessments of changes in levels of POPs over time.

(for time trends necessary: sampling of comparable cohorts over time, if more than 1 pooled sample prepared)

Sample preparation scheme (1)

- **Collection of 50 individual samples**
- **Preparation of**
 - **individual samples for analysis of basic POPs by country**
 - **pooled (mixed) samples (analysis by Reference Laboratory)**

1. Collection of 50 individual samples of 50 ml each.
Options for the collection of the individual samples:
 - ✓ if possible, in one collection, or
 - ✓ in portions over time (e.g. on several days), with preservation of the collected portions by freezing
2. These 50 ml have to be split into two portions of 25 ml each:



Individual samples for analysis
by country for basic POPs

Pooled sample (prepared of 25 ml of
each of the 50 individual samples)

Sample preparation scheme (2)

Preparation of individual samples for analysis of basic POPs by country and of pooled (mixed) samples



50 ml



25 ml



take 25 ml into 2000 ml bottle (50 * 25 ml ea = 1250 ml)



Send the 2000 ml bottle with frozen pooled samples to WHO/UNEP Reference Lab



Individual samples for analysis by country for basic POPs

For (deep-frozen) storage in and analysis by country. If no analysis in country possible and no storage capacity available, contact UNEP.

Sample preparation scheme (3)

Before taking an aliquot, shake intensely at room temperature and then take the aliquot immediately.

Options:

- Taking of 25 ml aliquot directly after collection of 50 ml sample in one collection at room temperature, if possible at place of collection (without freezing before aliquotation)
- Taking of 25 ml aliquot after thawing to room temperature at appropriate location, if samples are frozen.

➤ Important:

Storage and shipment of all samples **deep-frozen**.

Stabilization of human milk samples with dichromate

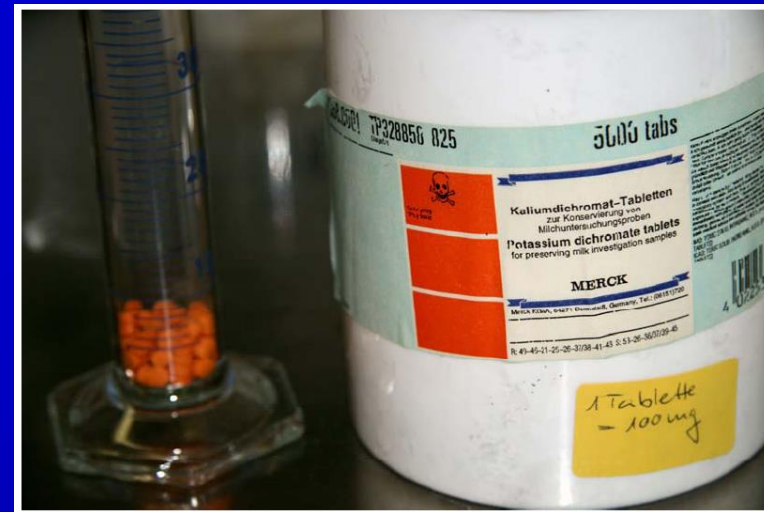
If refrigeration not available: Addition of dichromate to milk: 0.1 %
(140 mg potassium dichromate, containing about 100 mg dichromate, to 100 ml milk)
absolute accuracy is not important: finally an excess of dichromate in the milk (visible as yellow colour) which will be reduced to (green) Cr (III) before analysis.

Easiest: dichromate tablets

Merck "Kaliumdichromat-Tabletten zur Konservierung von Milchuntersuchungsproben" (potassium dichromate tablets for preservation of milk samples for analysis), 97 to 107 mg per tablet containing 32 - 24 mg dichromate per tablet.

0.1 % is equivalent to 3 tablets (= 100 mg dichromate) per 100 ml sample.

Very comfortable, avoids irritant reactions otherwise easily caused by handling of pure potassium dichromate powder



Arnold Schecter, Marian Pavuka, Olaf Pöpke and Rainer Malisch
Chemosphere 57 (2004) 1-7

The use of potassium dichromate and ethyl alcohol as blood preservatives for analysis of organochlorine contaminants

Comment to collection of samples

Respect the requested amounts:

- **Minimum amount: 50 ml / individual sample**
- **Pooled sample: 1250 ml**

Analytical quality control for pooled samples

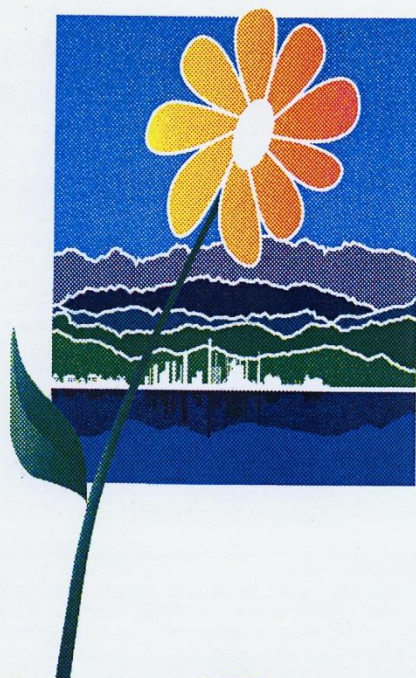
WHO-coordinated exposure studies on the levels of PCBs, PCDDs and PCDFs in human milk

1st Round	1987-1988	WHO-EURO	12 countries
2nd Round	1992-1993	WHO-EUR	19 countries

Preparation of next round (3rd round, start: 2000)

Interlaboratory Quality
Assessment of Levels of PCBs,
PCDDs and PCDFs in Human
Milk and Blood Plasma

Fourth Round of WHO-coordinated study



WHO European Centre for Environment and Health
Bilthoven

WHO quality assessment of PCB and PCDD/F analysis

Objectives of the study:

- **To assess the analytical quality of the participating laboratories based on**
 - ✓ **a statistical evaluation of between-laboratory comparability and**
 - ✓ **within-laboratory medium-term reliability of the analytical data**
- **To identify laboratories whose results can be accepted by WHO for exposure assessment studies**



CVUA Freiburg

(State Institute for Chemical and Veterinary Analysis of Food)



WHO/UNEP Reference Laboratory for dioxins, PCBs and halogenated pesticides (POPs) in human milk



EU Reference Laboratory (EU-RL) for dioxins and PCBs in feed and food

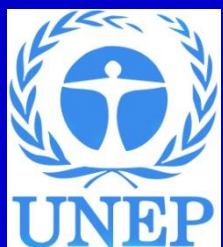


EU-RL for pesticides in food of animal origin and commodities with high fat content



WHO/UNEP-coordinated exposure studies on levels of PCBs, PCDDs and PCDFs in human milk

1st Round	1987-1988	WHO-EURO	12 countries
2nd Round	1992-1993	WHO-EUR	19 countries
3rd Round	2000-2003	WHO-EUR	26 countries
4th Round	2004-2007	WHO/UNEP	13 countries
5th Round	2008-2012	WHO/UNEP	49 countries
	2012-2015	UNEP	12 countries



Participating countries

3rd – 5th round (2000 – 2012)

Africa	Year	America	Year	Asia	Year	Australia, New Zealand, Pacific Islands	Year	Europe	Year
Congo, Dem.Rep.	2009	Antigua and Barbuda	2008	Hong Kong SAR	2002, 2009	Australia	2002, 2010	Belgium *)	2002, 2006, 2010
Côte d'Ivoire	2010	Barbados	2010	India	2009	Fiji	2002, 2006, 2011	Bulgaria	2001
Djibouti	2011	Brazil	2001-2002, 2012	Indonesia	2011	Kiribati	2006, 2011	Croatia	2001
Egypt	2001	Chile	2008, 2011	Israel	2012	Marshall Islands	2011	Cyprus	2006
Ethiopia	2012	Cuba	2011	Korea, Rep.	2008	New Zealand	2000, 2011	Czech Rep.	2001, 2006
Ghana	2009	Haiti	2004, 2011	Philippines	2002	Niue	2011	Finland	2001, 2007
Kenya	2009	Jamaica	2011	Syria	2009	Palau	2011	Georgia	2009
Mali	2009	Mexico	2011	Tajikistan	2009	Samoa	2011	Germany	2002
Mauritius	2009	Peru	2011	<i>total no:</i>	8	Solomon Islands	2011	Hungary	2001, 2006
Niger	2011	Suriname	2012	<i>no of country/year entries:</i>	9	Tonga	2008	Ireland	2001-2002, 2010
Nigeria	2008	Uruguay	2009			Tuvalu	2011	Italy	2001
Senegal	2009	USA	2003			<i>total no:</i>	11	Lithuania	2009
Sudan	2006	<i>total no:</i>	12			<i>no of country/year entries:</i>	16	Luxembourg	2002, 2006
Togo	2010	<i>no of country/year entries:</i>	15					Moldova	2009
Uganda	2009							Norway	2001, 2006
<i>total no:</i>	15							Romania	2001
<i>no of country/year entries:</i>	15							Russian Fed.	2001-2002
								Slovak Rep.	2001, 2006
								Spain	2001
								Sweden	2001, 2007
								Switzerland	2009
								The Netherlands	2001
								Ukraine	2001
								<i>total no:</i>	23
								<i>no of country/year entries:</i>	33

Round 3: 2000 - 2003 (only)
Round 4: 2004 - 2007 (+ 3 in some cases)
Round 5: 2008 - 2012 (+ 3 and/or 4 in some cases)

total number of countries:	69
total number of country/year en	88

Study	Period	No of countries	No of pooled samples
3rd round	2000 - 2003	26	102
4th round	2004 - 2007	13	18
5th round	2008 - 2012	49	54
Sum	2000 - 2012	88	174

*) in 5th round, only Flanders region
total no: 23
no of country/year entries: 33

Quality control programme (1)

Accreditation according to

- **DIN EN 17025**

(general request for accreditation of official control laboratories according to EU law)

Quality control programme (2)

Validation:

- **Blank samples**
- **Various quality control samples**
- **Participation in proficiency tests**

Quality control programme (3)

Duplicate analysis of breast milk samples as “overlapping sandwich method” (2000 – 2003)

From 69 samples, 38 as duplicates and 5 as triplicates.

