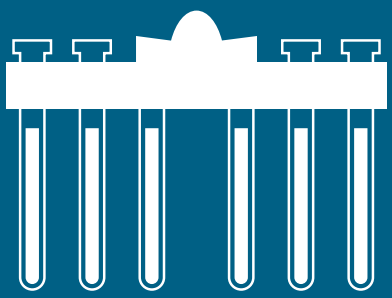
HUMAN BIO MONITORING



2nd International Conference on Human Biomonitoring, Berlin 2016
Science and policy for a healthy future

April 17 – 19, 2016
Langenbeck-Virchow-Haus
Berlin, Germany

Bundesministerium
für Umwelt, Naturschutz,
Bau und Reaktorsicherheit

Umwelt Bundesamt

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It gives us great pleasure to welcome you to the 2nd International Conference on Human Biomonitoring in Berlin entitled **“Science and policy for a healthy future”**.

Following on from the success of the conference in Berlin in 2010, the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety and the German Environment Agency are jointly organising the next international forum for an exchange on all aspects relating to human biomonitoring. Human biomonitoring is ideally suited to detecting human exposure to chemicals, recognising deficits in protection for the public against critical substances and measuring the success of measures for chemicals regulation. Human biomonitoring is therefore a key information and control instrument for health-related environmental protection.

International experts from the scientific sector, politics, authorities, industry and associations are invited to take a critical look at today’s chemicals that have the potential to harm human health and that should be investigated as a matter of priority, and to discuss the incorporation of human biomonitoring into national and international initiatives on the environment and health.

We also plan to organise more human biomonitoring conferences in future in order to promote and strengthen networking and cooperation between all stakeholders that are applying and further developing human biomonitoring to shape a healthy future.

Dr Barbara Hendricks
Federal Minister for the Environment, Nature Conservation, Building and Nuclear Safety

Maria Krautzberger
President of the German Environment Agency

Program

Sunday, April 17, 2016

5:00 pm – 7:00 pm	**Registration**
6:00 pm – 9:00 pm	**Welcome reception with scientific presentation** **Alexander Nies** Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany **Welcome address** **Per Magnus** Norwegian Institute of Public Health **The impact of the environment on health**

Monday, April 18, 2016

8:30 am	**Registration**
9:30 am – 10:10 am	**Opening session** **Barbara Hendricks**[1] Minister for the Environment, Nature Conservation, Building and Nuclear Safety, Germany **Human Biomonitoring – Why do we care?** **Maria Krautzberger**[2] President of the German Environment Agency **Human Biomonitoring across Europe – The way forward**
10:10 am – 10:40 am	Coffee break and poster viewing
10:40 am – 11:40 am	**Panel discussion 1** **Human Biomonitoring – a cornerstone of good political decisions** Moderator: **Andreas Gies**, German Environment Agency/UBA **Hermann Fromme**, German Human Biomonitoring Commission and Bavarian State Office for Health and Food Safety **Arnd Hoeveler**, European Commission, DG Research & Innovation **Sascha Gabizon**, Women in Europe for a Common Future/WECF **Elizabet Paunovic**, WHO European Centre for Environment and Health **Edgar Leibold**, BASF, Germany **Karl-Heinz Jöckel**, Institute of Medical Informatics, Biometry and Epidemiology, Essen University Hospital, Germany

German/English interpretation

[1] On the Minister's behalf: State Secretary Jochen Flasbarth
[2] On the President's behalf: Head of Division "Environmental Health and Protection of Ecosystems" Lilian Busse

Monday, April 18, 2016

11:40 am – 1:00 pm	Lunch and poster viewing
1:00 pm – 3:30 pm	**Session 1** **HBM programs – new developments** Chairs: **Robert Barouki,** Inserm-University Paris Descartes, France **Ovnair Sepai,** Public Health England, United Kingdom **Antonia Calafat** US Centers for Disease Control and Prevention, United States **Biomonitoring in NHANES – recent advances and future directions** **Douglas Haines** Health Canada **Health Canada's human biomonitoring initiatives – progress and uses** **Clémence Fillol** French Institute for Public Health Surveillance, Environmental Health Department **Prioritization of the biomarkers to be analyzed in the French biomonitoring program** **Break and discussion: 15 minutes** **Marike Kolossa-Gehring** German Environment Agency/UBA **The German Environmental Survey and the Environmental Specimen Bank – HBM for policy decisions** **Tamar Berman** Public Health Services, Ministry of Health, Israel **Human biomonitoring in Israel – recent results and developments** **Suejin Kim** National Institute of Environmental Research, Korea **Introduction of Korean National Environmental Health Survey (KoNEHS)**
3:30 pm – 4:00 pm	Coffee break and poster viewing
4:00 pm – 5:50 pm	**Session 2** **HBM in large scale birth cohorts** Chairs: **Birgit Wolz,** Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany **Michael Wilhelm,** Ruhr University Bochum, Germany **Ruth A. Etzel** Environmental Protection Agency, United States **Pediatric environmental health – the role of biomonitoring in birth cohorts**

	Shoji F. Nakayama National Institute for Environmental Studies, Japan **Japan's Environment and Children Study – lessons learned from incorporating HBM in a large-scale birth cohort study** **William D. Fraser** University of Sherbrooke, Research Center of Sherbrooke University Hospital/CHUS, Canada **Maternal-Infant Research on Environmental Chemicals (MIREC) – a Canadian biomonitoring birth cohort research platform** **Jun Jim Zhang** Shanghai Jiao Tong University, China **The Shanghai Birth Cohort – current status and results** **Sébastien Denys** The National Public Health Agency/ANSP, France **HBM in the ELFE birth cohort – results to date**
5:50 pm – 6:00 pm	End of the first day/Closing remarks

Tuesday, April 19, 2016

9:00 am – 10:30 am	**Session 3** **Broadening the HBM toolbox** Chairs: **Michael Bader**, BASF, Germany **Jana Klánová**, Masaryk University, Czech Republic **Gabriele Leng** Currenta GmbH, Germany **New specific and sensitive biomonitoring methods for chemicals of emerging health relevance** **Holger M. Koch** Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr-University Bochum/IPA **The quest for biomarkers of exposure to non-persistent chemicals** **Andy Nong** Health Canada **Pharmacokinetic modeling of health and exposure measures to support health risk interpretations** **Paolo Vineis** Faculty of Medicine, School of Public Health, Imperial College London, United Kingdom **The role of the "omics-techniques" in HBM, current and future applications**
10:30 am – 11:00 am	Coffee break and poster viewing

Tuesday, April 19, 2016

11:00 am – 12:15 pm	**Session 4** **HBM in health risk assessment** Chairs: **Lisbeth E. Knudsen**, University of Copenhagen, Denmark **Douglas Haines**, Health Canada **Martin Kraft** German Human Biomonitoring Commission and North Rhine Westphalian State Agency for Nature, Environment and Consumer Protection **HBM values derived by the German HBM Commission and their practical use** **Kembra Howdeshell** National Institute of Environmental Health Sciences/NIEHS, United States **Mixed exposure evaluation of pesticides and toxic substances, cumulative risk assessment** **Angelika Zidek** Health Canada **HBM data used in regulatory risk assessment under Canada's chemicals management program**
12:15 pm – 1:30 pm	Lunch and poster viewing
1:30 pm – 3:30 pm	**Session 5** **Harmonizing HBM approaches and data – progress in the international and European landscape** Chairs: **Argelia Castaño**, National Center for Environmental Health, Institute of Health Carlos III, Spain **Marika Berglund**, Karolinska Institutet, Institute of Environmental Medicine, Sweden **Greet Schoeters** Flemish Institute for Technological Research/VITO, Belgium **Results of the first Europe-wide HBM study** **Anke Joas** Consultancy for integrated solutions/BiPRO, Germany **Lessons learned from the COPHES/DEMOCOPHES process** **Leonardo Trasande** NYU School of Medicine, United States **Harmonizing approaches to burden of disease estimation due to environmental chemicals: endocrine disruptors as a case study**

	Megan Latshaw Association of Public Health Laboratories/APHL, United States **Harmonizing HBM approaches across the United States** **Sofie Nørager** European Commission, DG Research & Innovation **The European Commission's view on the EHBMI**
3:30 pm – 4:15 pm	Coffee break and poster viewing
4:15 pm – 5:30 pm	**Panel discussion 2** **Human Biomonitoring – the tasks ahead** Moderator: **Lilian Busse**, German Environment Agency/UBA **Peter van den Hazel,** Public Health Services Gelderland-Midden, Netherlands **Gerd Romanowski**, German Chemical Industry Association/VCI **Gertrud Sahler**, Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany **Catherine Ganzleben**, European Environment Agency/EEA **Carolyn Vickers**, World Health Organization/WHO
5:30 pm	**Summary and conclusion of the conference** **Jochen Flasbarth**[3], State Secretary, Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety, Germany

German/English interpretation

[3] On the State Secretary's behalf: Director General Gertrud Sahler

Welcome reception

The impact of the environment on health

Per Magnus
Norwegian Institute of Public Health

The presentation will take a bird eye's view on disease causality. Recent heritability estimates and findings from genome-wide association studies will be highlighted, and the framework for gene-environment interaction in the field of environmental medicine will be discussed. The global burden of disease project provides information that to some degree helps delineate the impact of the environment on health, but with several limitations. The impact of certain environmental factors can be ranked using etiologic fractions. These estimates are uncertain and depend on estimates of exposure levels as well as imprecise and often invalid relative risks associated with the exposures. Birth cohorts can provide important information on both the distribution of exposures as well as the risks associated with them. The experience of ten years of research on effects of environmental contaminants in the Norwegian Mother and Child Cohort Study will be summarized, including the presentation of a recent subproject on biomonitoring of human exposure. Despite all uncertainties, risk assessments based on research findings from toxicological and epidemiological studies remain the basis for public health actions.

Session 1

HBM programs – new developments

Biomonitoring in NHANES – recent advances and future directions

Antonia Calafat
US Centers for Disease Control and Prevention, United States

In modern societies, humans are exposed to a wide spectrum of environmental chemicals. Because some of these chemicals are toxic in experimental animals, understanding the extent of chemical exposures is of public health relevance and biomonitoring is increasingly used as a tool for exposure assessment.
In particular, biomonitoring programs are useful for investigating human exposure to environmental chemicals within populations. One of these programs, the National Health and Nutrition Examination Survey (NHANES) is conducted annually by the U.S. Centers for Disease Control and Prevention since 1999. NHANES collects data on the health and nutritional status of the general U.S. population, as well as biological specimens which can be used to assess exposure to select chemicals. NHANES biomonitoring data using blood from participants one year of age or older and urine from participants ≥6 years old have shown that exposure to some environmental chemicals is prevalent. In addition, NHANES data reveal that exposures to certain chemicals change as new compounds and products enter the consumers' market. NHANES data also suggest variability in exposure by sex, age, and race/ethnicity, all of which probably reflect lifestyle differences. This presentation will provide an overview of recent developments in the design of NHANES (e.g., include collection of urine from pre-school aged children since 2015). In addition, this presentation will also highlight the use of NHANES biomonitoring data to establish reference ranges, monitor trends of exposure (also to chemicals recently introduced in commerce), and provide exposure information for risk assessment (e.g., set intervention and research priorities, evaluate effectiveness of public health measures).

Health Canada's human biomonitoring initiatives - progress and uses

Douglas Haines
Health Canada

Human biomonitoring (HBM) is used to indicate and quantify exposure by measuring environmental chemicals, their metabolites or reaction products in biological specimens. The Canadian Health Measures Survey (CHMS) is the most comprehensive initiative providing general population HBM data in Canada.

The CHMS is an ongoing cross-sectional direct measures survey implemented in 2-year cycles. It provides nationally representative data on health, nutritional status, environmental exposures, and related risks and protective characteristics. The CHMS uses a stratified multistage household-based sampling strategy with sample size targets of 5,000 6-79 year olds for cycle 1 and 5,700 3-79 year olds for cycles 2 and beyond. The HBM component assesses blood, urine and hair collected from survey participants for chemicals. HBM blood and urine data are available for CHMS cycles 1 (2007-09), 2 (2009-11) and 3 (2012-13). Field collection has been completed for cycle 4 (2014-15), with cycle 5 (2016-17) in progress and cycle 6 planning (2018-19) being finalized.
HBM results for about 270 chemicals are expected over the six cycles of the CHMS (215 in individual blood, urine or hair, and 55 in pooled serum samples). The chemicals include metals and trace elements, PCBs, organochlorines, polybrominated flame retardants, perfluoroalkyl substances, volatile organic compounds and metabolites, environmental phenols, acrylamide, pesticides and metabolites, chlorophenols, PAH and phthalate metabolites, and tobacco biomarkers.

CHMS biomonitoring data have been used to: establish baseline concentrations in Canadians; inform public health, regulatory risk assessment and management decisions; and fulfil national and international reporting requirements. Concurrent efforts are underway in Canada to develop statistically- and risk-based concepts and tools to interpret HBM data.

Prioritization of the biomarkers to be analyzed in the French biomonitoring program

Clémence Fillol
French Institute for Public Health Surveillance, Environmental, Health Department

A national biomonitoring program has been implemented in order to estimate the exposure of the French population to various substances present in the environment:

- Analysis of biomarkers in the Elfe cohort (women who gave birth in 2011),
-Cross-sectional survey in the French metropolitan population aged 6-74 years called Esteban.

In 2009, a first set of compounds was selected by a working group included ministries (health, ecology and work) and public health agencies. Substances were included on the basis of analytical feasibility, toxicity and existing regulations. They were grouped by biomarkers sets (50 groups).
In order to reach a final list of biomarkers to be analyzed in both studies, we developed a method of prioritization based on consensual selection criteria applied through a formalized approach. Until the last step, anonymous was guaranteed to each expert.
1st step: Using a postal questionnaire, we submitted to each expert information items and asked for his opinion regarding the relevance of each one, using 0 if the item was not relevant until 10: totally relevant.
2nd step: We compiled the initial results into a second questionnaire asking each expert to comment upon all the answers, and modify its judgment on criteria relevance, if he thought it was necessary.
3rd step: Each expert confronted the results on criteria relevance with the list of 50 groups. Each expert had to grade each group for each criteria: 0.8 if the whole group of biomarkers fitted the criterion; 0.6 if the answer is rather yes; 0.4 if the answer is rather no and
0.2 if none of the biomarkers of the group fitted.
Total ratings were then calculated to rank the groups and thus produce a prioritized list.
4th step: A meeting was then convened to submit to the experts the prioritized list obtained. Discussions that took place during the meeting ended in the production of the list. Finally, more than 100 biomarkers belonging to 16 families were prioritized.

The German Environmental Survey and the Environmental Specimen Bank – HBM for policy decisions

Marike Kolossa-Gehring
German Environment Agency / UBA

Europeans of all ages are exposed to various chemicals via the environment, food, and consumer products. They are exposed to chemicals through a variety of oral, dermal and inhalative pathways. This results in an aggregated exposure to a mixture of chemicals. Safety of humans and the environment has to be safeguarded by producers and government. Human biomonitoring (HBM) has proven to be a powerful tool to quantify human exposure and support health risk assessment.

The German Environment Agency (UBA) employs two major HBM tools – the German Environmental Survey (GerES) and the German Environmental Specimen Bank (ESB). GerES is a population-representative study which has been carried out since the mid-1980s. The main study instrument is HBM in combination with ambient monitoring and the collection of information on exposure pathways and living conditions via interviews and questionnaires. The ESB is a permanent monitoring instrument following time trends of pollutants in humans and the environment. As samples are taken from typical ecosystems all over Germany, the ESB allows for analysing the transfer, accumulation and degradation of chemicals. The ESB is operated by UBA and subcontracted research institutes on behalf of the German Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB).

Moreover, UBA is involved in two HBM networks: 1) for using HBM for the development and assessment of policy measures in Europe within the European HBM Initiative and 2) as partner in a cooperation between BMUB and the German Chemical Industry Association (VCI) for developing new analytical HBM measures for substanc-

es with a potential health relevance and to which the general population might potentially be exposed to a considerable extent. In all its HBM activities UBA is advised by the German Human Biomonitoring Commission which statistically and toxicologically interprets exposure levels and derives HBM assessment values.

Human biomonitoring in Israel – recent results and developments

Tamar Berman
Public Health Services, Ministry of Health, Israel

The use of human biomonitoring (HBM) as a tool for environmental health policy and research is developing rapidly in Israel. Results from the 2011 Ministry of Health biomonitoring study showing relatively high urinary levels of cotinine and organophosphate pesticide metabolites in the general population were instrumental in supporting policy to reduce agricultural organophosphate pesticide use and to impose additional restrictions on smoking in public places. Results from the WHO-coordinated study in breast milk showing that exposure to persistent organic pollutants has declined in the last thirty years in Israel suggest that regulatory actions to reduce public exposure to these contaminants has been effective. Additional HBM data collected in Israel in recent years includes data on exposure to bisphenol A, phthalates, polycyclic aromatic hydrocarbons, and phytoestrogens in the general population; and on exposure to bisphenol A, phthalates, carbamate and organophosphate pesticides in a vegetarian community. A unique regional HBM collaboration project focused on exposure to organophosphate pesticides in Palestinian pregnant women. Currently, the Ministry of Health is collecting urine samples from children and adults in the framework of the National Nutrition and Health Study (MABAT), with the goal of combining HBM data on exposure to pesticides and environmental tobacco smoke with data on diet, health behavior, and health outcomes. In terms of research, there are three active birth cohort studies in Israel using HBM measures to study adverse health effects of phthalates, brominated flame retardants, and organophosphate pesticides. The Ministry of Health is working with partner organizations to develop a National Human Biomonitoring Laboratory. Future goals include collaboration with local NGOs to consolidate a long term national HBM plan for Israel and joining a regional HBM program in order to improve data harmonization.

Introduction of Korean National Environmental Health Survey (KoNEHS)

Suejin Kim
National Institute of Environmental Research, Korea

The Human Biomonitoring is a useful method to determine the level of exposure to hazardous environmental chemicals in human body as receptor, and identify the sources and exposure pathways as to make a proper countermeasures or policies. In Korea (Republic of), human biomonitoring survey (KoNEHS; Korean National Environmental Health Survey) was started from 2009, is based on the Article 14 of the Environmental Health Act. This survey is a nationwide population study, which has repeatedly been carried out every 3 years. The results of the KoNEHS are announced as National Statistics and are opened its raw data to researchers and the public. In 1st('09-'11) and 2nd survey('12-'14) were designed to determine the exposure level of environmental chemicals in Korean adults(19 years and older). Those were conducted 350, 400 nationwide sampling units, respectively. And participants scale was about 6,000. In the survey included questionnaires, biological sample collection such as blood and urine, some clinical analysis and the analysis of 16(1st), 21(2nd) environmental chemicals including metabolites. (Heavy metals, bisphenol-A, metabolites of phthalates/VOCs/PAHs, cotinine, etc.) Environmental chemicals in blood and urine samples were analyzed by AAS, GC/MS and HPLC/MS/MS etc. All participants were asked to complete a questionnaire by interview. The questionnaire was composed of 10 parts (including personal information, housing characteristics, indoor environment, transportation and usual dietary behavior and so on). Blood and urine samples were transported in a refrigerated state and were kept below -20 C until analysis. The chemicals and their metabolites analysis were carried out in 4 laboratories.

The 3rd survey is progressing from 2015 to 2017, this survey includes not only adults, also children and adolescents (3 years and older).

Session 2

HBM in large scale birth cohorts

Pediatric environmental health – the role of biomonitoring in birth cohorts

Ruth A. Etzel
Environmental Protection Agency, United States

Large scale studies of environmental influences on children's health and development are being planned or conducted in many places, including Japan, France, Shanghai (China), and Germany. The objective of these "next generation" studies is to better understand a broad range of environmental and social factors that influence the health and well-being of children. Some of these studies are designed to enroll tens of thousands of children and follow them for many years to investigate the influence of the environment on child growth, development and health. Environment is broadly defined in these studies and includes investigation of chemical, biological, physical and socioeconomic factors. An international group composed of study teams from Japan, France, Shanghai (China), and Germany has been meeting since 2011 to exchange information and work towards harmonization of processes that would provide the opportunity to compare methods and develop procedures to conduct combined analyses of results and data pooling procedures. Harmonization of infant health outcomes and biomarkers has been initiated. This presentation describes the progress of this work, and discusses the importance of biomonitoring as part of these birth cohort studies.

Japan's Environment and Children Study - lessons learned from incorporating HBM in a large-scale birth cohort study

Shoji Nakayama
National Institute for Environmental Studies, Japan

With rising concern over environmental effects on children's health and development, recent political initiatives, such as the G8 Environmental Ministers Meetings in 1997 and 2009, have encouraged the academic and government epidemiological research on children's environmental health. Many children's studies have conducted. worldwide. Nationwide large-scale birth cohort studies involving around 100,000 participants have taken place in several countries including Denmark, Norway and Japan (and until recently the U.S.). These studies collect environmental and biological samples to measure children's exposures during pregnancy and early childhood.

In Japan, the Ministry of the Environment started the Japan Environment and Children's Study or Jecs in 2011. Jecs is designed to evaluate the effect of the environment on children's health and development. In March 2014, the three-year recruitment was completed resulting in the registration of 103,106 pregnant women. Blood, urine, breast milk and hair samples were collected from mothers during pregnancy. Umbilical cord blood and children's hair were also sampled. Air and house dust samples are being collected from 5,000 households. Blood and urine samples will be collected from that 5,000 children at the ages of 2 and 4.

Available sample volume is limited while a vast range of chemical substances has to be evaluated for their effects on children's health and development. Especially due to the ethical consideration, it is challenging to collect samples in large volume and repeatedly from children. The number of samples to be analysed is also an important issue. New analytical methods should be developed to process huge number of samples in low cost. In Jecs, automated methods are being developed and applied to measure heavy metals, persistent organic pollutants, personal care products and nicotine metabolites and oxidative stress markers.

The Shanghai Birth Cohort – current status and results

Jun Jim Zhang
Shanghai Jiao Tong University, China

BACKGROUND: Certain environmental endocrine disruptors (EEDs), such as DDT and PCBs, are known to affect female reproductive health. Yet, the effects of emerging environmental pollutants on female reproduction are still unclear. OBJECTIVE: To assess the potential effects of bisphenol A (BPA), tricolosan (TCS) and certain pesticides on women's reproductive health. METHODS: This prospective cohort study recruited 1,183 couples who planned to conceive in Shanghai, China, between 2013 and 2015. The couples were interviewed and provided urine and blood samples. They were then prospectively followed every two months up to 12 months. BPA and TCS were quantified in preconception urine samples. The outcomes of interest included regularity of menstrual cycle, time-to-pregnancy and infertility. A nested case-control study was also conducted in 100 couples who tried to conceive continuously for 12 months but failed as cases and 100 couples who gave birth to a baby as controls. 76 pesticides were tested in preconception plasma samples. RESULTS: A total of 937 couples were followed up to 10 months or longer (follow-up rate 79.6%). Higher TCS levels were associated with approximately a 2-fold increased risk of abnormal menstrual cycle and 20–30% of reduction in fertility rate. But BPA had no effect on menstrual cycle or fecundity. Infertile women had higher levels of Naled (OR=4.3; 95% CI; 1.7-10.7), Cyanophos (1.62;1.20-2.17), Thiabendazole (1.91; 1.39-2.63) and Barban (1.67;1.05-2.67) than the controls. Clomazone was detected in all cases but in only 50% of the controls. CONCLUSION: In this prospective cohort study, TCS and certain pesticides were associated with abnormal menstrual cycle and reduced fecundity.

HBM in the ELFE birth cohort – results to date

Sébastien Denys
The National Public Health Agency/ANSP, France

As part of the French biomonitoring program, exposure biomarkers were measured in biological samples collected in 2011 from mothers of newborns randomly selected among the participants in the clinical and biological component of the cohort Elfe. The aim was to describe impregnation levels by a panel of chemicals, and their determinants, in mothers giving birth in continental France in 2011. For each biomarker, the geometric mean (GM) and 95th (P95) percentiles of the levels distribution were estimated, taking into account the sampling design and adjusting via calibration, in order to obtain estimates representative of this population. Multivariate analyses were conducted to search for the determinants of impregnation levels. Presentation will focus on a selection of organic and inorganic contaminants distribution and the main determinants of impregnation levels as well as a comparisons with the literature for the same population. These results provide a first global overview in a representative sample of French mothers giving birth. Form these data, reference internal exposure values will be defined in 2016. In the future, these values will be considered as the 2011 baseline levels of chemical impregnation for the studied population.

Session 3

Broadening the HBM toolbox

New specific and sensitive biomonitoring methods for chemicals of emerging health relevance

Gabriele Leng
Currenta GmbH, Germany

The Human Biomonitoring Project is a cooperation between the German Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB) and the German Chemical Industry Association (VCI). Aim of the project is the development of biomonitoring methods for selected substances for which by now no suitable analytical method exists. Substances are selected that might be taken in by the population in larger amounts or which could be of relevance to human health, e.g. plasticisers, foam components, flame retardants, antioxidants, UV filters.

In this presentation the challenges to cope for the aim to obtain innovative biomonitoring methods are visualized for the following chemicals: Di(2-propylheptyl)phthalate (DPHP), 2-Mercaptobenzothiazole (MBT), 4-Nonylphenol (NP), 4-tert-Octylphenol (OP), 3-(4-Methylbenzylidene)camphor (4-MBC), 3,5-Di-tert-butyl-4-hydroxytoluene (BHT), Climbazole, Mesamoll, 4,4´-Methylene diphenyl diisocyanate (MDI), 2,4- / 2,6-Toluene diisocyanate (TDI) and Hexabromocyclododecane (HBCDD). For these substances new specific markers were explored based on animal or human kinetic data with urine being the preferred matrix compared to blood. The determination of these markers was complex in all cases, because the sample preparation as well as the detection by LC/MS/MS or (HR)-GC/MS should enable the lowest possible detection limit by use of minimum biological sample. To get a first hint of a possible background level, the analytical methods were applied in about 40 persons for each chemical.

Moreover, for DPHP and MBT first results are presented here from population biomonitoring per-formed in the framework of The German Environmental Survey and the Environmental Specimen Bank on behalf of the German Federal Environment Agency. For these substances HBM values derived from the German HBM Commission are also available to evaluate population exposure.

The quest for biomarkers of exposure to non-persistent chemicals

Holger M. Koch
Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr-University Bochum (IPA)

Exposure biomarkers are increasingly used to provide an integrated measure of a person's chemical-specific exposure both, in environmental and occupational studies. However, the sole ability to measure a chemical in a human tissue does not necessarily make it a valid exposure biomarker. The quality of human biomonitoring (HBM) studies heavily relies upon the well-considered choice of the biomarker(s) and the matrix. Generally, urine is the preferred matrix for most non-persistent chemicals because of their toxicokinetic properties. Most non-persistent chemicals are metabolized and excreted quickly making urine the compartment with the highest concentrations of metabolites. When urinary metabolite excretion fractions are known, doses of the parent compound taken up can be reliably back-calculated from urinary metabolite levels. Selecting specific metabolites as exposure biomarkers in urine also minimizes contamination arising from collection, sampling, or analytical procedures. The non-persistent nature of many novel chemicals also creates new challenges in interpreting extent and duration of (transient) exposures in terms of inter- and intra-individual variabilities, short term vs. long term exposures and exposures during the time frame of biological or toxicological relevance. Special sample collection strategies (spot urines, 24h urines, biobanked samples) in conjunction with an appropriate set of biomarkers further strengthen the interpretative power of HBM data. The different aspects of appropriate exposure biomarker selection and application and de-novo exposure biomarker development will be illustrated on the example of parabens used as preservatives in personal care products, and the substance class of plasticizers.

Pharmacokinetic modeling of health and exposure measures to support health risk interpretations

Andy Nong
Health Canada

Consistent with initiatives in other countries, database of environmental contaminants measured in blood and/or urine from biomonitoring surveys and studies has been growing for the Canadian population. These biological measurements can provide exposure estimates to the population and help identify priority chemicals for which further action should be taken to protect the public's health. These results will require an extensive means to interpret population exposure to environmental contaminants. Since 2008, Health Canada has been developing Biomonitoring Equivalent (BE) to screen and evaluate biomonitoring measures from the general Canadian population. BEs are designed to leverage existing exposure guidance values and available pharmacokinetic models and data. The present work describes different applications and strategies of pharmacokinetic modeling and data to derive BE of environmental chemicals for the purpose of screening biomonitoring measures. A series of chemicals were screened with this approach and led to a series of communications and scientifically peer-reviewed publications that provide additional information for health assessment. Extensive work has also led to expand into provisional BE based on point-of-departures and doses that are defined into guidance values, including the use of extrapolated in vitro screening values extrapolated into biologically relevant exposure for the population. Lastly, this effort also led the development of a BE based hazard quotient to further help interpret biomonitoring data and rank exposure assessment priorities. The outcome of this research effort has led to the increased application of scientific biological data with BEs as a valuable exposure and biomonitoring screening tool for health risk assessment of environmental contaminants in Canada.

The role of the "omics-techniques" in HBM, current and future applications

Paolo Vineis
Faculty of Medicine, School of Public Health, Imperial College London, United Kingdom

The identification of hazardous environmental pollutants is complex, particularly in relation to chronic, non-communicable diseases. The main contributors to this complexity are the diversity of hazards that may exist, the typically low levels of environmental contaminants/pollutants, long latency periods, and largely unknown mechanisms of action. The unravelling of environmental causes of disease is also limited by the technical difficulties in defining, and accurately measuring exposures, and by considerable spatial, temporal, and intra-individual variation. The complex and partially unknown interaction with underlying genetic and other factors that modulate susceptibility and response to environmental exposures further complicates the process of delineating and understanding environmental hazards. To address such difficulties, the concept of the "exposome" was proposed, initially by Wild [2005], with more recent detailed development in relation to its application to population-based studies [Wild, 2012]. The original concept was expanded by others, particularly Rappaport and Smith [2010] who functionalized the exposome in terms of chemicals detectable in biospecimens. The exposome concept refers to the totality of exposures from a variety of sources including, but not limited to, chemical agents, biological agents, radiation, and psychosocial component from conception onward, over a complete lifetime, and offers a conceptual leap in studying the role of the environment in human disease [Exposome; Rappaport and Smith, 2010; Wild, 2012]. I will show examples from recent projects in the field.

