SESSION 4: CONTRIBUTION OF RESEARCH TO HUMAN BIOMONITORING

The contribution of research and how human biomonitoring activities provide information and lead to identify new knowledge gaps were discussed in this session. Several areas of research were covered: from the use and limitations of biomarkers of exposure and effects in population studies to advanced risk assessment modelling techniques. Research needs were highlighted through their challenging and stimulating potential contribution to HBM. Projects presented in this sessions are examples of current research projects funded by EU Member States (MS) or the European Commission's Research Directorate-General, which has been an important funding source for HBM projects for many years through the framework programmes of research. A large number of EU-wide projects including cohort studies are ongoing, focused on the development of exposure and effect biomarkers to a multitude of environmental contaminants.

The session was moderated by Sylvaine CORDIER from Inserm U625, Rennes, France.

Session Presentations

1. Overview of EU Research Projects Related to Human Biomonitoring
2. Pesticide Exposure of Pregnant Women in Brittany: The Pelagie Cohort Study
3. European Mother-Child Cohort Studies
4. Impact of Air Pollution on Biomarkers of Genetic Damage
5. Analytical Validation of Biomarkers: Laboratory Issues
6. Biomarkers of Estrogenic/Androgenic Activity in Connection to Breast Cancer: An Experience from Andalucía
7. Use of Biomonitoring Data to Improve Advanced Risk Assessment Models

Overview of EU Research Projects Related to Human Biomonitoring

Tuomo KARJALAINEN
European Commission, DG Research

The European Commission has funded a number of research projects relevant to Human Biomonitoring and many actors at the Commission address Environment and Health issues. The Directorate-General (DG) for Research promotes research. Under the DG for Research, there are several Directorates. I work in the Environment Directorate. We are not policy-makers. However, our research supports policies. Policy issues in this area are handled essentially by the DG Environment and the DG "SANCO" or DG Health and Consumers. These two DGs are responsible for the Environment and Health Action Plan (EHAP) as well as for many other public health policies, such as air pollution, indoor air, and food contaminants.

The Fifth and Sixth Framework Programs

In the Fifth Framework Program (FP5), 92 projects were funded with a budget of approximately 40 million euros per year. Many projects related to health risks of exposure to chemicals, projects on air pollution, and projects related to exposure to electromagnetic fields. For the Sixth Framework Program, most of the projects are still ongoing. The budget was approximately 10 more million euros per year. Projects included integrated environment and health risk assessment, on chemicals and health risks, and on exposure to nanoparticles.

Project focus	Number of projects	
	FP5	FP6
Health impacts and risk assessment of chemicals	43	18
Health impacts of air pollution	18	3
Health impacts of electromagnetic fields	8	2
Health impacts of noise	4	0
Health impacts of climate change	1	7
Health impacts of UV/radiation	5	0
Health impacts related to food and water contaminants	3	9
Integrated environment and health risk assessment, methods and tools; gene/environment interactions in disease development	7	13
Methods on cost/benefit, risk/benefit analyses	0	6
Environmental and health risks of exposure to nanoparticles	2	8
Total	92	64

Recently finished biomonitoring related projects

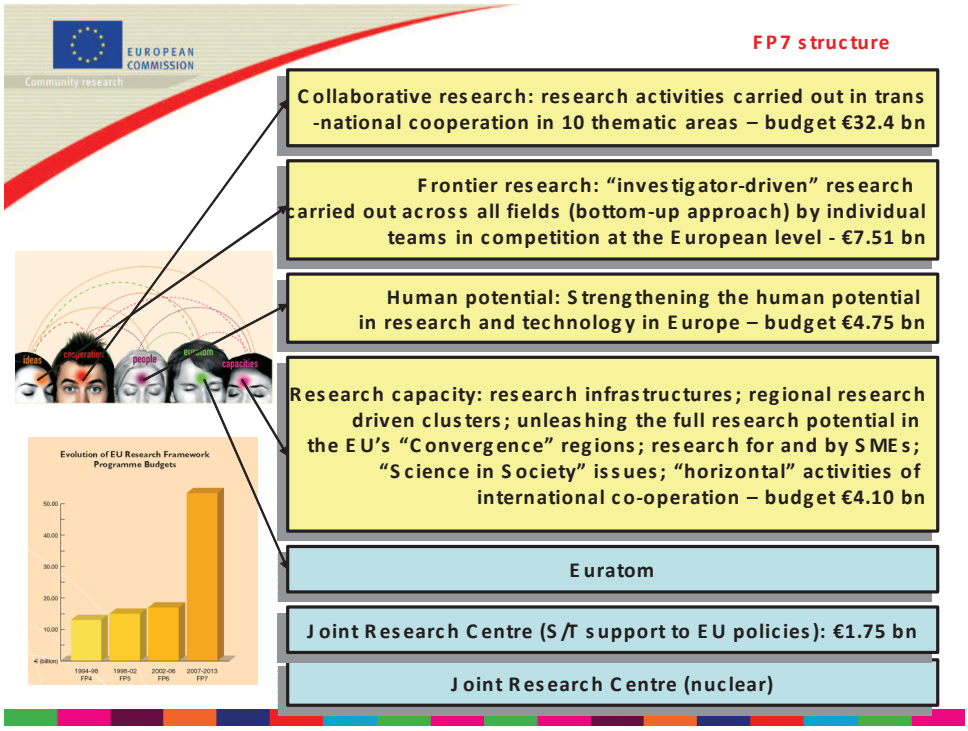
- **ESBIO:** Development of a coherent approach to human biomonitoring in Europe
- **PIONEER:** Puberty onset –influence of nutritional, environmental and endogenous regulators
- **DEVNERTOX:** In vivo and in vitro studies on the neurotoxic effects of mixture of neurotoxic seafood contaminants