CV for repeated analysis:

- **2.3 % for WHO-PCDD/F-TEQ**
- **4.0 % for WHO-PCB-TEQ**

Advantage

**Comparable analytical performance
over long period (> 15 years)**

Selection of laboratories for individual samples

1. Capacity building: focus on quality control programmes

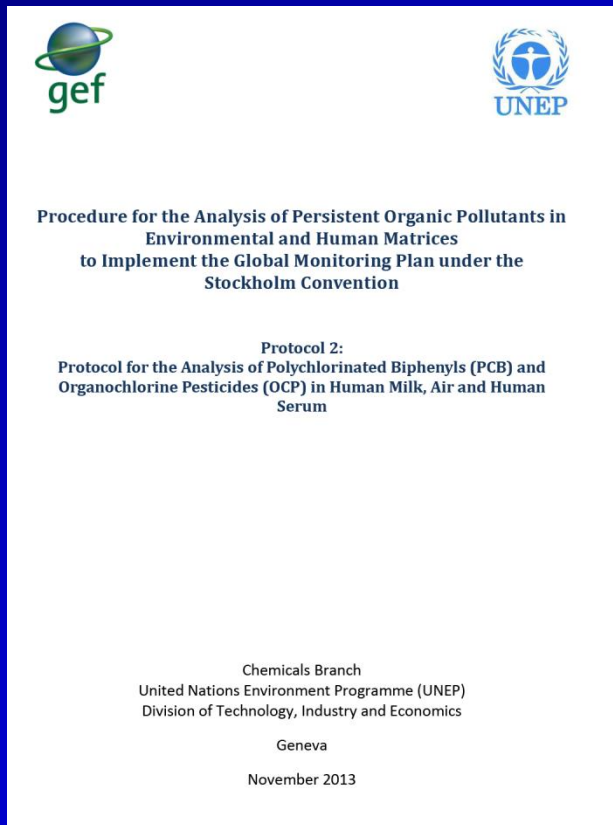
- **Blank samples**
- **Various quality control samples**
- **Participation in proficiency tests**

2. Contract laboratories:

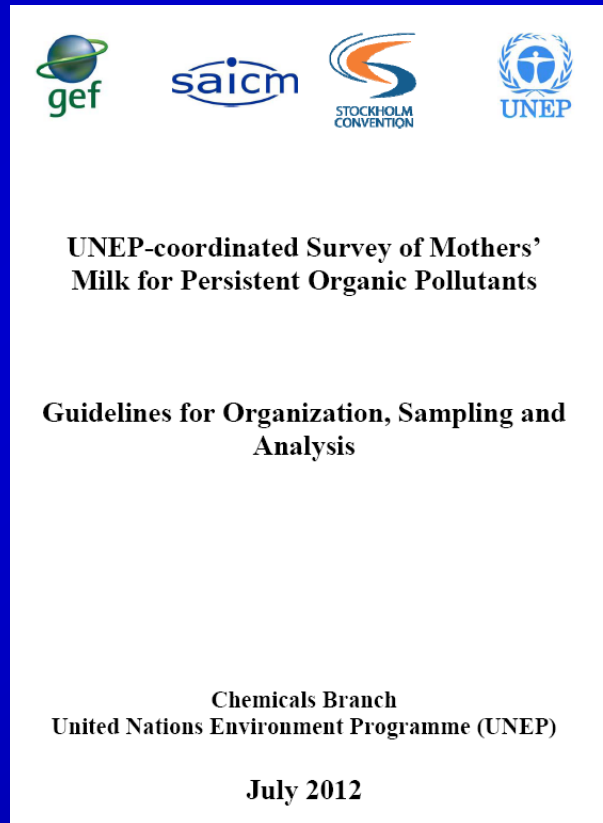
- **Accredited?**
- **Successful participation in proficiency tests?**

Harmonized methods – performance criteria

Two examples for established methods:



19 pages; air – human milk – human serum



p. 19 – 21 (basic POPs; PCDD/F+dl-PCBs)

Harmonized methods – performance criteria

Conclusion:

- Understand the methods and critical points
- validate, evaluate, validate ...
- meet the analytical performance criteria
(e.g. EU criteria for analysis of food and feed)

Project Cooperation Agreement (PCA) between UNEP and CVUA (2016 - 2019)

3 years project (2016 – 2019)

(planned according to state of play as of 01.06.2016)

- **Delivery of glassware containers
*by 31.12.2016***
- **Milk from donor mothers collected and
sent the pool sample to CVUA Freiburg
for POPs analysis *by 31.10.2017***
- **Analysis in pooled samples
*by 31.01.2019***

Project Cooperation Agreement (PCA) between UNEP and CVUA (2016 - 2019)

1. Preparation (cleaning) and shipment of glassware containers to countries according to UNEP project:

- 50 x 100 ml
- 1 x 2 l



Project Cooperation Agreement (PCA) between UNEP and CVUA (2016 - 2019)



Project Cooperation Agreement (PCA) between UNEP and CVUA (2016 - 2019)



Project Cooperation Agreement (PCA) between UNEP and CVUA (2016 - 2019)

3 years project (2016 – 2019)


- Delivery of glassware containers by 31.12.2016

➤ Requirement:


- ✓ Identification of participating countries
- ✓ nomination of national coordinators
- ✓ contact to CVUA Freiburg:
Dr. Karin Malisch
karin.malisch@cvuafr.bwl.de



Official letters to facilitate custom clearance



Chemisches und Veterinäruntersuchungsamt
Freiburg



World Health Organization

WHO/UNEP Reference Laboratory
For determination of Persistent Organic Pollutants (POPs) in human milk

Chemisches und Veterinäruntersuchungsamt Freiburg
Postfach 106462 • 79125 Freiburg

Address of Receiver: Freiburg, Phone: Contact: Dr. Karin Malisch, e-mail: Karin.Malisch@CVUAFFR.BWL.DE, reference: 5477.10-15 CRL-Dioxin

INVOICE 30/07/2010
Invoice No. 5477.10-15 006

Sender	WHO/UNEP-Reference Laboratory c/o State Institute for Chemical and Veterinary Analysis of Food Freiburg Karin Malisch
Address	Bissierstr. 5 D-79114 Freiburg
Phone No	+49 761 8855 109
Fax No	+49 761 855 100
Sender VAT#	
Receiver	
Address	
Phone No	Tel:593-2-2543588

Dienstgebäude der bearbeitenden Stelle:
Bissierstraße 5
79114 Freiburg
Trans-Line 3 (Händl) Haltestelle Bissierstraße

E-Mail:
poststelle@cvuafr.bwl.de

Sprechzeiten:
Mo-Do: 9^h - 11^h Uhr
14^h - 15^h Uhr
Fr: 9^h - 12^h Uhr


Bankverbindung:
Landesbankhaus Baden-Württemberg,
Baden-Württembergische Bank
(BLZ: 600 501 01), Kto. 746 95341 03

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←
incoming

Materials/
Sample

Outgoing
→



UNITED NATIONS ENVIRONMENT PROGRAMME
Programme des Nations Unies pour l'environnement
Programma de las Naciones Unidas para el Medio Ambiente
برنامج الأمم المتحدة للبيئة
聯合國環境保護計畫




Reference: Date: July 15, 2010

Subject: Statement of non-commercial nature of UN shipment to developing countries for capacity building and training purposes

To Whom It May Concern

Please note that UNEP has asked CVUA – the WHO Reference Laboratory in Freiburg, Germany, to prepare and ship to eligible countries and laboratories a box containing glassware and materials to collect national mothers' milk samples and prepare pooled samples for data generation in international context. This glassware and the methodology to collect the samples have been approved by the conference of the parties to the Stockholm Convention on persistent organic pollutants. The glassware is needed for the building of capacity for environmental monitoring of persistent organic pollutants (POPs) as part of the country's obligation under the convention.

The containers and the materials are part of the training materials supplied under the capacity building project GFL 4A 77 financed by the Global Environment Facility "Supporting the implementation of the Global Monitoring Plan of POPs in Latin America and Caribbean States (LAC)" and implemented by the United Nations Environment Programme (UNEP). These materials are a donation from UNEP to the assigned laboratory in your country for the capacity building purposes; they do not have commercial value.

Sincerely yours,

Dr. Heidelore Fiedler
Senior Scientific Affairs Officer
DTIE, Chemicals Branch
United Nations Environment Programme
e-mail: heidelore.fiedler@unep.org

Chemicals Branch, DTIE // Substances chimiques, DTIE
11-13, chemin des Acacias, CH-1219 Châtelaine, Geneva, Switzerland
Facsimile: +41 22 797 34 60 // E-mail: chemicals@unep.ch

Project Cooperation Agreement (PCA) between UNEP and CVUA (2016 - 2019)

3 years project (2016 – 2019) – cont'd

- **Collection of samples and shipment to CVUA Freiburg
31.10.2017**
- Exchange of information on State of Play on collection of samples and shipment of pooled sample
 - **Close contact to Karin Malisch, CVUA Freiburg:**
 - **Clarification of customs clearance**
 - **Express delivery: Deep frozen, cooling elements, no dry ice**
- **Analysis in pooled samples by 31.01.2019**

Project Cooperation Agreement (PCA) between UNEP and CVUA

**ECD amenable compounds: efficient cleanup?
AQC-Document SANTE 11945/2015 for pesticide analysis:
confirmation using 2 different columns possible**

Compounds to be analysed in pooled national mothers milk samples by CVUA under this Agreement

Initial POPs	
Aldrin	Aldrin
Chlordane	<i>cis</i> - and <i>trans</i> -chlordane; and <i>cis</i> - and <i>trans</i> -nonachlor, oxychlordane
DDT	4,4'-DDT, 2,4'-DDT and 4,4'-DDE, 2,4'-DDE, 4,4'-DDD, 2,4'-DDD
Dieldrin	Dieldrin
Endrin	Endrin
HCB	HCB
Heptachlor	Heptachlor and heptachlorepoxide
Mirex	Mirex
PCB	Σ PCB ₆ (6 congeners): 28, 52, 101, 138, 153, and 180
	PCB with TEFs* (12 congeners): 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, and 189
PCDD/PCDF	2,3,7,8-substituted PCD/PCDF (17 congeners)
Toxaphene	Congeners P26, P50, P62

Project Cooperation Agreement (PCA) between UNEP and CVUA

POPs listed at COP-4	
Chlordecone	Chlordecone
α -HCH	α -HCH
β -HCH	β -HCH
γ -HCH	γ -HCH
Hexabromobiphenyl	PBB 153
Pentachlorobenzene	PeCBz
c-penta BDE	BDE 47, 99, 153, 154, 175/183 (co-eluting)
c-octa BDE	Optional: BDE 100
POPs listed at COP-5	
Endosulfan	α -, β -endosulfan; and endosulfan sulfate
POPs listed at COP-6	
HBCD	α -HBCD, β -HBCD, γ -HBCD

**UNITED
NATIONS**



SC

UNEP/POPS/COP.6/INF/33

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Stockholm Convention on Persistent Organic Pollutants

**Conference of the Parties to the Stockholm
Convention on Persistent Organic Pollutants
Sixth meeting**

Geneva, 28 April–10 May 2013

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**

- ✓ **Parameters**
12 old, 9 new POPs
= 21 parameters
(without congeners, metabolites ...)