Session 4

HBM in health risk assessment

HBM values derived by the German HBM Commission and their practical use

Martin Kraft
German Human Biomonitoring Commission and North Rhine Westphalian State Agency for Nature, Environment and Consumer Protection

Human biomonitoring is an effective tool to assess the body burden of contaminants or their metabolites in the human population. However, the central question always arises, if these measured concentrations are related to potential health effects. In Germany, the Human Biomonitoring Commission (HBM Commission) derives health based standards for contaminants in body fluids, to harmonize the evaluation.

The HBM Commission represents a federal task force, and is affiliated to the German Environment Agency (UBA). It consists of experts of various scientific fields like toxicology, epidemiology, statistics, analytics and others. These experts meet twice a year to discuss and give advice on current issues of concern, to evaluate exposure data and to derive guidance values. The results of the HBM Commissions activities are published and can as well be found on the UBA-homepage.

On the Basis of toxicological or epidemiological data, two Human Biomonitoring values are derived. The HBM-I value represents the concentration of a substance in human biological material below which there is no risk for adverse health effects. In contrast, the HBM-II value represents the concentration of a substance in a human biological material above which there is an increased risk for adverse health effects. Consequently, there is an acute need for exposure reduction measures and the provision of biomedical advice. Thus, the HBM-II value should be regarded as an intervention or action level. So far, the HBM Commission derived 18 HBM-values for different contaminants like metals, phthalates or polychlorinated biphenyls.

In this presentation, the approach of the HBM-Commission in deriving the HBM values will be depicted, the practical use of the HBM values in different risk assessment processes will be given for selected examples and the benefit of HBM in the context of risk assessment will be elucidated.

Mixed exposure evaluation of pesticides and toxic substances, cumulative risk assessment

Kembra Howdeshell
National Institute of Environmental Health Sciences/NIEHS, United States

Toxicological studies of defined chemical mixtures assist human health risk assessment by characterizing the joint action of chemicals. This presentation will review the effects of anti-androgenic chemical mixtures on reproductive tract development in rats with a special focus on the reproductive toxicant phthalates. Observed mixture data are compared to mathematical mixture model predictions to determine how the individual chemicals in a mixture interact (e.g., response addition – probabilities of response for each individual chemical are added; dose-addition – the doses of each individual chemical at a given mixture dose are combined together based on the relative potency of the individual chemicals). Phthalate mixtures are observed to act in a dose-additive manner based on the relative potency of the individual phthalates to suppress fetal testosterone production. Similar dose-additive effects have been reported for mixtures of phthalates with anti-androgenic pesticides of differing mechanisms. Data from these phthalate experiments in rats can be used in conjunction with human biomonitoring data to determine individual hazard ratios. Furthermore, data from the toxicological studies can inform the analysis of human biomonitoring data on the association of detected chemicals and their metabolites with measured health outcomes. Disclaimer: This abstract does not necessary reflect US EPA policy.

HBM data used in regulatory risk assessment under Canada's Chemicals Management Program

Angelika Zidek
Health Canada

As a part of the Chemicals Management Plan launched in 2006, the Government of Canada is currently assessing and managing, where appropriate, the potential health and ecological risks associated with approximately 4300 substances under the Canadian Environmental Protection Act (1999). Since that time, nearly 3,000 substances have been assessed, with human biomonitoring (HBM) data playing an increasingly important role. A number of trends have been found in terms of the types of substances that have HBM data available, the types of sub-populations and matrices examined, as well as the impact HBM data can have in regulatory decision making. Case studies are presented, including both inorganic and organic substances (e.g. selenium, triclosan, phthalates), which highlight the impact and overall role HBM has had in regulatory decision making as well as criteria used in the application of HBM data in human health risk assessment. An overview of its limitations in terms of how and when HBM data can be applied across a wide spectrum of both data rich and data poor substances when assessing human health in a regulatory setting is discussed as well as the role HBM data can play in regulatory risk assessment and priority setting.

Session 5

Harmonizing HBM approaches and data –

progress in the international and European landscape

Lessons learned from the COPHES/DEMOCOPHES process

Anke Joas
Consultancy for integrated solutions/BiPRO, Germany

The potential of Human Biomonitoring (HBM) as policy tool is linked to availability of comparable data. Against this background the EU Environment and Health Action Plan asked explicitly for the development of a coherent approach to HBM in Europe in 2004.

After preparatory actions from 2005-2007 the European twin projects (COPHES & DEMOCOPHES www.eu-hbm.info) explored and tested an approach how to harmonise activities throughout Europe as an important step towards a sustainable EU HBM programme. COPHES established a harmonised study protocol and a functional expert network, whereas DEMOCOPHES tested feasibility of harmonised HBM in a pilot survey.

The pilot project clearly showed potentials and challenges of harmonising HBM within Europe that can form an important basis for future European HBM developments and international cooperation in the field. We will present key lessons learnt from the COPHES/DEMOCOPHES process in terms of comparability of data, study protocols, training and capacity building, data management and interpretation, quality assurance and communication, legal and ethical constraints, as well as infrastructural and funding needs. We will emphasise potentials and limitations of using harmonise HBM as policy tool, and provide overall recommendations from the projects for future priorities.

COPHES and DEMOCOPHES were funded by the EU (FP7 grant agreement 244237 and LIFE09 ENV/BE/000410). We would like to express our special thanks to all Consortium partners for the excellent cooperation throughout the project work.

Harmonizing approaches to burden of disease estimation due to environmental chemicals: endocrine disruptors as a case study

Leonardo Trasande
NYU School of Medicine, United States

Rapidly increasing evidence has documented that endocrine disrupting chemicals (EDCs) contribute substantially to disease and disability. We recently quantified a range of health and economic costs that can be reasonably attributed to EDC exposures in the European Union. A Steering Committee of scientists adapted the Intergovernmental Panel on Climate Change weight-of-evidence characterization for probability of causation based upon levels of available epidemiologic and toxicologic evidence for one or more chemicals contributing to disease by an endocrine disruptor mechanism. To evaluate the epidemiologic evidence, the Steering Committee adapted the WHO Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group criteria, while the steering committee adapted definitions recently promulgated by the Danish Environmental Protection Agency for evaluating laboratory and animal evidence of endocrine disruption. Expert panels used the Delphi method to make decisions on the strength of the data. Expert panels achieved consensus for probable (>20%) EDC causation for IQ loss and associated intellectual disability; autism; attention deficit hyperactivity disorder; childhood obesity; adult obesity; adult diabetes; cryptorchidism; testicular cancer; male infertility; female reproductive conditions and mortality associated with reduced testosterone. Accounting for probability of causation, using the midpoint of each range for probability of causation Monte Carlo simulations produced a median cost of €163 billion annually across 1000 simulations. We present here approaches to harmonize these estimates with those forthcoming for the United States, as well as for other environmental exposures.

Harmonizing HBM approaches across the United States

Megan Latshaw
Association of Public Health Laboratories/APHL, United States

For the last three decades, the US Centers for Disease Control and Prevention's (CDC) Environmental Health Laboratory has used biomonitoring to provide critical data about the US population's exposure to hundreds of environmental chemicals. These findings have been published in peer-reviewed literature and in CDC's National Report on Human Exposure to Environmental Chemicals, an ongoing assessment of exposure for the civilian, non-institutionalized US population.

CDC's current survey design does not allow calculation of exposure estimates on a state-by-state or city-by-city basis. For example, CDC cannot extract a subset of data and examine levels of blood lead that represent a state population. In order to produce such data, states need the capability and capacity to conduct their own biomonitoring assessments where chemical exposure is a concern. With this capability, states can produce community-specific exposure data, comparable to CDC's national biomonitoring data.

With support from the broader environmental health community, APHL finalized a five-year National Biomonitoring Plan for Public Health Laboratories in 2009. The plan sought to build an integrated network of public health laboratories, while also providing guidance and support in tracking the population's exposure to chemicals. Now, a loosely-organized structure exists, with comprehensive guidance documents to assist laboratories and epidemiologists interested in beginning a biomonitoring program, and an online toolkit featuring document libraries, a discussion board and relevant links.

APHL's newest National Biomonitoring Plan serves as a guide for formalizing a nation-wide, state-based system for biomonitoring. It will allow data comparison across multiple jurisdictional levels and will ultimately enable public health practitioners to better address community exposures.

Curricula vitae of chairs, speakers and panelists

Barbara Hendricks

Minister for the Environment, Nature Conservation, Building and Nuclear Safety, Germany

Name and Surname: Barbara Hendricks
Position: Federal Minister
Organisation: Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety

Brief CV Barbara Hendricks
Barbara Hendricks has been the Federal Minister for the Environment, Nature Conservation, Building and Nuclear Safety since December 2013. Before that she served as the federal treasurer of the Social Democratic Party beginning in 2007.

From 1998 to 2007 she was a Parliamentary State Secretary at the Federal Ministry of Finance. Since 1994 Barbara Hendricks, who has a doctorate in history, has represented her home district of Kleve in the German Bundestag. Prior to that she had gained political and professional experience working for the Deutsches Studentenwerk (National Association for Student Affairs) and in the administration of the Land North Rhine-Westphalia.

From 2001 to 2013 she was a member of the Executive Committee of the SPD.

Barbara Hendricks was born on 29 April 1952 Kleve in the Lower Rhine region, where she still lives.

Maria Krautzberger

President, German Environment Agency/UBA

Vocational training
1973 – 1976 Study of sociology and English area studies, LMU Munich
1976 – 1979 Study of public administration, University of Konstanz

Professional career
Oct 1979 – Sept 1980 Academic Staff, Seminar for Political Science, University of Bonn
Oct 1980 – Sept 1986 Scientific Manager and Section Head, City of Wuppertal urban administration
Sep 1986 – Nov 1989 Head of Division "Environmental Planning and Coordination", Office of Urban Development and Environmental Protection, City of Wuppertal urban administration
Nov 1989 – Feb 1992 Head, Deputy Head of Office of Environmental Protection, City of Wuppertal urban administration
Mar 1992 – Feb 1998 Senator for Environmental Affairs, Hanseatic City of Lübeck
Jan 1997 – Feb 1998 Deputy Mayor, Hanseatic City of Lübeck
May 1998 – Nov 1998 Staff member, VEAG, Marketing department
Dec 1998 – Dec 1999 Professional Deputy for City Planning, Building and Housing, City of Oberhausen
Dec 1999 – Dec 2011 Permanent Secretary, Senate Department for Urban Development and the Environment of the City of Berlin (Traffic, Environment, Berlin Forests, Urban Planning, Regional Planning)

Since May 2014 President, German Environment Agency

Michael Bader

BASF, Germany

Michael Bader studied chemistry at the University of Muenster (Germany) and received his doctoral degree in 1996 from the University of Erlangen-Nuremberg for his dissertation on quantitative GC-MS analyses of protein adducts of alkylating chemicals.

He specialized in human biomonitoring and analytical toxicology, and received the venia legendi in occupational and environmental toxicology in 2007 at Hannover Medical School.

Since 2010, he is responsible for the human biomonitoring group of the Occupational Medicine & Health Protection Department at BASF SE, Ludwigshafen/ Germany.

Michael Bader is a member of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) of the German Research Foundation (DFG) and its working groups Analyses in Biological Materials and Limit Values in Biological Materials. He is chairman of the ad-hoc working group Dermal Absorption of the MAK Commission, and a member of the Biological Exposure Indices Committee of the American Conference of Governmental Industrial Hygienists (ACGIH).

Robert Barouki

Inserm-University Paris Descartes, France

Professor of Biochemistry
Director Inserm unit 1124, University Paris Descartes
Head of metabolic biochemistry laboratory,
Necker Enfants maladies Hospital, Paris

Education/Training

1983 University of Paris 5, France: M.D.
1982 Ecole Normale Supérieure Ulm, France: Biochemistry Pharmacology
1982 University of Paris, France: Ph.D.; Pharmacology
1986 Johns Hopkins Medical School: Post-doc; Molecular biology
1992 University of Paris, France: Habilitation; Pharmacology

Biographical sketch

Robert Barouki is a biochemist and molecular biologist whose main research focus during the last fifteen years has been understanding the mechanisms of toxicity of environmental pollutants such as dioxin. In particular, he has studied the biological consequences following the activation of the dioxin receptor AhR. He studied the different effects triggered by different ligands of the AhR using in particular "-omics" technologies, suggesting that part of the toxicity may be related to the disruption of endogenous functions.

In addition, as head of the clinical metabolic biochemistry department, he has initiated and organized a shared mass spectrometry facility at the Necker.

Marika Berglund

Karolinska Institutet, Institute of Environmental Medicine, Sweden

Marika Berglund is deputy Director of the Institute of Environmental Medicine (IMM), Karolinska Institutet (KI), Stockholm. She has a PhD in Toxicology, and is associate professor in Environmental Medicine at KI. Research focus is on exposure assessment methodologies and environmental health risks. She is heading the Risk assessment secretariat at IMM, and is a member of the Steering Committee of the National Health Related Environmental Monitoring programme (HÄMI), coordinated by the Swedish Environmental Protection Agency. She is member of the interim management board of the European Human Biomonitoring Initiative; and was member of the former European Commission's European Human Biomonitoring Steering Group. She was a partner of the EU projects ESBIO and COPHES, and was Principal Investigator of the Swedish part of the European DEMOCOPHES project.

She has more than 20 years' experience in collaborating with and assisting national authorities (Swedish Environmental Protection Agency, National Food Agency, Swedish Board of Health and Welfare, Swedish Chemicals Agency) as well as European authorities and international organizations (EFSA, World Health Organization, United Nations Development Programme) in the field of exposure and health risk assessment of chemicals.

Tamar Berman

Public Health Services, Ministry of Health, Israel

Dr. Tamar Berman was born in Israel and completed her doctoral studies at the Hebrew University of Jerusalem. She is currently the Chief Toxicologist for Environmental Health at the Israel Ministry of Health. Dr. Berman headed the Israel Ministry of Health Human Biomonitoring Study conducted in 2011 and is currently heading the 2015 Israel Human Biomonitoring Study in children and adults. She is a researcher in longitudinal birth cohort studies using biomonitoring measures and in studies on exposure to environmental contaminants in Palestinian pregnant women. In addition to her role as a researcher, she is involved in regulatory toxicology and policy development related to a broad range of environmental health issues including pesticides and biocides; drinking water; and consumer products.

Lilian Busse

German Environment Agency/UBA

Head of Division,
Environmental Health and Protection of Ecosystems
German Environment Agency, Wörlitzer Platz 1,
06844 Dessau-Roßlau, Germany
Telefon: +49-340-2103-2299, Lilian.Busse@uba.de

Professional Experience
since April 2015 Head of Division, Environmental Health and Protection of Ecosystems, German Environment Agency, Germany

2006 – 2015	Lead Scientist, California Environmental Protection Agency, San Diego, USA
2002 – 2006	Scientist, Scripps Institution of Oceanography, San Diego, USA
2004-2006	Environmental Consultant, Weston Solutions, Carlsbad, USA
2000 – 2002	Postdoctoral Researcher, University of California Santa Barbara, USA
2001	Environmental Consultant, URS Corporation, Santa Barbara, USA

Education

1994 – 1999	Ph.D., Freshwater Ecology, Technical University Berlin, Institute of Environmental Engineering, Germany
1987 – 1993	M.S., Freshwater Ecology, Technical University Munich, Germany

Professional Affilations
Member of the Society of Freshwater Science
Reviewer for several scientific journals, and funding agencies
Secretary and Board member of the San Diego Stream Team

Antonia Calafat

US Centers for Disease Control and Prevention, United States

Antonia Calafat is the Chief of the Organic Analytical Toxicology Branch at the Division of Laboratory Sciences, National Center for Environmental Health of the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. She earned her Bachelor, Master and Doctoral degrees in Chemistry from the University of the Balearic Islands (Spain). Prior to her career at CDC, she was a Fulbright Scholar and a Research Associate at Emory University.

She currently leads CDC's biomonitoring programs for assessing human exposure to pesticides; polycyclic aromatic hydrocarbons; organophosphate flame retardants; persistent organic pollutants such as polyfluoroalkyl compounds; polybrominated diphenyl ethers; and polychlorinated dibenzo-p-dioxins, furans, and biphenyls; and chemicals added to consumer and personal-care products such as phthalates and phenols (e.g., bisphenol A, triclosan, parabens).

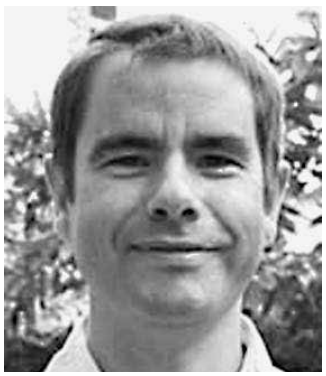
Antonia has developed and maintained extensive collaborative research with leading scientists in the fields of exposure science, epidemiology, toxicology and health assessment, and has coauthored more than 300 peer-reviewed publications. Her research has made relevant contributions to CDC's biomonitoring program including the CDC's National Reports on Human Exposure to Environmental Chemicals.

Argelia Castaño

National Center for Environmental Health, Institute of Health Carlos III, Spain

Coordinator and responsible for the Spanish National Program of Human Biomonitoring by mandate of the Ministry of Agriculture, Food and Environment. Under this mandate reference values for heavy metals, POPs and other pollutants were established for Spanish adult population.

At European level, belongs to the expert group on Human biomonitoring and has been leading the WP3 (Quality Assurance) in the FPVII-EU Project COPHES. She acted as Spanish National Focal point European project Life+ DEMOCOPHES. Member of the Technical Working Groups (TWG) heavy Metals and the TWG on Research needs for the preparation of the Environment and Health Action Plan 2004-2010. Temporary adviser for WHO, involved in the UNEP/WHO project on mercury human biomonitoring organized by WHO Regional Office for Europe.



Sébastien Denys

The National Public Health Agency/ANSP, France

Education

2011 Ability to be Head of Research (HDR, University of Lorraine) “Towards the Integration of the Bioavailability Concept in Soil Risk Assessment and Management”

2002 PH.D. in Agronomy (University of Lorraine, France)

Work Experience

Since 08/2015 French Institute for Public Health Surveillance (INVS), Environmental Health Department
Acting Director for the Environment and Health Department
Management of 50 persons (epidemiologists, statisticians, metrologists, sociologist,...)
Fields covered: surveillance of public health in relation with the environment (air, soil, water pollution); biomonitoring,...

2011-2015 French Agency for Food, Environment and Occupational Health Safety (ANSES), Risk Assessment Department
Head of unit “Method and studies”, 18 persons managed Fields covered biostatistics, modeling, food and environmental risk assessment

2002-2011 National Institute for Industrial Risk and Environment (INERIS) : Scientist and Project leader on risk assessment, contaminated sites and bioavailability concept

Ruth A. Etzel

Environmental Protection Agency, United States

Ruth A. Etzel, M.D., Ph.D. is the Director of the Office of Children's Health Protection at the US Environmental Protection Agency.

Previously she was Professor of Epidemiology at the University of Wisconsin Zilber School of Public Health. From 2009-2012 she served as Senior Officer for Environmental Health Research at the World Health Organization.

She completed medical school at the University of Wisconsin and residencies in Pediatrics and Preventive Medicine in Chapel Hill, North Carolina. After completing a pediatric residency, Dr. Etzel was a Robert Wood Johnson Clinical Scholar in Chapel Hill, and received her PhD in Epidemiology from the University of North Carolina School of Public Health. As a Commissioned Officer in the United States Public Health Service, Dr. Etzel served in numerous public-sector leadership positions including: Centers for Disease Control and Prevention (Founding Chief of the Air Pollution and Respiratory Health Branch), Department of Agriculture (Director of the Division of Epidemiology and Risk Assessment) and Indian Health Service.

Dr. Etzel is the founding editor of the popular AAP book Pediatric Environmental Health, of which a 3rd edition was published in 2012.

Clémence Fillol

French Institute for Public Health Surveillance, Environmental Health Department

Education

2010 PH.D. in Public Health (University of ParisDescartes) "Exposure of a population to arsenic; assessment of the attributable fraction of the soil"

2007 Pharmacist Doctor (University of ParisDescartes)

2001 - 2006 Pharmacy Residency

2005 Postgraduate Degree Following my Master: Assessment and Management of Environmental Risks and Professionals

Work Experience

Since 11/2009 French Institute for Public Health Surveillance (INVS), Environment Health Department

- Management of Esteban project (health study on the environment, biomonitoring, physical activity and nutrition);
- Participation in the analysis of the results of the perinatal component of biomonitoring program;
- Prioritization of biomarkers to be analyzed in the biomonitoring program;
- Preparation of the Study Esteban: protocol and questionnaires;
- Definition of the french national biomonitoring strategy

06/2005–11/2009 INVS, Environment Health Department Management of an arsenic biological study in the population of the eastern of the France

09/2004–06/2005 Laboratory Public Health and Environment (University of ParisDescartes) Participation in a study cohort of 3, 500 newborns Paris region

Jochen Flasbarth

State Secretary, Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety, Germany

Career

Since 2013 State Secretary at the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB), Berlin/Bonn

2009-2013 President of the Federal Environment Agency (UBA), Dessau
2003-2009 Director General of Nature Conservation and Sustainable use of Natural Resources, Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU), Berlin/Bonn
1994-2003 President of the Nature and Biodiversity Conservation Union (NABU)
1989-1994 Head of the editorial office of the Economica Verlag (publishing house)

Honorary Appointments (i.a.)

- German Council for Sustainable Development
- ZDF Television Board
- Supervisory board of the Wuppertal Institute for Climate, Environment and Energy
- Executive board of the German League for Nature and Environment

Hermann Fromme

Department of Chemical Safety and Toxicology, Bavarian Health and Food Safety Authority, Germany

Current position

since 2010 Head of the Department of Chemical Safety and Toxicology, Bavarian Health and Food Safety Authority, Munich

Education

1976-1977 Study of Social Sciences at the University of Goettingen
1977-1984 Study of Human Medicine at the Ludwig-Maximilians-University, Munich and the Free University, Berlin
1984 Degree: Medical doctor
03/1987 Dissertation on "Hypertension in a representative rural population" at the Ludwig-Maximilians-University, Munich
10/2002 Habilitation in Environmental Hygiene at the Free University, Berlin (Carcinogenic air pollutions – exposure and risk assessment using the example of Berlin)
since 12/2007 Associate professor at the Ludwig-Maximilians-University, Munich

Professional career

1985/1989 Working in the internal medicine unit of a hospital in Berlin and in different departments of local health authorities
1989/1994 Head of the Department of Air and Soil Hygiene, Human Biomonitoring, and Toxicological Assessments of the Berlin Senate Administration for Social Affairs and Health
1995/2000 Head of the Institute of Environmental Analysis and Human Toxicology, Berlin
2001/2003 Head of the Department of Environmental Health of the Senate Administration for Health, Berlin
2003-2010 Head of the Department of Environmental Health, Bavarian Health and Food Safety Authority, Oberschleissheim

Sascha Gabizon

Women in Europe for a Common Future/WECF

Sascha Gabizon, developed the organisation "WECF International" (with offices in Germany, France, Netherlands, Georgia) to become a major international network of 150 women and environment organisations working for a "Healthy Environment for All" see www.wecf.org. In Germany and other EU countries, the focus of WECF is on implementing and strengthening health and environment legislation, in particular regulations regarding chemicals, biocides and toys safety.

WECF informs consumers and in particular parents, on the vulnerability of the developing child to exposure of hazardous chemicals in daily use products and foods. At global level, Sascha Gabizon co-facilitates the Women's Major Group at the UN ensuring participation of over 600 Women's organisations in the UN Environmental Assembly and the Agenda 2030 for Sustainable Development (www.womenmajorgroup.org).

She is also engaged with in the Climate negotiations, promoting safe and sustainable energy. Before joining WECF she worked at the "Wuppertal Institute for Climate, Environment and Energy" where she worked on cooperation with social responsible businesses and was involved in research on the ecological footprint of consumer products. Sascha Gabizon has an MBA from the French Business School ESCP/EAP, and a degree from the Free University of Amsterdam. She has lived in Africa and Europe and is fluent in 5 languages.

Catherine Ganzleben

European Environment Agency/EEA

Catherine is responsible for work on chemicals and environment at the EEA, as well as the wider dimension of the relationships between environment, health and well-being. Her work sits within the programme on Integrated Environment Assessments, and is framed by the 7th Environmental Action Programme's vision that in 2050 we live well, within the planet's ecological limits. Catherine has been at the EEA since January 2014.

From 2008-2013, Catherine worked for a Brussels-based consultancy delivering projects on chemical policies and other environmental and public health issues to the Commission and other clients. She worked for two years for the chemicals and waste programme of UNITAR, United Nations Institute for Training and Research, delivering technical assistance projects to UN partner countries. Prior to that she reported on international negotiations on chemicals for the Earth Negotiations Bulletin, including SAICM and the POPs, PIC and Basel Conventions. Catherine has a D.Phil. in economic geography from the University of Oxford, a master of science in conservation biology and a degree in zoology.

Andreas Gies

German Environment Agency/UBA

Andreas Gies is head of the Department of Environmental Hygiene of the German Environment Agency. The department is responsible for almost all aspects of environment and health including human biomonitoring, indoor air quality, environmental medicine, human environmental exposure, burden of disease, and microbiology. The Institute looks back to more than 110 years of history, being founded in 1903. Thus it is the oldest part of the German Environment Agency.

Andreas Gies is also head of the WHO Collaborating Centre for Air Quality Management and Air Pollution Control.

Back in 1988 he worked for the German Health Agency and headed a project on acute vertebrate toxicology. At the German Environment Agency he worked in the fields of ecotoxicology, scientific planning and environmental reporting.

Andreas Gies is a native Berliner and studied biology and chemistry at Free University of Berlin. He received a Master's degree on "Biochemistry of the aging brain" and a doctorate on "Invertebrate muscle physiology". His research areas are human biomonitoring, assessment of health effects of environmental pollutants and exposure analysis. He published more than 40 scientific papers, including UBA reports and book chapters. Since 2010 he has been editor of the journal "Chemosphere, Environmental Toxicology and Risk Assessment".

Douglas Haines

Health Canada

Douglas Haines is a Science Advisor in Health Canada's Healthy Environments and Consumer Safety Branch. In his thirty year career in environmental health, he has been engaged in issues spanning air pollution, ecosystem health, climate change, and chemical surveillance and monitoring.

Under the Government of Canada's Chemicals Management Plan, he developed and implemented national human biomonitoring and environmental monitoring initiatives to track Canadians' exposures to environmental chemicals and their integration into health risk assessments. This includes the biomonitoring component of the Canadian Health Measures Survey and surveillance in Canada's north which is carried out in partnership with the federal Northern Contaminants Program.

Mr. Haines has managed Health Canada's Great Lakes Health Effects Program and the health component of the St. Lawrence Vision 2000 Program which focused on health and environmental pollution in these ecosystems.

In partnership with Statistics Canada, he developed the concept for the Canadian Health Measures Survey, launched in 2007, which is now providing human health data on a national scale.

He has published in peer reviewed journals and has presented at numerous Canadian and international, scientific, public and policy venues.

Arnd Hoeveler

European Commission, DG Research & Innovation

Prof. Arnd Hoeveler is Head of Unit – Advanced health research Directorate-General for Research and Innovation European Commission

Arnd Hoeveler received his PhD from the Institute of Genetics at the University of Cologne.
In 1991 he was awarded a full Professorship in Biochemistry and Molecular Biology in France. He served several positions in France before joining the Directorate-General for Research and Innovation at the European Commission in 1996.

Between 2001 and 2006 he served as Head of Unit, covering Infectious Diseases, and led several European programmes dealing with HIV/AIDS, Malaria and Tuberculosis.

Since 2007 he was Head of Unit of the European Commission's Health Biotechnology programme and is now in charge of the unit 'Innovative tools, technologies and concepts in health research' dealing with Regenerative Medicine, Advanced Tools and Technologies, Systems Medicine, Predictive Toxicology, Animal Replacement Strategies and Human Biomonitoring.

He is an observer on several International Advisory Boards.

Kembra Howdeshell

National Institute of Environmental Health Sciences/ NIEHS, United States

Kembra Howdeshell, Ph.D., is a Health Scientist in National Toxicology Program's Office of Health Assessment at the National Institute of Environmental Health Sciences (NIEHS) in the United States. She provides National Toxicology Program with expertise in endocrinology, reproductive biology, and toxicology.

She is primarily responsible for conducting literature evaluations using systematic review methodology on environmental chemicals or mixtures for which there is a concern for human health. Dr. Howdeshell earned her Ph.D. in Biology from the University of Missouri-Columbia in 2002.

Prior to joining the National Toxicology Program, she conducted postdoctoral studies at the University of Michigan-Ann Arbor, and the United States Environmental Protection Agency (EPA). Her research interests have focused on the effects of endocrine disruptive chemicals on reproduction and development in rodent and amphibian models. Specifically, her postdoctoral work at EPA and continued interest focus on the effects of individual and combinations of phthalates on reproductive development in rats. Her mixture work has used by the National Academy of Sciences in their report on Phthalates and Cumulative Risk Assessment: The Tasks Ahead (2008) and, more recently, by the United States Consumer Product Safety Commission's Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives.

Anke Joas

Consultancy for integrated solutions/BiPRO, Germany

Anke Joas (PhD) is member of the management board of BiPRO and head of department for sustainability and environment and health. She was educated as a medical doctor and has more than 20 years of professional work experience. After clinical work she has been providing consultancy services in the areas of environment and health policies since 1999.

Anke is expert in HBM, POPs, exposure and socio-economic impact assessment and circular economy. She has expertise in the field of prioritisation and substitution of chemicals of concern, and is involved in health impact assessment under REACH and regulations on occupational health.

Anke participated in the coordination of COPHES/DEMOCOPHES and was responsible for the work package on policy support, and has managed a number of large European consortia for policy advice and numerous European and national projects in different the fields of environment and health policies. Her particular focus is on policy advice.