Ongoing biomonitoring related projects

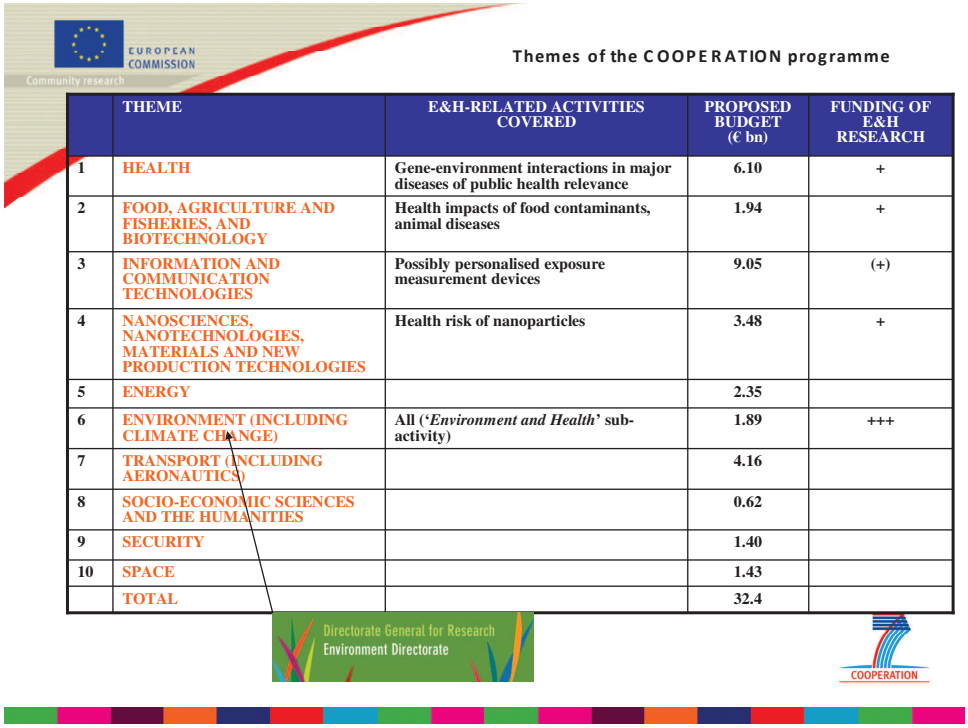
- **NewGeneris:** Newborns and Genotoxic exposure risks
- **PHIME**: Public health impact of long-term, low-level mixed element exposure in susceptible population strata
- **PHOEBE:** Promoting harmonisation of epidemiological bio banks in Europe
- **NORMAN:** Network of reference laboratories for monitoring of emerging environmental pollutants
- **INTARESE:** Novel methods for integrated risk assessment of cumulative stressors in Europe

EU Framework Programmes of Research

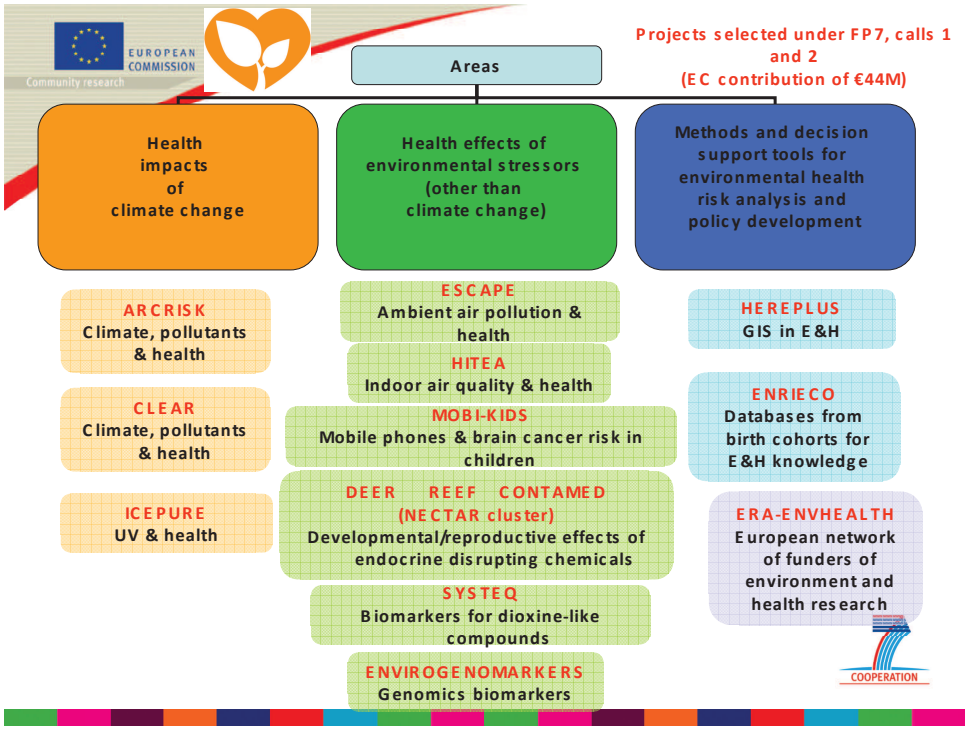
The 7th Framework Program was launched for the years 2006–2013. The main issues to be covered will most be likely investigations on the health risks of climate change, chemicals, electromagnetic fields, and exposure to nanoparticles.



