

United Nations Environment Programme Midterm Workshop of the UN Environment/GEF project 'Continuing Regional Support for the POPs Global Monitoring Plan under the Stockholm Convention' in the Africa Region Lusaka, Zambia, 23-25 July 2018

#### 2016-2019 round of UNEP-coordinated exposure studies on human milk in the Africa region

#### **Rainer Malisch and Karin Malisch**











- State Institute for Chemical and Veterinary Analysis of Food
- ✓ WHO / UNEP Reference Laboratory
- ✓ EU Reference Laboratory (EURL) for Halogenated POPs in Feed and Food
- ✓ EURL for Pesticides in Food of Animal Origin





# WHO/UNEP-coordinated exposure studies on levels of POPs in human milk

Pound	Voore		No of	
Round	Tears	Organized by	countries	Parameters
1	1987-1988	WHO-EURO	12	Dioxins and PCBs
2	1992-1993	WHO-EURO	19	Dioxins and PCBs
3	2000-2003	WHO-EURO	26	Dioxins and PCBs
				later Stockholm Convention Initial POPs
4	2004-2007	WHO/UNEP	13	Stockholm Convention POPs
5	2008-2011	WHO/UNEP	45	Stockholm Convention POPs
6	2012-2015	UNEP	17	Stockholm Convention POPs
7	since 2016	UNEP	42	Stockholm Convention POPs

### **Participants 2000 - 2015**

Africa					America					Asia					Australia, NZ, Pacific					Europe				
															Islands									
	2000-	2004-	2008-	2012-		2000-	2004-	2008-	2012-		2000-	2004-	2008-	2012-		2000-	2004-	2008-	2012-		2000-	2004-	2008-	2012-
	2003	2007	2011	2015		2003	2007	2011	2015		2003	2007	2011	2015		2003	2007	2011	2015		2003	2007	2011	2015
Congo (DR)			х		Antigua-Barb.			х		Hong Kong SAR	х		х		Australia	х		х	х	Belgium	х	х	х	х
Côte d'Ivoire			х	х	Barbados			х		India			х		Fiji	х	х	х		Bulgaria	х			х
Djibouti			х		Brazil	х			х	Indonesia			х		Kiribati		х	х		Croatia	х			х
Egypt	х				Chile			2 x		Israel				х	Marshall Islands			х		Cyprus		х		
Ethiopia				х	Cuba			х		Korea (Rep)			х		New Zealand	х		х		Czech Rep	х	х		х
Ghana			х		Haiti		х	х	х	Philippines	х				Niue			х		Finland	х	х		
Kenya			х		Jamaica			х		Syria			х		Palau			х		Georgia			х	х
Mali			х		Mexico			х		Tajikistan			х		Samoa			х		Germany	х			
Mauritius			х		Peru			х		total no: 8					Solomon Islands			х		Hungary	х	х		
Niger			х	х	Suriname				х						Tonga			х		Ireland	х		х	
Nigeria			х		Uruguay			х							Tuvalu			х		Italy	х			
Senegal			х		USA	х									total no: 11					Lithuania			х	х
Sudan		х			total no: 12															Luxembourg	х	х		
Тодо			х																	Moldova			Х	х
Uganda			х																	Netherlands	х			х
total no: 15																				Norway	х	х		
																				Romania	х			х
																				Russia	х			
																				Slovak Rep	х	х		
	4.0	4 - 1													00					Spain	х			
	to	tal	nun	npe	r or cou	Intri	es:								69					Sweden	х	х		
	fr	om	tho	20	narticin	otin	a													Switzerland			х	
				30	particip	aun	y													Ukraine	х			
	- (	onc	e												43					total no: 23				
	_ 1	twic	Ce												21									
													_											
	- three times										4													
	- 1	foui	r tin	nes											1									
	re	su	lting	n n	ımber o	of co	oun	try/	yea	r-data:					101									
	to	tal	nun	nbe	r of poo	bled	sa	mpl	les:						188									

Africa					
	2000-	2004-	2008-	2012-	2016-
	2003	2007	2011	2015	2019
Congo (DR)			х		Х
Côte d'Ivoire			х	Х	
Djibouti			х		
Egypt	Х				Х
Ethiopia				Х	Х
Ghana			х		Х
Kenya			х		Х
Mali			Х		Х
Mauritius			Х		Х
Morocco					Х
Niger			Х	Х	
Nigeria			х		Х
Senegal			х		Х
Sudan		Х			
Tanzania					Х
Tunisia					Х
Тодо			Х		Х
Uganda			х		Х
Zambia					Х
total no: 19	(2016	5-2019	): 15)		