Currently Anke is leading research work on how to integrate environmental health in European health information in the framework of the EU funded research project BRIDGE health http://www.bridge-health.eu/. This work will prepare background for the envisaged European HBM Initiative.

Karl-Heinz Jöckel

Institute of Medical Informatics, Biometry and Epidemiology, Essen University Hospital, Germany

Prof. Dr. Karl-Heinz Jöckel is Director of the Institute for Medical Informatics, Biometry and Epidemiology, University Clinics of Essen.

1972 - 1977 Study of Mathematics and Economics at Münster University Major: Mathematical Statistics and Probability Theory. Minor: Operations Research

1974 Vordiplom in Math. (comparable to B.A.)
1975 Vordiplom in Economics (comparable B.A.)
1977 Diploma in Math. (comparable to M.A.)
1982 Doctorate in Statistics (Dr. rer.nat.) at the Department of Statistics, Dortmund University
1989 Habilitation in Applied Statistics, Dortmund University

1977 - 1983 Research Assistant at the Department of Statistics, Dortmund University

1979 - 1983 Managing Director of the Statistical Consulting Centre at the Department of Statistics

1983 - 1994 Head, Division of Biometry and Data Processing and Deputy Managing Director of the Bremen Institute for Prevention Research and Social Medicine

1994 - now see above (I.)

2001 – 2002 Vice Rector and Rector of the University of Essen

2004 – 2008 Dean of the Medical Faculty of the University of Duisburg-Essen

Suejin Kim

National Institute of Environmental Research, Korea

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Address National Institute of Environmental Research, Hwangyung-ro 42, Seogu, Incheon, KOREA

Education

2000-2004 Ph.D. candidate, Graduate School of Engineering, Kyoto University, Kyoto, Japan

1992-1995 M.S., Department of Environmental Engineering, Graduate School of Engineering, Yonsei University, Seoul, Korea

Work Experience

1995-1999/2005-2010 Risk Assessment Research Division, National Institute of Environmental Research (NIER), Ministry of Environment (MOE), KOREA

2010-2013 Indoor Environment & Noise Research Division, NIER, MOE, KOREA

2014-present Environmental Health Research Division, NIER, MOE, KOREA

Project ongoing

NIER, MOE, KOREA, **2014~present**, "Korean National Environmental Health Survey (KoNEHS)"
NIER, MOE, KOREA, **2015~present**, "Korean Children's Environmental Health Study (Ko-CHENS)

Jana Klánová

Masaryk University, Czech Republic

- Full professor of Masaryk University in Brno, Czech Republic
- Director of the Research Centre for Toxic Compounds in the Environment (RECETOX), Regional Centre for Technology Transfer and Capacity Building in Central and Eastern Europe, and RECETOX research infrastructure which is a part of the Czech Roadmap of Large Research Infrastructures as well as ESFRI Roadmap
- Research interest: Fate of chemical compounds in the environment, transport and transformation processes, human exposure pathways, environmental determinants of health
- Bibliometric Indicators: 130 refereed international journal articles, 8 book chapters, more than 2000 citations, h factor of 28
- International Recognition: Member of the international Expert Group of advisors supervising implementation of the Global Monitoring Plan under the Stockholm Convention, Leading partner for the area of Health (HE-2) of the Global Earth Observation System of Systems (GEOSS), Czech Delegate in the Programming Committee of Horizon 2020
- Research projects: EU Structural Funds (2), HORIZON 2020 (2), EU FP7(3), EU InterReg, AMVIS/KONTAKT, NATO, UNEP/GEF, UNIDO, Granting Agency, Technology Agency, Ministry of Environment, Ministry of Education of the CR
- Teaching activities: Environmental chemistry, Genomics and Proteomics

Lisbeth E. Knudsen

University of Copenhagen, Denmark

M.Sc. in Biochemistry (1980). PhD in Biomedicine 1993.

1980- : Toxicologist at the Environmental Protection Agency, Copenhagen
1983- : Toxicologist at the Working Environment Agency, Copenhagen
1986- : Researcher, Phd student and senior researcher at the National Institute of Occupational Health
1998-: Preclinical assessor at the Danish Medicines Agency
2000-: Professor in Animal free Toxicology at the Institute of Public Health, University of Copenhagen
2015: Certified as European Registered Toxicologist(ERT)

Research in toxicology, genotoxicology, biomonitoring of environmental and occupational exposures, alternatives to animal experiments (replacement), ethical aspects of human biomonitoring.

At the national level Lisbeth coordinated major biomonitoring studies within occupational health: stainless steel welders, bus drivers and mail carriers. Past president in the European Consensus Platform for 3R Alternatives to Animal Experimentation (ECOPA) and current president of the European Mutagenesis and Genomics Society (EEMGS).

LEK participated in the coordination team of COPHES and was national contact point of DEMOCOPHES and now in BRIDGE-Health and the European Human Biomonitoring Initiative (EHBMI).

LEK published more than 200 scientific papers 156 with peer review.

Holger M. Koch

Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr-University Bochum (IPA)

Since 2006, Dr. rer. nat. Holger M. Koch is Scientific Head of the Human Biomonitoring Laboratories at the Institute for Prevention and Occupational Medicine (IPA) of the German Social Accident Insurance (DGUV) - Institute of the Ruhr-University Bochum, Germany. Dr. Koch is member of the Human Biomonitoring Commission of the German Environment Agency and also member of the Working Group 'Analyses of Hazardous Substances in Biological Materials' of the MAK-Commission of the Deutsche Forschungsgemeinschaft (DFG).
Since 2010, Dr. Koch is in the advisory board of the cooperation project on Human Biomonitoring between the German Ministry for the Environment, the German Environment Agency and the German Chemical Industry Association (VCI). In the U.S. he was member of the Chronic Hazard Advisory Panel on Phthalates (CHAP) of the Consumer Product Safety Commission (CPSC).

Dr. Koch has authored above 100 scientific publications in the field of human biomonitoring. Together with his research group (including four PhD students) he is constantly developing new biomonitoring methods for chemicals of emerging interest, such as parabens, phthalates, phthalate alternatives and sunscreens.

His interests span from underlying human metabolism investigations and analytical method developments to large scale population studies and experimental exposure pathway studies.

Marike Kolossa-Gehring

German Environment Agency/UBA

Dr. Marike Kolossa-Gehring, head of UBA Section II 1.2, "Toxicology, Health-related Environmental Monitoring", biologist/toxicologist.

She studied at the Christian-Albrechts-University Kiel where she also got her PhD in the field of toxicological research. She is in charge of the scientific lead and management of the German Human Biomonitoring Program consisting of the German Environmental Survey (GerES), the German Environmental Specimen Bank (ESB), the German Human Biomonitoring Commission, and the HBM cooperation between the German Chemical Industry Association (VCI) and the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB).

She was involved in the development of toxicological assessment strategies and methods at the national and international (EU, OECD) level.

She was member and work package leader of the Expert team to Support BIOmonitoring (ESBIO), a consortium for developing concepts for biomonitoring in Europe, as well as DEMOCOPHES and COPHES, the Consortium to Perform Human Biomonitoring on a European Scale preparing and piloting a European human biomonitoring study.

From to 2006 to 2010 she chaired the OECD Endocrine Disruptor Testing and Assessment Advisory Board.

From 2011 to 2014 she was Governmental Councillor of the International Society of Exposure Science (ISES).

Martin Kraft

German Human Biomonitoring Commission and North Rhine Westphalian State Agency for Nature, Environment and Consumer Protection

1989 – 1995 Diploma in Biology, University of Marburg and Ruhr-University Bochum, Institute for Hygiene and Environmental Medicine Thesis: Development of an in vitro digestion model for estimating the bioavailability of metals in soils

1995 – 1998 Doctorate in Natural Science (Dr. rer. nat.), Ruhr-University Bochum (Institute for Hygiene and Environmental Medicine) Thesis: Bioavailability of metals depending on different food components in a gastrointestinal in vitro testsystem

1998 – 2000 Consultant for occupational health and environment protection at the metal industry

2000 – 2002 Scientific advisor in the field of epidemiology and toxicology at the State Agency for the Environment North Rhine-Westphalia

2003 – 2009 Scientific consultant for environmental medicine at the Ministry for Environment, Conservation, Agriculture and Consumer Protection of the State of North Rhine-Westphalia

Since 2009 Head of the unit for environmental medicine, toxicology and epidemiology at the State Agency for Nature, Environment and Consumer Protection North Rhine-Westphalia

Collaboration German Human Biomonitoring Commission, since 2005 German Committee on Indoor Guide Values, since 2003

Megan Latshaw

Association of Public Health Laboratories/APHL, United States

As the Environmental Health Director at the Association of Public Health Laboratories, Dr. Latshaw works to strengthen environmental and public health laboratories. Her team focuses on creating a national biomonitoring system, testing for agents of chemical terrorism, and building a home base for environmental laboratories. Prior to that, she served as the Senior Director for Environmental Health Policy at the Association of State and Territorial Health Officials. While there Dr. Latshaw led the establishment of the State Environmental Health Directors group.

Her doctorate is in Environmental and Occupational Health from the Johns Hopkins University, where she continues to serve as a Faculty Associate. Additionally, she holds a Masters in Environmental Health Sciences, a Certificate in Risk Sciences and Public Policy, and a Bachelors in Biology from the same University. A massive, open, online course she developed on Chemicals & Health enrolled over 35,000 people.

Dr. Latshaw has served on over a dozen national committees and is Chair of the American Public Health Association's Environment Section. She has authored or co-authored eight peer-reviewed articles, served on over 20 committees, and presented at almost two dozen conferences or meetings.

Edgar Leibold

BASF, Germany

Dr. Edgar Leibold received his Diploma in biochemistry, physiological chemistry and pharmacology from the University of Tübingen and his doctoral degree from the Technical University of Munich. In 1993, he joined BASF SE working in various functions in the area of toxicology. With more than 20 years of experience in experimental and regulatory toxicology, Edgar Leibold is currently Vice President Product Stewardship at the Product Safety department of BASF SE being responsible for regulatory toxicology and ecology.

Gabriele Leng

Currenta GmbH, Germany

- Study of chemistry and medicine at The University of Western Ontario in London, Canada and the Universities of Bielefeld, Frankfurt and Duesseldorf
- Medical Specialist in Occupational Health as well as Hygiene and Environmental Health
- Habilitation on the topic biomonitoring of pyrethroids
- Since 2002 head of Institute of Biomonitoring, Department of Occupational Health, Currenta GmbH & Co.OHG (former Bayer AG)
- Since 2005 associate professor at the University of Duesseldorf
- Scientific work for:
  a) DFG: Member of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area
- Development of Analytical methods in biological material
- Assessment of Biological Exposure Values
  b) Federal Ministry of Labour and Social Affairs (BMAS)
- Member of Committee for Occupational Health
  c) Federal Ministry of Health (BMG)
- Member of Committee for gene diagnostics
  d) Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB)
- Member of Expert group of Human Biomonitoring Project
  e)DGAUM: Member of steering committee of German Association for Occupational and Environmental Medicine

Per Magnus

Norwegian Institute of Public Health

Per Magnus graduated from the Medical School at the University of Oslo in Norway in 1976. After internship in surgery, internal medicine and general practice as well as military service he became a specialist in medical genetics in 1985. In the same year he defended his PhD thesis on the causes of variation in birth weight.

Since 1985, he has been employed as a general epidemiologist at the Norwegian Institute of Public Health in Oslo. Main topics have been perinatal outcomes, asthma and allergies, HIV/AIDS, environmental hazards, cardiovascular diseases, genetics as well as neurodevelopmental disorders. He has participated in the conduction of a series of cohort and case-control studies.

Since 1998, he has been the principal investigator of the Norwegian Mother and Child Cohort Study (MoBa). He has published more than 370 papers in peer-reviewed scientific journals, with an H-index of 67. He is now Science Director in the Norwegian Institute of Public Health.

Shoji F. Nakayama

National Institute for Environmental Studies, Japan

Head, Integrated Health Risk Assessment Section,
Centre for Environmental Health Sciences,
National Institute for Environmental Studies, Japan

Dr Shoji Nakayama is a medical doctor and holds PhD in public health. His expertise is in exposure science, especially of compounds of emerging concern such as persistent organic pollutants, per- and poly-fluorinated compounds, endocrine disrupters and pharmaceuticals and personal care products.

In 2005, Dr Nakayama was invited to the U.S. Environmental Protection Agency (US EPA) and worked on exposure research on perfluorinated alkyl compounds. In 2009, he moved to EPA's engineering laboratory to help risk management of the contaminatns of emerging concern. Then in 2011, Dr Nakayama joined the National Institute for Environmental Studies in Japan. He is a lead exposure scientist for the Japan Environment and Children's Study (JECS), which is a longitudinal birth cohort study involving 100,000 mothers and children.

Alexander Nies

Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany

He is responsible for the Governmental Programme on Environmental Health; further key areas of work are human bio-monitoring, indoor air pollution, adaptation to climate change and environmental justice. His responsibilities in chemical safety include the legal and factual implementation of REACH in Germany, international (e.g. Stockholm and Rotterdam Conventions, SAICM, UNEP Governing Council) and national chemicals management, environmental effects of biocides, pesticides and drugs, nanomaterials and environmental contaminants in food. He holds this position since 1 August 2006.

Before his current position, he was the head of several divisions in the Ministry, including the division on radioactive waste management policy and on radioactive waste disposal where he was, inter alia, responsible for the development of a site selection procedure in co-operation with all involved stakeholders.

He is a mathematician by education and joined the Ministry in 1991. Before that he worked for two years at the Technical University in Berlin and for seven years in a national research center for environmental health.

Andy Nong

Health Canada

Objectives
Develop a health science research career by advancing the science and methods for health assessment of chemicals. Promoting an intergrative approach by applying modeling approaches such as QSAR, classical PK/PD, PBPK, population PK, Benchmark dosing, systems biology and IVIV Extrapolation.

Current Experience
Lead Computational Toxicologist (2009-current), Environmental Health Sciences and Research Bureau, Health Canada, Ottawa, Ontario, Canada.

Education
Philosophae Doctor, Public Health (Toxicology),

2002 – 2007 Université de Montréal, Montreal, Quebec, Canada. Master in Science, Pharmaceutical Sciences,

2000 – 2001 Université de Montréal, Montreal, Quebec, Canada. Bachelor of Science, Biochemistry,

1995 – 1998 McGill University, Montreal, Quebec, Canada.

Selected Publications
St-Amand A, Werry K, Aylward LL, Hays SM, Nong A. 2014. Screening of population level biomonitoring data from the Canadian Health Measures Survey in a risk-based context. Toxicol Lett. 231(2):126-34.
International Programme on Chemical Safety (IPCS), 2010. Characterization and application of physiologically based pharmacokinetic models in risk assessment, World Health Organization, International Programme on Chemical Safety, Geneva, Switzerland.

Sofie Nørager

European Commission, DG Research & Innovation

I am currently working as scientific officer in Environment and Health, in the Directorate General Research and Innovation (DG RTD) of the European Commission. I have been working for the European Commission since 2001 in areas such as eHealth, research coordination, ICT research strategy development and international cooperation for research. My academic degrees are a PhD in Physics with speciality in protein crystallography and NMR from the Joseph-Fourier University in Grenoble, France, a Master in crystallography and biological NMR from the same University, and a Master of Chemistry from the University of Konstanz in Germany. Before joining the European Commission, I worked as a Postdoc at the University in Copenhagen, Denmark at the Centre for Crystallographic Studies.

Elizabet Paunovic

WHO European Centre for Environment and Health

Dr Elizabet Paunovic is the head of WHO European Centre for Environment and Health. She is holding degrees from the Medical Faculty in Belgrade (Serbia) as the medical doctor, and postgraduate degree from Medical Faculty in Ljubljana (Slovenia).

Her working experience is covered by more than 30 years of experience in occupational and environmental health, as the main researcher in numerous projects related to occupational and environmental impacts on health. Dr Paunovic was serving as the chief coordinator of occupational and environmental health service in the biggest Serbian Electric Power Plant "Nikola Tesla", as the Secretary Deputy for Environment in the City of Belgrade and in the Ministry of Health of Serbia on different posts. Her main areas of professional expertise and activities are related to occupational and environmental health interventions and actions aimed to prevent and reduce occupational and environmental impacts on health.

At the current position Dr Paunovic is managing WHO Center for Environment and Health which is the major source of knowledge and normative guidance in the WHO European Region on matters of environment and health. The activities are performed through different partnerships by research and evidence development as science policy interface.

Gerd Romanowski

German Chemical Industry Association/VCI

1976 Final secondary school examination, Bremen, Germany

October 1977 to August 1983 Studied chemistry at the University of Bremen

August 1983 Diploma examination in chemistry
Thesis title: „Genertion and mass spectrometric study of clusters in a molecular ray"

January 1986 Received doctorate in the natural sciences (Dr. rer. nat.) from the University of Bremen
Dissertation title: „Mass spectrometric study of the reaction behaviour of bound carbon dioxide clusters"

January 1986 to March 1991 Scientist at Philips GmbH, Aachen, Research Laboratory

April 1991 to March 1993 Research and science policy manager in the Science and Research Department of the Chemical Industry Association (VCI)

April 1993 to Juni 1997 Head of the VCI Director General´s office

Since 1 January 1998 Director of the Science and Research Department at VCI, managing director ot the Chemical Industry Fund, managing director of the German Association of Biotechnology Industries (DIB)

Since 1 April 2001 Director of the VCI-Department Science, Technical and Environmental Affairs, Director of Chemical Industry Fund

5 April 2001 Appointed as Executive Director of VCI by the Presidial Board ("Präsidium") of VCI

Gertrud Sahler

Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany

1973 – 1979 Business Studies at University of Cologne

1979 – 1985 Dynamit Nobel AG

1985 – 1990 Federal Ministry of Justice

1990 – 1994 Press spokesperson at the Federal Ministry for Women and Youth

1994 – 1998 Press spokesperson at the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU)

1998 – 1999 Member of the National Climate Action Division at the BMU

1999 – 2009 Head of Division in Directorate-General Nature Conversation at the BMU

2009 – 05/2012 Head of Executive Staff at the BMU

06/2010 – 01/2014 Head of Directorate-General Nature Conservation and Sustainable Use of Natural Resources at the BMU

since 02/2014 Head of Directorate-General Environment and Health, Immission Control, Safety of Installations and Transport, Chemical Safety at the Federal Ministry of Environment, Nature Conservation Building and Nuclear Safety (BMUB)

Ovnair Sepai

Public Health England, United Kingdom

Principal toxicologist at Public Health England (www.gov.uk) –my role is to protect the public from adverse effects of chemicals in the environment, and involves developing an evidence base to support policy. I lead a group of 11 toxicologists and we provide advice to UK Government and the public on the health effects of chemicals in drinking water, land, consumer products including toys and cosmetics. I lead on the secretariat to government expert and independent advisory committees and am the UK National Coordinator for the OECD Test Guideline programme.

My group responds to incidents and events involving chemicals and offers toxicological evaluation of public exposure and human health risk assessment. One of the greatest challenges we face is evaluating public exposure and my research has focused on the development, validation and application of Human Biomonitoring (HBM) methods for the assessment of human exposure and uptake of anthropogenic and naturally occurring environmental chemicals.

I have been part of initiatives to harmonise HBM across Europe (COPHES/DEMOCOPHES (www.eu-hbm.info)) and advocate the development of a UK national HBM programme.

My PhD is in analytical chemistry and my postdoctoral training in toxicology in both academia and the UK Medical Research Council. Spent two years teaching in Ethiopia –public health problems are the same globally.

Leonardo Trasande

NYU School of Medicine, United States

Dr. Trasande's research focuses on identifying the role of environmental exposures in childhood obesity and cardiovascular risks, and documenting the economic costs for policy makers of failing to prevent diseases of environmental origin in children proactively. Dr. Trasande is perhaps best known for a 2012 Journal of the American Medical Association study associating Bisphenol A exposure in children and adolescents with obesity, and a 2011 study in Health Affairs which found that children's exposures to chemicals in the environment cost $76.6 billion in 2008. His analysis of the economic costs of mercury pollution played a critical role in preventing the Clear Skies Act (which would have relaxed regulations on emissions from coal-fired power plants) from becoming law. He serves on the Executive Committee of the Council for Environmental Health of the American Academy of Pediatrics, and on the Scientific and Technical Advisory Committee for the World Trade Center Health Program. He recently served on a United Nations Environment Programme Steering Committee which published a Global Outlook on Chemicals in 2013, and on the Board of Scientific Counselors for the National Center for Environmental Health at the Centers for Disease Control and Prevention.

Peter Jan van den Hazel

Public Health Services Gelderland-Midden, Netherlands

Peter Jan van den Hazel, MD, PhD, MPH. Trained as physician with specialization on Environmental Health. Peter van den Hazel has been president of the Dutch Association of Environmental Medicine, 1988–1998; Vice-President for Europe, International Society of Doctors for the Environment and president of ISDE 2001-2003; Member, WHO International Working Group on Children's environmental health; founder, chair of board of International Network on Children's Health, Environment and Safety (INCHES); consultant to the Environmental Impact Assessment Committee of the Netherlands, and in 2000 special advisor to Commissioner Wallström of the EU on the pre-work of the SCALE process. President Health and Environment Alliance (HEAL, Brussels); Member of National Health Council committee on New emerging diseases (2008 – present); Coordinator of EU-funded project PINCHE (QLK4-2002-02395), CHEST, PRONET, Climate-TRAP, PHEEDUNET, TOP and partner in projects AIRNET, Citi-sense, Sinphonie, HELIX, Esbio, NO-Miracle and Phenotype; Coordinator of Academic collaborative centres, 2006-current, the Netherlands. Van den Hazel acts as Health Advisor for Chemical Hazards in the East region of the Netherlands to advise on acute incidents and disasters for the regional safety and health services and for the emergency wards of the main hospitals.

Carolyn Vickers

World Health Organization/WHO

Carolyn Vickers leads the Chemical Safety Team in the World Health Organization Department of Public Health and Environment. The Team coordinates a global Chemical Risk Assessment Network, develops and harmonizes chemical risk assessment methodologies, assesses chemicals of international public health concern, promotes prevention of poisoning, develops guidance on and responds to chemical incidents and emergencies, and promotes health in international conventions and agreements.

Prior to joining WHO in 2002, Carolyn held various positions in the Australian government related to the regulation of chemicals, including Manager of the Existing Chemicals Program in the National Industrial Chemicals Notification and Assessment Scheme, and overseeing pesticide assessments in the National Occupational Health and Safety Commission. As well as being responsible for the publication of numerous government and WHO publications, Carolyn has individually authored articles on methods for chemical risk assessment and the burden of disease attributable to chemicals. She has a BSc with Honors in Toxicology from the University of Queensland, Australia and a Master of Toxicology Degree from the University of Surrey.

Paolo Vineis

Faculty of Medicine, School of Public Health, Imperial College London, United Kingdom

Professor Paolo Vineis is a leading researcher in the fields of molecular epidemiology and exposomics. His latest research activities mainly focus on examining biomarkers of disease risk, complex exposures and intermediate biomarkers from omic platforms (including metabolomics and epigenetics) in large epidemiological studies as well as studying the effects of climate change on non-communicable diseases. He has more than 800 publications (many as leading author) in journals such as Nature, Nature Genetics, Lancet, Lancet Oncology. He is a member of various international scientific and ethics committees (including the Committee of the US National Academy of Sciences on 21st Century Risk Assessment) and vice-chair of the Ethics Committee at the International Agency for Research on Cancer (IARC,WHO). He has been a member of the Scientific Council of IARC. Professor Vineis has extensive experience in leading International projects.

He is currently coordinating the European Commission funded Exposomics project (valued at €8.7m, started in 2012) and the Horizon 2020-funded project Lifepath (valued at €6 million, started in 2015). He is a Principal Investigator/Co-investigator of numerous international research projects, such as the European Commission funded GENAIR, ECNIS2, Envirogenomarkers, Hypergenes, ESCAPE and Transphorm networks, in which he has led WorkPackages. In addition he has attracted grants from the Leverhulme Trust, MRC, Cancer Research UK, and the US National Cancer Institute. He is the director of the Unit of Molecular and Genetic Epidemiology, HuGeF Foundation, Torino, Italy and leads the Exposome and Health theme of the MRC-PHE Centre for Environmentand Health at Imperial College. http://www1.imperial.ac.uk/medicine/people/p.vineis

Michael Wilhelm

Department of Hygiene, Social Medicine and Environmental Health, Ruhr University Bochum, Germany

Academic Education

1978-1984 University of Hamburg Degrees: Diploma in Biology (1978), German Approbation in Medicine (1984), Medical degree Dr. med. (1984)

Professional Career

1984-1997 Heinrich Heine University Düsseldorf Scientific Assistant Institute of Toxicology and Pharmacology Assistant Professor (C2), Deputy Director Institute of Hygiene

Further Degrees

German Habilitation in Toxicology (1991), Medical Specialist (German Facharzt) in Toxicology and Pharmacology, Hygiene and Environmental Health, Environmental Medicine

Further professional Career

Since 1997 Professor (C4) and chair of the Department of Hygiene, Social and Environmental Medicine, Ruhr-University Bochum

1997-2002 Head of Department Toxicology/ Molecular Biology at former BGFA (Research Institute for Occupational Medicine) Bochum

2007-2013 Member of Executive Board Institute for International Law of Peace and Armed Conflict, Bochum

About 100 Publications in peer-reviewed journals in the main Research Areas Toxicology, Hygiene, Environmental Health, Human Biomonitoring, Environmental Virology

Editor-in-Chief of International Journal of Hygiene and Environmental Health

Birgit Wolz

Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany

Birgit Wolz holds a PhD in law and a master degree in public administration (Harvard), She has worked for the University of Kiel (research assistant in criminal law) and the European Bank for Reconstruction and Development in London (Personal Assistant, Vice President for Project Evaluation). In the Federal Ministry for Environment, Nature Conservation, Building and Nuclear Safety she has held a range of positions including negotiating the Environmental Protocol to the Antarctic Treaty, preparing the Rio Conference and working for the German EU Presidency.

A Director since 1999, she drafted legislation on radiation protection and for the domestic implementation of EU law on bathing waters and flood protection. Since 2008 she heads the Environment and Health Division which is i.a. responsible for human-biomonitoring, indoor air pollution, environmental food contaminants, the German Environmental Surveys (GerES) and the German Environmental Specimen Bank.

In 2010, she started a ten-year cooperation project with the German Chemical Industry Association to develop new human biomonitoring methods for modern chemicals of concern.

She is engaged in a number of international processes relevant for environment and health involving i.a. the EU-Commission, WHO, the World Bank and the International Children's Environmental Health Birth Cohort Working Group (ECHIBCG).

Jun Jim Zhang

Shanghai Jiao Tong University, China

Jun Jim Zhang graduated from Shanghai Medical University, China, in 1988 and obtained PhD degree in epidemiology from the University of North Carolina at Chapel Hill, U.S. in 1993.

He was an Investigator and Senior Investigator at the National Institutes of Health (NIH) from 1997 to 2011. He was granted NIH tenure in 2005 and received NIH Merit Award twice. Currently, he is a K. C. Wong Chair Professor of Shanghai Jiao Tong University, and the Director of Ministry of Education Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine.

His research focuses on reproductive and perinatal epidemiology. He has conducted several large, multicenter observational studies in the U.S. eg "Consortium on Safe Labor", which established a new standard for normal labor. In a multicenter randomized controlled trial, he and his collaborators compared the efficacy and safety of medical management for early pregnancy failure with misoprostol. He launched a multicenter study to establish the national standard for normal fetal growth.

Currently, he is leading a large prospective study "Shanghai Birth Cohort", and a multidisciplinary, multicenter study on environmental endocrine disruptors and female reproductive function. He has published over 200 papers in professional journals.

Angelika Zidek

Health Canada

As part of Health Canada's Existing Substances Risk Assessment Bureau, Angelika Zidek leads the development of regulatory risk assessments and exposure methodology in support of human health risk assessment.

For the last 7 years, as a Canadian delegate on the OECD Working Party on Exposure Assessment, Angelika has worked with other OECD member countries on ways to share tools and information related to environmental and human health exposure, harmonizing and collaborating on approaches related to chemical risk assessment. Angelika has worked in the field of exposure, risk assessment, and pollution abatement for over 15 years.

Her experience includes occupational and general population exposure to pesticides and industrial chemicals, waste management, as well as environmental compliance programs. She has published in peer reviewed journals and has presented at numerous Canadian and international, scientific, public and policy venues.

Poster Abstracts

P101-P123: Existing and emerging HBM programs

P201-P208: HBM in cohorts

P301-P317: Developing the HBM toolbox

P401-P407: HBM in health risk assessment

P501-P518: HBM exposure measurements

P601-P608: Miscellaneous

P101-P123: Existing and emerging HBM programs

P101 - Canadian Health Measures Survey: Reference values for metals and trace elements in the general Canadian population

Cheryl Khoury [1], Morie Malowany [1], Gurusankar Saravanabhavan [1], Kate Werry [1], Mike Walker [1]

[1] **Health Canada,** Ottawa, Canada

Introduction: Reference values (RV95) for environmental chemicals, computed based on population representative human biomonitoring datasets, indicate the upper bound of background exposure of the general population to a given substance at a given time. RV95s can be used to identify individuals or sub-populations with increased exposures, changes in exposure over time, and the effectiveness of actions to reduce exposures. The nationally representative Canadian Health Measures Survey (CHMS) is the most comprehensive, direct health measures survey conducted in Canada. Here we report the RV95s developed for metals and trace elements measured as part of the CHMS. **Methods:** Data from three cycles of the CHMS (2007-2013) were used to derive RV95s for 12 metals and trace elements in blood and 14 in urine based on guiding principles from the International Union of Pure and Applied Chemistry and the International Federation of Clinical Chemistry and Laboratory Medicine. For each metal or trace element a reference population was constructed based on an a posteriori selection approach with specific criteria for exclusion and partitioning of the data and an evaluation of the quality of the analytical methods used for measurements. **Results:** Exclusion criteria were fasting (molybdenum, cadmium, copper, zinc, fluoride), fish consumption (arsenic, dimethylarsinic acid, mercury), dental amalgams (mercury), and cotinine levels (cadmium). Nine urinary and eight blood biomarkers were partitioned by age. Four urinary and one blood biomarker were partitioned by sex. No exclusion criteria or partitioning were applied to cobalt, nickel, antimony or cesium. Blood RV95s ranged from a value of 0.18 ug/L for cadmium in 3-5 year olds to 7900 ug/L for zinc in males aged 20 -79 years. In urine, RV95s ranged from 0.17 ug/L for antimony in 3-79 year olds to 1400 mg/L for fluoride in those 20-79 years of age. **Conclusions:** RV95s derived for CHMS results can be compared to those from other national surveys, as well as results from sufficiently large sub-population studies. These RV95s are not fixed but can be updated using future cycles of the CHMS.