- ✓ **Regions**
 - **Continents**
 - **Countries**

- ✓ **Time trends**

**Aspects for
differentiation**

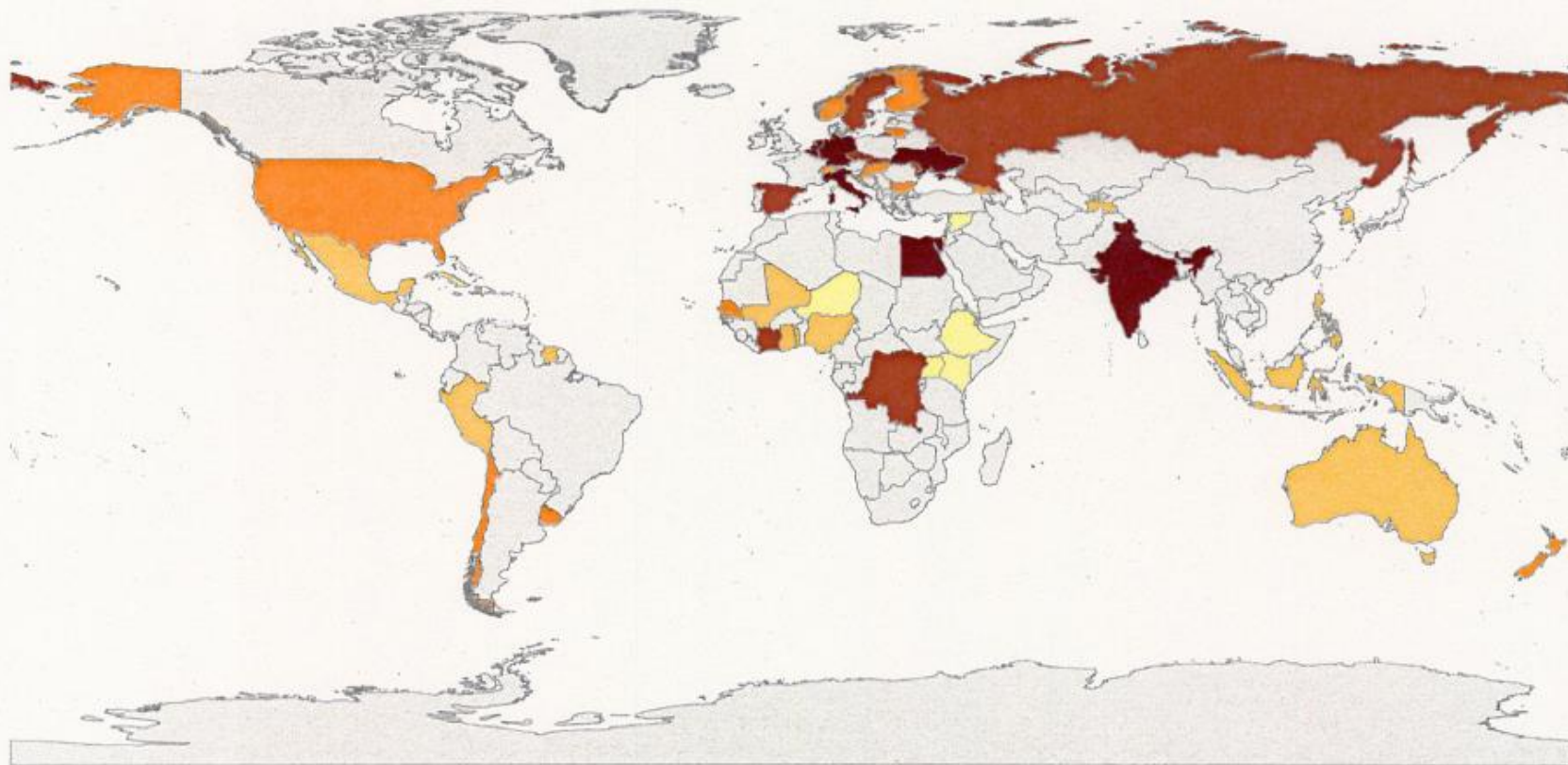


WHO-PCDD/F-PCB-TEQ



Breast milk (2000 – 2012)

WHO2005 - TEQ total



Legend



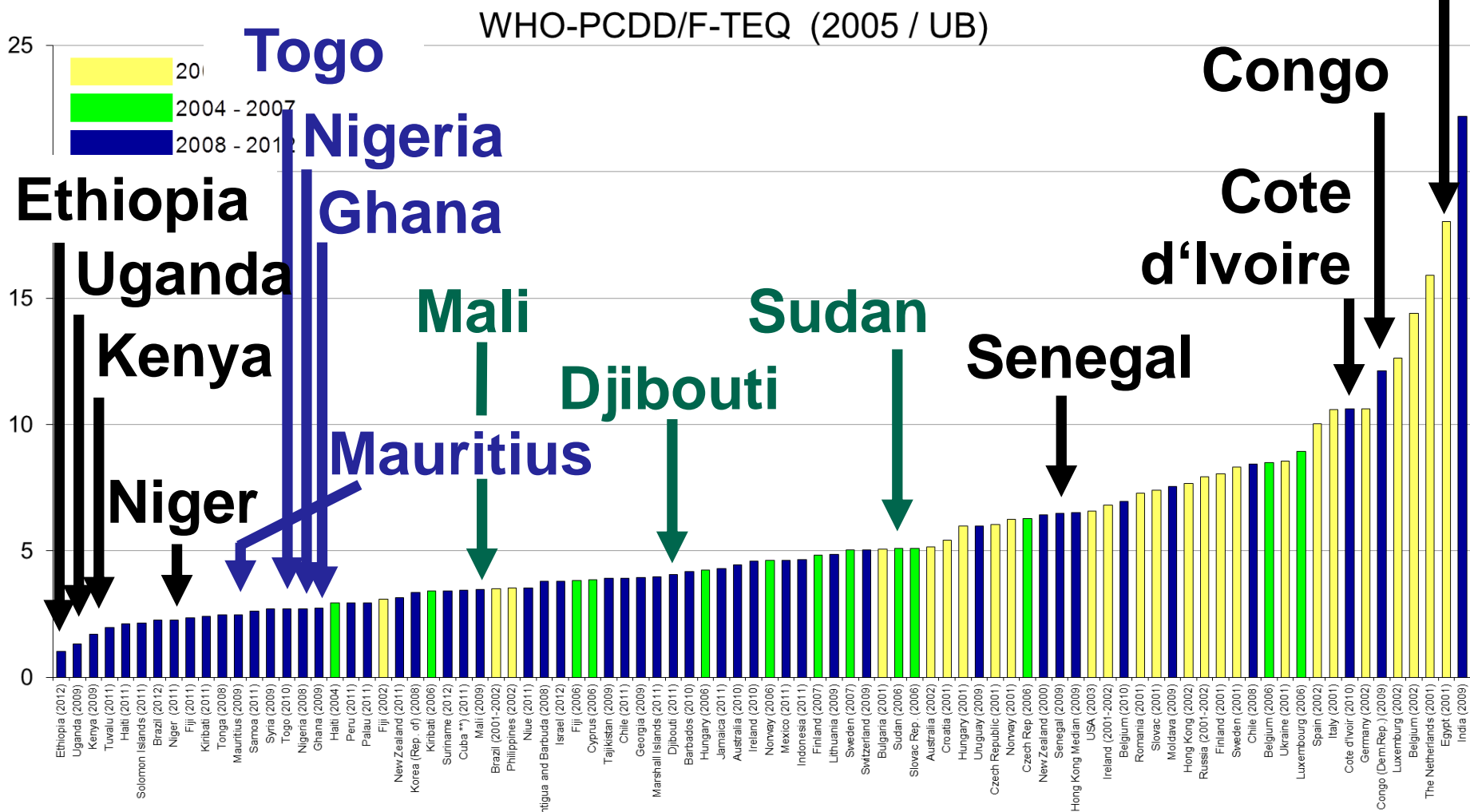
pg WHO-PCDD/F-PCB-TEQ (2005)/g lipid

Comparison of levels between countries

- NO „ranking“ between countries
- But identification of lower / middle / upper ranges
 - ✓ **Goal: findings allow setting priorities in different regions and countries**

Africa

Egypt



Egypt

Ministry of State for Environmental Affairs
Egyptian Environmental Affairs Agency

EEAA-EIMP



- Main source of dioxins is waste incineration

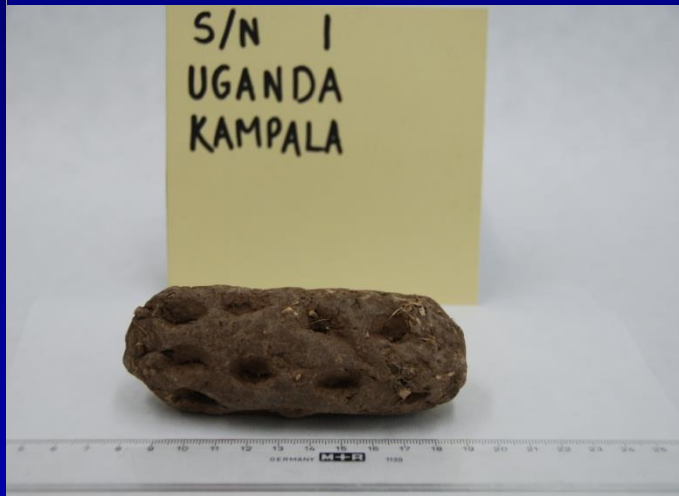


Geophagia

- **Consumption of clay** quite common among ethnic minorities in the Netherlands, UK and certain parts of the population in Africa
- **Consumption of clay by pregnant women**
 - use against morning sickness, but also source of minerals



Clays collected from Africa (n=20)



- Increased dioxin levels in some of the clays with a highest observed level of 103 ng TEQ/kg



Ball clay / caolinitic clay I

Food and Drug Administration (USA),
1997:

- **Ball clay (bentonite) as source of dioxin contamination in poultry, commercial catfish and eggs**
- **Used as feed additive (to soybean meal, as flowing or anticaking agent)**
- **Origin: mine in Mississippi**



Ball clay / caolinitic clay II

EU, 1999:

- ✓ **Caolinitic clay as source of dioxin contamination**
- ✓ **Feed additive (anticaking agent)**
- ✓ **Origin: mine in Germany**
- ✓ **Same PCDD/F pattern as in clay from Mississippi (OCDD-dominated; no furans; similar to PCP)**
- ✓ **Range of contamination:**
> 100,000 to > 500,000 pg WHO-TEQ/kg

Ball clay / caolinitic clay III

Obvious: natural source

- Possibly, geological processes formed this unique pattern of dioxins over time from organic material and chlorine.



Conclusions for breast milk from Ivory Coast and Congo

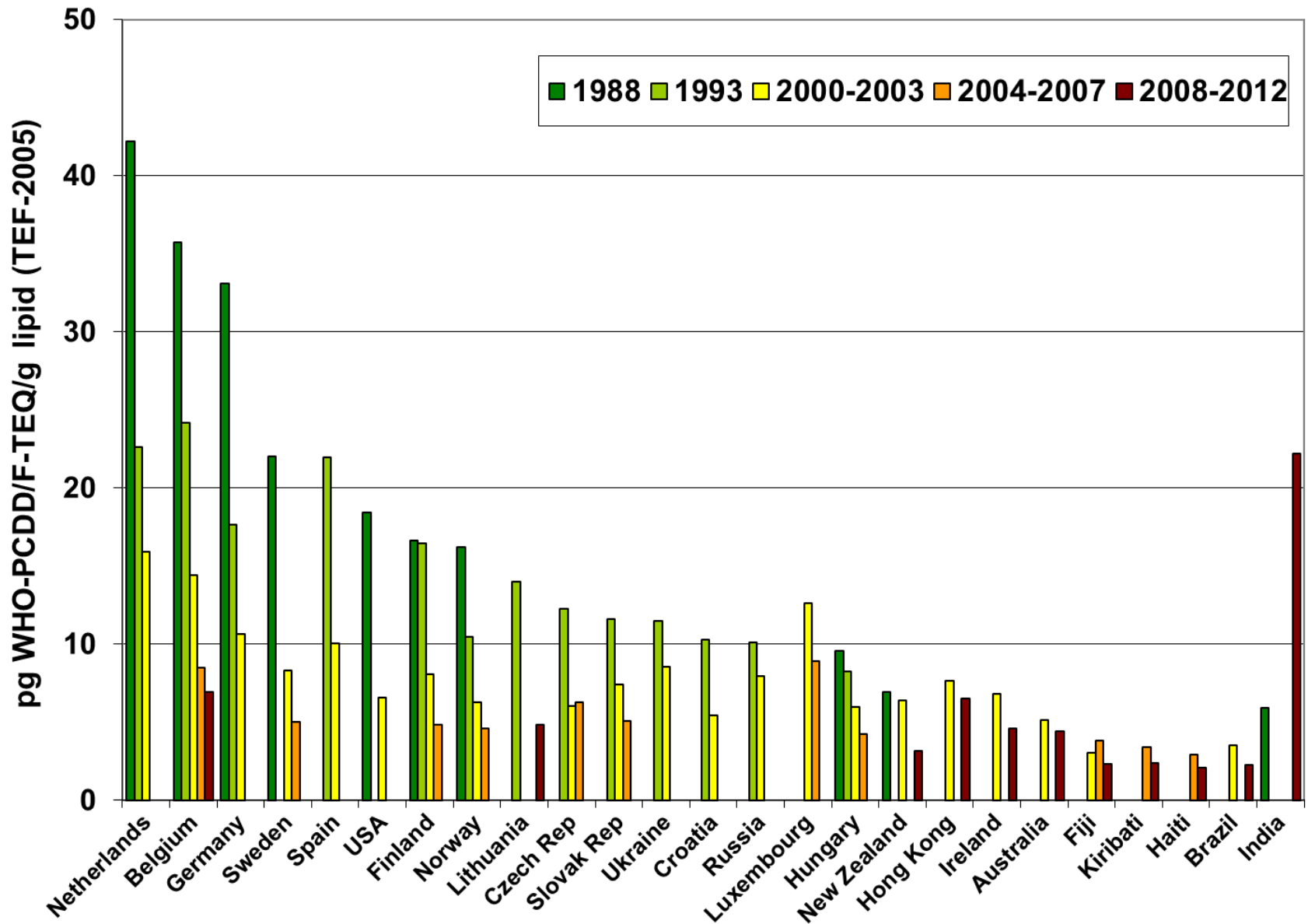
- Dioxin pattern in clays can explain pattern in human milk
- Use of clay likely to be responsible for elevated dioxin levels in breast milk from some African countries
- Potential risk