## Participants from Africa 2000 - 2019

#### Key aspects for human milk monitoring

- Effectiveness evaluation (time trends)
- Inclusion of new POPs
- Cost-effective approach to evaluate relevance of individual POPs
- Support of capacity building (quality control in labs)

Human tissues as indicators of human exposure to POPs

Human samples as suitable indicators for bioaccumulation of POPs :

✓ Breast milk

✓ Blood

✓ Adipose tissues

**Comparable results on fat basis** 

#### Advantage of <u>breast milk</u> samples

- non-invasive mean to estimate the exposure
- Less toxicological concern (relatively high risk of contacts with infectious agents: AIDS virus, hepatitis) than for human blood
- human milk has higher fat content than blood

For analysis: available amount of lipids important factor with regard to number of analytically covered POPs and LOQs

- Lipid amount of type of sample
- Mixing (pooling)

# Standardized protocol



- Collection of human milk from representative individuals (since 2007: n = 50)
- Preparation of <u>one</u> pooled (=mixed) sample <u>representative</u> for a country / region
- Analysis by Reference Laboratory for reliable and comparable data
  - (+) Cost-effective and useful non-invasive mean to estimate the overall exposure of a local population
  - Possible to get a rough estimate on the exposure in different regions of the world and time trends with only very few samples

## **Standardized protocol**

- **Collection of human milk from representative individuals** (since 2007: n = 50)
- Preparation of <u>one</u> pooled (=mixed) sample <u>representative</u> for a country / region
- Some flexibility:
  - 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.
  - Small countries: less?

### Support of capacity building

Sample preparation scheme: Preparation of individual samples for analysis of basic POPs by country and of pooled (mixed) samples (Before taking an aliquot, shake intensely at room temperature and then take the aliquot immediately. Storage and shipment of all samples deep-frozen.)



Mean of individual samples should be comparable to concentration found by reference lab





#### **Guidelines**

UNEP-coordinated Survey of Human Milk for Persistent Organic Pollutants

> Guidelines for Organization, Sampling and Analysis

January 2017

#### Prepared by:

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#### and

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for:

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Page 1 of 38

#### Video on guidelines

#### https://youtu.be/7LwJ0x2\_PXQ

Preparing the video:

Alejandra Torre Gabriela Medina Virginia Santana



#### **Project Cooperation Agreement (PCA),** part I: shipment of glassware containers

(here: 15 countries from Africa)

Activity	Comments for 2016	Comments for 2017				
Activity 1						
Supply of samplers for human milk for 9 countries of Pacific Islands	Purchase and cleaning of glassware for 9 countries, shipment to 8 countries	Shipment to 1 country; with 1 country (Fiji) not accepting the first shipment; therefore a second shipment necessary				
Supply of samplers for human milk for 7 countries of Asia-Pacific	Purchase and cleaning of glassware for 7 countries, no shipment in 2016	Shipment to 7 countries, with 1 country (Philippines) not accepting the first shipment; therefore a second shipment necessary				
Supply of samplers for human milk for 15 countries in Africa	Purchase and cleaning of glassware for 15 countries, shipment to 13 countries	Shipment to 2 countries				
Supply of samplers for human milk for 12 countries of GRULAC	Purchase and cleaning of glassware for 12 countries, no shipment in 2016 (one country not selected, so far)	Shipment to 11 countries (1 country not responding)				