P102 - Czech human biomonitoring system enters the third decade of its activity

Milena Černá [1], Lenka Sochorová [2], Lenka Hanzlíková [2], Mája Čejchanová [2], Darina Lanková [3], Marek Malý [2]

[1] **Charles University in Prague, Third Faculty of Medicine**, Prague, Czech Republic, [2] **National Institute of Public Health,** Prague, Czech Republic, [3] **University of Chemistry and Technology, Faculty of Food and Biochemical Technology,** Prague, Czech Republic

Introduction: The Czech Human Biomonitoring (CZ-HBM) started in 1994 as part of the nation-wide Environmental Health Monitoring System. Generally, a broad spectrum of biomarkers reflecting exposure to environmental pollutants has been included in the CZ-HBM. The spectrum of monitored biomarkers has been continuously updated to reflect the current level of knowledge and the impact of the exposure on human health. In 2014 and 2015, the CZ-HBM activity were concentrated primarily on emerging substances such as brominated flame retardant (BFRs), and perfluorinated alkylated substances (PFASs) in human milk and blood serum. **Methods:** BFRs and PFASs were analyzed in serum of adults and in human milk of breastfeeding mothers. In hair of breastfeeding mothers total and methylmercury content was also analyzed. Volunteers received written information, signed informed consent and filled in a short questionnaire. Recruitment, sampling and sample handling reflect COPHES/DEMOCOPHES recommendations. Analyses were performed in accredited laboratories according to standard operating procedures in compliance with external quality assurance and control. Principally, LC-MS/MS, GC-MS and ICP-MS methods were used according to particular analyte. **Selected results:** Concentration of PFOS and PFOA in human milk were in 95 – 95 % of samples above the LOQ. PFASs concentrations in human milk ranged from LOQ (0.001 ng/ml) to 0.128 ng/ml for Br-PFOS; from LOQ (0.001 ng/ml) to 0.096 ng/ml for L-PFOS; and from LOQ (0.003 ng/ml) to 0.159 ng/ml for PFOA. In comparison with our data

from 2006 and 2010/2011, PFASs suggested a downward trend. BFRs compounds were in more than 50% of samples below the LOQ. Only congeners 47, 99 and 153 were detectable. The content of mercury in hair of altogether 180 mothers (median and 95th percentile were 0.13 g/g and 0.48 g/g, respectively) was below the health-related limit values and does not reflect health risk. **Conclusion:** The levels of PFASs in human milk of Czech females are relatively lower than those reported from other European countries. Exposure to mercury revealed a continuous downward trend.

P103 - Toxic metal impregnation in children residing in Tunis: A pilot biomonitoring study project

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[1] **National Agency of Sanitary and Environmental Control of Products, Ministry of Health,** Tunis, Tunisia

As a part of environmental health surveillance programs related to ensuring health and environment safety, a human pilot biomonitoring project have been established in the National Agency of Sanitary and Environmental Control of Products (ANCSEP), to assess exposure to lead and cadmium in children between 6-11 years old living in Tunis. Actually, few national data on the levels of heavy metal exposure are available. Although this study is regional, it will represent the only source of systematic data on childhood exposure to heavy metals in our country, making its significant production and publication of results. Our Purpuses are to describe the exposure state to heavy metals and draw a portrait of the child impregnation with comparisons between girls and boys and between regions; to Determine the percentage of children exceeding the limit values or are likely to have high levels of lead and cadmium; to Set priorities on health problems related to the environment and to issue measures to protect vulnerable populations; to Use the results of this pilot study to prepare for the implementation of an extensive study of human biomonitoring and finally the acquisition of this biomonitoring tool for the development of the evaluation approach to risk. This pilot study will help to produce the first national results on childhood exposure to heavy metals (Pb and Cd), in Tunisia. Results will be used to: - The implementation of precautionary measures to prevent contamination from biological samples by external sources. - Prioritization of biomarkers to be assayed in the biomonitoring component of a national study.

P104 - HBM approach and preliminary results in LIFE PERSUADED project

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Introduction: One of the main objectives of the LIFE PERSUADED project (Phthalates and bisphenol A biomonitoring in Italian mother-child pairs: link between exposure and juvenile diseases, http://www.iss.it/lifp/) is the evaluation of the exposure to plasticizers, such as Diethylhexyl phthalate (DEHP) and Bisphenol A (BPA), in mother-child pairs. DEHP and BPA are non-persistent environmental contaminants recognized as endocrine disruptors (EDs), thus potentially affecting human health, in particular children because of their susceptible phase of development. The internal levels are determined through the biomonitoring study involving a representative number of mother-child pairs from urban and rural areas of the Italian geographical macro-areas (North, Centre, South). **Methods:** Urban and rural areas within each macro-area were identified by using urbanization and population density data provided by the Italian Institute of Statistics. Ninety family pediatricians were trained to recruit the 2160 mother-child pairs according to enrollment criteria and urine sampling methods. Data on lifestyles, food preparation, storage and consumption are collected through a structured questionnaire and a food diary (also in electronic format). BPA and DEHP metabolites (MEHP, 5OH-MEHP and 5oxo-MEHP) levels are determined by LC–ESI-MS in urine samples. **Preliminary**

Results: To date 1129 questionnaires, food diaries and urine samples are collected. Descriptive preliminary results on internal level of BPA and DEHP will be presented. **Conclusions:** LIFE PERSUADED fills the data gap on DEHP and BPA exposure in Italian children by setting background levels for susceptible groups of population and implementing the EU database. Data integration for EDs risk assessment, the evaluation of determinants of exposure as well as the creation of a biobank for urine samples will represent relevant output of HBM. **Acknowledgment:** The study is supported by LIFE13 ENV/IT/000482.

P105 - Phthalates and bisphenol A biomonitoring in Italian mother-child pairs: link between exposure and juvenile diseases - LIFE PERSUADED: new European project linking HBM and health risk assessment

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Introduction: Diethylhexyl phthalate (DEHP) and Bisphenol A (BPA), used as plasticizers, are non-persistent environmental contaminants recognized as endocrine disruptors (EDs), potentially affecting human health. EDs exposure deserves attention during childhood, a susceptible phase of development: studies associated DEHP and BPA exposure to endocrine-related diseases in children. The PERSUADED project is focused to improve risk assessment, identifying measures to reduce children DEHP and BPA exposure and health effects. The goal is reached through the integration of biomonitoring approach, case control studies and innovative in vivo study (www.iss.it/lifp). Methods: Human biomonitoring study. Healthy 2160 children and adolescents (both sexes), aged 4-6, 7-10, 11-14 years, and their mothers, are enrolled from urban and rural areas in North, Centre and South Italy. Urine samples are analyzed for BPA and DEHP metabolites levels by LC–ESI-MS. Case-control studies. Idiopathic premature thelarche and precocious puberty (30 girls for each group, aged 2-7 years) and idiopathic obesity (30 boys and 30 girls, aged 6-10 years) studies are carried out. Urine samples are analyzed for BPA, DEHP metabolite levels; clinical and toxicological biomarkers related to puberty onset and obesity are assessed in serum samples. Juvenile rodent toxicological study (same life stage as children in biomonitoring study). Rats are exposed for 28 days to BPA and DEHP, at dose levels recorded in children population. At sacrifice, blood and tissue samples are collected to evaluate DEHP/MEHP/BPA-responsive endpoints: reproductive and metabolic biomarkers, histopathological findings, selected genes expression. Expected Results: • Reference ranges for DEHP and BPA exposure in Italian children, • Characterization of EDs determinants of exposure and biomarkers of effect, • Potential correlation between EDs exposure and children diseases, • DEHP and BPA exposure effects related to postnatal developmental lifestages • Data evaluation and integration for EDs risk assessment, • Targeted tools for risk communication to stakeholders and general population

P106 - The Norwegian Environmental Biobank – Status and future perspectives

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One of the duties of the Norwegian Institute of Public Health (NIPH) is to have an overview of the health status of the Norwegian population and factors influencing public health. This includes the surveillance of the intake of nutrients and environmental

contaminants and their possible effects on health. A Human Environmental Biomonitoring program has recently been established and will use the Norwegian Mother and Child Cohort Study (MoBa) as a basis for recruitment. The MoBa cohort is an ongoing prospective study which includes 114,500 children, 95,200 mothers and 75,200 fathers. Part 1 of our biomonitoring program includes analyses of 11 elements (including heavy metals) in 3,000 stored blood samples collected from women during mid-pregnancy. In addition, iodine, sodium and potassium will be determined in urine and several nutrients and hormones in plasma. The results will be available early 2016. Part 2 of the program includes both children and their parents from Part 1 of the study. They have been invited to answer questionnaires and donate new blood and urine samples. The collection is currently ongoing. Here, a number of organic environmental contaminants like PFASs, PCBs and PBDEs will be analysed in addition to the components mentioned for Part 1, as well as a number of less persistent organic pollutants in urine. However, the bulk of the samples in Part 2 will be stored in the biobank for future studies, both to allow for analyses of hitherto not studied contaminants and for the purpose of studying trends in exposure. An advantage of using the MoBa cohort is that extensive health information is already available. This opens for a number of studies on possible health effects of both nutrients and environmental contaminants.

P107 - Contribute of the MYCOMIX project and future perspectives for Human Biomonitoring and health risk assessment in Portugal

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There is a growing concern within public health about mycotoxin involvement in human diseases, namely those related to children. The MycoMix project (2012-2015), funded by the Portuguese Foundation for Science and Technology, gathered a multidi€sciplinary team aiming at answering several questions: 1) Are Portuguese children exposed daily to one or several mycotoxins through food? 2) Can this co-exposure affect children´s health? and 3) Are there interaction effect between mycotoxins? Mycomix results revealed that Portuguese children (< 3 years old, n=103) are exposed to multiple mycotoxins through food consumption. Cumulative risk assessment results revealed a potential health concern for the high percentiles of intake, especially for aflatoxins which are carcinogenic compounds. This fact assumes particular importance considering the interactive effects found in in vitro bioassays. These results highlight the need for a more accurate approach to assess the human exposure to mycotoxins. Within the Mycomix project the assessment of mycotoxin exposure was based on calculations combining mycotoxin data in food with population data on food consumption. This approach does not consider some aspects as the inter-individual metabolism variation, the exposure through sources other than food and the heterogeneous distribution of mycotoxins in food. Exposure assessment of mycotoxins in Portuguese population through biomarkers is still missing and further studies are urgent to be developed. The European Human Biomonitoring Initiative (EHBMI), a proposal within the European Joint Programme, aims to advance the understanding of the extent of exposure to environmental chemicals across Europe and the impact on human health, by gathering national expertise in human biomonitoring domain. At national level Mycomix project uncovered the potential health risk of exposure of Portuguese children to multiple mycotoxins. The risk assessment expertise acquired within Mycomix, namely in analysis and toxicology of chemical mixtures, will be brought together as a contribute to EHBMI objectives.

P108 - Human biomonitoring for lead levels in Korean: 1st and 2nd stage of the Korean National Environmental Health Survey (KoNEHS)

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Human biomonitoring is a well-recognized tool for estimating the exposure of human populations to environmental pollutants. Therefore, Korea Ministry of Environment (MoE) has recently funded a human biomonitoring study (Korean National Environmental Health Survey, KoNEHS) on the general population (male and females aged 19 years over). This study aims to determine reference levels for several biomarkers, especially heavy metals, metabolite of endocrine disrupting chemicals (EDCs), polynuclear aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs), 3-PBA and cotinine in urine or whole blood. Lead (Pb) is well-known naturally occurring pollutants whose environmental levels have increased as a result of human activity. Lead can be toxic to humans and produce multiple adverse health effects, even at low levels of exposure, due to their ability to accumulate in the environment and organisms (WHO, 2007). KoNEHS has been observing whole blood lead levels for six years. Blood lead levels were analyzed by graphite furnace-atomic absorption spectrometer. The samples were diluted (1:5) using solution (Triton X-100 and ammonium phosphate dibasic). The method detection limit (MDL) was 0.3 μg/dL. For the results of the first survey (2009-2011) for whole blood reference value and 95th percentile value, the determined concentrations were 1.77 and 3.90 μg/dL. The results by year were 1.81, 1.86, 1.91 μg/dL and male shows higher value than female. According to the second survey (2012-2014) results, concentrations of reference and 95th percentile were both higher than those of 1st survey to 1.94, 4.09 μg/dL, respectively. The results by years were 2.01, 2.02, 2.07 μg/dL and male shows higher value than female as same as the result of the first survey. Although the whole blood lead levels of Koreans had been declined since 1993 when government enforced unleaded gasoline policy, it shows an increasing tendency recently. Therefore, continued survey will be conducted to find the cause of increased whole lead levels of Koreans.

P109 - First Portuguese Health Examination Survey and HBM: future opportunities

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Population based health examination surveys collect information by a detailed questionnaire complemented with objective information from physical examination and laboratory tests of biological samples. These surveys provide more accurate and better quality information for many health indicators, some of which cannot be obtained through other methods. In Portugal, population-based epidemiological studies including a physical examination component have been developed to measure the prevalence of obesity, diabetes and hypertension. Although highly relevant these studies are specific to certain specific disorders, some are not nationally representative and none of them followed the methods of the European Health Examination Survey. The First Portuguese Health Examination Survey (INSEF) is being developed as a cross-sectional population-based study representative at regional and national level that aims to expand knowledge of health status, health determinants and use of health services. By the end of INSEF a nationally representative probabilistic sample of more than 4500 individuals with the respective biological samples (whole blood, serum, plasma and DNA) and with integrated epidemiological data (physical exam and health questionnaire) will be available for future research. This presentation highlights the work already done and describes the opportunities INSEF presents and how it can contribute to the gathering of exposure data from the Portuguese population. The collected biological samples could be used for the accurate evaluation of the internal exposure of the Portuguese population to environmental chemicals such as metals/trace elements, PCBs, PFCs, PBDEs, organochlorine pesticides, flame retardants and other compounds. On the other hand, the possibility to re-contact INSEF's participants opens a window for the collection of additional questionnaire data needed to properly interpret the biomarker values. INSEF is being developed as part of the Pre-defined project of the Public Health Initiatives Program that benefits from a 1.500.000 Euro€Grant from Iceland, Liechtenstein and Norway through the EEA Grants.

P110 - The role of National Institute of Public Health in existing and emerging human biomonitoring programmes in Slovenia

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The National Institute of Public Health (NIPH), the main Slovenian public health institution, has been involved in existing and emerging human biomonitoring (HBM) programmes. In 2007, the NIPH prepared a proposal for the national HBM programme aiming to establish the national reference values, determine exposure of adults to selected chemicals and exposure of babies via maternal milk, to establish the geographical differences in exposure, to identify and evaluate the sources of exposure, to compare the data internationally, to generate data for risk assessment and risk reduction measures (Perharic and Vracko, Int J Hyg Environ Health 2012;215:180-4). Former Regional Institutes of Public Health, since 2014 part of the NIPH, were involved in recruitment and sampling phase of the national HBM (Mazej et al. Proceedings of the 2nd Congress of the Slovenian Society of Toxicology, 2015, p. 28; http://www.tox.si/attachments/article/189/merged_document.pdf). We used the results of national HBM to develop an environmental health indicator Dioxins in human milk (Perharic et al, Toxicol Lett 2012; 211S:S53). Based on the results of a risk assessment in an area of central Slovenia polluted from previous mining and industrial activities (Juričič et al. [Exposure of residents of Zagorje by Sava, Trbovlje and Hrastnik to environmental pollutants – heavy metals in soil and vegetables.] Institute of Public Health Ljubljana, Final report, 2013), we prepared a protocol for an epidemiological study. In 2016, we plan to recruit 80 children of both genders, aged 3-5 years, living in the municipality of Zagorje by Sava, part of which is polluted with arsenic due to former antimony mining. Determination of arsenic species in urine will be done in spring and in early autumn to establish seasonal variations in arsenic exposure, to refine our initial risk assessment, and assess the exposure reduction measures proposed in 2013. In the forthcoming European Human Biomonitoring Initiative (EHBMI) the NIPH plans to play a central role as the national hub including active participation in a number of the proposed EHBMI pillars and work packages.

P111 - Measurements of concentrations of organophosphate insecticide metabolites in urine extracted from used diapers in 1.5-year-old children

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Introduction: Recently, epidemiological studies linking exposure to insecticides and effects on neurodevelopment have been drawing worldwide attention. Central nervous system rapidly develops in early childhood. Nonetheless, reports about biological monitoring of insecticides exposure in diapered children are limited. Accordingly, we measured urinary concentrations of organophosphate insecticide metabolites in 1.5-year children which were extracted from used disposable diapers. **Methods:** We recruited 18-month-old children participating in Japan Environment and Children's Study (JECS) at the Aichi Regional Center of JECS, and we collected used diapers from 104 children (18-21 months of age, 53 males and 51 females) from June 25 to July 31 in 2015 (Consent rate was 82%). The children wore designated disposable diapers during night and the used diapers were collected as refrigerated cargoes. Afterward, urine samples were extracted from the diapers by acetone, dried up with a gentle nitrogen stream, and were stored at -80 ºC until analysis. Urinary dimethylphosphate (DMP), diethylphosphate (DEP), which passed through the solid-phase extraction (SPE) column, and dimethylthiophosphate (DMTP), diethylthiophosphate (DETP), dimethyldithiophosphate (DMDTP), and diethyldithiophosphate (DEDTP) which were extracted from SPE column using 2.5% NH_3 water including 50% acetonitrile, were analyzed by ultra-performance liquid chromatography with tandem mass spectrometry. Respective deuterium-labeled dialkylphosphates (DAPs) were used as internal standards. **Results:** The geometric values of the urinary DMP, DMTP,

DMDTP, DEP, DETP, DEDTP, and total DAPs (∑DAPs) were 6.6 (0.74-98.2), 1.9 (ND-78.3), 1.6 (ND-117.1), 0.2 (ND-88.2), 0.2 (ND-5.9), 0.1 (ND-1.5) µg/L and 116 (8.8-1389.0) nmol/L, respectively. Between-individual variability of ΣDAP was about 160 times. **Conclusions:** This is the first study which describes urinary concentrations of OP metabolites in 1.5-year-old Japanese diapered children.

P112 - Time trend of organochlorine contaminants and brominated flame retardants in breast milk of women from Northern Germany (2006-2014)

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While organochlorine substances in breast milk have significantly decreased during the last 30 years due to early regulatory restrictions, brominated flame retardants gained more and more attention because of their similar chemical characteristics like persistence, bioaccumulation and toxicity. In many studies their occurrence in human breast milk has been shown. Meanwhile further regulatory restrictions came into force. To determine possible time trends of substance concentrations in breast milk of mothers from Northern Germany (Schleswig-Holstein), we analyzed yearly pooled milk samples from 2006-2014 of in total 445 single specimens (30-61 per year), which where pooled according to their milk lipid contents, by means of capillary gas chromatography with high resolution mass spectrometry (GC-HRMS) for polychlorinated dibenzo-p-dioxins (PCDD), dibenzofurans (PCDF), polychlorinated /-brominated biphenyls (PCB / PBB) and diphenylethers (PBDE). Hexabromocylcododecanes (HBCDD) were analyzed applying HPLC-tandem mass spectrometry (MS/MS). Isotope labelled internal standards were used for all analyses. During the last decade (2006-2014) concentrations of PCDD/PCDF and dioxin-like PCB showed a further decreasing trend from 15.0 to 7.2 pg/g on a fat basis (WHO (2005) PCDD/F-PCB-TEQ) and for indicator PCB from 126 to 62 ng/g fat. PBDE 28, 47, 99, 100, 183 and PBB 153 decreased between 2006 and 2014 from 850 to 350 pg/g fat and from 160 to 70 pg/g fat, respectively. No continuous decrease could be observed for PBDE 153 (range 480 – 950 pg/g), PBDE 154 (range 7-19 pg/g) and PBDE 209 (range 150-650 pg/g). The concentrations of alpha-HBCDD are ambiguous and a tendency of a rising body burden cannot be excluded yet (2006 to 2010 mean value 1.27 ng/g; 2011 to 2014 mean value 3.06 ng/g fat). Beta- and gamma-HBCDD were detected in none of the samples. Data show that most of the PBDE have decreased in our human milk samples during the last decade. Nevertheless, this does not account for PBDE 153, 154 and 209 as well as for alpha-HBCDD so far. The time series will be continued for the next years also in consideration of ongoing regulatory changes.

P113 - German Environmental Survey 2014-2017: Human Biomonitoring (HBM) within the Framework of a Cross-sectional Population Study – First Fieldwork Experiences

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Introduction: The German Environmental Survey for Children and Adolescents (GerES V) conducted by the German Environment Agency is the fifth nationwide study that aims to generate sound data on the internal and external exposure of children and adolescents to environmental stressors at home and in their residential environment in Germany. **Methods:** GerES V is conducted in cooperation with Wave 2 of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS W2) of the Robert Koch Institute. It aims to include approx. 2,500 children and adolescents ages 3 to 17 years from 167

representative locations in Germany. GerES V started in 2014; data collection will end in 2017. The main element of the study program is human biomonitoring (HBM). Additional priorities are indoor air pollution, pollutants in house dust, tap water quality, noise exposure, residential environment, environmental justice, and environmental burden of disease. During home visits urine, water, dust and air samples are collected and ambient measurements are conducted. Interviews of the children and their parents focus on the residential environment, behaviors and health complaints. Blood samples are taken during KiGGS W2. Urine and blood samples are analyzed i. a. for heavy metals, plasticizers, perfluorinated compounds, solvents, and pesticides. **Results:** In the first study year 933 children participated, the response rate was 74%. 95.3% provided a valid morning urine sample and 77% agreed to blood sampling. So far, 3.6% of the participants exceeded at least one HBM reference value and 0.1% exceeded a health-based HBM value. Conclusion: GerES V demonstrates how HBM studies can be complemented by study modules on exposure factors and ambient monitoring. GerES V data provide further insight into key sources of human exposure and on associations between internal and external exposure of the young generation and their behaviors. **Acknowledgements:** GerES V is funded by the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety as well as the Federal Ministry for Education and Research. Further information is available at www.uba.de/geres.

P114 - Reference level of blood mercury in Korean adults: results from the Korean National Environmental Health Survey(KoNEHS), 2012-2014

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The Korean National Environmental Health Survey (KoNEHS) as a nationwide study launched in 2009, and for the purpose of identifying the human exposure status to environmental contaminants and helping assess the environmental health policies to reduce exposure to chemicals. The present study aims to determine the representative values for Blood Mercury levels in the Korean population, with the distribution by potential exposure factors. 6,457 participants were eligible for these analyses after exclusion of subjects without blood sample. Blood mercury was analyzed using the mercury analyzer with the gold-amalgam collection method. The detection level of 0.10 ug/L was achieved, sufficient for measuring blood mercury levels in non-occupationally exposed participants. Data analysis was conducted using SAS procedure SURVEYMEANS. The geometric mean (GM) in the 2nd survey was 3.11 ug/L, similar to the levels in the 1st survey (3.08 ug/L). Whereas the level of 95th percentile in the 2nd survey was 9.05 ug/L, lower than that in the 1st survey (9.91 ug/L). The GM levels increased with age except among individuals ≥60 years and was lower in female than in male. Also, the blood mercury concentrations showed a strong association with residence areas and smoking habits. The mean and 95 percentile of blood mercury levels in the general Korean population were higher than those in American and Canadian populations. In addition, these two studies showed no differences in the concentration between male and female, unlike our survey results. 22.5% of the total participants exceeded the HBM I and 1.3% exceeded the HBM II, which decreased by 3.3% and 0.6% respectively from the 1st survey. According to the analysis results of risk factors for those who exceeded the HBM II, mercury levels were higher in men, those who live in coastal areas and those who more frequently consume small fish. In this study, we presented the geometric means of the blood mercury in the Korean population and also identified the distribution of several factors. Seafood diet as food culture has been identified as a major route of blood mercury exposure in the Korean population and domestic standards on mercury levels have not yet been set up, which requires concerted actions among Government ministries to develop countermeasure for reducing its exposure.

P115 - French biomonitoring program: the Esteban study, data collection and milestones

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Introduction: As part of the French biomonitoring program, a cross-sectional survey called Esteban, combining health exams and a nutrition study with biomarker dosages is ongoing. Its aims are to describe and establish reference values for the levels of biomarkers of exposure to chemical agents present in the environment (incl. food); to analyze the determinants of exposure biomarkers levels and to compare with results from studies conducted abroad. **Method:** Esteban is a descriptive cross-sectional study conducted on a national sample of children from ages 6-17 and adults from ages 18-74, residing in metropolitan France. Three levels stratified random sampling was used to select households to be proposed with participation in the study. Each participant answers a « questionnaire survey » (sociodemographic data, use of medical care, exposures to environmental pollutants), and undergo a « biological and clinical exam » including collection of biological samples (blood, urine and hair, collected either at home during a visit by a nurse, or in a clinic). Biological samples are prepared and send to a biobank, for long term conservation at -80°C. An iterative consensus process (adapted from Delphi) among experts was used to obtain a list of biomarkers to analyzed. **Results:** Inclusions have begun since April 2014, and full size implementation of data collection will continue until the end of March 2016. As of February 19th, 2016, 2, 312 adults and 1, 010 children have been included in the study. More than hundred chemicals prioritized and belonging to biomarkers' families (Metals, Benzene, Perfluorochemicals, Pesticids, Polybrominated compounds…) are obtained by the Delphi process. **Conclusion:** This survey will offer a unique opportunity to assess the levels of impregnation of the French population by many chemicals. It will then allow comparison across time, and will be complementary to other national initiatives (e.g. biomonitoring in children as part of the Elfe cohorte). Perspectives are to monitor time trends in biomarkers levels, when previous results are available and to monitor the impact of public health policies and regulations aiming to reduce environmental exposures to chemicals.

P116 - Success factors of HBM in Flanders

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Introduction: Since 2002 more than 50 biomarkers of exposure and effect were measured in the general population (3 age groups) and selected hot spots in Flanders, Belgium in the successive FLEHS studies (I –IV). The combination of cross sectional and cohort studies, including in total more than 5500 participants, has led to a substantial storage of samples in a biobank. **Methods:** Several biomarkers of exposure were measured in blood or urine samples, including heavy metals, dioxins and 'new' pollutants such as phthalates and musks. Biomarkers of effect included genotoxicity markers, hormone levels and fertility markers. A participatory process for policy translation was developed (phased action plan) to translate scientific results of the FLEHS studies to concrete policy measures. **Results:** The HBM-program resulted in more than 120 publications and 12 PhD's and a collaboration between all Flemish universities, PIH and VITO within the Policy Research Centre of Environment and Health. This collaboration developed a co-creation of knowledge based on interdisciplinary research including epidemiologists, toxicologists, food scientists, social scientists, chemists and medical doctors. More than 20 policy orientated scientific research projects in Flanders were grafted on the HBM-program, e.g. coupling of HBM data with effect oriented air measurements. The Flemish HBM program also served as input for several international scientific research projects such as OBELIX, ENRIECO and CHICOS which led to a strong scientific capacity building in an international context. The HBM program has until now generated answers on more than 60 questions from the Flemish parliament posed to the minister of environment. Each HBM cycle ended with a phased action plan, leading to concrete policy actions communicated by the ministers for environment and health (e.g. source-related measures, optimization of (environmental) monitoring programs and communication en sensitization of the public). **Conclusions:** The FLEHS studies led to a better understanding of the complex relation between environment and health in Flanders and served as basis for concrete policy action plans.

P117 - Levels and trends of contaminants in human populations in the Arctic

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The Arctic Monitoring and Assessment Programme (AMAP) is one of six working groups established under the Arctic Council. AMAP is tasked with monitoring the levels of contaminants present in the Arctic environment and people as well as assessing their effects on a continuous basis, and reporting these results regularly. This presentation provides an excerpt of the human biomonitoring data reported in the 2015 Human Health Assessment Report. Most of these data have been collected over the last twenty years and are from all eight circumpolar countries. Levels of contaminants are declining in the monitored Arctic populations, but not consistently across the Arctic. Certain populations are experiencing more rapid declines than others, and certain populations have concentrations that are remaining stable or are still increasing. Most Arctic populations described in this chapter continue to experience elevated levels of these contaminants compared to other populations monitored worldwide, for example, mercury, where 7 to 85% of Inuit women 18 to 39 years of age in Arctic Canada and Greenland exceed the Canadian provisional blood guidance value of 8 µg/L established for children and women of childbearing age. There are certain contaminants, like perfluorinated compounds (PFCs) and polybrominated diphenyl ethers (PBDEs) which are still increasing in Arctic populations. These and other emerging contaminants require more investigation to find the predominant and important sources of exposure, and whether they are being transported to the Arctic through long range transport in the environment. Coordinated, international biomonitoring must continue in the future to determine if levels of these contaminants, and others, are changing in Arctic populations. This work also supports the objectives of Canada's Chemicals Management Plan.