Time trends

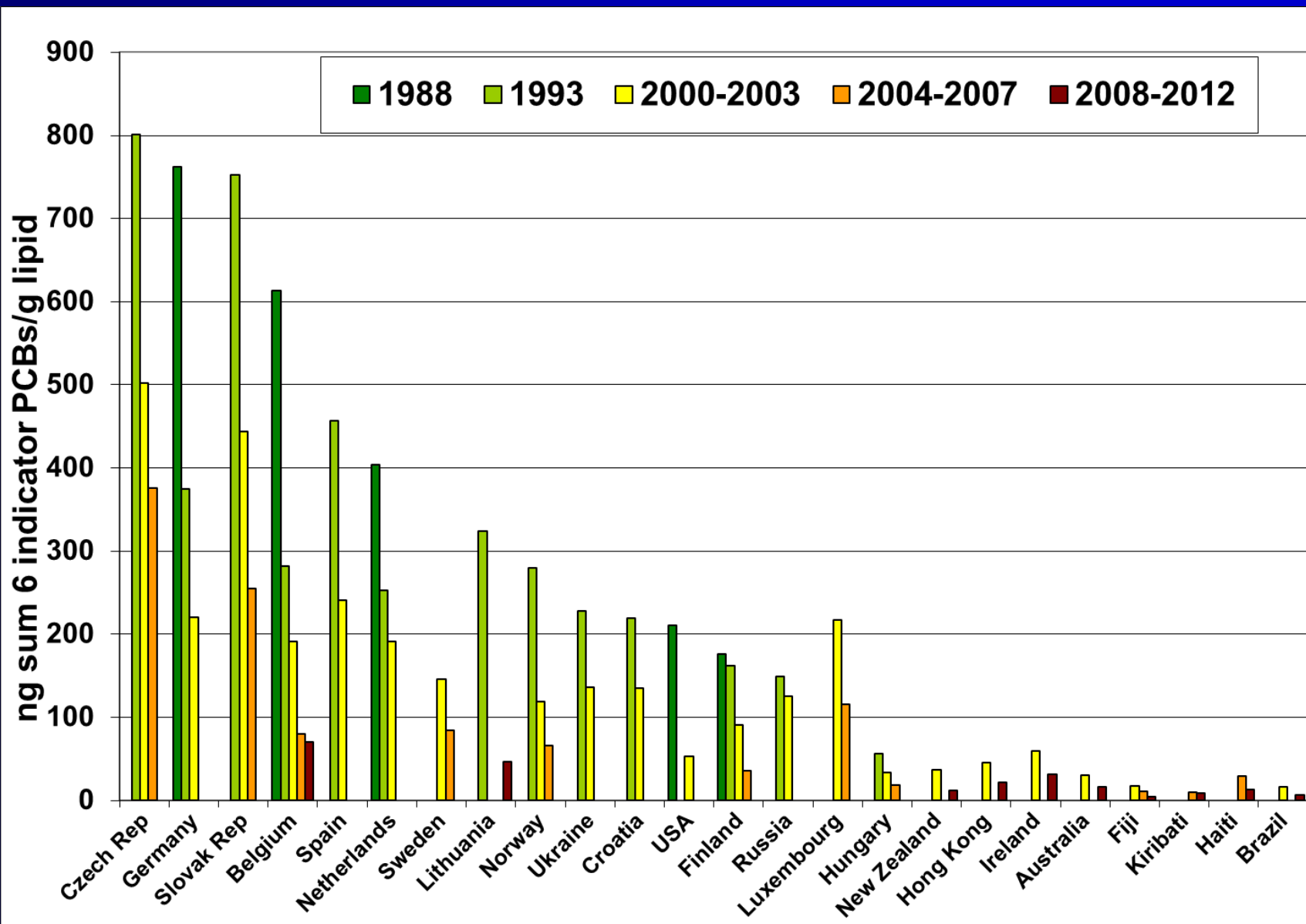


Temporal trend of PCDD/F in human milk

(pg WHO-PCDD/F-TEQ/g lipid; TEF-2005)