### All countries received glassware (60 x 100 ml; 1 x 2000 ml);



# Participation of African countries 2016-2019

No	Country	Shipment of	Date of	Receipt of	Announcement /	additional infos of UNEP	Date of shipment of	Receipt of	amount of milk
		glassware	shipment	glassware	info on shipment of		samples	samples (date)	sample
			of		human milk samples				
			glassware						
1	DR Kongo	yes	08.12.2016	15.03.2017	planned 13.11. 2017	done	14.11.2017	22.11.2017	1150 ml
2	Egypt	yes	08.12.2016	25.12.2016		Started in October 2017, finished hopefully first quarter of 201	8		
3	Ethiopia	yes	08.12.2016	27.02.2017		going through ethical clearance			
4	Ghana	yes	08.12.2016	11.01.2017		going through ethical clearance			
5	Kenya	yes	08.12.2016	13.02.2017	planned April 18	going through ethical clearance, planned end of April			
6	Mali	yes	08.12.2016	13.02.2017		planned to start soon			
7	Mauritius	yes	08.12.2016	11.01.2017	clearance . 28.02.18:	details; Waiting for ethical clearance to start sampling, donor	planned 16 06 2018	21.06.2018	1200 ml
8	Morocco	yes	08.12.2016	13.01.2017		planned to start soon			
9	Nigeria	yes	08.12.2016	07.02.2017	01. 2018: ethical clearar	started			
10	Senegal	yes	15.12.2016	16.03.2017		ongoing	28.03.2018	03.04.2018	1200 ml
11	Tanzania	yes	15.12.2016	28.12.2017		planned to start soon			
12	Тодо	yes	15.12.2016	03.01.2017	13.11.2017	done	13.11.2017	16.11.2017	1250 ml
13	Tunisia	yes	15.12.2016	22.05.2017		ongoing			
14	Uganda	yes	10.01.2017	03.02.2017		planned shipment end of May	10.06.2018	14.06.2018	1200 ml
15	Zambia	yes	10.01.2017	01.03.2017		ongoing, hopefully finished February 2018			

✓ 15 participants received glassware
 ✓ 5 countries sent human milk samples



## Supply of dichromate tablets via distributor of chemicals in Germany?



The shipment of the pooled samples should be done in close cooperation with Karin Malisch who should be informed about date of shipment and tracking number for follow-up of the shipment and in particular solving possible problems at customs in Germany and to avoid any problems of possible delays due to shipment at inappropriate times Contact e-mail: pops@cvuafr.bwl.de For questions: karin.malisch@cvuafr.bwl.de Address: Dr. Rainer Malisch



Chemisches und Veterinäruntersuchungsamt (CVUA) Freiburg (State Institute for Chemical and Veterinary Analysis of Food) Bissierstr. 5 D-79114 Freiburg Germany

- Shipment of samples in close contact with Dr Karin Malisch
- Coordination before shipment preferably on Monday; no holidays
- Express; frozen; cooling elements
- Tracking number allowing to contact to customs in Germany !!!

# Project Cooperation Agreement (PCA), part II: analysis – compounds to be analysed in pooled national mother's milk samples

Compounds to be analysed in pooled r	national mothers milk samples by CVUA under this Agreement
Initial POPs	
Aldrin	Aldrin
Chlordane	cis- and trans-chlordane; and cis- and trans-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
НСВ	НСВ
Heptachlor	Heptachlor and heptachlorepoxide
Mirex	Mirex
РСВ	ΣPCB <sub>6</sub> (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
* PCB with TEFs (Toxic Equivalency Factors) assign	ned by WHO in 1998
POPs listed at COP-4	
Chlordecone	Chlordecone
α-HCH	α-HCH
β-НСН	β-НСН
γ-ΗCΗ	γ-ΗϹΗ
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	$\alpha$ -, $\beta$ -endosulfan; and endosulfan sulfate
POPs listed at COP-6	
HBCD	α-HBCD, β-HBCD, γ-HBCD



Expert meeting to update the Global Monitoring Plan guidance document

Brno, Czech Republic, 7-9 November 2017

2. Introduction and context:

(a) Outcomes of COP-7 and COP-8 relevant to the update of the global monitoring plan (GMP) guidance document;

- (b) Mandate and process for updating the GMP guidance document;
- 3. Experiences from monitoring programmes in sampling and analyzing the newly listed POPs in core matrices and other media:
  - (a) Hexachlorobutadiene;
  - (b) Pentachlorophenol and its salts and esters;
  - (c) Polychlorinated naphthalenes;
  - (d) Decabromodiphenyl ether (BDE-209);
  - (e) Short-chain chlorinated paraffins;



# Aim of CVUA Freiburg: inclusion also of voluntary POPs (COP 7, COP 8) (except PFAS, analysed at University Örebro)

mandatory (according to PCA)

1) Initial POPs: aldrin, chlordane, DDT, dieldrin, endrin, HCB, heptachlor, mirex, toxaphene, PCB, PCDD, PCDF

2) POPs listed at COP-4: chlordecone, HCH (alpha, beta, gamma), hexabromobiphenyl (PBB 153), Pentachlorbenzene, PBDE (47, 99, 153, 175/183-co-eluting); optional: BDE 100; PFOS

3) POPs listed at COP-5: endosulfan

4) POPs listed at COP-6: HBCDD (alpha, beta, gamma)

voluntary:

5) POPs listed at COP-7: Hexachlorobutadiene (Annex A), pentachlorophenol + salts + esters, polychlorinated napthalenes

6) POPs listed at COP-8: Decabromodiphenyl ether, SCCP, hexachlorobutadiene (Annex C)

7) possible candidates at COP-8: dicofol, pentadecafluorooctanoic acid (PFOA) and salts, perfluorohexane sulfonic acid (PFHxS)

Selected results and discussion – examples for a complex picture

Participation of <u>African</u> countries <u>2016</u>-2019

As part of a more complex picture of

Global WHO/UNEP-Studies 2000 - 2019

#### **Aspects for differentiation**

Parameters
 23 parameters
 (without congeners, metabolites ...)