Nine thematic Priorities a few of them new as compared to FP6.



	THEME	E&H-RELATED ACTIVITIES COVERED	PROPOSED BUDGET (€ bn)	FUNDING OF E&H RESEARCH
1	HEALTH	Gene-environment interactions in major diseases of public health relevance	6.10	+
2	FOOD, AGRICULTURE AND FISHERIES, AND BIOTECHNOLOGY	Health impacts of food contaminants, animal diseases	1.94	+
3	INFORMATION AND COMMUNICATION TECHNOLOGIES	Possibly personalised exposure measurement devices	9.05	(+)
4	NANOSCIENCES, NANOTECHNOLOGIES, MATERIALS AND NEW PRODUCTION TECHNOLOGIES	Health risk of nanoparticles	3.48	+
5	ENERGY		2.35	
6	ENVIRONMENT (INCLUDING CLIMATE CHANGE)	All (‘*Environment and Health*’ sub-activity)	1.89	+++
7	TRANSPORT (INCLUDING AERONAUTICS)		4.16	
8	SOCIO-ECONOMIC SCIENCES AND THE HUMANITIES		0.62	
9	SECURITY		1.40	
10	SPACE		1.43	
	TOTAL		32.4	



Conclusion

DG Research is committed to support science related to policy-making, including in the field of Human Biomonitoring and undertake do extensive collaboration with international organisations such as WHO.

Pesticide Exposure of Pregnant Women in Brittany: The Pelagie Cohort Study

Cécile CHEVRIER
Inserm U625, Rennes, France

Results of an epidemiological study carried out in Brittany (France) and the results of the link between levels of urinary metabolites from herbicides and organophosphorus insecticides and birth outcomes was presented.

Context in the Brittany Region

As Brittany is an agricultural region, 90% to 95% of the exposure to pesticides comes from agricultural activities. Non-agricultural sources of exposure to pesticides include community needs and domestic uses. The contamination in water, air, soil, plants, and food is transferred to humans by ingestion, inhalation, and dermal contact of pesticide residues. Other studies, based on questionnaires, have been carried out to assess the consequences of pesticides on reproduction. Some suggested an increased risk of stillbirths and congenital anomalies and a negative impact on intrauterine growth.

Aim

The aim of the study was to assess the impact to prenatal exposure to pesticides on intrauterine growth, using biomarkers of exposure to the herbicide atrazine and to organophosphorus insecticides.

Method

The study was conducted in Brittany during the period 2002-2005 from a mother-child cohort (Pélagie cohort). The Pélagie cohort involved 3421 pregnant women. Researchers collected questionnaires filled out by the mothers from the beginning of the pregnancy, took urine samples of the pregnant woman, and medical data on pregnancy, delivery, child health from the time of birth with a follow-up biomonitoring studies during childhood planned. 52 pesticide metabolites were selected for study. Chemical analyses were carried out at IDHESA, a French laboratory. For statistical analysis, they worked in molar concentration and used linear regression adjusted for various factors. The first results revealed a slight decrease in birth weight, birth length and especially in head circumference, among babies of mothers with higher urinary levels of atrazine mercapturate, a marker of exposure to atrazine. Further results revealed decreases in birth weight and birth length of mothers with higher urinary levels of organophosphorus insecticides (DAP) metabolites and specific chlorpyrifos metabolites.

Conclusions on the use of biomarkers

Positive Points: The results are only preliminary. However, there was a consistency within studies using indirect exposure assessment. More knowledge on the specificity of biomarkers, timing, and the amount of pesticide exposure was acquired. They were able to link biomarkers, questionnaires, and environmental data.

Limitations: There are limitations within and between individual variability. There is no straightforward interpretation of urinary metabolites or sufficient knowledge of metabolism.

European Mother-Child Cohort Studies

Lisbeth E. KNUDSEN
Institute of Public Health, University of Copenhagen, Denmark

Critical Windows of Exposures and Vulnerability

The unborn and newborn child is susceptible to adverse exposures of pollutants. The exposures can be associated with adverse effects on growth and metabolism, on the immune, neurological, and reproductive systems. Induction of DNA damage early in life may increase the risk of development of chronic diseases such as cancer and immunological disorders later in life. In addition, there are gaps in our understanding of the potential links between maternal exposures, in uterus exposures and adverse health effects.