P118 - Organochlorinated pesticides levels in a representative sample of the Spanish adult population: The bioambient.es project

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Introduction: Organochlorine pesticides (OCPs) are chlorinated hydrocarbons used extensively from the 1940s to 1970s, mainly, in agricultural applications. Most OCPs are persistent in the environment, lipophilic, toxic at low concentrations and can be transported long distances from the emission source, so they are considered as Persistent Organic Pollutants (POPs) and therefore regulated internationally in the framework of the Stockholm Convention. Methods: In 2009, the Ministry of Agriculture, Food and Environment funded the BIOAMBIENT.ES project, the first national-level HBM survey on environmental pollutants carried out in Spain to estimate the levels of selected pollutants in a representative sample of Spanish adults. In summary, participants were recruited among employed people older than 16 years, which underwent their annual occupational medical check-up. Participants were selected through a stratified cluster sampling which covered all geographical areas, gender, and activity sectors. Analysis of human serum was carried out using GC-qMS (NCI mode). The compounds included in this study were Aldrin, Endrin, Dieldrin, Heptachlor, Heptachlor-epoxide, Dichlorodiphenyldichloroethylene (DDE), Dichlorodiphenyltrichloroethane (DDT), hexachlorocyclohexanes (HCHs) and hexachlorobenzene (HCB). Results: 4,4-DDE and HCB presented the highest levels in serum, being detected in 99.5% and 83.8% of the samples. Geometric mean and 95th percentile for 4,4-DDE were 158.8 ng/g lipid and 717.7 ng/g lipid respectively, whereas for HCB 28.50 ng/g lipid and 160.4 ng/g lipids levels were obtained. In addition, the geographical distribution showed significant differences ($p < 0.05$) depending on the OCP. Conclusions: In general, the concentrations of OCPs in this study were in the same range or lower than those reported from other European countries. This study represents the first nationwide survey of exposure to OCPs in Spain and provides a background reference range for exposure to OCPs in the Spanish workforce. Acknowledgments: MAGRAMA-ISCIII Projects SEG 1251/07 ; 1210/10 and 1321/15.

P119 - Human biomonitoring survey of the Spanish adult population: BIOAMBIENT.ES

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Introduction: BIOAMBIENT.ES is the first Human Biomonitoring study made in Spain at national level including Canary Islands and the autonomous African province of Ceuta. The study was coordinated by the National Center for Environmental Health (Institute of Health Carlos III) and funded by the Ministry of Environment. **Methods:** The survey was a nationwide cross-sectional study, with a stratified cluster sampling designed to cover all geographical areas, gender and occupational sectors. Participants, age 18 to 67, were recruited from the annual occupational medical examination survey March 2009–July 2010. A biobank of urine, blood, serum and blood clots was established. Biological sampling was complemented with a short questionnaire on environmental- and lifestyle-related exposures. Additionally, clinical information from the participants was included. Geometric means and 95% percentiles are reported for: metals (Cd, Co,Pb,Tl, Se, Hg), POPs (PAH metabolites, PCBs 138, 154 and 180, Perfluorinated compounds(PFA), Organochlorine Pesticides(OCP) and Poly Brominated Flame Retardants). Values are grouped after regions, gender, age and life-style determinants. **Results:** The study represents 1,892 individuals. Cadmium, Lead, Mercury, PAH metabolites, PCBs and OCPs showed differences by age, gender and geographical region. PFAS showed differences by gender and life style. Fish consumption was associated with an increase of Hg, PFAS and ΣPCB138,153,180 exposure. Smoking was a determinant for Cd, Pb and PAH exposure. **Conclusions:** In general, the Spanish population showed similar exposure patterns in comparison to other European countries and in some cases (for example Cd) lower than Canada and USA. The exception is mercury in which is much higher in the Spanish participants, probably because of a high consumption of fish and other marine products. The information obtained here represent the first baseline data for the Spanish adult population and will serve as bases for study effectiveness of environment and health policies as well as exposure trends of Spanish population. Acknowledgments: MAGRAMA-ISCIII Projects SEG 1251/07 ; 1210/10 and 1321/15.

P120 - Living with Lead - Heritage of the past centuries

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The Upper Meža Valley with 6951 inhabitants is situated in northern Slovenia. Due to long lasting lead mining and smelting the area is polluted with lead. The studies conducted in 2002 and 2004 showed high blood lead concentrations (≥100 µg/L) in children. Since 2004 regular blood lead monitoring has been in place. In 2007, a special remediation programme started with the aim to protect human health. The results of blood lead monitoring in children aged 2 - 4 years are used to evaluate the efficacy of exposure reduction measures. The goal is to reduce blood lead levels in children to < 100 µg/L until 2022. Blood lead levels have been determined annually (2004-2015) in children aged 2 - 4 years from the Upper Meža Valley. In 2008 and 2013, children aged 1- 6 years and 9 years have also been included. Blood was analysed by electro thermal atomic absorption spectrometry (2004-2013) and by inductively coupled plasma mass spectrometry (2014-2015). The surveillance was approved by the National Medical Ethics Committee. Comparison of the results for 2008 and 2013 showed lower blood lead concentrations in 2013 for all age groups of children. On both occasions the highest blood lead concentrations were found in age group 2-3 years, confirming

that age group to be most suitable for annual monitoring. In total 849 blood lead samples have been analyzed. In the period from 2004 until 2010 blood lead levels gradually declined. In 2004, the levels < 100 µg/L were found in only 15%; in 2007 in 55% and in 2010 in 90% of children. The median value declined from over 100 µg/L to < 50 µg/L in the same period. From 2011 to 2015 the results stagnated. Median value varied from 45 to 50 µg/L, and the proportion of children with the levels < 100 µg/L varied from 83 to 91%. Parental occupational exposure was the most important risk factor. Extensive risk reduction measures (asphalting the roads, reducing the use of home grown vegetables, soil replacement in playgrounds, hygiene measures, promotional activities) contributed significantly to exposure reduction. To achieve further exposure reduction targeted work with small groups and individual children would be required.

P121 - The German Environmental Specimen Bank: Unveiling the Data Treasure on Inter-individual Variation in Human Biomonitoring

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Introduction: In addition to individual environmental exposures, human biomonitoring (HBM) results are influenced by behaviors, e. g. smoking and food consumption as well as anatomical or physiological factors, e. g. sex and urine volume. Assessing environmental sources of pollutant levels in human samples must therefore also consider these influencing factors, as well as their inter-correlations. **Methods:** The German Environmental Specimen Bank (ESB) regularly collects human samples which are analyzed for various substances before being cryo-archived. Analyses of physiological sample parameters, e.g. urinary creatinine, are additionally performed. Each year samples from 480 adults (20-29 years) from four German cities are acquired. All participants fill in standardized questionnaires on their exposure relevant behaviors and report on their anthropometrics. **Results:** 1) Bivariate analysis yielded significant correlations between levels of perfluorinated compounds (PFAS) and protein in plasma. No association resulted for PFAS and body-mass-index. PFAS are higher in males. 2) Multivariate evaluation of Hg in urine resulted in significant associations with dental amalgam and fish consumption, explaining more than 50% of variation. 3) Mainly due to reduced emissions, lead in blood (PbB) decreased on average from 77.5 in 1985 to 11.7 µg/L in 2013. Smokers tend to have higher PbB levels. PbB is also constantly higher in males. 4) Mean Cu in blood differs substantially by sex: (2013: females: 1.4 vs. males: 0.9 mg/L), with oral contraceptives as one possible reason. For urinary Cu no such differences are observed. **Conclusions:** ESB data allows for analyzing associations between HBM data, environmental exposures, physiological/anatomical parameters and individual behaviors. This data support the further improvement on HBM studies in environmental health research and contribute to a better standardization of HBM data. Further augmenting HBM trend analysis by multivariate evaluation is warranted. **Acknowledgements:** The ESB is funded by the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety.

P122 - Human biomonitoring studies in Flanders to support policy action

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Introduction: Human biomonitoring (HBM) is part of the Flemish Environment and Health Surveys (FLEHS). In FLEHS I (2002-

2006) 4458 participants of 3 different age groups were recruited in 8 areas with different environmental pressures. Results show significant geographical differences. In rural areas, expected to represent background levels, higher persistent organic pollutants (POPs) levels were observed. New questions emerged: what are the factors influencing exposure? How do we manage knowledge gaps and uncertainty? Which policy measures can be taken? **Methods:** In cooperation with the Flemish government a structured and participatory procedure was developed to translate FLEHS data into policy action. This procedure is based on an analytic-deliberative and iterative approach involving experts, policy makers and stakeholders. After prioritizing the importance of HBM results on the basis of health, social and policy criteria, the top priorities are subjected to further interpretation and policy formulation. **Results:** The higher POPs blood levels in rural areas were selected as one of the priorities of FLEHS I. More detailed data analysis identified consumption of locally grown food and combustion habits as contributing factors. This evidence, together with expert consultations and stakeholder debate, led to the formulation of policy measures by the risk managers, such as changes in legislation on residential combustion and open fires, expansion of the monitoring network for dioxins and polychlorinated bifenyls (PCBs) in ambient air to include residential and agricultural sites, investments in new research on chemical contamination of home-grown food resulting in tools for custom-made citizens' advice, collection of old chlorinated pesticides and promoting healthy gardening. More recent FLEHS HBM data showed declining time trends for POPs, suggesting the success of these actions. **Conclusions:** Interpreting HBM results by using a combination of analysis and deliberation in a structured and participatory procedure yields a broadened spectrum of policy options to address environmental health issues and leads to well-informed and socially robust policy.

P123 - Danish participation in European Human Biomonitoring Program

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Danish participation in the large European Human biomonitoring (HBM) pilot project DEMOCOPHES Demonstration of a study to Coordinate and Perform Human biomonitoring on a European Scale investigated the exposure to 65 different biomarkers in a group of Danish school children aged 6-11 years and their mothers from rural and urban areas in 2011. The environmental exposure to chemicals from a variety of different sources including foods, plastics, electronics, cosmetics, and housing was investigated. Nine polychlorinated biphenyls (PCBs), 4 dichlorodiphenyltrichloro-ethane (DDT) metabolites, hexachlorobenzene (HCB) and beta-hexachlorocyclohexane (ß-HCH), 6 polyfluoroalkyl substances (PFASs) and 7 polybrominated diphenyl ethers (PBDEs) were analysed in plasma samples. The blood samples were also analysed for dioxin-like activity and the biomarker of effect, micronuclei frequency. Hair samples were analysed for mercury. Urine samples were analysed fifteen phthalate metabolites, 7 parabens, and 9 phenols as well as cadmium, paracetamol and cotinine. There was a significant association between the intake of fish and mercury hair concentrations. The exposure seems to follow a family related pattern and the chemicals within the same groups are significantly correlated. As some of the compounds were measured in higher levels in children compared to mothers, increased focus on the exposure in young children is needed. The study gives rise to further investigations of the correlation between biomarkers of exposure, as well as follow-up studies of the participants with repeated biomarker measurements and register-based investigations. For more detailed investigation of specific exposure sources more studies with increased power and detailed questionnaire is needed. Denmark was the only country of 17 participating countries including blood sampling and biomarkers of effect as well as health information related to pain and use of analgesics (paracetamol). The Danish experiences from the extended test may provide valuable information for the planned European Human Biomonitoring Initiative.

P201-P208: HBM in cohorts

P201 - New Possibilities for Urinary Biomarker of PCB exposure: Determination of hydroxylated polychlorinated biphenyls (OH-PCBs) in a highly occupationally exposed German Cohort.

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Introduction: Polychlorinated biphenyls (PCBs) are among the most ubiquitous pollutants in the environment and their metabolism can lead to the formation of OH-PCBs. Most phenolic compounds are known to be readily conjugated and excreted in the urine, although some congeners have been also shown to be strongly retained in human blood causing endocrine-related toxicity, particularly on the thyroid system. **Method:** This study evaluates for the first time the determination of OH-PCBs in urine as a biomarker of PCB exposure in humans. Thereby, a fast, sensitive and selective online SPE method coupled to LC-MS/MS was developed and validated for the separation and quantitation of OH-PCBs in human urine. The study was conducted in three different group, which were distinctly separated as non-exposed to known sources of PCBs (N=21), highly occupationally exposed workers of a transformer recycling plant (N=25) and relatives and residents exposed to low-to-moderate levels of PCBs (N=25) in a German cohort. **Results:** Limits of quantification (LOQ) ranged from 0.01 to 0.19 ng mL-1 and average extraction recoveries from 79-125% for all congeners. Intra- and inter-assay coefficients of variation were between 2 and 17 %. Extraction recovery tests were also performed in urine with different creatinine values (0.52-3.92 mg dL-1) for an estimation of matrix influences and ranged between 69 and 125%. Tri-chlorinated OH-PCBs were the predominant congeners in urine with concentrations up to 174 ng mL-1. High chlorinated OH-PCBs were also frequently detected in urine samples from non-exposed and occupationally exposed individuals, although levels were in general very low or lower than LOQ. **Conclusions:** The method required minimal sample preparation and less solvent consumption being previously successfully applied for OH-PCBs in human plasma. In general, OH-PCB elimination profile in urine followed the same pattern as in plasma with a significant decreased in concentrations over the years (2010-2014). Statistical analyses showed a positive correlation between OHPCB congeners in plasma and urine, as well as between the parent PCBs and their possible metabolites.

P202 - Comparison of colostrum versus urine as biomarkers of pregnant women exposure to chlorinated derivatives of Bisphenol A

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Introduction: Bisphenol A (BPA) is a widespread industrial chemical, frequently used in production of plastic products, classified as an endocrine disruptor (ED). BPA has been found throughout the environment, in particular in water. Chlorine present in drinking water may react with bisphenol A to form chlorinated derivatives (Clx-BPA), which have demonstrated a heightened level of estrogenic activity. Therefore, assessment of Clx-BPA exposure is essential, especially in pregnant women due to the high sensitivity of fetus to ED. **Materials and methods:** The aim of this work was to compare colostrum versus urine as biomarkers of pregnant women exposure to BPA and Clx-BPA. Pregnant French women were enrolled in the Endocrine Disruptors Deux-Sèvres (EDDS) cohort study. Urine samples were collected during the 2nd and 3rd trimester of gestation; colostrums were collected just after the birth. BPA and Clx-BPA were assessed through online solid-phase extraction coupled to ultra high-per-

formance liquid chromatography tandem mass spectrometry (Xevo® TQS). Both biomarkers were compared by concordance analysis (Kappa coefficient). **Results:** Twenty-nine colostrum and corresponding pair of urine samples were analyzed. BPA was detected in 13 colostrums (45%) and in 21 urine samples (71%), while at least one Clx-BPA was found in 17 colostrums (58%) and in 27 urine samples (93%). Among Clx-BPA, dichloro-BPA was the most frequently detected in colostrum, whereas in urine trichloro-BPA was the most frequent derivative. BPA and Clx-BPA were quantified at a level of few ng/ml. Kappa coefficients were ranging from 0.026 (poor agreement) to 0.26 (fair agreement). **Conclusion:** The analytical methods developed for this study are in accordance with the requirements applicable to biomonitoring of BPA and Clx-BPA in colostrum and in urine of pregnant women. The results confirm that pregnant women are widely exposed to BPA and Clx-BPA. These data are preliminary results since only 29 out of 109 pregnant women have been assessed. Complete analysis of the EDDS cohort study is required in order to determine which biological specimen best reflect internal exposure to ClxBPA.

P203 - Transport of Persistent Organic Pollutants across the human placenta

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Prenatal life is the most sensitive stage of human development to environmental pollutants. Early exposure to Persistent Organic Pollutants (POPs) may increase the risk of adverse health effects during childhood. The mechanisms of transference of POPs during pregnancy are still not well understood. The present study is aimed to investigate the transfer of POPs between mother and fetus. The concentrations of 14 organochlorine pesticides, 7 polychlorinated biphenyls (PCBs) and 14 polybromodiphenyl ethers (PBDEs) congeners have been measured in 308 maternal serum samples, their respective umbilical cords and 50 placental tissues from a mother-infant cohort representative of Spanish general population. In general, the adjusted lipid-basis concentrations were higher in maternal serum than in cord serum and placenta. The concentrations of most pollutants between maternal serum and cord serum and between maternal serum and placenta were significantly correlated. These distributions were consistent with a predominant maternal source that transfers the pollutants into the placenta and the fetus. However, this distribution did not correspond to passive diffusion of these compounds between these tissues according to lipid content. The compounds more readily metabolized were higher in newborns, which suggest that differences in metabolic capabilities may be responsible of the observed variations in POP distributions between mother and newborns. Prenatal exposure to 4,4'-DDT and some PBDEs such as BDE 99 and BDE 209 is much higher than it could be anticipated from the composition of venous maternal blood. POP exposure assessment studies of newborns may overlook the effects of some of these pollutants if they only consider maternal determinations.

P204 - Factors related to organophosphate pesticide exposure during pregnancy in a Spanish birth cohort study. INMA-Valencia Project

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Background: Organophosphate pesticides (OP) are widely used in Spain and the Valencia Region is the 2nd largest agricultural area in this country. Early OP exposure could affect infant neurodevelopment. We aimed to investigate OP exposure in pregnant

women from the Spanish general population, as well as its associated factors. **Methods:** Study subjects were 355 pregnant women participating in the INMA cohort from Valencia (2003-2005). Socio-demographic, dietary and environmental factors were collected using questionnaires. OP metabolites were analysed in urine at the 32nd week of gestation by liquid chromatography-high resolution mass spectrometry. The analysis included generic metabolites (three diethyl phosphates (DEP) and two dimethyl phosphates (DMP)), and the specific metabolites: 3,5,6-trichloro-2-pyridinol (TCPY), 2-diethylamino-6-methyl-4-pyrimidinol (DEAMPY), 2-isopropyl-4-methyl-6-hydroxypyrimidine (IMPY), and para-nitrophenol (PNP). The association between OP (those detected in at least 30% of the samples and sum variables) and covariates was analysed using multivariable interval censored regression. **Results:** Only one generic (dimethyl thiophosphate (DMTP): 63.7%) and one specific (TCPY: 33.5%) metabolite were detected in more than 30% of the samples. The geometric means for DMTP, sum(DEP), sum(DMP), and sum(specific OP) were 5.2, 9.5, 7.4, and 4.4µg/g creatinine, respectively. Higher OP levels were found in summer, in non-smokers, and with lower body mass index. Living near fields was associated with higher levels of specific metabolites. Vegetables and fruit intake were both associated with OP levels. **Conclusions:** OP levels were low compared with other US longitudinal studies. Only DMTP was detected in more than half of the samples. Very few studies have investigated factors associated with pesticide exposure in pregnant women. This is the first study that evaluates prenatal OP exposure in Spain. The longitudinal design of the INMA Project will allow the evaluation of postnatal OP exposure and the possible effects on child health. **Funding:** FP7-ENV-2011cod 282957, FIS-FEDER (PI13/1944, PI14/0891), Miguel Servet-FEDER (CP11/0178 and CP15/025)

P205 - Exposure to mercury in a Spanish birth cohort study. INMA Project

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Introduction: Mercury (Hg) is a ubiquitous heavy metal that may negatively affect human health. Vulnerability of the central nervous system is increased during early development. Therefore, it is desirable to investigate Hg exposure in vulnerable populations. The aim of this study is to describe pre and postnatal exposure to Hg and its associated factors. **Methods:** Study subjects were pregnant women and their children participating in the INMA birth cohort study. Women from 4 areas of Spain (Valencia, Sabadell, Gipuzkoa and Asturias) were recruited (2003-2008) during the 1st trimester of pregnancy and followed up until delivery. Their children were followed up until 9 years of age. Total Hg (THg) was measured in the cord blood (n=1883) of newborns from the 4 regions and in the hair of children from Valencia aged 4 (n=580) and 9 (n=405) years. Socio-demographic and dietary information was obtained by questionnaires. Multivariate linear regression models were built in order to study the associated factors. **Results:** The geometric mean (GM) of cord blood THg was 8.2µg/L, with 24% of newborns having levels above the WHO Provisional Tolerable Weekly Intake (PTWI) and 64% above the US EPA Reference dose. Higher cord blood THg was found in children from mothers with higher fish intake during pregnancy, older age, lower parity, Spanish origin, higher education, and employed. The GM of THg in hair was 1.10µg/g at 4 years and 0.89µg/g at 9 years. The intake of large oily fish was the main contributor to Hg exposure. **Conclusions:** Children participating in this birth cohort study presened a high prenatal and postnatal exposure to Hg compared with other European countries and similar levels to those reported in other countries with high fish consumption. We observed a decreasing trend in THg levels from birth to the age of nine. Prospective birth cohort studies such as INMA allow the exposure to Hg to be evaluated longitudinally while also enabling us to perform biomonitoring studies, to evaluate dietary recommendations, and to assess its possible effects on children's health. **Funding:** FIS-FEDER (PI13/1944, PI14/0891), Miguel Servet-FEDER (CP11/0178, CP15/0025)

P206 - Exposure to Organochlorine Compounds during Pregnancy and Mother-Child Transfer: The INMA cohort (Spain)

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Background: During pregnancy, organochlorine compounds (OCs) can cross the placenta and reach the fetus. **Objectives:**To measure OC levels in maternal (week 12 of pregnancy) and umbilical cord serum and to study mother-child transfer of these compounds in four INMA-cohorts (Asturias, Gipuzkoa, Sabadell and Valencia), Spain (2003-2008). **Methods:** 4,4´-dichlorodiphenyldichloroethylene (4,4´-DDE), hexachlorobenzene (HCB), and polychlorinated biphenyl (PCB) congeners (138, 153, and 180) were determined by gas chromatography with electron capture detection in 2369 maternal and 1140 cord samples. Placental transfer was evaluated by calculating the Pearson's partial correlations between log2(OC) levels adjusted by cohort, and the ratios of maternal/cord OC levels (n=1102). **Results:** OCs were detected in >82% of samples. The most predominant contaminants were 4,4´-DDE and PCB-153 (99.2% and 96.2% in maternal serum and 98.3% and 91.6% in cord serum, respectively). Maternal medians were: 0.83 (141), 0.29 (50), 0.17 (29), 0.28 (48), and 0.20 (34) ng/mL (ng/g lipid) for 4,4´-DDE, HCB, PCB-138, PCB-153, and PCB-180, respectively. Respective cord medians were 0.38 (154), 0.16 (61), 0.08 (34), 0.12 (48), and 0.08 (34) ng/mL (ng/g lipid). Pearson's correlation coefficients between maternal and cord log2(OC) levels (in ng/mL or ng/g lipid) ranged between 0.38 and 0.77 (p<0.001). Maternal serum levels (ng/mL) of 4,4´-DDE, HCB, PCB-138, PCB-153 and PCB-180 averaged 2.46, 2.11, 2.41, 2.55, and 2.79 times those of cord serum, respectively. Ratios were close to 1 when OCs were lipid-adjusted. Stratified by cohort, 4,4´-DDE and HCB levels were higher in Valencia and Asturias and PCBs lower in Sabadell. Placental transfer of OCs was similar among cohorts. **Conclusions:** OC levels were 2-3 fold higher in maternal than cord samples on a wet-weight basis, but similar when lipid-adjusted. The correlations between maternal and cord OC levels were from moderate to high.
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P207 - Mycotoxin exposure in a developing country: The case of Bangladesh

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Introduction: Surveillance of mycotoxin contaminants in food is insufficient in developing countries as Bangladesh. Since biomonitoring covers intake from all sources, urinary biomarkers of mycotoxin exposure were analysed in various cohorts. Methods: LC-MS/MS multi-method served to select major mycotoxins, i.e. aflatoxin B1 (AFB1), ochratoxin A (OTA), citrinin (CIT), deoxynivalenol (DON). Then sensitive specific methods for AFM1 (AFB1 metabolite), OTA, CIT and dihydrocitrinon or DON, were used to determine biomarker concentration ranges in urines from Bangladeshi cohorts and from a German cohort. **Results:** Main findings of this first systematic biomonitoring study in the Bangladeshi population are presented with comments on possible risks from mycotoxin exposure. AFM1 was not detected in German urines, but it was found in >40% of Bangladeshi urines (range 1.7-190 pg/mL). AFM1 biomarker data show frequent exposure of the Bangladeshi population to the hepatocarcinogen AFB1, and at levels which raise concerns. As AFB1 is a potent mutagenic carcinogen, no "safe" intake values can be defined,

and exposure should be kept as low as possible. Biomarkers of exposure to the nephrotoxins CIT and OTA were present in most urines, with total CIT (mean 3.8, max 48.1 ng/mL) and OTA (mean 0.2, max 1.8 ng/mL) in Bangladeshi urines in winter. In German urines, the OTA level (mean 0.2, max 1.8 ng/mL) is similar, whilst CIT (total mean 0.14, max 0.6 ng/mL) is clearly lower than in all Bangladeshi samples. The new data indicate frequent concomitant exposure to OTA and CIT. Exposure to both mycotoxins should be further monitored, including also other groups (e.g. children), and in light of possible combined effects. Analysis for all Bangladeshi cohorts reveal low DON exposure, but higher urine DON levels (mean 9.0, max 38.4 ng/mL) in German adults. Probable daily DON intake calculated for persons in both countries is below a TDI of 1 µg/kg/d set by WHO, indicating that present DON exposures are not of concern. **Conclusions:** The cohort studies illustrate the usefulness of human biomonitoring in characterizing exposure to mycotoxins, an important group of hazardous food contaminants.

P208 - Development of UPLC-MS/MS methods for endocrine disrupting chemicals (EDCs) in placenta in an ongoing mother-birth cohort in Belgium

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Introduction: The placenta is the first organ to be fully developed during pregnancy. It is in contact with all nutritional, hormonal and other chemical stress factors throughout the pregnancy. Currently, only limited data on levels of EDCs in placenta exist. We initiated the development of techniques to measure EDCs in placental tissue in an ongoing mother-birth cohort. In a further stage, we plan to explore the impact of in utero and early life exposures to EDCs on growth and early development. **Methods:** Within an existing and ongoing birth cohort (ENVIRONAGE, Hasselt University), mother-child pairs are recruited from Hospital East Limburg, the largest hospital of the province. Till now, over 950 mother-child pairs have been enrolled. Comparison of basic characteristics with the National Health Interview Survey shows that the cohort is representative. Each mother-child pair contributing to the study provides maternal and umbilical cord blood, urine, as well as 5 placental biopsies. The selected EDC are analytically measured in the obtained placenta samples and correlated with the health effect parameters of a child (after birth and at the age of 4 years). **Results:** A prioritization of compounds with known or suspected endocrine disruptor properties to be developed at WIV-ISP was performed by a multidisciplinary team of toxicologists and public health experts (REACH) in combination with experts having background in human biomarkers. The development of a high throughput analytical approach to determine a first batch of multiple chemical compounds (bisphenols, parabens and alkylphenols) in placental tissue by Ultra-Performance Liquid Chromatography coupled to tandem-mass spectrometry (UPLC-MS/MS) was set-up. Currently, a good separation and sensitivity for all selected chemical compounds using a Xevo TQ-S mass spectrometer in negative ionization mode is achieved after minimal sample pretreatment. **Conclusion:** This ongoing study is one of the first to measure prenatal exposure to EDCs by using placenta as matrix, developing a multi-analyte method, and annotation with health outcomes at individual level.

P301-P317: Developing the HBM toolbox

P301 - New external quality assessment scheme for the measurement of monohydroxy polycyclic aromatic hydrocarbons (OH-PAHs) in urine presented through a sensitive method by GC-MS/MS

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Introduction: No complete quality assessment scheme, covering all the main OH-PAHs found in urine, exists for the evaluation of laboratory performance. The CTQ has developed a new program for these metabolites in urine giving the opportunity for the laboratories to measure the effectiveness of their method. **Methods:** This program, called OSEQAS (Organic Substances Exernal Quality Assessment Scheme), incorporates the following OH-PAHs: OH-phenanthrenes (1, 2, 3 and 4-OH-phenanthrene), OH-fluorenes (2, 3 and 9 OH-fluorene), 1 and 2-naphthol, 1-OH-pyrene in addition to bisphenol-A, triclosan, 2,4-dichlorophenol and 2,5-dichlorophenol. The concentration range for OH-PAHs to evaluate laboratories is between 0.0069 to 50 µg/L. Two proficiency testing materials are distributed twice a year. **Results:** This poster presents the OSEQAS program and the analytical method used by the CTQ to determine 19 OH-PAHs in urine by GC-MS/MS. Method validation is presented as well as a stability study on the conjugated and free forms of OH-PAHs, the stability of these metabolites during freeze and thaw cycles and finally the stability of the derivatized extracts. **Conclusion:** The analytical method shows a good sensitivity with limits of detection (LODs) lower than 0.004 µg/L for almost all OH-PAHs except for 1 and 2 naphthol. **Keywords:** Organic substances external quality assessment scheme, monohydroxy polycyclic aromatic hydrocarbons, gas chromatography tandem mass spectrometry, stability in human urine.

P302 - Interlaboratory and intraindividual variability analyses in measurements of urinary metabolites of organophosphorus insecticides

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Introduction: Single spot urine is often used for estimating organophosphorus insecticide (OP) exposure. However, most insecticides used today have short half-lives and diet is main exposure source of OP, indicating that urinary concentrations of OP metabolites have large inter-day variations. In addition, quality control of measured values among institutions which analyze OP exposure is necessary in a large-scale epidemiological study. This study aimed to clarify 1) an interlaboratory variation in measured concentrations of urinary OP metabolites, and 2) adequate frequencies of collecting urine samples for estimating OP exposure. **Methods:** Interlaboratory variations. Twenty-three spot urine samples from five pregnant women who participate in Japan environment and children's study (each spot urine was collected in second and third trimester of pregnancy) and from thirteen 3-year-old infants were used for measuring urinary OP metabolites. Four urinary dialkylphosphates, common OP metabolites, were analyzed by liquid chromatography-tandem mass spectrometry after solid phase extraction. Intraindividual variations. Urine sample was collected from 9 preschool children (3 to 5 years old) twice per a day (first-void morning urine and spot urine in the afternoon), 4 days per 2 weeks. Six urinary dialkylphosphates were analyzed by liquid chromatography-tandem

mass spectrometry after solid phase extraction. **Results:** As for interlaboratory variations, good correlation of measured values of four dialkylphosphates were observed in between two laboratories except one urine sample. For the sample, one outlier was observed for each dialkylphosphate, suggesting the effects of urinary matrix. Diethyldithiophosphate concentrations in all subjects were below the limit of quantitation. Intraclass correlation coefficients (ICC) is low in the remaining five dialkylphsphates and three-time repeats in measuring urinary OP metabolites almost satisfy ICC>0.4. **Conclusion:** Urinary OP metabolites should be measured in spot urines taken on three different days for better estimation of OP exposure. Effects of urinary matrix should be further investigated.