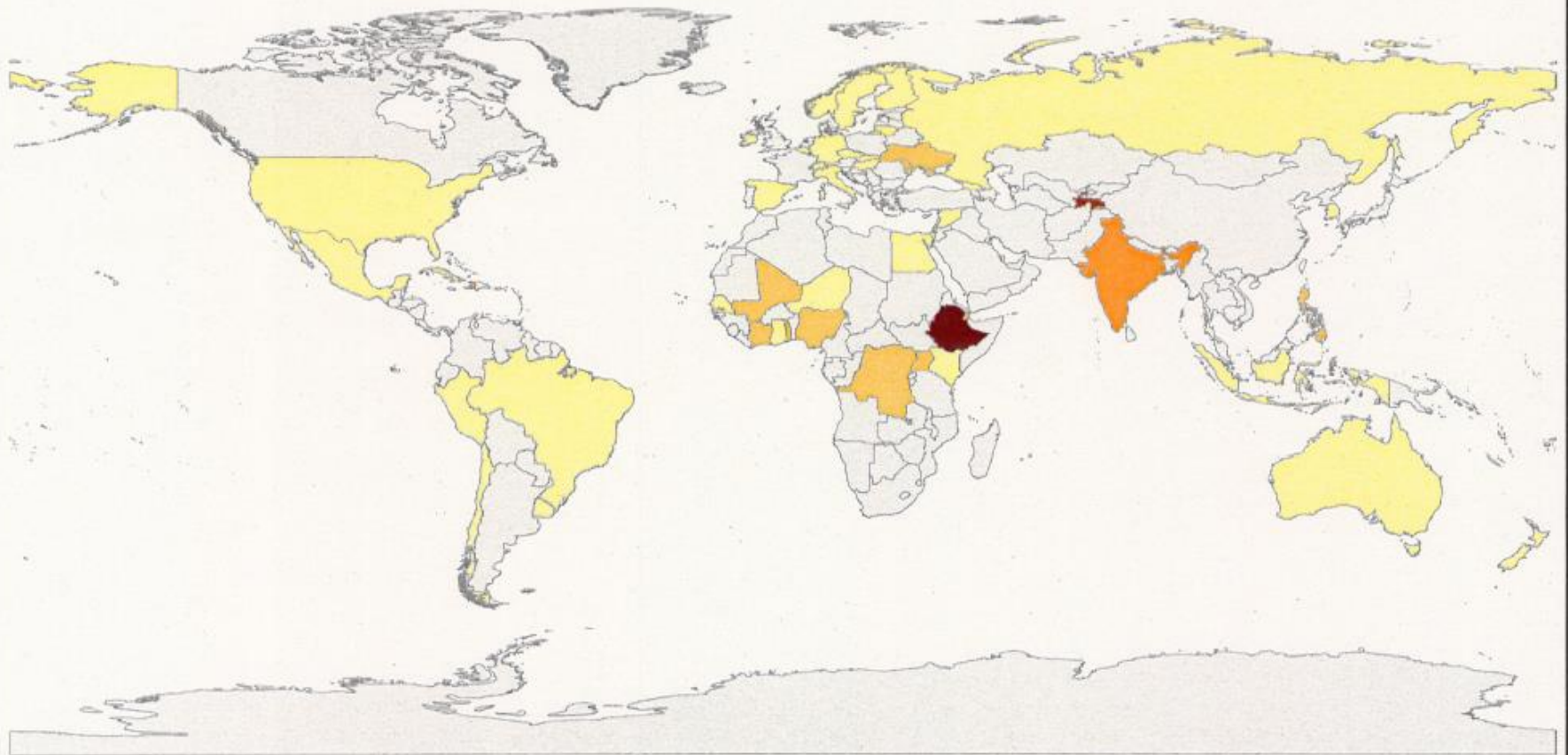
Sum 6 Indicator PCB



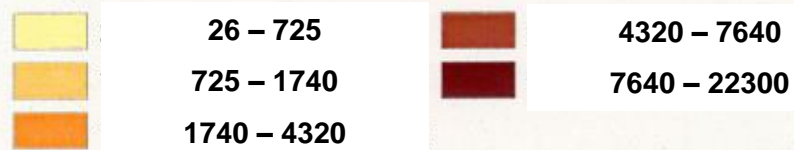
DDT



SUM DDTs



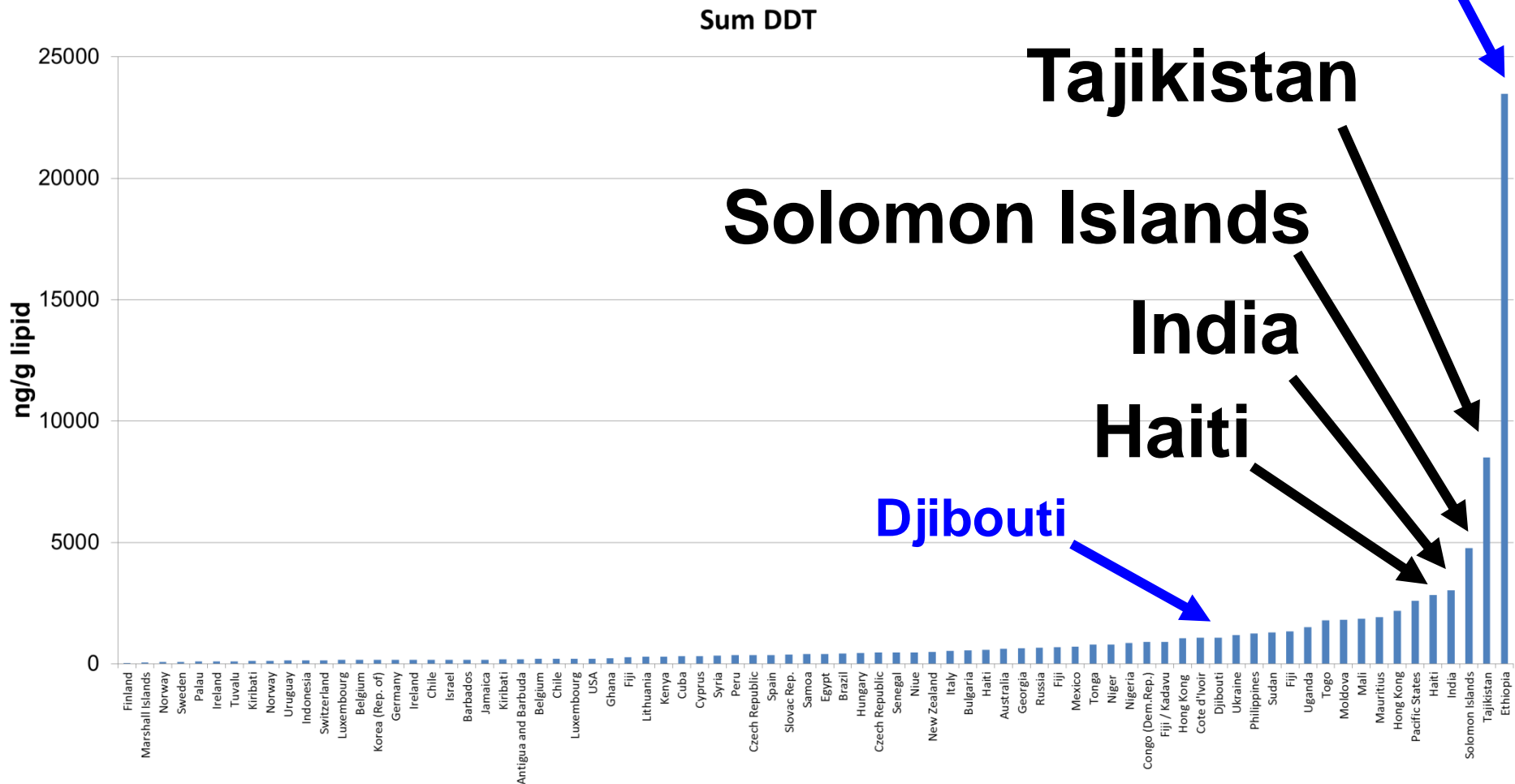
Legend



ng Sum DDT/g lipid

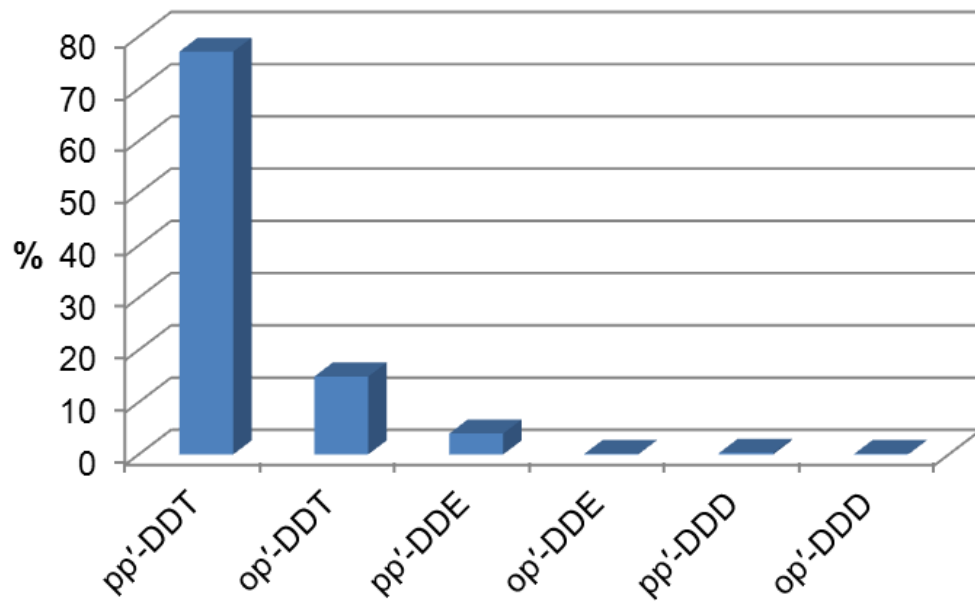
Median levels of DDT (ng/g lipid)

Ethiopia

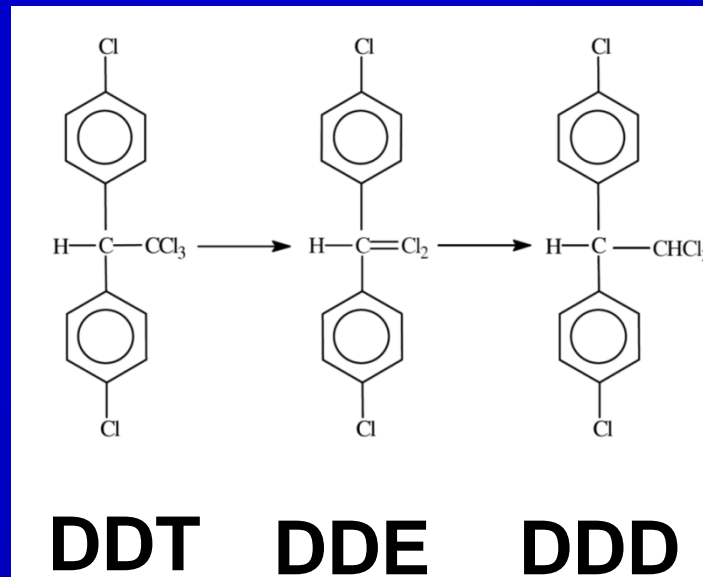
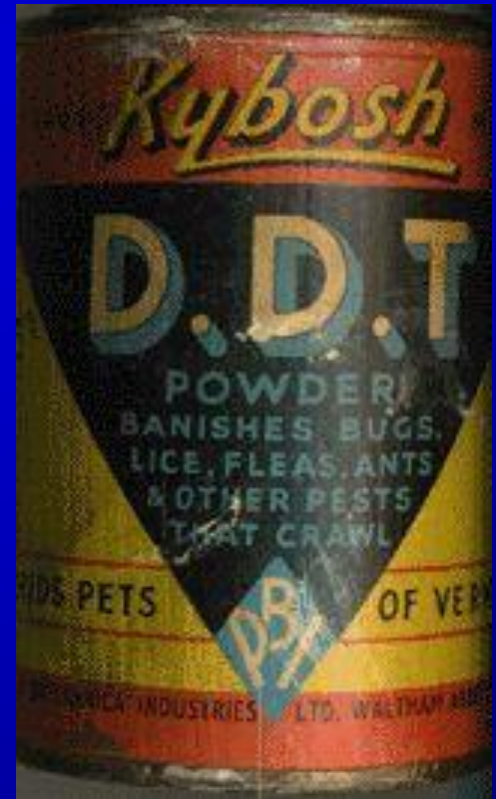


Max: 23500 ng sum DDT/g lipid (= 23.5 mg/kg)

DDT



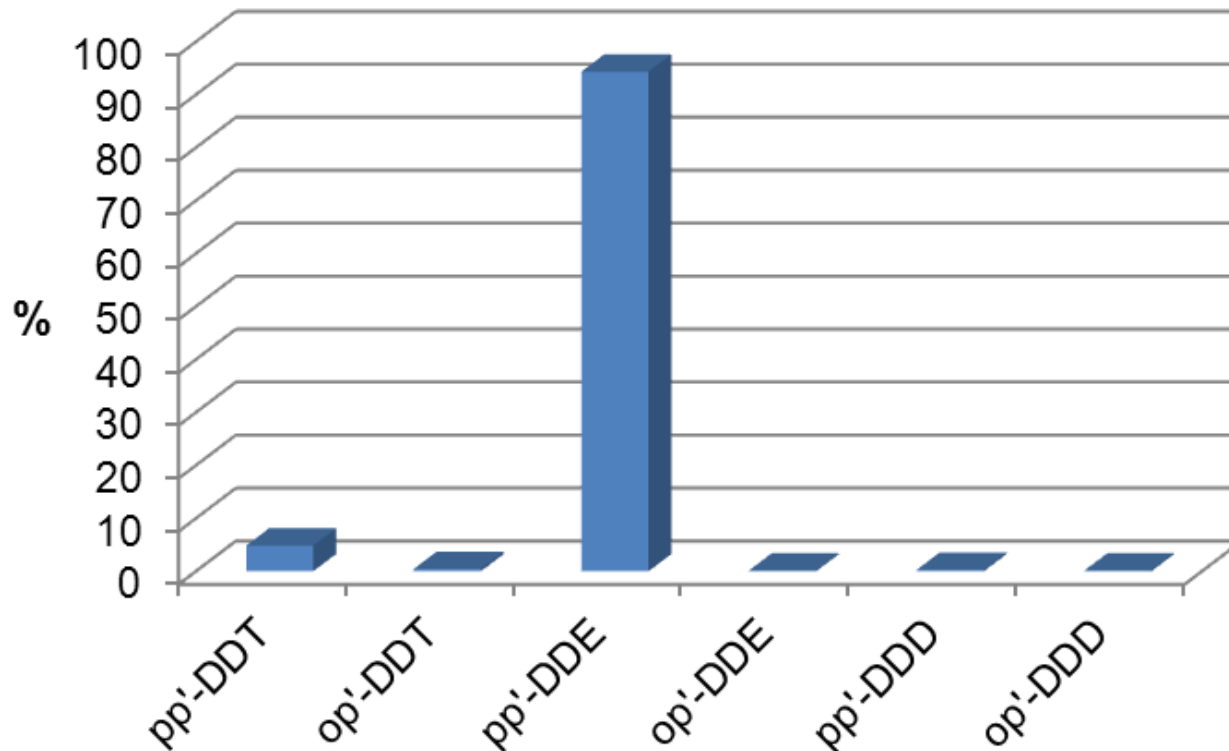
Composition of technical DDT (%)