Pros and Cons of Using Mother-Child Cohorts for Biomonitoring

The use of mother-child cohort studies has pros and cons.

Pros: In this kind of study, we can focus on the most sensitive developmental process of the foetus. The studies provide essential data for prenatal epidemiology, taking account of environment, life style, and gene interactions. Due to the fact that the pregnant mothers are under specific surveillance and attention, the studies provide opportunities for establishing cohorts, follow-ups, and nested case-control studies. The results may provide evidence for future prevention of adverse environmental exposure early in life and recommendation for the optimization of health.

Cons: Large sample sizes are required for the case-control (i.e., most cost-efficient way to utilize biological samples from cohort studies). Therefore, the data and samples for biomonitoring may not always be collected or processed in the most optimised manner. Most importantly, there are numerous ethical issues, which need to be addressed, and which are not always foreseen at the time of the informed consent, such as the right of the child who participated.

Collaboration on Existing and New Cohorts

Within Europe, a number of birth cohorts have been established and there are approximately 400,000 mother-child cohorts in European countries. A network and website provides an overview of these cohorts for the ease of collaboration between the birth cohorts is available in Europe at (http://birthcohortnet.net aims to facilitate collaborations. The idea behind www.birthcohorts.net is to encourage collaborative studies focusing on a specific genotoxic exposure or on a specific outcome suspected to arise from gene-environment interactions. The advantages of this approach are the feasibility and low costs associated with it. A prerequisite for this strategy is that the cohorts are well documented and that information about design and data on the existing cohorts is collected in a comparable form and easily accessible

~ 400 000 participants in different European birth cohorts

European mother-child cohort studies – contribution of research to human biomonitoring

Further Collaboration Needed

Collaboration on existing and new cohorts is needed:

To increase statistical power to evaluate new hypotheses, sufficient know-how, and a wide spectrum of exposures, diseases, and genetic backgrounds

To allow for selective sampling for outcomes, exposures and genetic traits using cohort or nested case-control designs could be done so as to maximize efficiency

To replicate results in independent cohorts

To evaluate differences in contextual and environmental factors between populations are obvious and prominent, and these differences are valuable when biological pathways are to be distinguished from social pathways (Kogevinas *et al.,* 2004)

Collaboration may also be an alternative to large new cohorts. For specific purposes, data from multiple cohorts could be successfully pooled together and be linked in the future for biomonitoring studies.

The existing birth cohorts are heterogeneous in design and focus, but for specific purposes data from multiple cohorts could be successfully pooled together

The number of existing and planned mother-child cohorts is increasing

In principle, any group of children followed over time or with a possibility to be followed up, and for whom any kind of information on their mother was collected, could create a mother-child cohort. In addition, intervention studies carried out during pregnancy are potential mother-child cohorts

NewGeneris – An Example of Mother-Child Cohort Research

The NewGeneris (Newborn and Genotoxic Exposure Risk) project http://www.newgeneris.org is developing an application of biomarkers of dietary exposure to genotoxic and immunotoxic chemicals, and of biomarkers of early effects, using mother-child birth cohorts and biobanks in a number of countries (Norway (MoBa), Denmark (DNBC), Spain (IMNA), United Kingdom (UK women & BiB) and new mother-child cohorts in Greece (RHEA) and Denmark (DKB). Approximately 1000 mother-child pairs will donate samples for measurements of biomarkers related to the FFQs etc. and early biological effects such as heterocyclic amines, nitroamines, vitamins, dioxin and dioxin-like activity, hemoglobin adducts, gene expression profiles, proteomics, DNA damage & repair, DNA adducts, micronuclei and genotypes of selected SNPs.

The project will examine the possible role of exposure to toxic chemicals during pregnancy in the risks of cancer and immune disorders during childhood. It will investigate the development of biomarkers of dietary exposure to genotoxic and immunotoxic chemicals, and of biomarkers of early effects, using mother-child birth cohorts.

The biological samples, including placental tissue and maternal and foetal blood at the time of birth, come from already existing biobanks in five different European countries. Three new bio banks will be created. The subjects will come from regions with a wide diversity of environmental conditions and dietary and lifestyle habits.

Perspectives

The perspectives of carrying out biomonitoring within mother-child cohorts includes the possibility of having background exposure levels in an identified comparable group of pregnant mothers at the relevant same age, willing to complete questionnaires and have the possibility of controlling most of the confounding factors.

The gene-environment-life style interaction are obvious and by having set up harmonized and comparable protocols for the data collection and for the data processing research will be able to make share data and pool the data for meagre cohort studies which will increase your power. In such kind of initiatives have already been established however not with biomarkers within the world wild network collecting data from a number of birth cohorts (I4C) and the first study protocol of associations of leukaemia and environmental exposures have already been forwarded for approval.