✓ Regions

- Continents
- Countries
- ✓ Time trends

#### UNITED NATIONS



# SC

#### UNEP/POPS/COP.6/INF/33

Distr.: General 26 March 2013



Stockholm Convention on Persistent Organic Pollutants

English only

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<sup>\*</sup>

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

## WHO-PCDD/F-PCB-TEQ

#### **Comparison of levels between countries**

<u>NO</u> "ranking" between countries
 But identification of lower / middle / upper ranges

 Goal: findings allow setting priorities in different regions and countries



5	C



#### PCP and dioxins in guar gum from India

RASFF, July 2007, notification from Switzerland:

Very high contamination levels of dioxins and pentachlorophenol (PCP) found in certain batches of guar gum from India:

about 1000 times the level of what can be considered as normal background contamination

9 EU Member States affected

## Guar gum

- extracted from guar bean
- use as thickening, emulsifying, binding, gelling additive
- India produces about 80 % of world market
- Food grade guar gum: authorised as food additive
- Industrial grade guar gum: for non-food uses, e.g. in printing and textile industry
  - Technical note (2004): guar gum used as printing thickener for printing inks on textile (in particular in textiles made from polyester).
    Frequently/often preserved with pentachlorophenol (PCP).

#### Two EU missions to India (2007, 2009)

Na-PCP extensively used in India for industrial grade guar gum > either sold as food grade

or cross-contamination from industrial to food grade gums

Detection in food grade guar gum points to use for textiles –

elimination of sources is quite complex (environment, food, ...)



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



According to Ministry of State for Environmental Affairs, Egyption Environmental Affairs Agency:

#### > 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

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journal homepage: www.elsevier.com/locate/chemosphere

## Dioxins (polychlorinated dibenzo-p-dioxins and polychlorinated dibenzo-furans) in traditional clay products used during pregnancy

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#### HIGHLIGHTS

- ► We determined PCDD/F levels of clays taken orally during pregnancy.
- ▶ PCDD/F levels in some clays were high, up to 103 ng TEQ kg<sup>-1</sup>.
- ▶ We compared congener patterns of clay and human milk samples from Africa.
- ▶ PCDD/F patterns in some breast milk suggest a relationship with clay consumption.
- ▶ Use of contaminated clay presents a health risk for the developing fetus.

## **Time trends**









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	pp'-DDE	pp'-DDT						
	µg/kg lipid	%	%						
Djibouti	1080	69	26						
Ethiopia	23500	50	46						

Two pillars: Air and human milk – comparison

#### Air

Report on Passive Air Sampling under the Global Monitoring Plan for Persistent Organic Pollutants - GMP Projects 2010-2011

#### Adsorbent: polyurethane foam (PUF)







**HCH** 

Alpha-HCH
 (65 – 70 %)



✓ Beta-HCH
 (7 - 20 %)



✓ Gamma-HCH
 (14 – 15 %)









## **HCH** in air

# Contribution (%) to "Sum HCHs" in air of Latin America and Caribbean \*):

	%
Alpha-HCH	41
Beta-HCH	2
Gamma-HCH	56



\*) calculated on basis of median for all samples



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

#### Perfluorinated compounds (PFCs)

- Lack of lipophilicity results in relatively low levels in milk compared to serum/blood (distribution milk/serum ~1:100).
- Distribution varies for different PFCs.
- More reliable data would be generated using blood/serum.