P303 - Oxidative stress biomarkers in human biomonitoring as intermediates between exposure and disease.

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Introduction: Many environmental contaminants have been shown to cause oxidative stress (OS) and are associated with disease states (Korean J Intern Med, 25, 282-287, 2010; Food Chem Tox, 90, 30-35, 2016). In addition, the redox status of humans can also be affected by environmental exposures. In the FP7 project CHANCES, serum biomarkers of OS and redox status have been validated and will now be applied in environmental studies. **Methods:** ROM (Reactive Oxygen Metabolites) is used as biomarker of oxidative stress (hydroperoxides) and SHp (thiol groups in proteins) for the redox status. All assays were obtained from Diacron, Italy. **Results:** The assays for the biomarkers ROM and SHp in serum were adapted on a clinical auto-analyzer (Beckman-Coulter) with very good reproducibility. The biomarkers were stable in serum on short- and long-term storage up to 5 years at -800C (Biomark Med, 9, 425-432, 2015). These biomarkers were successfully applied in large-scale European studies on aging and diseases in total 20,000 samples. The results regarding cause-specific mortality, strong associations were found between ROM and cardiovascular (Relative Risk=5.2) and cancer mortality (RR=4.3). SHp was only associated with CVD mortality (BMC Medicine, 13, 300, 2015). In addition, the use of an auto-analyzer allows also determination of biomarkers of general health status concerning liver, kidney, inflammation, lipid, carbohydrate and antioxidant status in the same serum sample. **Conclusions:** • a set of biomarkers of OS was validated in human studies and correlated with disease endpoints, • the use of an auto-analyzer guarantee a good reproducibility, low sample volume and cost-effectivity, • this set of biomarkers of OS can be applied in environmental studies as intermediate biomarkers, • in addition, other biomarkers of health status can be determined in the same sample. **Acknowledgement:** This study was performed in project SOR/340006 of the National Institute for Public Health and the Environment and in the FP7 project CHANCES financed by the European Commission.

P304 - Metabolism study of 1-vinyl-2-pyrrolidone after respiratory and dermal exposure of Sprague Dawley rats

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1-Vinyl-2-pyrrolidone (VP) is a chemical which is produced in great industrial scale and with a wide variety of applications. The metabolism of VP is only vaguely described in the literature. No biomarker for human biomonitoring methods has been established so far. The authors postulated the generation of a specific VP-mercapturic acid (VPMA) and proposed two selective oxidation metabolites of VP, N-(2-Hydroxyethyl)-2-pyrrolidone (N-2-HE-2-P) and N-(2-Hydroxyethyl)succinimide (N-2-HESI) thus being potential biomarkers. Analytical methods for the quantification of VPMA, N-2-HE-2-P and N-2-HESI have already been established. The aim of this study was to enlarge knowledge about VP metabolism exposing rats to defined concentrations of VP and analyzing obtained urine samples for the target compounds. The desired turn out of this work was to pioneer the way for the establishment of a human biomonitoring method for VP metabolites in human urine. Animal experiments with 20 female Sprague Dawley rats (age 8 to 10

weeks) were performed. Two exposure pathways, one respiratory and one dermal, as well as according control groups were investigated with subgroups of 5 animals. Urine samples gathered from SD rats in metabolic cages were collected, limited to a total time of 24 h in 6 h intervals. Respiratory exposure was performed with an air concentration of 5 ppm VP for 6 h resulting in a total dose of approximately 1.7 mg VP/rat. Ambient monitoring ensured the accurate VP air concentration. The dermal group was exposed to 40 µL VP/kg rat which is equal to 10.4 mg VP/rat. We could demonstrate that VPMA and N-2-HE-2-P are metabolic products of VP. N-2-HESI could not be identified as a metabolite of VP. Given the low transformation rates of VP to VPMA (appr. 10 ppm) and N-2-HE-2-P (appr. 1000 pm) it remains questionable if one of them will be applicable as a biomarker for environmental or occupational questions. Anyway, due to its higher transformation rate, N-2-HE-2-P might serve as a biomarker for occupational monitoring with regard to the dermal VP exposure with the restriction of being highly selective but not necessarily specific.

P305 - A fast and simple analytical method for human biomonitoring (HBM) studies on parabens in urine

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Introduction: Nowadays, humans are exposed to a wide spectrum of environmental chemicals. One class of substances with endocrine acitivties are parabens. Parabens are extensively used in personal care products as well as in food and pharmaceuticals for preservation. The exposure of humans was accounted for approximately 76 mg total parabens per day in the US. Water solubility, antimicrobial activity and estrogenic acitvity depend on the length and the structure of the alkyl chain of the ester group. Therefore, analytical methods used for HBM of parabens need to distinguish not only between parabenes of different chain lengths but also between alkyl chain isomers of propyl- and butyl parabens (n-, iso- and sec-isomers). **Methods:** Here, we present a quick and simple method for the quantification of 8 parabens in human urine by isotope-dilution UHPLC-MS/MS. Cleavage of paraben conjugates (glucuronide as well as sulfates) is completed within 30 min enzymatic incubation by the support of ultrasound. Moreover, the enzyme removal before analysis is simplified by the use of centrifugation devices. The new method shows high accuracy, high precision and is sensitive enough to analyze exposure of the general population. The fast processing allows to analyze larger sample numbers as required in epidemiological studies. **Results:** Findings in 39 urine samples (female and male adults) were in agreement with previous studies in Germany demonstrating the feasibility of the method and applicability for HBM studies. We have furthermore analyzed urine samples from 150 pregnant women from the LINA cohort showing concentration ranges between 1.7-360 µg/L and <LOQ-60 µg/L (5th - 95th percentile) for methyl- and ethyl paraben, respectively. The frequency of detection was highest (≥ 85%) for methyl-, ethyl-, n-propyl- and n-butyl paraben. **Conclusion:** A rapid method has been developed for the deconjugation and determination of 8 parabens in human urine. The human exposure, in particular in pregnant women differs substantially between individuals and might be of relevance for health outcomes of their children. This aspect is currently under investigation.

P306 - Human metabolism and excretion kinetics of methyl, n- and iso-butyl paraben after oral dosage

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Introduction: Parabens are used as preservatives in personal care products, food and pharmaceuticals. Their use is controversial because of suspected endocrine disrupting properties. Human biomonitoring studies have proven ubiquitous exposure of the general population to parabens by measuring the parent compounds (parabens) in urine as biomarkers of internal exposure. However, information on human metabolism is sparse. We present first human metabolism data and elimination kinetics of methyl- (MeP), iso-butyl- (iso-BuP) and n-butyl paraben (n-BuP) after oral dosage of deuterium-labeled analogs. The thus

obtained urinary conversion factors enable us to reliably extrapolate from urinary paraben levels to actual paraben doses taken up. **Methods:** We orally dosed three volunteers with 10 mg labeled MeP, iso- and n-BuP and collected their urines over 48h. Administration of the parabens followed at least a week apart to avoid interferences from shared metabolites. Metabolites were determined using online LC-MS/MS with quantification by isotope dilution. **Results:** MeP represented 17% of the dose excreted in urine, while iso-BuP represented only 6.8% and n-BuP 5.6%. In addition to the parent parabens and the non-specific metabolites p-hydroxybenzoic acid (PHBA) and p-hydroxyhippuric acid (PHHA), we identified new, oxidized metabolites with hydroxy groups on the alkyl side chain (3OH-n-BuP and 2OH-iso-BuP) and with oxidative modifications on the aromatic ring. For iso-BuP, about 16% was excreted as 2OH-iso-BuP and for n-BuP about 6% as 3OH-n-BuP. Less than 1% was excreted as ring-hydroxylated metabolites. In all cases, PHHA was identified as the major but non-specific metabolite (57–64%). PHBA represented 3.0–7.2%. For all parabens, the majority of the oral dose captured by the above metabolites was excreted in the first 24h. **Conclusions:** With this study we provide essential data on human metabolism including urinary metabolite conversion factors to be used for exposure and risk assessment. Complementary to the parent parabens, alkyl-chain-oxidized metabolites of the butyl parabens are introduced as valuable and contamination-free biomarkers of exposure.

P307 - Analysis of 18 Urinary Mercapturic Acids by two Multiplex-LC-MS/MS Methods

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Introduction: Mercapturic acids (MAs) are metabolic end-products formed from conjugates between glutathione (GSH) and electrophilic compounds. MAs are, therefore, suitable biomarkers of exposure to toxicants, which are either electrophiles by themselves or are converted to reactive metabolites. We developed and validated two LC-MS/MS methods which allow the complementary, rapid and sensitive determination of MAs derived from acrolein, acrylamide, acrylonitrile, benzene, 1,3-butadiene, crotonaldehyde, N,N-dimethylformamide, ethylene/ethylene oxide/vinylchloride, propylene oxide, styrene, toluene, and alkylating agents. **Method:** Since separate determinations of single or only a few MAs are time-consuming and expensive, we multiplexed several different methods into two LC-MS/MS methods. Method validation according to FDA guidelines showed excellent results in terms of sensitivity, reproducibility and robustness. Moreover, the use of a minimal, simple and straightforward sample clean-up accelerated the analytical workflow, which allows a time- and cost-efficient analysis of up to 18 MAs derived from the toxicants mentioned above under environmental exposure levels. **Results:** The methods were applied to urine derived from a diet-controlled clinical study including 25 smokers and 25 non-smokers. For smokers, MA concentrations correlated significantly with the smoking dose for the majority of analytes, except for the MAs of alkylating agents, ethylene/ethylene oxide and toluene ($p > 0.05$). Furthermore, a significant increase was observed in smokers as compared to non-smokers for the MAs of acrolein, acrylamide, acrylonitrile, benzene, 1,3-butadiene, crotonaldehyde, N,N-dimethylformamide and styrene ($p < 0.05$). Currently, analysis of MAs derived from acrylamide is performed in the course of the German Environmental Survey 2014 - 2017 (GerES V) organized by the German Environment Agency (UBA) using these methods. **Conclusion:** The newly developed assays represent a powerful tool for the reliable and fast quantification of MAs, which are suitable biomarkers of exposure to environmental toxicants.

P308 - Identification of new mercapturic acid biomarkers based on non-target screening

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One of the major challenges for modern medicine is the prevention and treatment of so-called civilisation diseases such as dementia or allergies. These diseases might be influenced by electrophilic stress in the human body, caused by the uptake of

chemicals from air, water, and food, as well as the application of cosmetics and pharmaceuticals. In this study, we characterised the electrophilic burden by analysing mercapturic acids (MA) which are breakdown products of glutathione conjugates.
We established a non-target neutral loss screening method for the analysis of MA in human urine using direct injection LC-MS/MS. We analysed 600 urine samples of pregnant women in the LINA cohort study (Life style and environmental factors and their Influence on Newborns Allergy risk). Data on lifestyle and health state was used for prioritisation of 368 different peaks found in the samples. For 32 prioritised signals structure elucidation was carried out by LC-high resolution MS. For 20 out of 32 prioritised peaks, a mercapturic acid could be definitely assigned and molecular formulas could be calculated. Most of the tentatively assigned structures found were not reported before and current work is focusing on a definite confirmation and suggestion of possible precursor compounds of the MA. In conclusion, MA screening is a promising tools for the evaluation of human exposure to chemicals and the identification of so far unknown, but potentially harmful compounds. It could be useful for the establishment of biomarkers that can help to diagnose and prevent future diseases in an early life stage.

P309 - Assessment of mercapturic acid profiles using non-targeted neutral loss scanning LC-MS

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Mercapturic acids (MAs) are a degradation product of glutathione conjugates of electrophiles which are excreted with human urine. Therefore, a screening for MAs can be used as a measure of a person's overall electrophilic burden, but most studies so far addressed only a limited number of targeted MAs. Thus, it was our aim to develop a method to determine nontargeted MA profiles in human urine by liquid chromatography–tandem mass spectrometry, which should be capable to analyse a large number of samples from cohorts. Sample preparation of urine was limited to filtration and dilution. For LC a gradient separation on a C18 with a runtime of 13 min was applied. For detection, an AB Sciex QTrap 6500 was operated in constant neutral loss scan mode for the diagnostic loss of MAs. Chromatograms were processed with MZmine 2.10 for peak picking and alignment. Parameters were optimized based on the recovery of 12 MA standard compounds in spiked urine samples. For method evaluation 600 urine samples obtained from expectant mothers enrolled in a cohort study were analysed. For quality control the mixture of the MA standards was analysed three times with each batch of 30 samples. Despite the limited sample preparation quality control samples showed a good stability over the time of analysis of 14 days. The SD was about 0.01 min for retention times and the RSD between 19 and 50% for signal intensities. The MA profiles showed a large difference in the number of peaks ranging from 11 to 110 peaks, while 50% of the samples contained between 20 and 30 peaks. Also intensities of peaks varied between individuals up to a factor of 2300. Overall the screening resulted in 368 potential MA peaks, although some of these might stem from other compounds doing the same neutral loss. The developed method enabled a high throughput of samples. The detection of several hundred of potential MA and a wide range of peak number and intensities in the cohort population reflects the variation of MA profiles among individuals. This method acts as first step towards the identification of new MA biomarkers linking individual exposure to adverse outcomes.

P310 - Human Urinary Biomarkers of the UV Filter Octocrylene

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Octocrylene (OC) is a UV filter substance used in the majority of sun screen formulations and in other personal care products in concentrations up to 10% (maximum authorized concentration within the USA and the EC [1])[2]. OC has been reported to cause photocontact allergy and is of concern owing to possible formation of reactive oxygen species (ROS) in vivo [1,3]. Because of the likely exposure of the general population, OC was selected as a substance of interest by the cooperation project between the German Federal Ministry for Environment (BMUB) and the German Chemical Industry Association (VCI), which has the aim

to provide biomarker based exposure data for fifty emerging substances of concern. We investigated metabolism and renal excretion of OC after oral dosage (5 mg) and separately after dermal application. Consecutive urine samples were collected for a period of 48 h or 96 h after dosage, respectively. We obtained 2-cyano-3,3-diphenyl acrylic acid (CPAA – the breakdown product of OC, obtained by ester cleavage) and two alkyl chain oxidized metabolites (the 5-OH and dinor carboxylic acid metabolites) as analytical standard substances and analyzed urine samples with online-SPE-LC-MS/MS after enzymatic deconjugation. We could clearly identify the postulated metabolites in post dose urine samples. Elimination characteristics (kinetics), and specificity seem appropriate to use these postulated metabolites as biomarkers of OC exposure for future human biomonitoring studies both in the environmental and occupational field. Preliminary urinary conversion factors were calculated. So far, our results hint towards a low dermal penetration of OC and a background exposure of the general population towards OC.The study has been approved by the ethical review board of the Ruhr-University Bochum (Reg. No.: 4288-12). **References:** [1] Gilbert et al. International journal of cosmetic science 2013;35:208–19; [2] Kerr et al. Clinical and experimental dermatology 2011;36:541–3; [3] Manová et al. The British journal of dermatology 2014;171:1368–74.

P311 - Human excretion kinetics of N-methylmalonamic acid after oral dosing of the biocidal active substances 2-methyl-3-isothiazolinone (MIT) and 5-chloro-2-methyl-3-isothiazolinone (CIT)

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Introduction: Methylisothiazolinone (MIT) and the mixture of chloromethylisothiazolinone and methylisothiazolinone CIT/MIT (3:1) are important biocidal active substances (ASs) and are used widespread as preservative agents in industrial applications, cosmetic and household products. Both ASs have skin-sensitizing properties and are well absorbed orally and dermally. An increasing frequency of contact allergies to MIT and CIT/MIT (3:1) in recent years has raised concerns about the use of these ASs. Human biomonitoring might help to evaluate the extent of exposure to these ASs in the general population and to elucidate main exposure pathways. The main urinary metabolite of MIT and CIT in rats was reported to be N-methylmalonamic acid (NMMA). However, data on human metabolism of both substances and kinetics of urinary excretion of NMMA are lacking. Therefore, it was the aim of our study to fill this gap by the investigation of the urinary excretion of NMMA after oral dosage of isotopically labeled MIT and CIT to human volunteers. **Methods:** Four volunteers (2 m/2 f) received one dosage (2 mg) of 13C3-MIT and d3-CIT separately and at least 2 weeks apart. Consecutive urine samples were collected over 48 h. For the quantification of urinary NMMA, a newly developed GC/MS/MS-method was applied. The study has been approved by the institutional review board of the RWTH Aachen University (EK 336/14). **Results:** According to first results, both substances are rapidly metabolized with peak excretions of urinary NMMA 2 - 4 h after dosing and estimated half-lifes of urinary excretion of 8 – 10 h. Concerning MIT, excretion of NMMA accounts for 18 – 31 % of the dose with app. 91-97 % thereof excreted within the first 24 h. For CIT, urinary NMMA accounts for 11 – 14 % of the dose with 82 – 91 % excreted within the first 24 h. **Conclusion:** The present study is the first to investigate human metabolism of the biocidal ASs MIT and CIT. The results of this study confirm their rapid metabolism and the excretion of NMMA as major human metabolite and biomarker of exposure. The pharmacokinetic data obtained in this study are useful for exposure assessment in the general population.

P312 - Human Biomonitoring of the Exposure to the Flavorant Lysmeral

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Introduction: 2-(4-tert-Butylbenzyl)propionaldehyde also known as "Lysmeral" is a synthetic chemical mainly used as fragrance material in a variety of consumer products like cleaning agents, fine fragrances, cosmetics and fresheners. Due to its broad application in various fields, lysmeral was selected for the development of a biomonitoring method for the quantitative exposure assessment within the frame of the cooperation project of the Federal Ministry for the Environment (BMUB) and the Association of the chemical industry (VCI). **Method:** A method based on UPLC-MS/MS was developed for the simultaneous determination of potential biomarkers of lysmeral in human urine samples. Sample clean-up was performed by liquid-liquid extraction (LLE). Quantification was achieved by standard addition using stable-isotope labeled, authentic reference standards. The method is characterized by its robustness, reliability and excellent sensitivity as proven during method validation according to FDA and DFG guidelines. **Results:** The validated method was applied to urine samples derived from a Human study including 5 subjects after oral application of Lysmeral. The study was approved by an ethical commission and conducted at the IPA Institute, Bochum under the direction of Dr. Holger Koch. The following four lysmeral metabolites were identified as suitable biomarkers of exposure for lysmeral in human urine samples: lysmerol, lysmerylic acid, hydroxylated lysmerylic acid and tert-butylbenzoic acid (TBBA). The urinary excretion had its maximum (Tmax) after 2 - 5 h, showing faster kinetics for the primary (lysmerol, lysmerylic acid) as compared to the secondary metabolites (hydroxylated lysmerylic acid, TBBA). An exposure dose of 0.1 – 2 mg of lysmeral per day was observed in volunteers by making use of conversion factors determined from the human metabolism study. **Conclusion:** We successfully developed a biomonitoring method for the assessment of the exposure to lysmeral under real-life conditions. Sensitivity was found to be sufficient for assessing the background exposure to this chemical in the general population.

P313 - Is nontarget screening a feasible approach for detecting new compounds in human biomonitoring?

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Humans are exposed to thousands of anthropogenic chemicals present in food, consumer products and the environment. Recent achievements in high-resolution mass spectrometry (HRMS) instruments have triggered research towards a comprehensive analysis of such contaminant mixtures in environmental samples by nontarget screening approaches. Human biomonitoring, in contrast, has so far mainly focused on a small number of compounds or related biomarkers, which does not reflect the huge number of chemicals. Thus, we explored the capabilities of LC-HRMS nontarget screening in combination with generic sample preparation procedures for the detection of contaminants in human biomonitoring. Based on a set of known human contaminants, we developed generic sample preparation methods for blood and urine samples. LC-HRMS acquisition and data processing comprised a full scan acquisition in positive and negative ESI mode, software-assisted peak detection, blank peak removal and assignment of adduct and isotope peaks. The application of the developed methods was tested on 16 blood and urine samples from the German Environmental Specimen Bank. A good coverage of a large compound domain was achieved by salt-assisted liquid-liquid extraction of blood and urine samples (QuEChERS) and an additional direct LC injection of urine for the more hydrophilic compounds. The recoveries of spiked analytes and internal standards showed significant matrix effects, but sufficient signal intensities could be achieved despite the limited sample preparation. A large number of more than 5000 peaks per sample could be detected, but all high-intensity peaks were likely internal biochemical compounds rather than contaminants. Thus, evaluation was focused on compounds showing a Cl or Br isotope pattern, and several new compounds could be detected, among them 4-hydroxy-chlorothalonil in blood. In conclusion, generic sample preparation in combination with LC-HRMS for allow for screening for a large compound domain in blood and urine. The main challenge remains the development of methods for a priorization of detected peaks for contaminants among the large number of internal biochemical compounds.

P314 - Analytical Quality Requirements in Human Biomonitoring: trace elements in human blood

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Introduction: Metrological comparability of the measurement results obtained in laboratories is one of the most critical issues in Human Biomonitoring (HBM) studies to assure appropriate quality of measurement results. To demonstrate the equivalence of the measurement results obtained by different laboratories, a case study including inter-laboratory comparison exercises was implemented within a cross-sectional survey, in which exposure to metals in school-age children was addressed. **Methods:** Total mercury (Hg), cadmium (Cd) and lead (Pb) were determined in 6-11 year old children (n=50) in the same laboratory. Fifteen laboratories then determined concentrations of selected metals in 4 sets of blood samples differing in metal concentration. Power calculations were applied to assess sample size required to detect significant differences in mean concentrations of selected metals between given populations, taking into account inter-laboratory variability as determined within the inter-laboratory comparisons. **Results:** Concentration of total Hg, Cd and Pb in blood in the study population of school-age children was the following (geometric mean ± SD): 0.94 µg/L ± 0.54 µg/L; 0.14 µg/L ± 0.04 µg/L; and 13.4 µg/L ± 4.68 µg/L, respectively. Based on the observed population variability, the sample size required to observe 10 % difference in concentrations between two study populations would be 298, 70 and 105, respectively; and for 20% difference 71, 18 and 27, respectively. Adding the inter-laboratory variability to the population variability, the sample size would increase for 2-10% in the case of total Hg, 67-172% in the case of Cd, and for 0-42% in the case of Pb, depending on concentration range determined in blood. **Conclusions:** In order to follow geographical- and/or time-trends in the levels of environmental pollutants in selected populations and also differences between sub-populations, analytical performance of measurements should be carefully controlled. Our case study showed that variability arising from analytical measurements contributes significantly to the overall variability in the studied populations, especially at lower levels of exposure.

P315 - Determination of enzymatic deconjugation marker in plasma and urine using an HPLC-MS/MS method

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Introduction: In plasma and urine, micropollutants (MP) may appear as conjugated and unconjugated forms due to hepatic metabolism. In biomonitoring study, to determine the total content of MP (unconjugated + conjugated), an enzymatic hydrolysis step is required. In order to check the deconjugation using ß-glucuronidase and/or sulfatase the 4-methyl-umbelliferone (MU) and its conjugates: 4-methylumbelliferyl-glucuronide (MUG) and 4-methylumbelliferone sulfate (MUS) have been proposed as markers. However, no analytical method is available in the literature in order to assess the concentration of MU formed and the decrease of MUG and MUS concentrations. The purpose of this study was to develop and validate an UPLC-MS/MS method to determine their concentrations in plasma and urine. **Method:** Heat-inactived glucuronidase/sulfatase was added to plasma or urine which was spiked with MU, MUS, MUG and umbelliferone used as internal standard. Plasma samples were precipitated with acetonitrile before injection. For plasma, final standards concentrations in vials ranged from 0.5 to 8 nmol/mL for MUS and MUG and from 1 to 16 nmol/mL for MU. For urine, final standards concentrations in vials ranged from 0.625 to 10 nmol/mL for MUS and MUG and from 1.25 to 20 nmol/mL for MU. The concentrations of the 3 markers were determined using UPLC (Shimadzu) coupled to a triple quadrupole mass spectrometer (3200 QTRAP Applied Biosystems). Trueness and precision were determined by quality control analysis at three different concentrations. **Results:** The chromatographic conditions allow the separation of the four compounds. Linearity of the method was demonstrated over the concentration range: r2>0.99 for plasma and urine. The method was accurate (bias <15%) and precise (Coefficient of variation <9%) in both matrices. The developed method was applied with success to deconjugation assay using active glucuronidase/sulfatase in plasma and urine. **Conclusion:** Con-

jugated and non-conjugated forms of MP having different chemical characteristics and properties, it is important to separately identify the two forms. The analytical methods developed in this study are suitable to assess the deconjugation of MP metabolites using MU, MUS and MUG as deconjugation markers.

P316 - 2,3-Dihydroxypropyl Mercapturic Acid (DHPMA): no urinary Biomarker for the Background Exposure to Glycidol and 3-Monochloropropane-1,2-diol (3-MCPD)

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Introduction: Glycidol and 3-monochloropropane-1,2-diol (3-MCPD) are carcinogenic food contaminants, which are present in heat-processed oils and fats mainly in form of fatty acid esters. Due to incomplete data on the occurrence of these fatty acid esters in food stuffs it is difficult to assess the exposure to humans and the consequential health risk. An alternative strategy for the estimation of external exposure is the monitoring of the internal exposure. Urinary metabolites may be useful as internal biomarkers of a short-term exposure. We have studied the application of the metabolite 2,3-dihydroxypropyl mercapturic acid (DHPMA), which is generated from glycidol or 3-MCPD due to conjugation with glutathione. **Methods:** The urine of a male volunteer was collected quantitatively over 8 days (4- to 12-hour fractions, 45 samples). After avoiding food containing refined fats for two days, a relatively high amount of glycidol fatty acid esters (100 g of a commercial frying fat containing 1.1 mg of glycidol equivalents), 1.1 mg glycidol (as isolated substance) and 1.1 mg 3-MCPD (as isolated substance) were taken up orally in the morning on day 3, 5 and 7, respectively. The quantification of DHPMA was performed with a LC-MS/MS multiple reaction monitoring technique in urine samples with the isotope-labeled reference compound 13C2-DHPMA. **Results:** The limit of quantification for the analysis of DHPMA was 10 µg/l. The average concentration in urine samples of the male volunteer collected over 8 days was relatively constant (mean ± SD: 154 ± 21 µg DHPMA/g creatinine, n=45). Following the oral intake of the frying fat (containing 1.1 mg of glycidol equivalents), 1.1 mg glycidol or 1.1 mg 3-MCPD, an unequivocal increase of the urinary DHPMA excretion could not be recognized. **Conclusion:** Our findings support the hypothesis that DHPMA may be formed from an endogenous C3-metabolite, as already suggested by Eckert et al. (2011). Oral exposure to food with high background levels of glycidol or 3-MCPD fatty acid esters is not able to increase the urinary excretion of DHPMA – in contrast to the much higher doses used in animal experiments (Appel et al. 2013).

P317 - Analyzation of all 209 PCB congeners in blood – can indicators be used to calculate the total PCB blood load?

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Introduction: For Human Biomonitoring (HBM) regularly PCB 138, 153 and 180 are analyzed in blood samples. The German "HBM Commission" assumes that the sum of these indicator congeners multiplied by two represents the total PCB burden. This norm is based on data taken from exposure studies after dietary intake. Data from indoor air shows a different congener pattern, which might lead to a relatively higher intake of lower chlorinated PCBs. We analyzed all 209 congeners in blood samples from employees exposed to elevated PCB indoor air levels. We examined whether the three indicator congeners would also represent 50 % of the PCB burden if relevant exposure comes from indoor air. **Methods:** Blood samples have been collected from 44 adults working in public buildings with elevated concentrations of PCB in indoor air. In questionnaires we asked for other possible exposure sources and time budgets. The blood samples have been analyzed by HRGC/HRMS, which allows quantifying 141 individual PCB-congeners. Others could only be co-eluted. Therefore in total 172 results per blood sample could be reported. Results: 63 different congeners could be quantified in each blood sample, another 96 congeners in at least one. Most rele-

vant were PCB 153 and the co-eluted congeners PCB 189/193 and PCB 138/160. To 14 others relevant shares (> 1%) could be attributed. The median relative contribution of the indicator congeners was 49%; but their relative share varied over the 44 different samples (24% to 61%). 4 samples showed higher percentages than 55% and in 8 samples the indicator PCBs shared less than 45% of the burden. Total PCB, calculated by multiplying the sum of the indicator congeners by 2, showed a strong and highly significant correlation to the sum of all 209 measured congeners for each sample. A slightly stronger correlation could be achieved by choosing six indicator congeners, including the lower chlorinated congeners (PCB 28, 52 and 101) into the calculation. **Conclusions:** The norm issued by the "HBM Commission" to calculate the total PCB body burden on the base of three indicator congeners leads to quite good results, also in groups exposed mainly by indoor air.

P401-P407: HBM in health risk assessment

P401 - The applicability of human biomonitoring in chemical exposure assessment for food safety

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Introduction: There is strong evidence that human biomonitoring (HBM) can be applied in human exposure assessment, but the impact of HBM in food risk assessment needs to be better understood. Specifically, there has been a lack of knowledge about the current practice of linking body burden to potential dietary exposure sources. **Method:** In order to highlight the state of the art of dietary intake assessment in current HBM programmes, we performed a literature review of national HBM programmes over the past 20 years and conducted further analysis on food monitoring and food intake assessment methods used in HBM. **Results:** Here we provide a detailed compilation of the HBM outcomes related to potential dietary exposure sources and any environmental monitoring employed in the HBM programmes. All of the investigated HBM programmes have collected information on dietary intake, and a number of associations have been made between food intake and increased body burden such as positive correlation between seafood intake and methylmercury detected in hair and blood. However, only a few programmes have conducted concurrent measurements in drinking water or food. Also, there are considerable deficits in the methodological approach and data quality regarding dietary intake. The customised 24-hr food recall method, as recommended by the European Food Safety Authority (EFSA), has been used by France, the Czech Republic and the USA so far. **Conclusion:** While HBM can serve as a tool for chemical exposure assessment in food safety and can significantly contribute to policy making in this field, the interpretability of current HBM programmes for food safety is suffering from deficits in dietary intake assessment methods. More outcomes from this project can be found in a EFSA supporting publication (2014:EN-724). **Acknowledgement:** We would like to thank EFSA for funding this work.