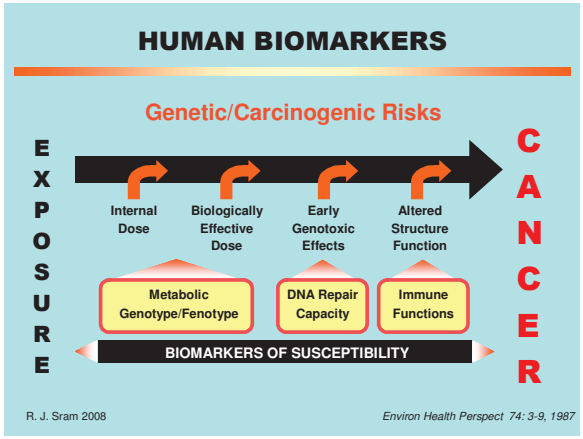
Impact of Air Pollution on Biomarkers of Genetic Damage

Radim SRAM
Institute of Experimental Medicine, Czech Republic

Biomarkers of genetic damage are rarely mentioned but it is essential to include them in future European projects. The hope is that biomonitoring of the genotoxic potential of air pollution will be included in the chosen topics of priority concerning the health effects of toxins on the European population. Such studies are essential for ensuring primary prevention of human cancers and damage of genetic material.

Biomarkers of Genetic Damage

In most European countries, levels of heavy metals such as lead or cadmium have found in increasing levels in the population. The scheme for representing the relationship of biomarkers of carcinogen exposure to biomarkers of effect is well known. It is possible to use the same scheme to demonstrate the genotoxic effects of exposure. It is also essential to investigate biomarkers of susceptibility.

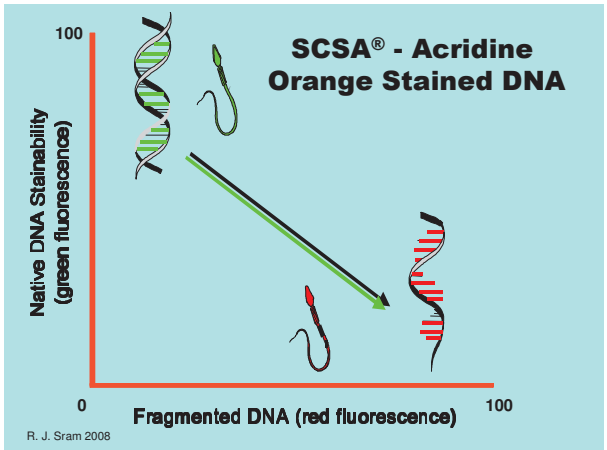


Analyses

In environmental exposure studies, cytogenic analyses have been carried out both by conventional methods and by FISH analyses (whole chromosome painting and fluorescence in situ hybridisation), determining the genomic frequency of translocations. Biomarkers of susceptibility have been investigated, including chromosomal aberrations, genetic polymorphisms, DNA repair genotypes, single cell gel electrophoresis (SCGE), oxidative damage, lipid peroxidation and protein oxidation.
We investigated the reactive oxygen species, and discovered the impact of rare, very small particles (PM2.5) in the air we breathe. Our studies are related to nanotechnologies.

Air Pollution and Human Studies

Data was gathered data on gene expression in children from polluted and unpolluted areas to show the impact of air pollution on gene expression. They observed that air pollution affected DNA adducts in placenta and cord blood as well as birth weight. Data analyses of studies on policemen and bus drivers in Prague demonstrated that environmental exposure to such fine particles (PM2.5) and to carcinogenic Polycyclic Aromatic Hydrocarbons (c-PAHs) increased DNA adducts and the genomic frequency of translocations, suppressed DNA repair in the peripheral lymphocytes, and had particularly adverse effects of sperm and fertility.



Risk Assessment

The level of air pollution must be assessed on the basis of information from data obtained from stationary measuring stations as well as from personal sampling devices. According to molecular epidemiology studies, environmental exposure to pollution concentrations higher than 1 ng B[a] P/m^3 represent a risk of DNA damage.

Analytical Validation of Biomarkers: Laboratory Issues

Holger M. KOCH
Research Institute of Occupational Medicine (BGFA), Germany

In Germany, laboratories that perform quantitative determinations in biological materials are obliged to carry out internal and external quality assurance and includes both ambient and biological monitoring.

Ambient Monitoring: Ambient monitoring is the investigation of pollutants or residues that might enter the human body: chemicals in air, soil, and water.

Biological Monitoring: Biological monitoring, or Biomonitoring, is the surveillance of the pollutants or residues that have actually entered the human body. It depends on different qualities of biomarkers.

There are three types of Biomonitoring:

1. Dose monitoring of biomarkers in pollutants or metabolites in blood, urine, and exhaled air;
2. Biochemical effect monitoring of reaction products in DNA or protein adducts;
3. Biological effects monitoring of more complex gene expressions and cytogenic parameters.

As ambient monitoring is quite far from the disease, it is not possible to calculate risk. Biomonitoring methods are much closer to disease and have more precise impact on risk assessment and management. Biomonitoring involves a wide choice of biometric parameters with varying explanatory power regarding time and duration of exposure. It is possible to deduce a great deal of information.