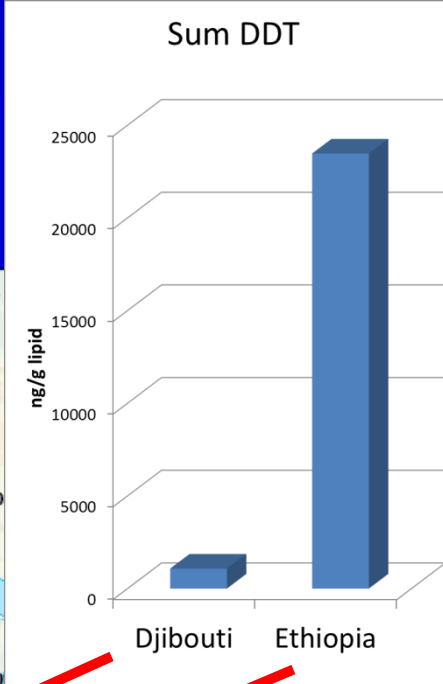
Contribution (%) to Sum DDT in humans



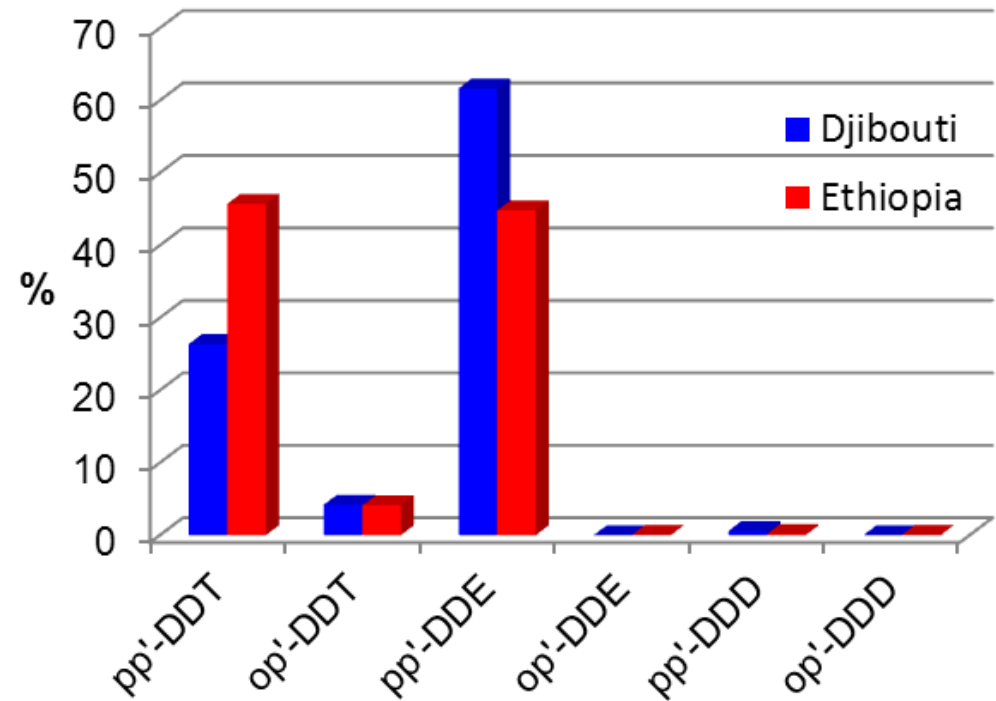
(all samples except from Ethiopia and Djibouti, median of 97 samples)



Sum DDT (ng/g lipid) in breast milk from Ethiopia and Djibouti



Contribution (%) to Sum DDT in breast milk from Djibouti and Ethiopia



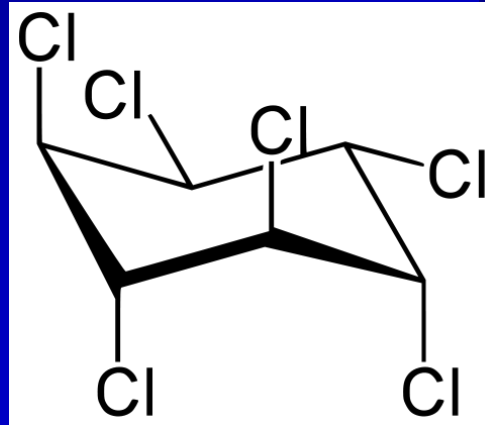
HCH



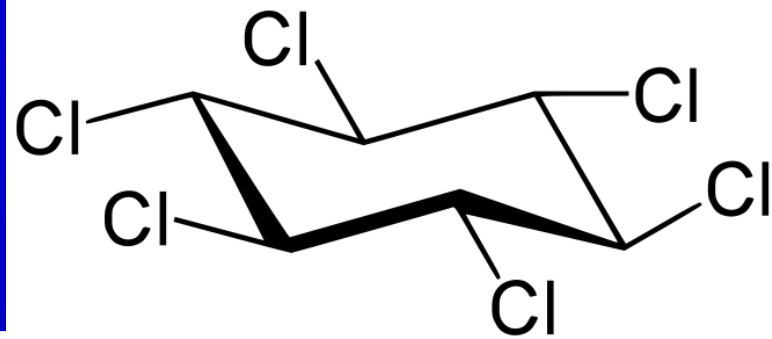
HCH

Technical HCH:

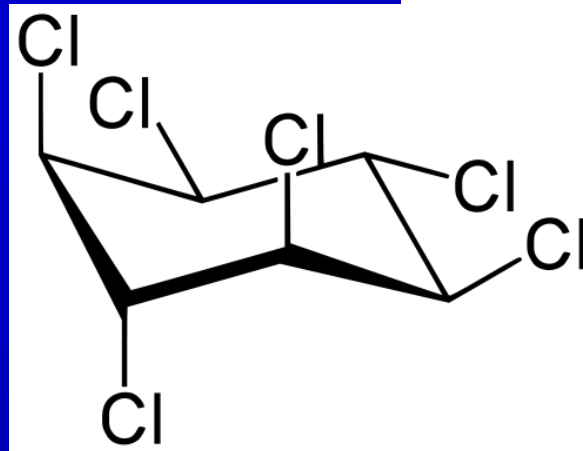
✓ **Alpha-HCH**
(65 – 70 %)



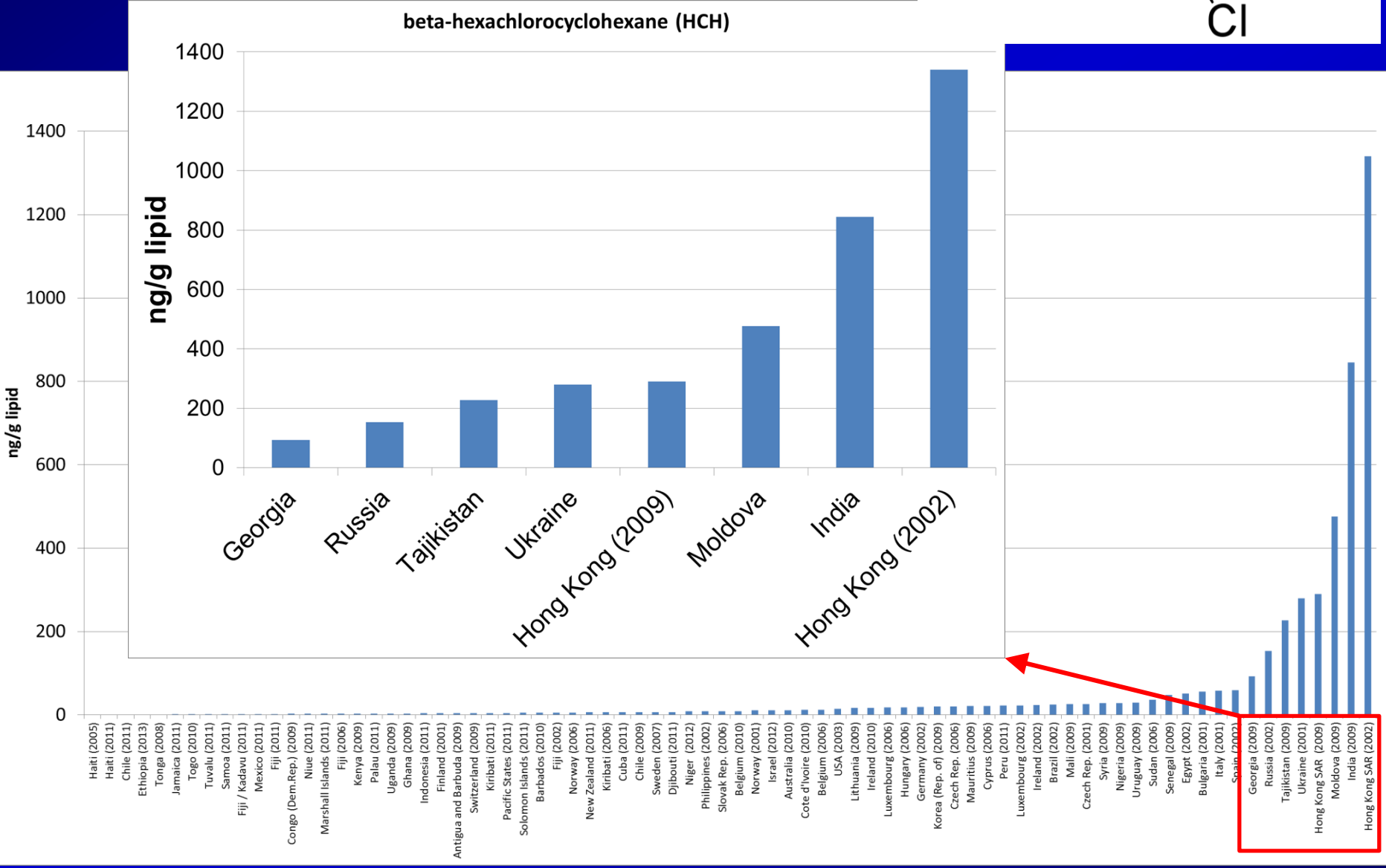
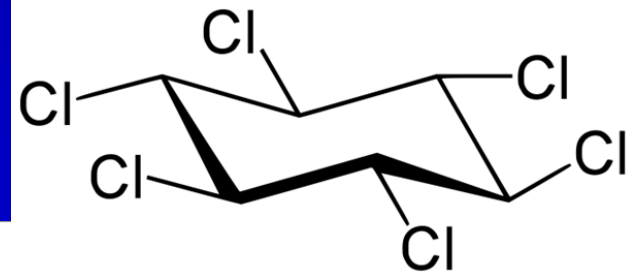
✓ **Beta-HCH**
(7 – 20 %)