P402 - Accelerated telomere shortening in peripheral blood lymphocytes after occupational polychlorinated biphenyls exposure

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Introduction: Polychlorinated biphenyls (PCBs) are organochlorine pollutants with a worldwide dissemination. PCBs have been classified as human carcinogens and immunologic dysfunctions have been linked to PCB exposure in several epidemiological

studies. **Methods:** We examined telomere length of 207 individuals with a high body burden of PCBs by Flow Cytometry based fluorescence in situ Hybridization (Flow-FISH). Participants of the study were included in the medical surveillance program HELPcB (Health Effects in High-Level Exposure to PCB), which was initiated by a German Statutory Accident Insurance and a district council. **Results:** We found that the age-adjusted TL in lymphocytes (TLLymph) of exposed individuals was significantly shorter than expected (-0.77 kb; 95% confidence interval [CI], -0.9316;-0.6052; p=0.0001). The rate of telomere shortening in lymphocytes of PCB exposed individuals was dependent both on the PCB-congener profile as well as on the concentration of PCBs found in peripheral blood plasma of individuals. A high plasma concentration of lower chlorinated PCBs led to more accelerated telomere shortening than a low concentration. In addition, when used in a lymphoproliferation assay, blood plasma of PCB exposed individuals inhibited the expression of telomerase, the telomere extending enzyme. In addition, 3-OH-CB28, a metabolite of PCB-28, detected in the blood plasma of PCB exposed individuals, inhibited telomerase expression when used as a single agent and accelerated telomere shortening in long-term in vitro cell expansions studies.**Conclusion:** PCB exposure has been linked to several immunological dysfunctions including diminished host resistance to infection and reduced antibody responses in vaccination studies. Furthermore, cellular aging of the immune system represented by telomere shortening has been shown to contribute to decreased immunoresponsiveness. We therefore conclude, that accelerated telomere shortening due to PCB exposure may lead to limitations of cell renewal and clonal expansion of lymphocyte populations and contribute to the observed adverse effects of organochlorines on the immune system.

P403 - Human biomonitoring as a tool for objective exposure assessment: A case-study of a major train accident with acrylonitrile in Belgium

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Introduction: Following a train derailment, 60 tons of acrylonitrile (ACN) exploded, inflamed and part of the ACN ended up in the sewage system of the village of Wetteren (Belgium). The objectives of the present study are: 1) To assess the human exposure to ACN in the local population with the highest suspected exposure; 2) To describe the short-term health effects that were reported by the residents following the train accident; and 3) To explore the association between biomarkers and the self-reported short-term health effects. **Methods:** 2-3 weeks after the accident, 242 residents participated in the study. N-2-cyanoethylvaline (CEV), a biomarker that is highly specific for ACN exposure, was measured in the blood. To account for potential influence by smoking, cotinine was determined in the urine. Participants also filled in a questionnaire with short-term health effects. **Results:** In the evacuated zone, 37.3% of the non-smokers and 40.0% of the smokers had CEV concentrations above the reference values of 10 and 200 pmol/g globin, respectively, at the time of the train accident. Spatial mapping of the CEV concentrations depending on the residential address showed a distribution pattern following the sewage system. The most frequently reported symptoms were local symptoms of irritation. In the non-smokers, a dose-response relation was observed between the CEV concentrations and the reporting of short-term health effects. Overall, the value of self-reported symptoms to assess exposure was limited, with exception of some local symptoms that are known to be prominent for the specific chemical compound studied. Even then, the reporting of symptoms was only absolute in case of exposures that resulted in CEV values exceeding 10 times the reference value. For the lower exposure ranges, there was no clear relationship between symptom reporting and exposure. **Conclusion:** The present study is one of the first to relate accidental exposure and short-term health effects. The results of this study confirm that a critical view should be taken when considering self-reported health complaints and that ideally biomarkers are monitored to allow an objective assessment of exposure.

P404 - The German Human Biomonitoring Commission – Reference and HBM values

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Introduction: The German Human Biomonitoring Commission (HBM Commission) was established in 1992 and has the mandate to advise the German Federal Environment Agency on all HBM related issues. **Methods:** One important field of the HBM Commissions work is the description of the chemical background exposure of the population by reference values. These values are statistically derived and defined as the 95th percentiles of the measured concentrations of selected substances in human biological material (e.g. blood, urine). Accordingly they allow for an appraisal if the body burden of individuals or population groups is comparatively elevated or not, they cannot serve to assess health risks. Another key activity of the HBM Commission is the derivation of health-related biological exposure limit values (HBM values). The HBM-I value represents the concentration of a substance in human biological material at or below which, according to the current knowledge and assessment by the HBM Commission, there is no risk of adverse health effects, and, consequently, no need for action. In contrast, the HBM-II value describes the concentration of a substance in human biological material at or above which adverse health effects can't be excluded for persons affected. Consequently, attaining the HBM-II value means an acute need for exposure reduction measures and the provision of biomedical advice. **Results:** An overview is given of all substances for which reference values are available. Furthermore an update of HBM values is presented. **Conclusions:** Reference and HBM values are valuable tools for the evaluation of the internal exposure to chemical substances in environmental medicine as well as in health related protection of the environment.

P405 - Human Biomonitoring for emergency responders with potential contact to hazardous substances

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Human Biomonitoring (HBM) is increasingly applied after incidental release of hazardous substances. The HBM Commission of the German Federal Environment Agency (UBA) recommends HBM as a useful approach to exposure analysis in case of chemical incidents. To address this topic with a practical approach, and to gain experience with its strengths and limitations, a standardized HBM program was initiated at a large chemical production site in Germany. Post-exposure sampling was offered and carried out for altogether 36 different substances, including aromatic hydrocarbons, isocyanates, amines, phenols and alkylators. Prerequisites for HBM were: known CAS number of the substance, validated analytical methods, toxicology-based assessment values. Additional information was collected by questionnaire (e.g. distance to source of exposure, duration and location of operations, PPE used and time of sampling). In 2015, 241 analyses were carried out in 70 samples of 61 firefighters collected after ten emergency operations. In most cases, specific biomarkers were analyzed, or 1-hydroxypyrene (1-OHP) as an exposure marker for pyrolysis products. While exposure was low in most cases, excursions of the action value for 1-OHP (1 µg/g crea.) were observed in 4 samples (3–45 µg/g crea.) after an operation with dermal exposure to contaminated surfaces being the most likely route of uptake. The standardized program tackles critical aspects of HBM for emergency responders after chemical incidents. It enables the optimization of procedures and adds to the preparedness in case of large incidents. Furthermore, HBM provides information on the efficacy of the protection equipment, and allow for a differentiation between exposed and non-exposed persons.

P406 - Using biological monitoring and physiologically-based pharmacokinetic modelling to quantify human exposure to selected metals resulting from allotment land-use

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Current exposure models used in contaminated land risk assessment are highly conservative. Use of these models may lead to over-estimation of actual exposures, which could result in negative financial implications from unnecessary remediation. A study is being carried out to improve our understanding of human exposure to selected soil-bound elements (As, Cd, Cr, Pb and Ni) resulting from allotment land-use. The research employs physiologically-based pharmacokinetic (PBPK) modelling and human biological monitoring to quantify human exposure to these elements. Biological monitoring is being carried out with thirty six participants across Scotland. Preliminary PBPK models have been developed; using literature data from similar models previously developed and validated by others using data from human studies. We have used the models to estimate the distribution and accumulation of the elements in key body compartments, thus indicating the internal body burden. The models were also used to predict the concentrations of the elements in blood and urine. Simulating low metal intake (based on soil and allotment produce test results from a pilot study), the predictive models suggest that detection of these elements in participants' blood and urine would be possible within a given period of time following exposure. This information is being used to plan the biological monitoring and in the subsequent interpretation of test results from biological samples. These models will be validated using biomonitoring data currently being gathered. With improved understanding of human exposure to these elements, the findings of this study will promote sustainable management of contaminated land.

P407 - Evaluation of urine and blood Cd levels and their associations to renal proteins, at low level of exposure

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Introduction: Reliability of urinary cadmium (U-Cd) as a long-term exposure biomarker and its use in human health risk assessment, which currently relies on relationship between excretion of Cd and biomarkers of renal dysfunction in urine, has recently been questioned, especially at low levels of exposure. Our objectives were to assess the associations between Cd exposure biomarkers and four biomarkers of kidney function, and to identify factors that might influence these associations in order to estimate the appropriateness of Cd in urine and/or blood (B-Cd) as biomarker(s) of choice at low environmental exposure. **Methods:** Data on levels of B-Cd, U-Cd, and four urinary renal proteins (albumin, α1-microglobulin (A1M), N-acetyl-β-glucosaminidase (NAG) and immunoglobulin G (IgG)) from 1081 healthy occupationally unexposed individuals aged 18-49 years (533 primiparous post-partum females and 548 males) was used in the assessment of correlations between the selected biomarkers. Univariate and multiple linear regression was performed using biomarker urinary levels expressed per volume and per creatinine or specific gravity. **Results:** In our study population exposed to low Cd levels (geometric means: B-Cd 0.27 ng/g; U-Cd 0.20 µg/g Crea) clear significant positive correlations between U-Cd and all four renal proteins, irrespective of gender, age or smoking status, were observed. U-Cd and B-Cd were positively correlated (r_p~0.2, $p<0.001$), but among the studied renal proteins only A1M in men correlated significantly with B-Cd (r_p~0.16, $p<0.001$) and was mainly confounded by current smoking. Current smoking significantly increased levels of both U-Cd and B-Cd and of A1M (irrespective to Cd levels). Moreover, B-Cd but not U-Cd was influenced by former smoking. **Conclusions:** We provided further evidence that U-Cd alone is not a reliable biomarker in Cd health risk assessment at low levels of exposure, since its excretion could be influenced by various factors, such as recent exposure and co-excretion with renal proteins. Therefore, B-Cd as a biomarker of exposure, and its correlation to renal proteins need to be addressed as well, but also with a lot of caution.

P501-P518: HBM exposure measurements

P501 - Concentrations of urinary pyrethroid metabolites in Japanese women between 1994-2011

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Synthetic pyrethroids (PYR), a major insecticide group, are used worldwide to control agricultural and household pests. Although many researchers have maintained continuous interests in PYR exposure level in daily lives, few studies has been done to actually monitor its historical change. The present study was undertaken in order to reveal the changes in the levels of human exposure over the last two decades by means of measurements of urinary PYR metabolites. We quantified urinary concentrations of six PYR metabolites, 3-phenoxybenzoic acid (3-PBA), 1R-trans-chrysanthemumdicarboxylicacid (tCDCA), and cis/trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (DCCA), in 95 adult females aged 45–75 in 1994, 2000, 2003, 2009, and 2011 (n = 17–20 different individuals in each year) in Japan. The geometric means (geometric standard deviation) of 3-PBA were 0.66 (3.2), 1.02 (2.5), 0.77 (3.0), 0.80 (2.4), and 0.51 (2.5) μg/g creatinine in chronological order. There was no significant association between the urinary 3-PBA concentration and the year of sampling. Similar statistical results were also found in tCDCA and DCCA. Although the urinary concentration level of neonicotinoid, the fastest growing class of insecticides in modern crop protection, in the same samples we used in this study has risen steadily (Ueyama et al., Environ Sci Technol. 2015, 49, 14522-8.), the PYR exposure level has remained virtually unchanged over the past 20 years in Japanese adults.

P502 - Human biomonitoring in occupational exposure: application of genotoxicity biomarker

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Biological monitoring in occupational health has three main goals: individual or collective exposure assessment, health protection, and occupational health risk assessment. It consists of standardized protocols aiming to the periodic detection of early biological signs, referred as biomarkers. Biomarkers, provided by cytokinesis-block micronucleus (CBMN) assay: micronucleus (MN), nucleoplasmic bridges (NPBs) and nuclear buds (NBUDs), can detect the genotoxic effects, being very sensitive and capable of integrating the effects of multiple interactions and molecular genotoxic events on genome stability. Comet assay identifies DNA damage, namely oxidative DNA damage. These two genotoxicity biomarkers were applied in two case-control studies in two different occupational exposure settings – formaldehyde and cytostatics exposure. In the formaldehyde study, the group of cases was constituted by 55 workers in histopathology laboratories and 80 controls. All the biomarkers measured by CBMN assay presented statistical significant differences between exposed and controls (Mann-Whitney test), namely MN (4.02±0.53 vs 0.85±0.18, p≤0.001), NPB (0.70±0.19 vs 0.28±0.10, p=0.013) and NBUDs (0.37±0.12 vs 0.06±0.03, p=0.002), respectively. In the

cytostatics study, the group of cases was constituted by 46 workers in pharmacy laboratories and nurses, and 46 controls. All the biomarkers measured by CBMN assay showed statistical significant differences between exposed and controls (Mann-Whitney test), namely MN (9.83±1.28 vs 5.09±0.89, p≤0.0001), NPB (0.65±0.140 vs 0.11±0.05, p=0.001) and NBUDs (2.43±0.37 vs 1.37±0.32, p=0.006), respectively. It was found higher mean levels of % DNA in tail and DNA oxidative damage in the exposed group (15.18±1.40 vs 5.32±0.54) in comparison with controls (12.42±1.24 vs 4.59±0.59), however no statistically significant differences were found. The results suggest that workers studied showed increase frequency of genotoxicity biomarkers in comparison with non-exposed. It is important in human biomonitoring to take in account all the possible confounding factors since they may modify the levels of DNA damage, thus modifying individual cancer risk.

P503 - Occupational exposure to Bisphenol S via thermal paper. Preliminary results

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Introduction: Bisphenol A (BPA) is widely used in the production of diverse industrial and consumer products. BPA also has been shown to occur in the paper industry as color developer in thermal paper. Human exposure to BPA is widespread and has been associated with an array of adverse health outcomes. However, controversial discussions around the effects of BPA are still ongoing. Given the societal pressure and the regulation put forward to limit its applications, BPA is gradually being replaced by alternative chemicals to produce “BPA-free” products. In thermal paper, Bisphenol S (BPS) is the primarily replacement for BPA. Limited information on the hazards of BPS is available. Moreover, data on the occurrence of BPS in human specimens are scarce. In this study, we investigated the urinary BPS levels of cashiers and controls from 2 hypermarkets. **Methods:** Total (unconjugated and conjugated forms) BPS was measured urine samples, using liquid chromatography tandem mass spectrometry (LC-MS/MS). Spot urine samples, including pre-shift and post-sift samples and first morning void were collected from each participant. BPS concentration in thermal paper was also measured from each hypermarket and the number of receipts handled by cashiers was estimated. **Results:** Urine samples were collected from 17 cashiers and 15 controls. The estimated number of receipts handled was highly variable among cashiers, ranging from 10 to 400 for a working day. The mean concentration of BPS in thermal paper was 13 mg/g. Total BPS was detected in 95 % of samples in the control group and a significant increase was found in urinary total BPS concentration for cashiers compared to controls. **Conclusion:** The detectable levels of BPS in urine of controls would suggest the exposure of general population to BPS. More, frequent contact with thermal paper would be associated with an increase in urinary total BPS concentration in cashiers.

P504 - Maternal and newborn blood endocrine disruptor levels related to cryptorchidism

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Introduction: Early life in utero cannot provide a safe place for newborns. Placenta cannot hold all agents and the first acquaintance with chemicals takes place in utero and/or with mother milk after delivery, leading to alterations in development, growth, and/or reproduction in an organism. Cryptorchidism (a failure of one or both testicles to descend) is one of the relatively common newborn male genital congenital anomaly and evidence shows that frequency is increasing globally. There is a suggestion that increasing rates of cryptorchidism may be caused partly by early exposure to endocrine disrupting chemicals in the envi-

ronment. The aim of this study was to determine the levels of endocrine disruptors in mothers and newborns to investigate any possible chemical exposure pattern. **Methods:** 29 organochlorine pesticide (OCP) and 18 polychlorinated biphenyl (PCB) congeners in blood samples of healthy (n=37) and cryptorchidic (n=20) newborn babies with their mothers are investigated. Concentrations of all examined OCPs and PCBs were determined by the isotope dilution method with High Resolution Gas Chromatography / High Resolution Mass Spectrometry (HRGC/HRMS). **Results:** Pentachlorobenzene (p=0.0032), 4,4'-DDD (p=0.0498) and 4,4'-DDD (p=0.0284) mother blood levels of cryptorchidic children were found to be significantly higher when compared with control group's blood levels.ß-BHC (p=0.0077), ΣHCH (p=0.0079), hexachlorobenzene (p=0.0020), ΣDDT (p=0.0019), 4,4'-DDT (p=0.0092) and 4,4'-DDE (p=0.0025), cis-heptachloroepoxide (p=0.0025), dieldrin (p=0.0113) blood level of cryptorchidic children were found to be significantly higher when compared with control group children blood levels. **Conclusions:** This study is very important as it is the first information presented about these chemicals levels in blood of healthy and cryptorchidic newborns and their mothers in Turkey while showing that, children are being exposed to endocrine disruptor chemicals in utero and these chemicals may have an active role in the etiology of cryptorchidism. **Acknowledgment:** This project is a part of and granted by TUBİTAK-Helhmholtz Research Institute joint research project.

P505 - Birth weight in relation to maternal blood levels of selected elements in Slovenian mothers

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Introduction: Literature suggests that trace exposures to some elements may influence birth weight. Objective of the present study was to evaluate impact of maternal blood levels of selected toxic and trace elements (manganese (Mn), copper (Cu), zinc (Zn), arsenic (As), selenium (Se), cadmium (Cd), lead (Pb) and mercury (Hg)) on birth weight of their babies, taking into account maternal socio-demographic characteristics and dietary habits. **Methods:** 535 delivering women (19-39 years) from 12 regions all-over Slovenia were recruited. Maternal blood was collected 4-6 weeks after delivery. Associations between new-borns weight and a) predictors obtained through the questionnaires and b) levels of selected elements in maternal blood samples were tested using univariate and multiple linear regression. **Results:** The level of exposure to selected elements was in general low and did not represent any health risk for the mother-child pairs. Multiple regression model showed that gender of the baby, gestational age, maternal age and pre-pregnancy body mass index (BMI) were the main predictors for the baby birth weight, and that Mn in maternal blood was significantly and positively associated with the birth weight. Dietary habits showed insignificant correlations with birth weight. **Conclusion:** Associations between new-borns weight and the main predictors of birth weight (gender of the baby, gestational age, maternal age and pre-pregnancy BMI) was in agreement with the literature data. Positive association observed between birth weight and Mn in maternal blood could be explained by essentiality of Mn in foetal development as an important cofactor in enzymatic reactions in bone formation and metabolic regulation for amino acid, lipid, protein and carbohydrate. This work was supported by the National Human Biomonitoring program financed by the Ministry of Health of Republic of Slovenia and the Slovenian Research Agency.

P506 - LUPE III: An interstate cooperation assessing exposure to chemicals by biomonitoring preschool children from German daycare centers

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Introduction: Interstate research programs offer the possibility to combine resources and knowledge while focusing on shared critical health issues. Human-biomonitoring is thereby an effective tool to assess body burden of the population. In an interstate cooperation we examined phthalate exposure of preschool children in the German states Bavaria, Berlin and North Rhine-Westphalia (LUPE III). Phthalates are substances added to plastics and cosmetics to improve chemical properties. Therefore, exposure can occur ubiquitous from numerous sources. Only few data is available on the magnitude of preschool children's exposure to phthalates, especially in daycare centers. **Methods:** We collected indoor air samples as well as urine samples for analyzation of 10 phthalates metabolites in 63 day-care centers. In winter 2011 / 2012, urine samples from 663 children were examined (after and in part before their stay in daycare centers). A total daily intake was calculated from the concentration in urine specimens and was compared with tolerable daily intake (TDI) values. **Results:** Results show that nearly all children (> 95%) in this study had urine concentrations equal to or above the limit of quantification for five most common phthalate- metabolites (MnBP, MiBP, 5OH-MEHP, 5oxo-MEHP, 7oxo-MiNP). In general, concentration in the morning urine samples were slightly higher compared with those collected after their stay in the facility. **Conclusion:** Our study displays a widespread exposure of preschool children to various phthalates in all three states. There was no hint of an increased uptake of phthalates by visiting daycare centers. For some individuals the calculated daily intake for DiBP is close to or even above the TDI. These results demand a further reduction in exposure. Preschool children exposure to phthalates is not a critical issue on local level, but a general topic for environmental state agencys and an opportunity to perform further interstate cooperation. This project showed that interstate project cooperation is a good instrument to assess human exposure and save monetary and personal resources all at once. The results of our next cross sectional human-biomonitoring study (phase 2014/2015) with preschool children will be published soon.

P507 - The content of toxic and essential trace elements in biological samples of children and adolescents is effective environmental pollution monitoring

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Introduction: Establish of causal relationship between the health effects and content of toxic and essential chemical elements in environmental samples studied is extremely complicated procedure. Routine tests involve biomonitoring study of objects of environment: soil, water sources and plants. **Aim:** To assess the possibility of carrying out a biomonitoring of the environmental situation. **Method:** 310 children13-16 aged from 3 different groups of territories. In Chelyabinsk region had been examined in 2014-2016. 1-st is located near some of the largest copper smelting plant; the 2-nd group of territories is conventionally clean area, free from large industrial facilities; the 3 group of territories is part of the East-Ural radioactive trace. The samples of hair, blood, saliva were collected and tested by method of determination of trace elements in bio substrates by mass spectrometry with inductively coupled plasma. **Results and Conclusion:** Maximum high levels of toxic elements As, Cd, Pb were in all biological samples of children, living near a smelting plant. Children living on the territory of East-Ural radioactive trace show (mostly girls) the general trend toward slightly lower content in the hair most studied chemical elements. The content of Cs in girls from Russian Techa were not significantly different from other settlements. Although Sr in girls from Russian Techa it slight-

ly (not significantly) higher. Homeostasis saliva is highly dependent on oral health and demonstrates the pronounced dynamics after sanitation caries and non-carious lesions. Significant variation in the elemental composition of blood serum appear less frequently reported in children from all areas. Comparative analysis of the samples confirmed that the elemental composition of hair are seen as an integral component of balance in the body of chemical elements and better than blood test reflects a chronic accumulation of toxins in the body, including in the early stages. It is can be recommended as a non-invasive biomonitoring in children and adolescents living in adverse environmental conditions.

P508 - Occupational exposure to environmental tobacco smoke in hospitality venues: are genetic- or proteomics-based biomarkers predictive of respiratory diseases?

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Environmental tobacco smoke (ETS) is recognized as an occupational hazard in the hospitality industry. Although Portuguese legislation banned smoking in most indoor public spaces, it is still allowed in some restaurants/bars, representing a potential risk to the workers' health, particularly for chronic respiratory diseases. The aims of this work were to characterize biomarkers of early genetic effects and to disclose proteomic signatures associated to occupational exposure to ETS, with potential to predict respiratory diseases. A detailed lifestyle survey and clinical evaluation (including spirometry) were performed in 81 workers from Lisbon restaurants. ETS exposure was assessed through the level of PM 2.5 in indoor air and the urinary level of cotinine. The plasma samples were immunodepleted and analysed by 2DIGE and LC/M/MS - based proteomics approaches. DNA and chromosome damage was analysed in lymphocytes and exfoliated buccal cells from 19 cigarette smokers, 29 involuntary smokers, and 33 non-smokers not exposed to tobacco smoke. Also, the DNA repair capacity was evaluated by an ex vivo challenge comet assay with the alkylating agent EMS. All workers were healthy and recorded normal lung function. Interestingly, following proteomics analysis 19 plasma proteins were found differentially expressed in ETS-exposed non-smokers. Some of these proteins have been related with cancer and other conditions associated with tobacco smoke exposure. On the other hand, those individuals showed neither an increased level of DNA/chromosome damage on lymphocytes nor an increased micronucleus level in buccal cells, when compared to non-exposed non-smokers. Noteworthy, lymphocytes challenge with EMS resulted in a significantly lower level of DNA breaks in ETS-exposed as compared to non-exposed workers ($P<0.0001$) suggestive of an adaptive response elicited by the previous exposure to low levels of ETS. Overall, changes in proteome may be promising early biomarkers of exposure to ETS. Likewise, alterations of the DNA repair competence observed upon ETS exposure deserves to be further understood. Work supported by Fundação Calouste Gulbenkian, ACSS and FCT/Pluriannual Program.

P509 - Bisphenol A in urine of preschool children - results of a human biomonitoring study in North Rhine-Westphalia, Germany

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Introduction: Bisphenol A (BPA) is a high production volume chemical used in the manufacture of polycarbonate plastics and epoxy resins. As a result of the presence of BPA in many consumer products, human exposure is widespread. The adverse ef-

fects of BPA especially in doses relevant for human exposure are still part of an ongoing debate which is also shown by the lowering of the Tolerable Daily Intake (TDI) (50 µg/kg BW per day) to a temporary-TDI (4 µg/kg BW per day) by the European Food Safety Authority (EFSA) in early 2015. Due to their rapid development, their in-creased food intake per kg body-weight and child specific exposure routes like mouthing young children are considered to be more susceptible to BPA exposure than the general population. Therefore we aimed to investigate exposure to BPA in preschool children. **Results:** We analyzed urine specimens - collected in 2011/2012 - from 253 preschool children aged from 20 to 80 (mean: 54) months from 23 different day-care centers in North Rhine-Westphalia, Germany. Overall, 94 % of the urine samples had BPA concentrations equal to or above the limit of quantification (LOQ, 0.5 µg/l). The geometric mean (GM) and the arithmetic mean (AM) concentration of urinary BPA levels were 2.3 µg/l and 4.3 µg/l respectively. The maximum BPA level found was 72.4 µg/l and the 95%-percentile 14.6 µg/l. **Discussion:** The measured urinary BPA concentrations in our study population were in range with results reported by several European and North American studies surveying children in age groups from 6 to 10 years (GM range from 2.0 to 3.4 µg/l). Two studies conducted in Canada and the US with a similar range of age showed GM values of 1.4 µg/l and 4.8 µg/l. Furthermore, our results showed slightly lower levels compared to those of older studies from Germany (GM 3.6 µg/l) and Spain (median 4.2 µg/l) which were used to estimate the average daily exposure to BPA of children aged 3-5 years by EFSA. Additional data like food consumption habits and use of personal care products were obtained via questionnaire. These data will be used to investigate associations between the urinary levels of BPA and potential exposure factors.

P510 - Lead intoxicated children in Kabwe / Zambia

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Introduction: Kabwe was an important lead and zinc mining town in Zambia for over 90 years, leaving waste lead contaminated tailings behind. Lead is a well-known serious health hazard, causing anemia, seizures, encephalopathy and death. Soil in Kabwe's housing areas is highly contaminated with lead, especially children from neighboring townships ingest toxic lead dust. **Methods:** The environmental assessments and the health data for Kabwe's children were collected and analyzed. Data is available from three different sources: Copperbelt Environment Project; Blacksmith Institute/ Pure Earth and University of Zambia / Hokkaido University in Sapporo/ Japan. **Results:** In most housing areas the tolerable soil lead levels of 400 ppm were surpassed. Children's blood lead levels were in the most affected townships in over 95% of children increased (≥ 10 µg/dL). Most children did have blood lead levels where urgent action to reduce blood lead levels is required. Exposure to the toxics urgently needs to be reduced. Over ≥ 45 µg/dL medical treatment is recommended, in the most affected townships > 50% of the children showed such high levels. The existing data clearly proves the severity of lead exposure in Kabwe.**Conclusion:** Large proportions of children are not only highly exposed, but actually have high to extremely high levels of lead in their bodies. According to threshold levels and international recommendation they need to be treated and the exposure must be considerably reduced.
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P511 - Aflatoxin B1 can also be an occupational risk factor! How bio-monitoring helped to evidence this.

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Among all aflatoxins, aflatoxin B1 (AFB1) is normally predominant in food cultures and products and is also the one with highest toxicity. It is the most potent hepatocarcinogen known in mammals and due to that is classified by the International Agency of Research on Cancer as Group 1 carcinogen. Although dietary exposure to AFB1 has been extensively documented, only a small number of studies examined exposure in occupational settings. Workers can be exposed by inhalation and dermal absorption in specific occupational settings and during some tasks. A study was developed aiming to know exposure to AFB1 in four occupational settings: poultry and swine production, poultry slaughterhouse, and waste management. A biomarker of internal dose that measures AFB1 in serum was used. 114 workers were enrolled: 34 from poultry farms, 30 from poultry slaughterhouses, 11 from swine production farms and 40 from waste management industry. A control group (n = 30) was also considered in order to know AFB1 background levels for Portuguese population and to discard exposure by ingestion of contaminated food in the workers group. In the control group, the AFB1 values were all below 1 ng/ml. Eighteen workers (58.6%) from poultry farms showed detectable levels of AFB1 with values ranging from <1 ng/ml to 4.23 ng/ml and with a median value of 1.36 ng/ml. Fourteen workers (47.0%) from the slaughterhouse showed detectable levels ranging from <1 ng/ml to 4.03 ng/ml, with a median of 1.73 ng/ml. In swine, six workers (54.5%) had detectable levels with values ranging from <1 ng/ml to 8.94 ng/ml and with a median value of 1.05 ng/ml. In waste management, all the workers had detectable levels of AFB1, ranging from 2.52 ng/ml to 25.99 ng/ml with a median value of 9.75 ng/ml. Data showed that occupational exposure to AFB1 occurs in all these settings with the waste management being the most problematic. Besides a food contaminant, the use of a biomarker allowed to recognize AFB1 as an occupational risk factor. **Keywords:** Aflatoxin B1; occupational exposure; biomarker; poultry farms; poultry slaughterhouse; swine farms; waste management

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P512 - N-acetyl-4-aminophenol (paracetamol) in urine samples of 6-11-year-old Danish school children and their mothers.