Analytical Validation of Biomarkers

It is mandatory that the biomarkers be quality assessed and assured before they can be used in exposure assessment, risk assessment, and risk management. The analytical validation of biomarkers requires a wise selection of biomarkers and biological matrix based on recent scientific knowledge. It necessitates toxicological research in animals and humans and the identification and synthesis of target analyses. We need to synthesise internal standards, establish valid analytical methods, and perform human metabolism studies in order to make interpretations. Internal quality control involves the systematic check of the precision and accuracy of the determinations within each laboratory. External quality assessment schemes are essential for checking the accuracy and ensuring the worldwide comparability of the results.

Summary and Outlook

Biomonitoring has proven to be essential tool in exposure assessment, risk assessment, and risk management, and can be used even without ambient data. Quality assurance is an integral part of Biomonitoring. It is necessary to identify and validate new biomarkers through scientific research. They will need to be applied to population-based studies.

Biomarkers of Estrogenic/Androgenic Activity in Connection to Breast Cancer: An experience from Andalucía

Nicolás OLEA SERRRANO
University Hospital, University of Grenada, Spain

Breast Cancer Trends in the Western World

We are all aware of the fact that breast cancer is a problem in the entire Western world and although the overall mortality rate is decreasing in some countries, temporal trends in breast cancer incidence are rising.

Known and Unknown Risk Factors

Only slightly over 40% of breast cancer incidences seem to be related to known risk factors, such as nulliparity, late age at giving first birth, family history, or high income. Speculation on possible causes of the remaining cancer incidences have resulted in tests on high fat diets, alcohol consumption, and human exposure to environmental pollutants. The "estrogen hypothesis of breast cancer" is now widely accepted. Under this hypothesis, the cumulative number of ovulations, as well as the cumulative estrogen dose that reaches the breast over a lifetime, determines risk. Exposure to environmental "endocrine-like" pollutants has therefore been considered a possible cause of breast cancer. Such chemicals include not only polychlorinated persistent organic pollutants (POPs), but also phthalates, parabens, bisphenols, and UV sunscreens.

Studies on Environmental Pollutants

Up to the present time, most studies have concentrated on only a small number of chemicals, such as DDTs and DDEs. There have been very few studies on polychlorinated biphenyls (PCBs) and a total neglect of more polar endocrine disrupting compounds. Studies in a highly polluted region in southern Spain on the "full effect of the combined mediums" demonstrated that no individual chemical present in an extracted sample could be associated with hormonal activity in the samples, but that the combined effect of the chemicals is most likely responsible adverse effects.

Conclusion

Most human studies of pollutant exposure have ignored the combined effects of mixtures. The estrogen hypothesis of breast cancer should be extended to encompass the multitude of weak "estrogenic" agents. The challenge for epidemiology is therefore to take account of a specific exposure scenario relevant to breast cancer: the low-level exposure to large numbers of chemicals.

Use of Biomonitoring Data to Improve Advanced Risk Assessment Models

Frédéric Y. BOIS
INERIS, France

Global Analysis of Individual Biomarkers

A global analysis of individual biomarkers is possible. In that context, correct extrapolations to populations are done via multilevel modelling which is the best way to analyse individual data. Such a method requires mastering models and Bayesian numerical methods for statistical inference. It can be done with existing software. The challenge is to bring together experts in exposure assessment, pharmacokinetics, metabolism, epidemiology and statistics. However, it must be noted that biomarker integration is complex and not everything on the main pathways leads to disease.

Analysis and Modelling

To deal with such complexity, it is important to avoid analysing the various biomarkers independently of each other. If nothing is known of the causal links between variables and data, we can rely on the multivariate analysis and modelling to make inference about the existence of links between variables.
If we know some of the links, as in fundamental biology, we can make structural models to make parametric inference, such as in physiologically based pharmacokinetic (PBPK) modelling. This modelling technique helps in the prediction of absorption, distribution, metabolisation and excretion of a compound. We can gain in statistical power. The problem is that usually we know only part of the links and we need to merge the two types of modelling. This is a topic of active research.

Linking the Models

One solution is to link PBPK, metabolic pathway, and disease progression models. In such a case, the body is described as a set of compartments corresponding to organs or tissues. PKPK models can be treated as general non-linear multivariate models in a Bayesian statistical framework. They can be introduced as a complex link function in conditional independence models. To go from internal dose to effect, additional models can be included and treated in the same way. They can be usefully embedded in a multilevel hierarchical framework to estimate and dissociate variability from uncertainty, and to extrapolate inference from a sample to a larger population.

Perspectives for Biomarker Analysis and Design

The general concepts of these models have been applied to studies of dioxins, nanoparticles, metal fumes, and butadiene. The studies have been mostly in occupational health, but recent developments have also been in clinical and environmental health.

We can conclude that it is possible:

- To integrate prior biological knowledge seamlessly and to fuse exposure models and biomarker data,
- To obtain estimates of internal exposures with measures of uncertainty,
- To use a calibrated model to estimate the optimal biomarkers' sampling times, the number of samples, etc., to reconstruct external exposure.