![](_page_56_Picture_4.jpeg)

### **Chlorinated Paraffins (CPs)**

![](_page_57_Figure_1.jpeg)

✓ general formula CnH2n+2-zClz

- ✓ variation of chain length, number and position of chlorines
  - Short chain CPs (SCCP; C10 C13)
  - > medium chain CPs (MCCP; C14 C17)
  - Iong chain CPs (LCCP; > C17)
- ✓ complex mixtures: > 10.000 compounds
- chlorine content of commercially available mixtures
  between 30 70 %

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

![](_page_58_Figure_1.jpeg)

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

![](_page_59_Figure_1.jpeg)

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

![](_page_60_Figure_1.jpeg)

WHO recommendation over last decades

 Support and promotion of exclusive breastfeeding for the first six month Risk evaluation of breast feeding with regard to concentrations of PCDDs, PCDFs, PCBs and DDTs

CrossMark

Arch Toxicol DOI 10.1007/s00204-016-1802-z

**REVIEW ARTICLE** 

![](_page_62_Picture_3.jpeg)

Martin van den Berg<sup>1</sup> · Karin Kypke<sup>2</sup> · Alexander Kotz<sup>2</sup> · Angelika Tritscher<sup>3</sup> · Seoung Yong Lee<sup>3</sup> · Katarina Magulova<sup>4</sup> · Heidelore Fiedler<sup>5</sup> · Rainer Malisch<sup>2</sup>

#### August 2016

Risk evaluation of breast feeding with regard to concentrations of PCDDs, PCDFs, PCBs and DDTs

**Conclusions from several studies:** 

Prenatal exposure to these compounds is more important for effects than breastfeeding itself

#### Safety standards for human milk

#### **Recommended intake for (PCDD/F + dl-PCB)-TEQ**

- European Commission, Scientific Committee on Food (2001): tolerable weekly intake (TWI) of 14 pg WHO-TEQ/kg bw
- Joint FAO/WHO Expert Committee on Food Additives (JECFA) (2001): provisional tolerable <u>monthly</u> intake (PTMI) of 70 pg WHO-TEQ/kg bw/month

#### ➢ US EPA (2010):

oral reference dosis (RfD) of 0.7 pg TCDD/kg bw/day

#### **Recommended intake for DDT**

➢ WHO (2001):

provisional tolerable <u>daily</u> intake (TDI) of  $10 \,\mu g/kg$  bw

US EPA and ATSDR (2011): oral reference dosis (RfD) of 0.5 µg/kg bw/day

#### **Recommended daily intake**

- TDI, TWI, PTMI, RfD: meant for chronic life time exposure
- Not applicable to breastfeeding situation (covering a much shorter period of life – with exceedance of TWI/PTMI with one or two order of magnitudes)

#### Comparison of results for human milk from WHO/UNEP studies (2000 – 2012) with "safe" levels

			Ranges in human milk (pooled samples)								
	unit	safety standards as "Equivalent milk level"	Min	25th perc.	Median	75th perc.	90th perc.	95th perc.	Max		
WHO-PCDD/F-PCB-TEQ (2005 / UB)	pg/g lipid	0.2 - 0.9	1,5	5,6	9,4	14,3	20,3	23,7	49,0		
Total PCBs *)	ng/g lipid	7	2	18	38	121	223	347	1009		
Sum DDT **)	ng/g lipid	2300	23	171	396	1015	1849	2616	23472		

\*) in human milk as sum of 6 indicator PCBs

\*\*) in human milk calculated after correction of metabolites for molecular weight

# Risk-benefit assessment for PCDDs, PCDFs, PCBs and DDTs

#### CONCLUSIONS (1):

- Human milk levels of PCDDs,PCDFs and PCBs are still significantly above those considered safe
- ΣDDTs are below or around those considered safe in most countries.
- In comparison to pooled samples, individual samples will show some variation.
- Picture gets more complex, if other POPs included.

# Risk-benefit assessment for PCDDs, PCDFs, PCBs and DDTs

#### CONCLUSIONS (2):

- With respect to potential adverse health effects, <u>in utero exposure</u> is more important than lactational exposure.
- If potential adverse effects are balanced against positive health aspects for (breastfed) infants, the advantages of <u>breastfeeding</u> far outweigh the possible disadvantages.
- In view of the importance of *in utero* exposure due to maternal body burdens, all efforts should still be directed to further reducing human dietary and environmental exposure to these POPs.

### Outlook

Complex evaluation possible after performance of 7th round based on cost-effective study with pooled human milk samples (as end-point of bioaccumulation)

- Regional differentiation allowing identification of priorities for follow-up with regard to wide range of POPs (including new POPs)
- Effectiveness Evaluation: Time trends for countries with repeated participation

## Thank you !

![](_page_70_Picture_1.jpeg)

![](_page_70_Picture_2.jpeg)

![](_page_70_Picture_3.jpeg)

![](_page_70_Picture_4.jpeg)

![](_page_70_Picture_5.jpeg)