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Recent studies indicate an association between the use of paracetamol during pregnancy and reproductive disorders in male and female offspring as well as behavioral effects on the children. Furthermore, N-acetyl-4-aminophenol (NAAP, paracetamol) has been shown to be ubiquitously excreted in urine samples of the general population. To investigate the internal body burden of the Danish population to NAAP for the first time, 288 morning urine samples from 6-11-year-old Danish school children and their mothers were analyzed for NAAP. NAAP was measurable in all mothers and all of the children except for one child. Results showed that there is a ubiquitous body burden of NAAP in Danish mothers and children even when paracetamol analgesics have not been used recently. Hence, several unknown sources of NAAP/paracetamol exposure have to exist. We found an association in NAAP excretion between the mothers and their children which could indicate common lifestyle related exposure (e.g. via food or indoor air sources). However, we did not detect any association between lifestyle data from questionnaires and levels of NAAP excretion in this study. The knowledge about possible sources of exposure leading to this omnipresent paracetamol excretion is limited and further investigation is wanted. Nielsen JKS, Modick H, Mørck TA, Jensen JF, Nielsen F, Koch HM, Knudsen LE. (2015) N-acetyl-4-aminophenol (paracetamol) in urine samples of 6-11-year-old Danish school children and their mothers Int J Hyg Environ Health. 218(1):28-33. Jensen JF, Gottschau M, Siersma VD, Graungaard AH, Holstein BE, Knudsen LE. (2014) Association of maternal self-medication and over-the-counter analgesics for children. Pediatrics.133(2):e291-8.

P513 - Perfluorinated alkylated substances and brominated flame retardants in serum of the Czech adult population

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Introduction: Persistent organic pollutants such as perfluorinated alkylated substances (PFASs) and brominated flame retardants (BFRs) are widespread in the environment and most of them are bioaccumulating in wildlife and human. Some of these chemicals are also subjects of the Stockholm convention. The present study was focused on the monitoring of these substances in human serum samples. **Method:** A total of 300 samples were collected in 2015 from the blood donors in four cities of the Czech Republic. All participants completed a detailed questionnaire to provide information on their lifestyle factors. The mean age of the participants was 40.8 ranging from 18 to 64 years. In all samples 19 PFASs and 33 BFRs including some of their metabolites were analyzed. The analyses were performed using ultra high performance liquid chromatography coupled with tandem mass spectrometry or gas chromatography with mass spectrometry (according to the type of analyte). **Results:** None of BFRs was detected at levels above the LOQ in more than 50 % of serum samples. The most frequently found representatives of this group were congeners of polybrominated diphenyl ethers, namely BDE-47 (in 8.7 %; range: 0.484-5.37 ng/g lipid), BDE-99 (in 6.0 %; range: 0.818 – 9.35 ng/g lipid), BDE-153 (in 7.3 %; range: 0.698-6.10 ng/g lipid) and BDE-209 (in 7.0 %; range: 16.8-2939 ng/g lipid). Longer-chain PFASs, with the carbon chain length C6 and higher were dominated in all samples. The detection frequency declined in the following order: perfluorooctanesulfonate (PFOS)> perfluorooctanic acid (PFOA)> perfluorononanoic acid (PFNA)> perfluorohexanesulfonate (PFHxS)> perfluoro-n-decanoic acid (PFDA)> perfluoroundecanoic acid (PFUdA); median concentrations were 1.15, 0.756, 0.325, 0.184, 0.145, 0.0580 ng/ml, respectively. We observed statistically significant associations ($p<0.05$) between selected PFASs and locality, sex and education. **Conclusion:** This study is the first investigation to reveal the PFASs and BFRs levels of serum samples in the general population of the Czech Republic. The levels of PFASs and BFRs in serum samples are relatively lower than those reported from other European countries.

P514 - Lower Saxony's human milk research program

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Introduction: Breastfeeding represents the best nutrition for infants. In Lower Saxony, mothers can obtain a free of charge chemical analysis of their human breast milk (HM) in order to detect exposure to environmental contaminants. The main objective of the program is to give mothers a breastfeeding recommendation. **Methods:** HM is routinely analyzed in our lab for polychlorinated biphenyls (PCBs), pesticides, polybrominated diphenyl ethers (PBDEs), and nitromusks. In cooperation with partners special analyses were performed for polychlorinated dibenzodioxins/-furans (PCDDs/PCDFs), dioxin-like polychlorinated biphenyls (dl-PCBs), perfluoroalkyl alkyl substances (PFASs), ochratoxin A (OTA), and glyphosate. Data from chemical analysis and questionnaires were evaluated using multivariable regression models. **Results:** Since 1999, an average of ff 550 samples p.a. was analyzed. For organochlorine compounds, an ongoing decrease in their concentrations is noted. Based on data for 2005 to 2007 (n=1,658), the following reference value estimators were derived: PCBs 0.45 mg/kg fat, DDT 0.25 mg/kg fat (solely mothers from West Germany), HCB 0.06 mg/kg fat, BDE-47 1.5 ng/g fat, and BDE-153 1.3 ng/g fat, respectively. In 2010 to 2012 (n=1,566), reference values were exceeded by 2.2 % for PCBs, 0.4 % for HCB, and 2.9 %for DDT. PFASs and OTA concentrations ranged from < 10 to 270 ng/L (n=110, 2010/11) and < 10 to 78 ng/L (n=60, 2009/10), respectively. Glyphosate levels were < 0.02 µg/L (n=97, 2015). Regression models were used to assess whether individual characteristics of the mother (origin of birth, age, previous lactation periods as provided by questionnaires) were associated with the concentration. **Conclusions:** The HM research program ensures scientifically based information for breastfeeding mothers about their individual body burden. It

can furthermore help to identify potential contaminants in Lower Saxony´s general population. With the exception of only a few cases, the measured concentrations were not of toxicological relevance. The available extensive data base permits to modify the program´s study design as well as to respond to emerging contaminants of public health concern.

P515 - Perfluorobutan sulfonate (PFBS) and perfluoroheptanoic acid (PFHpA) seem to be bioaccumulating

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Introduction: Many perfluorinated alkyl acids (PFAA) are known to be bioaccumulating, especially those with longer chain lengths. Thus, perfluoro alkyl carboxylic acids with less than seven carbons and perfluoro sulfonic acids with less than six carbons are considered to be “short chained” due to the fact that they are not considered to bioaccumulate. The aim of this study was to investigate if some of the more-short chained PFAA are bioaccumulating. **Methods:** In the community Ronneby, Sweden many thousands of people have been exposed to high levels of PFAA in the drinking water, probably for more than 20 years. Among the PFAA in the water, high levels of PFBS and PFHpA was found. When the PFAA was detected in the drinking water this was changed to another water source without PFAA contamination immediately. More than 2 months after the water supply was changed to un-contaminate water, serum samples were collected from 20 eleven years old children that lived in the area with contaminated water and going to a school where they had been drinking the contaminated water. Serum was also collected from 17 similar aged children drinking water both at home and in school from a non-contaminate area. The serum samples were analyzed by liquid chromatography tandem mass spectrometry. **Results:** The median levels of the serum in the 20 children drinking the contaminated water was 0.27 (range <LOD-1.4) ng/ml for PFBS while that for the other 17 children was 0,018 (range <LOD-0.075) with a 15 times difference. For PFHpA the same numbers was 0.38 (range <LOD-1.6) and 0.018 (range <LOD-0.072) ng/ml with a 21 times difference. **Conclusions:** PFBS and PFHpA seem to be bioaccumilating agens. The definition of what should be considered as long chained or short chained PFFAs must be changed if this is depending on bioaccumulation.

P516 - UV filters monitored in urine from Danish children and adolescents

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Introduction: Experimental studies indicate that some chemicals with UV blocking properties (known as UV filters) can act as endocrine disruptors and are suspected to have estrogenic and/or anti-androgenic effects. Exposures to some UV filters have been associated with pubertal development, thyroid and reproductive functions. UV filters are used in sunscreens and other cosmetic- and personal care products, as well as in other consumer products such as in food packaging, clothing and furniture textiles to protect the products against UV radiation. Here we present the urinary excretion of suspected endocrine active UV filters in Danish children and adolescents recruited from the general population. **Methods:** The content of benzophenone (BP), benzophenone-1 (BP-1), benzophenone-2 (BP-2), benzophenone-3 (BP-3) and 4-hydroxybenzophenone (4-HBP) were monitored in 24-hour urine and two consecutive first morning samples from 129 healthy Danish children and adolescents (6-21 yrs). All samples were collected at winter time (Nov. 2007) and were analyzed by a new on-line TurboFlow-LC-MS/MS method developed for simultaneous biomonitoring of UV filters in urine and other human matrices, such as serum and amniotic fluid. **Results:** BP-3 and BP-1 were measured in more than 80% of the 24-hour samples and were significantly correlated (R2=0.815), followed by BP, 4-HBP and BP-2 measured in 43, 15 and 5% of the samples. The median (range) concentrations of the UV-filters in 24-hour urine were as follows: BP-3, 0.92

(LOD-115); BP-1, 0.54 (LOD-44.6); BP, <LOD (LOD-48.5); 4-HBP, <LOD (LOD-10.5); and BP-2, <LOD (LOD-8.43) ng/mL. Around two time higher concentrations of BP-3 and BP-1 were measured in first morning urine compared to 24-hour urine, while the concentration of BP was similar in both first morning and 24 hour urine. **Conclusion:** This biomonitoring study on UV filters in Danish children and adolescents shows that the children were exposed to multiple UV filters simultaneously and the high amount of children exposed during winter time indicates that the sources for exposure might be others than sun protection products.

P517 - Associations between plasma concentrations of PCB 28 and possible indoor exposure sources in Danish school children and mothers

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Polychlorinated biphenyls (PCBs) are ubiquitously present in the environment and are suspected of carcinogenic, neurotoxic and immunotoxic effects. Significantly higher plasma concentrations of the congener PCB 28 occur in children compared to adults. Exposure in schools may contribute to this difference. PCB 28 was analyzed in plasma samples from 116 children aged 6-11 years and 143 mothers living in an urban and a rural area in Denmark and participating in the European pilot project DEMOCOPHES (Demonstration of a study to COordinate and Perform Human Biomonitoring on a European Scale). In Denmark, PCBs were used in construction in the period 1950-1977, and year of construction or renovation of the homes and schools was used as a proxy for indoor PCB exposure. Linear regression models were used to assess the association between potential PCB exposure from building materials and lipid adjusted concentrations of PCB 28 in plasma, with and without adjustment for potential confounders. Amongst the 116 children and 143 mothers, we were able to specify home construction period in all but 4 children and 5 mothers leaving 111 children and 138 mothers for our analyses. The median lipid adjusted plasma PCB 28 concentration was 3 (range: 1-28) ng/g lipid in the children and 2 (range: 1-8) ng/g lipid in the mothers. Children living in homes built in the PCB period had significantly higher lipid adjusted plasma PCB 28 concentrations compared to children living in homes built before or after the PCB period. Following adjustment for covariates, PCB 28 concentrations in children were 40 (95% CI: 13; 68) percent higher than concentrations of children living in homes constructed at other times. Our results suggest that PCB exposure in the indoor environment in schools and homes constructed during the PCB period may contribute significantly to children's plasma PCB 28 concentration. Efforts to minimize PCB exposure in indoor environments should be considered.
Egsmose EL, Bräuner EV, Frederiksen M, Mørck TA, Siersma VD, Hansen PW, Nielsen F, Grandjean P, Knudsen LE. (2016) Associations between plasma concentrations of PCB 28 and possible indoor exposure sources in Danish school children and mothers. Environment International 87: 13-19.

P518 - Efficiency control of dietary pesticide intake reduction by human biomonitoring

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In spite of food safety controls for pesticide residues in Europe, a regular diet still leads to a noticeable exposure of the general population to several pesticides. A dietary shift to organic food may result in a decrease of the public exposure to pesticides. To assess the success of dietary interventions on the internal pesticide burden several human biomonitoring (HBM) parameters are available. In a pilot study the response of exposure reduction by dietary shift on the urinary levels of pesticide metabolites was investigated. In the study two adult individuals were kept on a common diet for 11 days and morning urine voids were collected at the last four days of the period. Afterwards, the participants switched to exclusively on organic food for

18 days and likewise morning urine samples were collected at the last four days of this period. In the urine samples pyrethroid metabolites, dialkylphosphates phenolic pesticide metabolites, 6-chloronicotinic acid (ClNA) and glyphosate were quantified using GC-MS methods. Some HBM parameters were not found in any or hardly any of the samples, whereas other parameters were detected in each or almost each sample. Generally, the comparative analyses revealed greater shares as well as higher levels of the parameters in the samples of the common diet period compared to the organic diet period. Considerable decrease of the urinary levels was found for pyrethroid metabolites, for dialkylphosphates, for 4-nitrophenol and for 3,5,6-trichloropyridinol. In contrast, higher values were found for the organic diet period by tendency for ClNA. HBM enables the efficiency control of exposure reduction by a dietary shift. Generally, switching to organic food consumption results in a considerable reduction of pesticide exposure. However, the unexpected increase of ClNA demonstrates that reliable information on the effect can only be ascertained by larger intervention studies or cross-sectional studies with accurate nutrition data.

P601-P608: Miscellaneous

P601 - Sex/gender in environmental health research: relevance, interdisciplinary approaches and transdisciplinary perspectives

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Introduction: Though gender inequalities in environmental exposures and their health impacts have been described, systematic consideration of sex/gender in environmental health research is still missing. It is assumed that systematic integration of both biological and social dimensions of sex/gender and their interactions into health research will enhance significance and validity. However, there is often a mismatch between theoretical concepts and analytical approaches used in practice as well as a conceptual muddle in the use of the terms 'sex' and 'gender'. Contrary to gender theorized as a multidimensional, context-specific factor that changes according to time and place, a homogeneous dichotomic category measured by a single check box is often used in research. **Aim:** An interdisciplinary research network GeUmGe-NET, funded by the Federal Ministry of Education and Research in Germany, was created to (1) systematically evaluate the current state of knowledge, underlying concepts, and methods used in research on sex/gender and environmental health, (2) develop interdisciplinary approaches to integrate theoretical concepts of sex/gender into environmental health research, and (3) discuss implications for environmental health monitoring and develop recommendations for environment and health authorities. Research network and approach: Researchers from environmental and genetic epidemiology, toxicology, environmental medicine, public health, gender studies and social-ecological gender research constitute the research network. In a first workshop in February 2016 a common agreement on terms and concepts was developed and examples of good practice as well as knowledge gaps were discussed. The next step is the systematic assessment of how sex/gender is currently considered in biomedical and public health research on environmental health. Potentials for further development of methodology in the field of environmental health research by integrating sex/gender concepts will be analysed. Finally, transfer from science to practice is intended with recommendations useful for environmental health monitoring, promotion, and protection.

P602 - Exposure and risk assessment of pesticides

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Introduction: Dietary intake of pesticides is one of the main routes of exposure to different pesticides. The widespread applications of plant protection products (PPPs) causes the risk to produce negative effects on the health. Some pesticides used in agriculture are classified as carcinogenic, mutagenic or causing hormonal system disorders. The present research was conducted to assess the cumulative health risk associated with consumption of vegetables and fruits contaminated with pesticides. **Material and Methods:** Samples from the harvest of 2014 and 2015 years were selected. Selected samples of fruits and vegetables were analyzed by using of GC/MS. **Results and Discussion:** According to our results, obtained in 2014 [1], the maximum residue level (MRL) exceedance for dimethoat, tebufenpyrad, phosalone, carbendazim, and indoxacarb was registered in 31% of all detected pesticides in analyzed commodities. The estimated daily intake (EDI) have been ranged between 0.000015 and 0.0012 mg/kg of body weight/day. Calculated values of EDIs are lower than the levels of acceptable daily intake (ADI) of detected pesticides. Obtained data of the sum of EDI were used to calculate the hazard index for the tested compounds. The calculated hazard indices (EDI/ADI) ranged from 0.00041 and 0.42 for the analyzed pesticides. The sum of hazard indices is 0,6. According to the results of 2015, the MRL exceedance of pesticides was not registered in analyzed commodities. The calculated hazard indices ranged from 0.001 and 0.031 for the analyzed pesticides. The sum of hazard indices is 0,4. **Conclusions:** Our results of the hazard indices show that the long-term consumption of tested vegetables and fruits could not pose a health risk for the population of Moldova as the hazard indices for all the detected residues were less than one. 1 – Raisa Sircu, Iurie Pinzaru, Nicolae Opopol, Raisa Scurtu. Health risk related to the intake of pesticides in the Republic of Moldova. International Journal of Advanced Research (2015), Volume 3, Issue 7, 628-633.

P603 - A need for coordinated European human biological monitoring in Lithuania and Europe

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Human biological monitoring (HBM) used to evaluate exposure and risks for different chemicals has the main objective to determine the internal dose of chemical absorbed by an individual. Because of the growth of industry and an increase in use of chemicals, this objective is important and relevant for all countries of the European Union, especially Eastern European and the Baltic countries. The urgent need for HBM and subsequent translation of the results into legislative measures is based on knowledge about certain pollution trends in our countries. Lithuania is a border country facing pollution sources from Belarus and Russia via rivers and air. Air pollution is also affected by domestic combustion and traffic. European Environmental Agency report on Air Quality in Europe – 2015 states that population-weighted concentration of benzo(a)pyrene is above 1.5 ng/m3 in large regions of Central and Eastern Europe. The study by Baltic Environmental Forum found indoor air affected by formaldehyde, toluene, aromatic molecules exceeding the allowed levels up to 10 times. HBM of a huge spectrum of chemicals in a randomly selected population from each country and possibility to determine chemicals, according to standardized methodology and protocols could provide a real picture about an internal dose of chemicals. Internal dose determined would let to look for biomarkers of susceptibility and effects. The relationships found out between exposure, dose, effects and responses would be the base for toxicological risk estimations. A standardized questionnaire could be used to assess exposure routes, socioeconomic and lifestyle factors. The results could be used to determine threshold values, ban the use of hazardous substances and make political decisions related to improvement of environment and human health. The database could be linked to the registries of the diseases, giving an opportunity to have European cohort survey estimated the causal relationships between exposure and health effects. European HBM could be a basis for a comprehensive picture on levels of hazardous substances in biological media of the European population and subsequently better and cleaner environment.

P604 - Environmental exposure to toxicants mixtures from a multi-purpose estuary: perspectives for a biomonitoring study in Portugal

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The present work was focused on a multi-purpose estuarine environment (river Sado estuary, SW Portugal) around which a number of activities (e.g., fishing, farming, heavy industry, tourism and recreational activities) coexist with urban centers with a total of about 200 000 inhabitants. Based on previous knowledge of the hazardous chemicals within the ecosystem and their potential toxicity to benthic species, this project intended to evaluate the impact of estuary contaminants on the human and ecosystem health. An integrative methodology based on epidemiological, analytical and biological data and comprising several lines of evidence, namely, human contamination pathways, human health effects, consumption of local produce, estuarine sediments, wells and soils contamination, effects on commercial benthic organisms, and genotoxic potential of sediments, was used. The epidemiological survey confirmed the occurrence of direct and indirect (through food chain) exposure of the local population to estuarine contaminants. Furthermore, the complex mixture of contaminants (e.g., metals, pesticides, polycyclic aromatic hydrocarbons) trapped in the estuary sediments was toxic to human liver cells exposed in vitro, causing cell death, oxidative stress and genotoxic effects that might constitute a risk factor for the development of chronic-degenerative diseases, on the long term. Finally, the integration of data from several endpoints indicated that the estuary is moderately impacted by toxicants that affect also the aquatic biota. Despite data pointing to a potential human health risk, its assessment requires a biomonitoring study including the quantification of contaminants (or metabolites) in biological fluids as well as biomarkers of early biological effects (e.g., biochemical, genetic and omics-based endpoints) and genetic susceptibility in the target population. Data should be supported by a detailed survey to assess the impact of the contaminated seafood and local farm products consumption on human health and, particularly, on metabolic diseases or cancer development. Work supported by the Portuguese Foundation for Science and Technology (PTDC/SAU-ESA/100107/2008).

P605 - Apolipoprotein E (ApoE) genotypes in relation with Hg, As, Pb and Se levels in mothers and their newborns

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Introduction: Apolipoprotein E (ApoE, gene APOE) is a lipid binding plasma glycoprotein with central roles in lipid metabolism and neurobiology. Some studies point on its antioxidative, metal-binding and immunomodulatory/anti-inflammatory properties. It has three major isoforms (ApoE2, ApoE3 and ApoE4 encoded by alleles ε2, ε3 and ε4). The purpose of present work was to estimate relations between ApoE polymorphisms (ε4 carriers vs no-carriers) and conc. of metal(loid)s (Hg, As, Pb, Se) in mothers and their newborns chronically exposed to low or moderate amounts of Hg, mostly through fish consumption. **Methods:** We used DNA extracts and metal concentration data-set of Croatian mothers (n=209, aged 19-44y, sampling 3rd trimester) and their newborns (n=176, sampling at delivery) from a wider prospective birth cohort study PHIME ('Public Health Impact of long-term, low-level, mixed element exposure in susceptible population strata'; EU project 2006-2011). Database consisted of Hg, MeHg, Se, As, Pb, Cd, Cu and Zn levels in maternal urine, breast milk, hair, peripheral and cord blood (CB), and child urine. Archived

DNA extracts from maternal leukocytes and cord tissue were used for APOE genotypization by TaqMan® pre-designed SNP assay for rs429358 and rs7412 (Applied Biosystems, ZDA). Statistics: STATA/SE 12 package. **Results:** Mothers and newborns were divided in Apo ε4 carriers (genotypes ε3/4 and ε4/4) and ε4 non-carriers (genotypes ε3/3, ε3/2 and ε2/2). We identified 17% and 20% ε4 carriers among mothers and newborns, respectively. Mothers with allele e4 have significantly higher conc. of: i) blood Se, Hg and As; ii) plasma Se, iii) hair Hg and iv) CB Hg. In CB the additional positive association was found between Pb and the presence of ε4 in newborns. For Se only the observed associations persisted after taking into account the influence of possible cofounders like fish intake, parity, age, presence of other metals ect. **Conclusion:** Observed superior Se status in healthy pregnant females with genotypes Apo ε4/3 and ε4/4 in comparison with Apo ε3/3, ε3/2 and ε2/2 group is enigmatic, but it could be linked to Apo ε4 'beneficial effects early in life'. The presence of detrimental metals in maternal blood didn't affect plasma Se level in sense of its decrease.

P606 - HBM data related to age – Children and elderly

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Introduction: HBM data related to age are of special interest as children and elderly are considered vulnerable.
Method: We performed a literature review of National HBM programs over the past 20 years (poster by Choi et al), and collected data related to HBM data and age. Among the reviewed HBM programs, phthalates have shown to be a major concern for children as both the GerES and NHANES previously showed that children had higher body burden of several phthalate metabolites compared to adults. In addition, GerES IV found that levels of organochlorine pesticides such as HCB, hexachlorocyclohexane (HCH), and dichlorodiphenyldichloroethylene (DDE) in children decreased with increasing age, and data analysis from the NHANES showed that children aged 6-11 had the highest urinary level of the PAH metabolite 1-hydroxypyrene compared to adolescents and adults. Other scientific HBM studies also indicated higher levels of PBDEs and PFCs in children aged 1.5-9 than other subjects aged 9 or older. These findings emphasize the need of HBM in children in order to generate the data appropriate for accurate risk assessment and management regarding children's exposure to chemicals. Among the HBM programs, it has been observed that several metals appear to accumulate in the elderly population. FLEHS findings showed that the highest levels of total Hg in blood were found in the elderly (aged 50-65) and the PROBE study also showed that both blood lead and palladium concentrations increased with age). The Slovenian HBM study found that the blood cadmium, blood lead, and hair mercury levels were the highest among the older women (aged 50-60) compared to children or adults Aside from metals, urinary levels of phthalates also appeared to be higher among subjects with older age in the South Korean KorSEP study (Lee et al., 2011), and a scientific HBM study from Australia observed the highest level of PFOS in the serum of subjects aged 60 or older These findings suggest slower clearance of these chemicals out of the body. Therefore, it is likely that the elderly is at a higher risk of developing adverse effects from exposure to chemicals, making it important to monitor the chemical levels in the elderly within a HBM program.**Conclusion:** Age must be considered when designing HBM programs. More outcomes from this project can be found in a EFSA supporting publication (2014:EN-724). **Acknowledgement:** We would like to thank the European Food Safety Authority (EFSA) for funding the review.

P607 - Using Human Biomonitoring data to quantify the burden of disease due to environmental risk factors in children and adolescents – the UKAGEP project

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Introduction: Human Biomonitoring (HBM) data are a rich source to estimate the population exposure towards several environmental hazards. These data can further serve as the basis to quantify the environmental burden of disease (EBD). Here, health effects are assessed by using summary measures of population health which can be of additional value to inform policy-makers about the major environmental risk factors causing ill-health. However, national up-to-date EBD estimates are currently not available for Germany. Therefore it is planned to fill this gap by a research project, called UKAGEP. This project aims at estimating the EBD of 16 risk factors for children aged between 3 and 17 years in Germany. **Methods:** The UKAGEP project uses the EBD methodology and its core measure, the disability-adjusted life year (DALY). Current HBM data derived in the population-representative German Environmental Survey (GerES 2014-2017) are used to estimate the internal exposure of German children for eight hazards (e. g. lead in blood, arsenic in urine, endocrine disruptors in urine). Combined with exposure-response functions, which are derived or updated by meta-analysis, and data on the related health effects, DALYs will be calculated. To take into account long lag periods between exposure and effect and the cumulative chronic effects of stressors probabilistic modeling will be performed which also includes estimates of the future burden. **Expected results:** The concentration of most environmental hazards is expected to be rather low. However, some of the stressors might still pose a considerable threat on the population level, especially if both, effects of mortality and morbidity are reflected in the summary measure of population health. Furthermore the project updates the scientific evidence on adverse health effects of the stressors in a qualitative and quantitative way (DALYs). **Conclusions:** Though the UKAGEP study was just recently launched, we expect new insights in the EBD of children in Germany. High quality HBM data from the new GerES-study will inform the models and help to identify the major drivers of EBD.

P608 - Exposure to bisphenol A related to hemodialysis treatment

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Bisphenol A (BPA) is an endocrine disruptor (ED) found in food containers, in plastic beverages and in some dialyzers. The aim of this study is to investigate for the first time, the overall potential exposure to BPA during hemodialysis (HD) treatment of patients suffering from end stage renal disease. Samples were collected on the water loop, dialysis machine, and dialyzer. In order to avoid contamination by BPA, samples (250 mL) were collected into calcined glassware (500°C for 5 h). The concentrations of BPA were determined using a LC/MS/MS system consisting of a Solid-phase extraction system. We studied 5 commonly used dialyzers. These dialyzers are manufactured with different synthetic compounds representative of what is most commonly used in industry. Before HD sessions dialyzers were rinsed using a 2000 mL clear-flex of 0,9% sodium. We confirm that significant amount of BPA may migrate from dialyzers and demonstrate that BPA is also provided by water used for dialysate production (8.0 ± 5.2 ng.L-1 on average) and by dialysis machine and dialysate cartridge leading to a dialysate contamination of 22.7 ± 15.6 ng.L-1 on average. Taking into account all sources of BPA contamination during HD session, the estimated highest exposure could reach 140 ng/kg b.w/day for HD patients, directly available for systemic exposure. Our study shows that HD patients are exposed to BPA through the water used for HD, the internal circuit of the generator and the dialyzer itself. As regards the water processing loop, BPA is not removed by this treatment. If the dialysis machine also salts out BPA, this is probably due to the composition of the tubes in which the water circulates. All dialyzers salt out. BPA could come from the plastic polymers that

form the fibers and the case. The rinsing of dialyzers greatly reduces the quantities of BPA, so it is essential that this be done before each HD session. The absence of BPA in dialyzers could become a standard of choice when purchasing these medical devices. Our perspectives are associated with the future development of a marker in patients' blood that most accurately reflects degree of exposure.

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Chairs:

Michael Bader, BASF, Germany
Robert Barouki, Inserm-University Paris Descartes, France
Marika Berglund, Karolinska Institutet, Institute of Environmental Medicine, Sweden
Argelia Castaño, National Center for Environmental Health, Institute of Health Carlos III, Spain
Douglas Haines, Health Canada, Canada
Jana Klánová, Masaryk University, Czech Republic
Lisbeth E. Knudsen, University of Copenhagen, Denmark
Ovnair Sepai, Public Health England, United Kingdom
Michael Wilhelm, Ruhr University Bochum, Germany
Birgit Wolz, Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany

Panelists:

Lilian Busse, German Environment Agency/UBA, Germany
Hermann Fromme, German Human Biomonitoring Commission and Bavarian State Office for Health and Food Safety, Germany
Sascha Gabizon, Women in Europe for a Common Future /WECF
Catherine Ganzleben, European Environment Agency/EEA
Andreas Gies, German Environment Agency/UBA, Germany
Arnd Hoeveler, European Commission, DG Research & Innovation
Karl-Heinz Jöckel, Institute of Medical Informatics, Biometry and Epidemiology, Essen University Hospital, Germany
Edgar Leibold, BASF, Germany
Elizabet Paunovic, WHO European Centre for Environment and Health
Gerd Romanowski, German Chemical Industry Association/VCI, Germany
Getrud Sahler, Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany
Peter van den Hazel, Public Health Services Gelderland-Midden, Netherlands
Carolyn Vickers, World Health Organization/WHO

Speakers:

Tamar Berman, Public Health Services, Ministry of Health, Isreal
Antonia Calafat, US Centers for Disease Control and Prevention, United States
Sébastien Denys, The National Public Health Agency/ANSP, France
Ruth A. Etzel, Environmental Protection Agency, United States
Clémence Fillol, French Institute for Public Health Surveillance, Environmental Health Department, France
Jochen Flasbarth, Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety/BMUB, Germany
William D. Fraser, University of Sherbrooke, Research Center of Sherbrooke University Hospital/CHUS, Canada
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Kembra Howdeshell, National Institute of Environmental Health Sciences/NIEHS, United States
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Suejin Kim, National Institute of Environmental Research, Korea
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