SESSION 5: SUSTAINABLE ORGANISATION OF HUMAN BIOMONITORING

If countries are willing to implement programmes, they will need to design resources, programmes and funding in a coherent way. This will mean, among others, exchanging and harmonising practices between countries in order to avoid duplication. This session helped to understand in which context the national programmes were planned, the role of regulatory instruments and the underlying national policies as well as the importance of ensuring comparability across Europe.

This session was moderated by Moderato Pierre BIOT from the Federal Public Service Health, Food Chain Safety and Environment in Belgium.

Session Presentations

1. Framework for a European Pilot Study.
2. The current activities of JRC in human biomonitoring.
3. The European Health Examination Survey and Human Biomonitoring.
4. Potential use of human biomonitoring for Reach.
5. Overview on European specimen banking activities: taking the past into the future.
6. Biomonitoring of environmental chemicals in the Canadian Health Measures Survey.
7. Public health impact of biomonitoring studies in the United States.
8. Human biomonitoring in the Slovenian Chemical Act.
9. The 2003 Flemish Parliament Act on preventive health policy.
10. Stockholm Convention and WHO Milk Survey.
11. Requirements for a European Human Biomonitoring programme for priority assessment of environmental chemicals.

Framework for a European Pilot Study

Reinhard JOAS
BiPRO GmPRO GmbH, Germany

The framework for a European Pilot study was presented by Joas Reinhard who led us on a journey up a snow-covered mountain to illustrate how it is possible to arrive at a European Pilot Study. The path is slippery, dangerous, exhausting but in any case we have to be careful and we have to do this exercise together to see that we can arrive at a European approach.

In 2003, there was the European Environment and Health Action Strategy with the following objectives:

- To reduce the disease burden caused by environmental factors,
- To identify and prevent new health threats caused by environmental factors,
- To strengthen EU capacity for policy making in health and the environment.

It presents a NEW VISION on how to address environment and health in an integrated way and puts health in the centre of environment policy. In the framework of Action 3, the European Commission committed to develop, in close cooperation with the Member States, a coherent approach to Human Biomonitoring in Europe. Given the complexity of the approach, it was clear that it needed to be a step-by-step approach.

The first step, 2005

The first step was the ESBIO project, which involved the technical preparation of the EU Pilot Project and the recommendations of an Implementation Group (IG) on Human Biomonitoring in Europe for Human Biomonitoring experts and close contact with national policy makers. The ESBIO (Expert team to Support Biomonitoring) Project www.eu-humanbiomonitoring.org , a consortium of 22 institutes coming from 17 Member States and Croatia, was created. Numerous surveillance and research projects are carried out in Europe and it is necessary to aim for a common line of development between Member States with advanced HBM research and newcomers to the field, and to have as many Member States as possible participating in the Pilot Project.

In addition, there was political support for and EU pilot project including:

June 2007: Communication of the Commission

- First call for proposals under FP7 reserved funding for an EU network on HBM to fund the EU Pilot Project.

- The pilot phase will focus on capacity building and harmonisation of procedures, on the future policy role of HBM, and on appropriate communication at individual and at Community level.

- For the post-pilot phase the Commission is exploring the possibility of embedding future HBM activities in an established framework such as the EU Health Examination Survey

- They will ensure that HBM is linked to the existing regulatory frameworks.

December 2007: Council Conclusions

- Discussed under the Portuguese Presidency of the EU

- The Council invites the Commission : "to ensure adequate funding for the EU pilot project on human biomonitoring (HBM), as endorsed by the Mid Term Review, in order to implement this project as early as possible, fulfilling the commitment established in the European Environment and Health Action Plan 2004-2010, providing therefore data to develop, adapt and evaluate environmental policies."

January 2008: Position of the European Parliament

- Letter of support to Commissioner Potocnik addressed by the Committee on the Environment, Public Health and Food Safety
- European Parliament resolution
- Lagging behind the United States
- Political priority for funding under FP7

September 2008: European Environment and Health Action Plan 2004-2010

"The European Parliament having regard to the importance of human biological monitoring as a tool for assessing the European population's degree of exposure to the effects of pollution and the determination (repeatedly expressed by Parliament in Paragraph 3 of its aforementioned resolution of 23 February 2005 and in the conclusions issued at the end of the 20 December 2007 Council meeting of Environment Ministers) to expedite the introduction of a biological-monitoring programme at EU level,"

"Deeply regrets the fact that the Commission (and in particular its Research DG) has not provided sufficient funding for human biological monitoring in 2008 to enable it (as it had promised Parliament and the Member States) to introduce a consistent approach to biological monitoring within the EU;"

Framework for a European Human Biomonitoring Program Pilot Project

At present, there is no European HBM program, but various activities exist in different countries. There are many surveillance and research projects that are ongoing but they are not coordinated or harmonised. There is an inventory available www.hbm-inventory.org that gives an overview of all the activities but again the message is that there are no European results and no European input for policymaking based on surveillance activities. That is the challenge and the requirements for the pilot project.