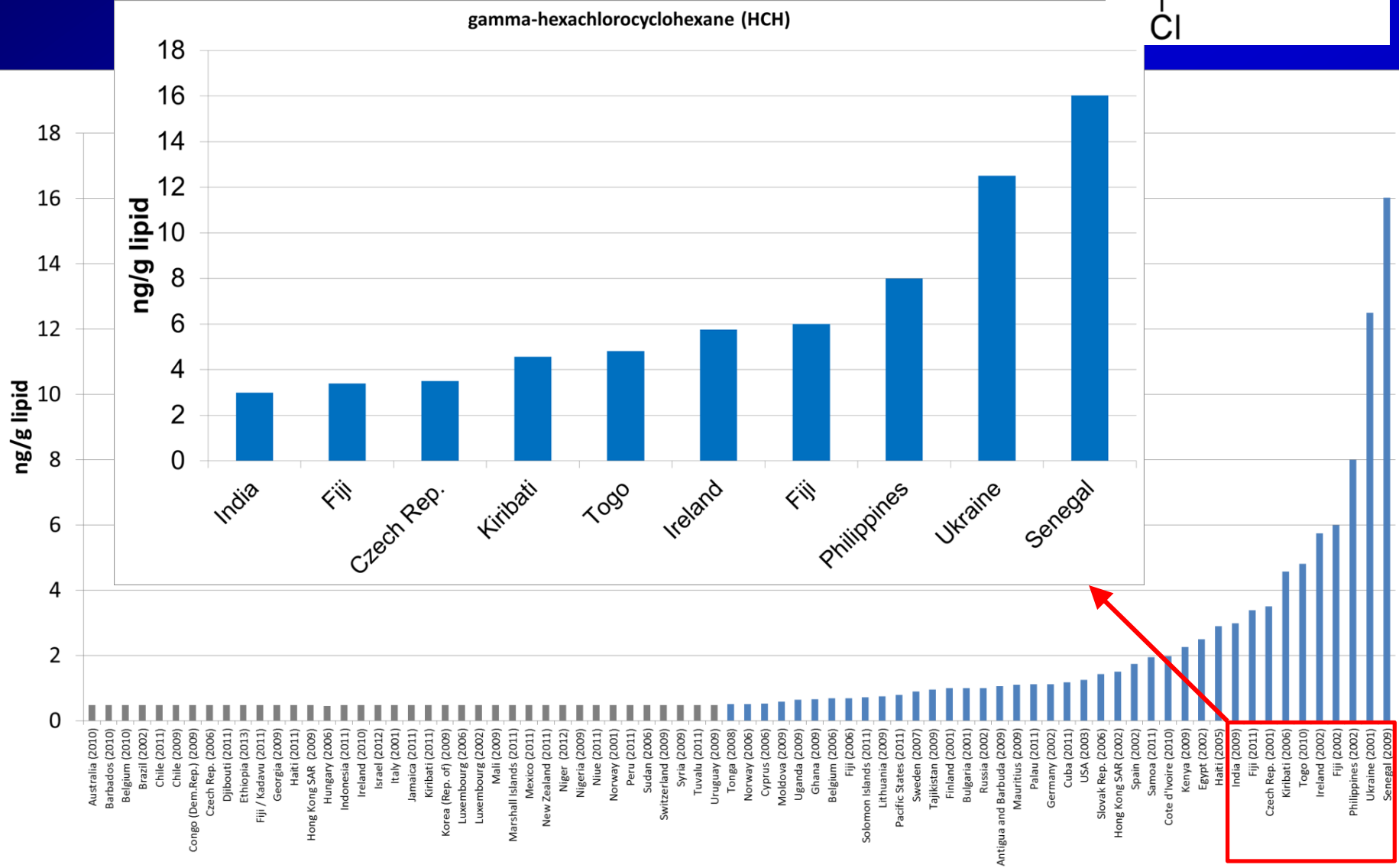
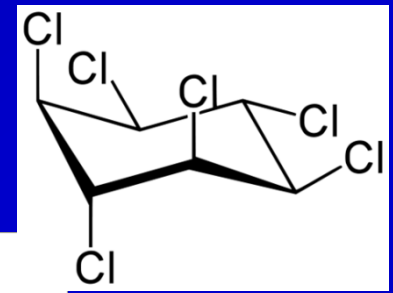
✓ **Gamma-HCH**
(14 – 15 %)



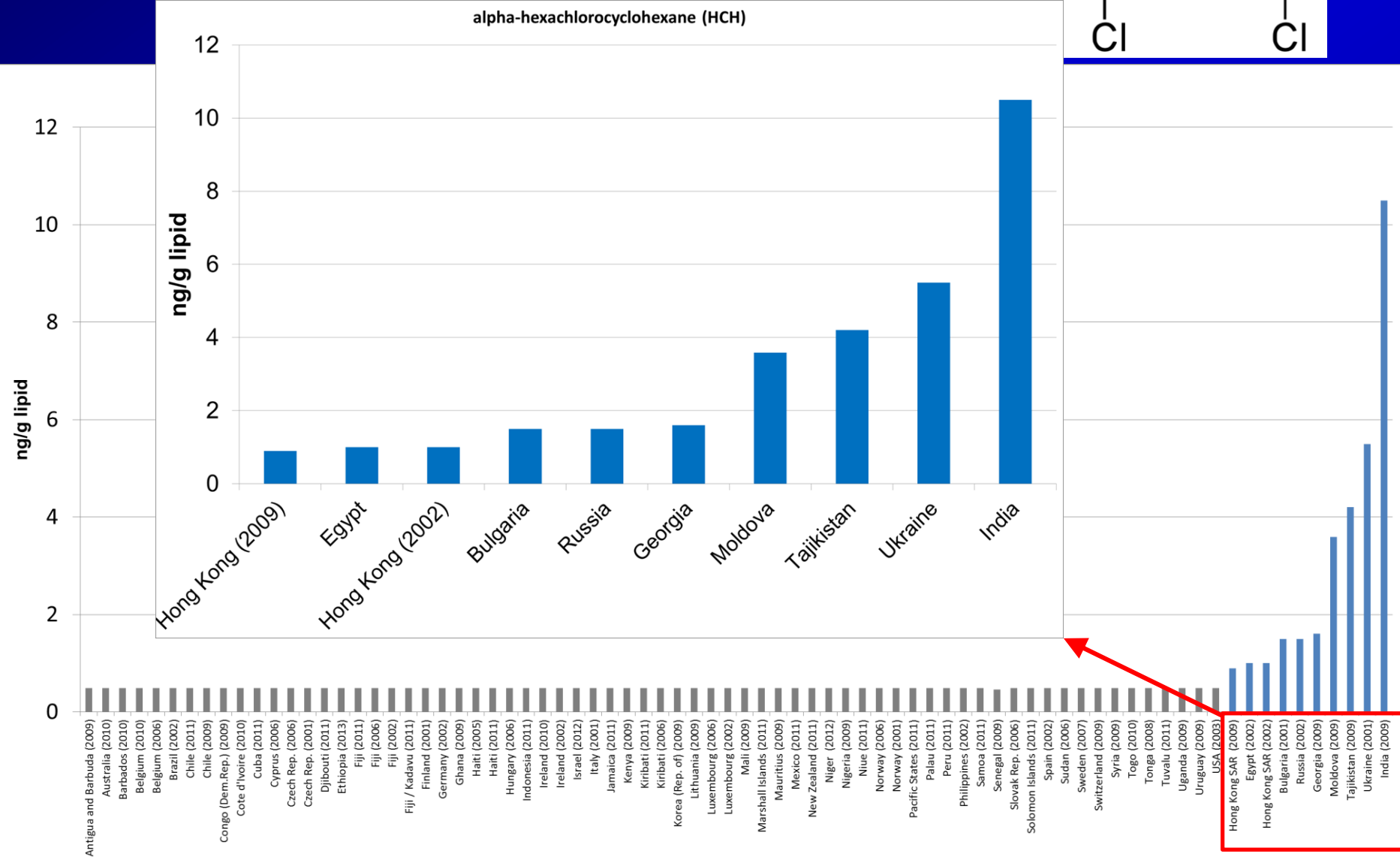
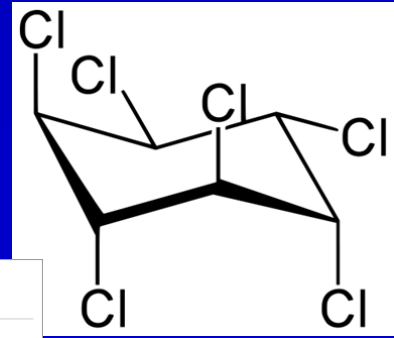
Beta-HCH



Gamma-HCH



Alpha-HCH



Difference environment - human

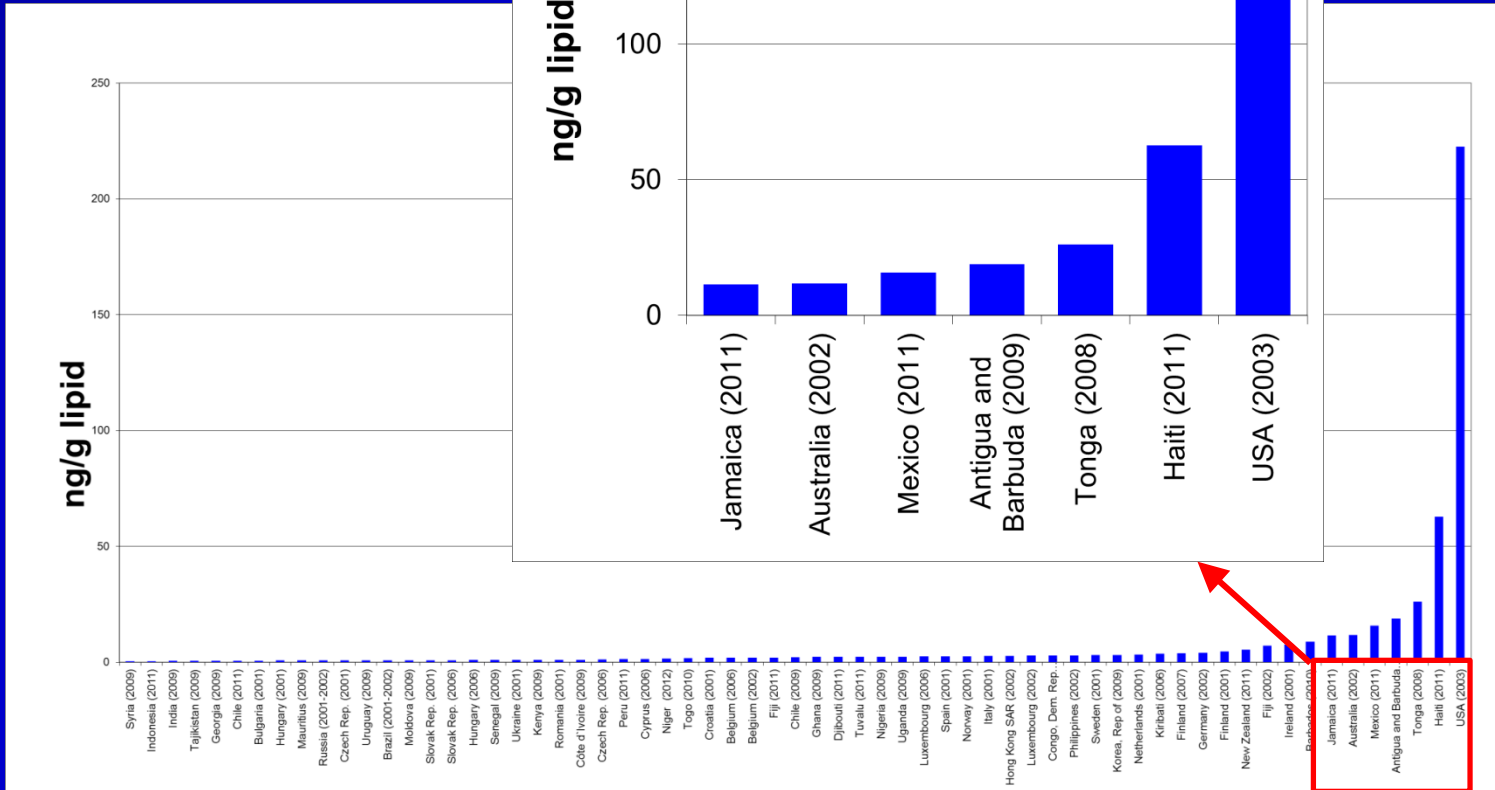
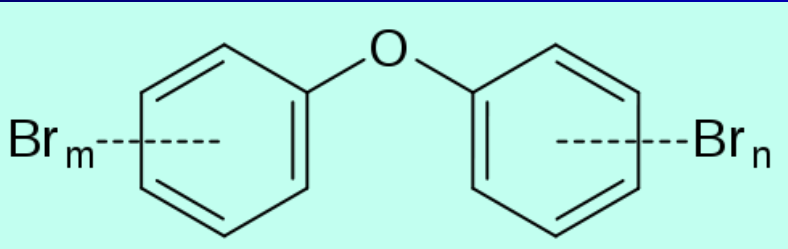
- Metabolization in mammals can change patterns of technical mixtures in comparison to the emission source, air, water or fish

(beta-HCH; alpha-HBCDD; DDE; PCDD/F; ...)

Other POPs

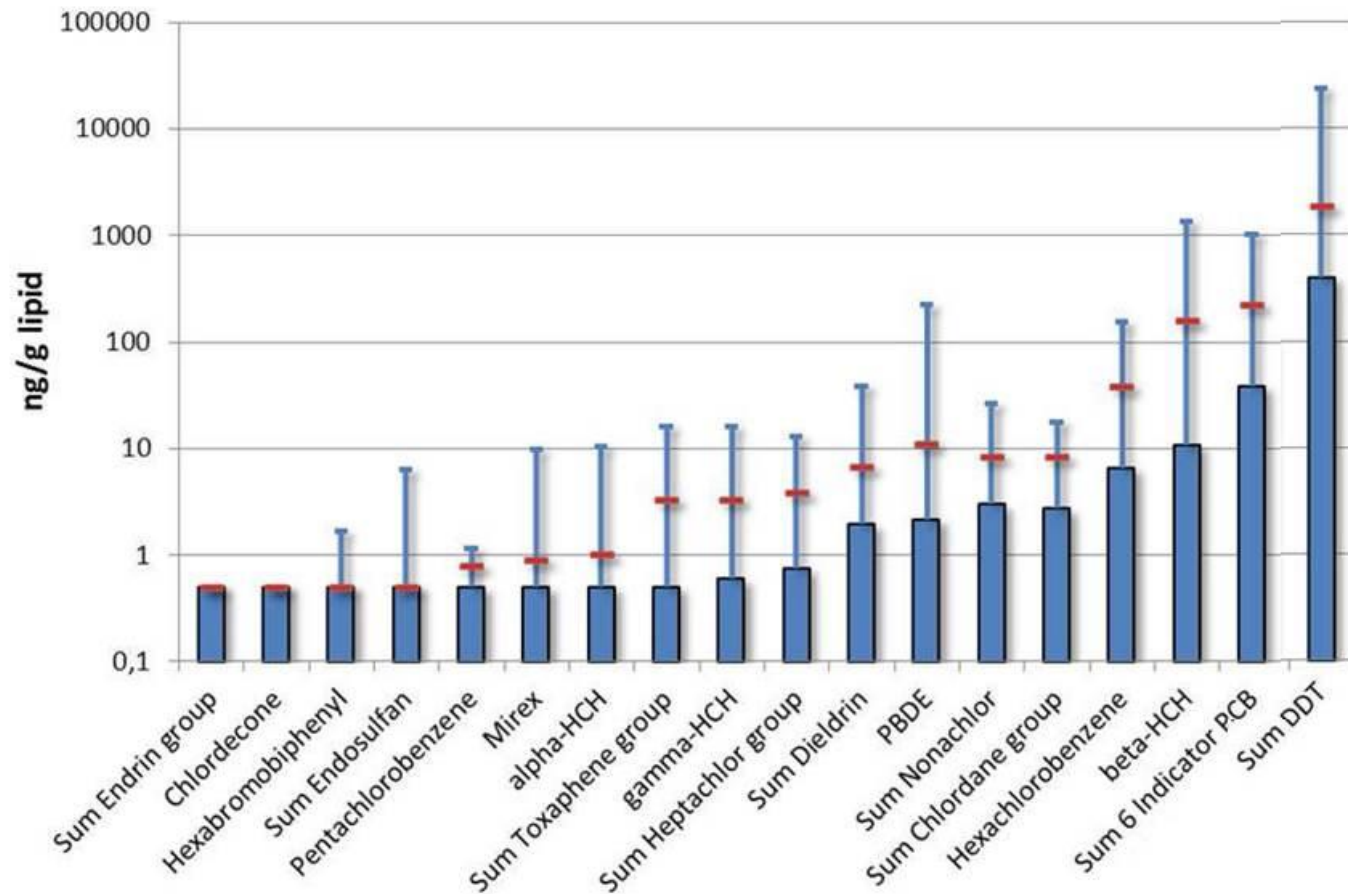


Sum PBDE



No increase of PBDD/F-levels with increasing PBDE levels

Stockholm Convention POPs in breast milk (ng/g lipid)

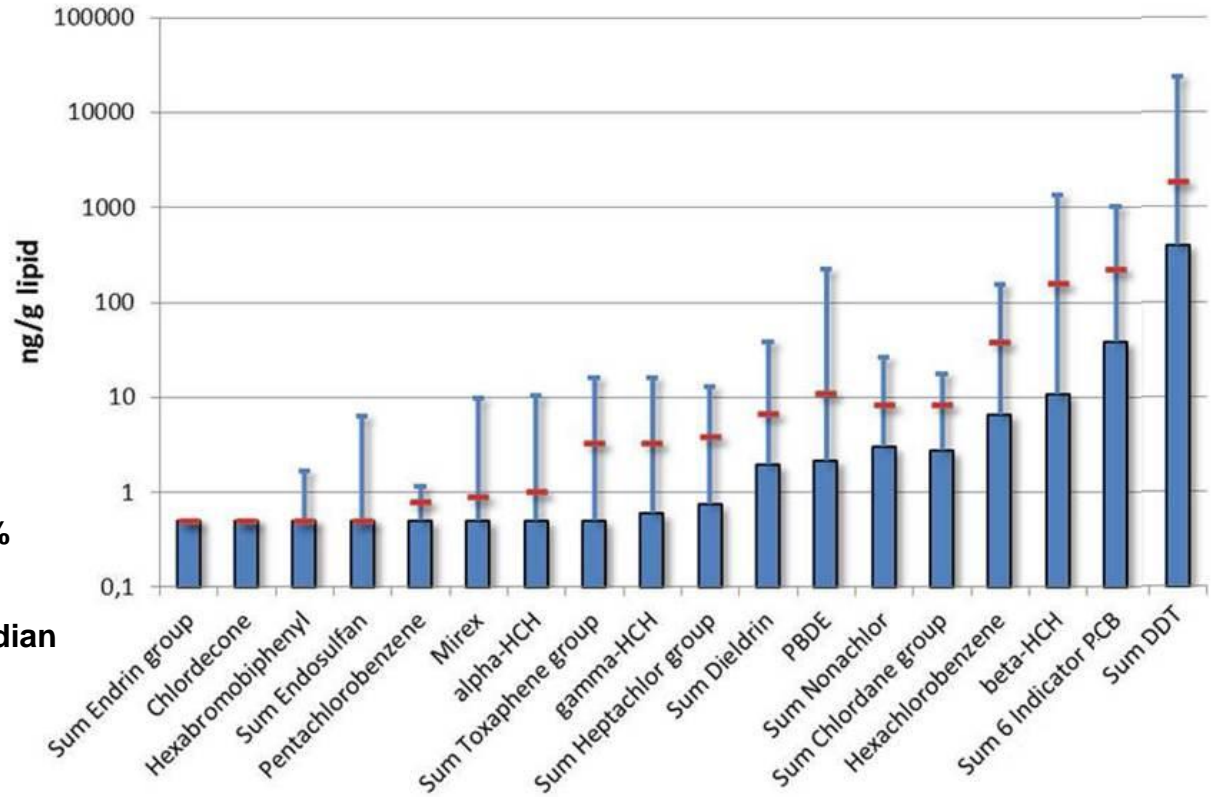
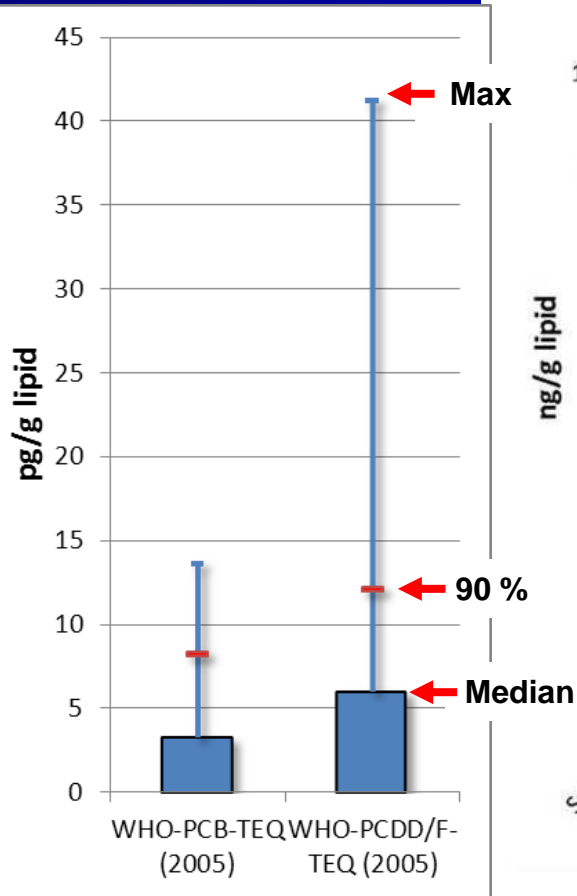


← Max

← 90 %

← Median

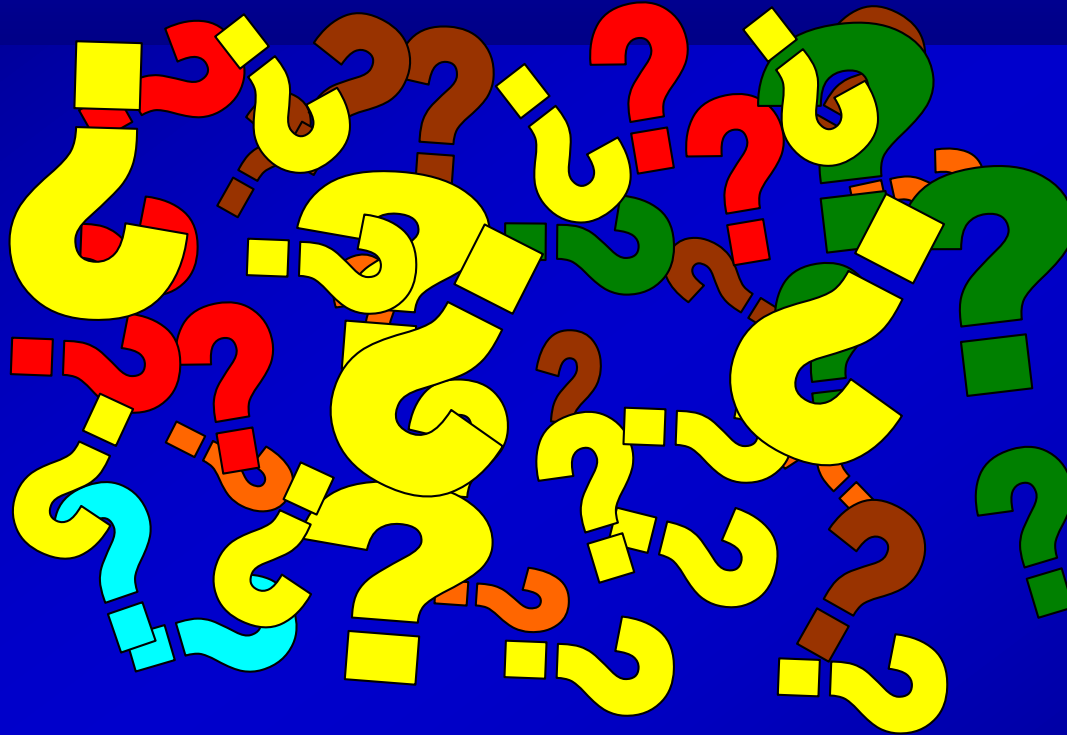
Stockholm Convention POPs in breast milk (pg/g lipid resp. ng/g lipid)



Thanks



Final



Thank you for your attention