We now need to define the framework and make decisions on how such a pilot project should look like. Concentrating on our climb to the top of the mountain, we are entering into the difficult part. We cannot run or hurry through this as we see many wholes in the ice and we need a strong team with a rope to prevent anyone disappearing and getting lost. In addition, we have no formal path and no clear administrative or legal framework that shows us the road to the peak so we have to find it, design it, and elaborate what is possible. There are questions that need to be addressed for such a pilot project including whether we should follow the philosophy of having as many Member States as possible or should we do a first step with only a few Member States. After discussions, it was decided to have as

many members as possible. Then the challenge becomes to find a common line between very advanced MS and newcomers and a system where Member States can learn from each other. Another important aspect is to find consensus about pollutants/biomarkers. This is not an easy task because MS problems are different, political priorities, and technology is different so a consensus is necessary. We need to fine a balance between surveillance and research. Research provides us with answers that are requested, on the other hand, the limitations of research are obvious if we go to a European scale and want to do a European survey. Solutions are required for representativeness and needs of regions as not all Member States have the same regional distribution. We need to find proper ways to integrate stakeholders and to comply with different ethical requirements and to find a balance for different financial resources.

An Approach for a Second Step, 2007

A second step was implemented with the COPHES (Consortium to Perform Human Biomonitoring on a European Scale) proposal. Fifty-five institutions from 24 EU Member States formed the consortium and applied for the EU call of May 2007 for an EU network on Human Biomonitoring to test out a harmonised approach. MS committed themselves to contribute more than 50% of the calculated budget in terms of cash, manpower and existing infrastructures (~ more than 8 Million € from MS).

After discussion, the Implementation Group on HBM in Europe came up with recommendations and proposed two different scenarios to take into account the different level of expertise in Member States (an obligatory and optional scenario).

Scenario 1: Obligatory for all participating MS

- Recommended substances: Lead, Methylmercury, Cadmium and Cotinine

Scenario 2: Optional but at least 5 MS intending to participate

- From MS requested substances: Phthalate, PAHs, tinorganic sub., arsenic, BFR, PFOS

Unfortunately, COPHES was not selected for funding, as the focus was more on fundamental research and topics such as climate change.

Advantages of a coordinated European HBM Pilot Project

Member States and the COPHES team are motivated to continue to push for a HBM Pilot Project. This is necessary in order:

1. To gain practical knowledge of access to study populations, recruitment procedures and response rates

2. To test the developed guidelines, protocols and technical procedures for field work, questionnaires, chemical analyses, data handling and processing

3. To test ethical guidelines and gain experience on ethical rules, within the frame of social and legal aspects of the different Member States

4. To receive practical information on, evaluate and improve overall performance of participating Member State units including the laboratories involved
   (e.g. inter-laboratory comparison)

5. To collect HBM data from different European countries, coordinate with stakeholder activities and move in the direction of European reference values

6. To link HBM values with environment and health data

7. To assess the costs of the applied HBM-programme, preferably including a concept to improve time and cost efficiency

8. To develop practices and guidelines for effective communication and raise awareness for the wider public and policy makers

9. To develop guidelines and seek to establish protocols for the translation of HBM results into policy recommendations.

10. To support new future oriented HBM approaches with a common European basis

The Current Activities of the Joint Research Centre in Human Biomonitoring

Claude GUILLOU
Institute for Health and Consumer Protection (ISTRA), Italy

Overview of the Joint Research Centre

The Joint Research Center (JRC) is a body of the European Commission, located in Italy that works on consumer protection. In September 2005, JRC organised a European Working Group on Human Biomonitoring. In addition, JRC joined the Physical and Chemical Exposure Unit to conduct research on the metabonomics on human biofluids and on cells exposed to chemicals. After the COPHES rejection of the project by the Commission, JRC had discussions with DG Environment to see what could be done to make the project more feasible and it was decided to have an administrative link between DG Environment and the JRC.

Preparation of the EU Human Biomonitoring Pilot Project

JRC is assisting in the preparation of the EU Human Biomonitoring Pilot Project, based on the results of the ESBIO project and on the recommendations of the Implementation Group. In order to carry out the preparation, a number of technical meetings and workshops are planned with the final outcome being to a smooth start of the EU Pilot Project. To assist in this five tasks were identified:

- **Task 1:** The preparation of a harmonised protocol to be used in an EU-wide Human Biomonitoring Pilot Project.
- **Task 2:** Elaboration of source identification for Human Biomonitoring and integration with Environment and Health monitoring.
- **Task 3:** Organisation and follow-up of two technical meetings for each task.

  A first Experts Working Group technical meeting was held in July 2008 to provide an overview of current protocols. The second Experts Working Group meeting was held in Brussels at the end of November 2008. An inventory was made on the state-of-the-art of Biomonitoring. The next step was the drafting of a questionnaire on ongoing and planned activities related to Human Biomonitoring in the European Member States that was sent to 22 Member States.
- **Task 4:** Analytical measurements on biologic fluids (Metabonomics and Metabolomics).
- **Task 5:** Organisation of a final workshop.

The European Health Examination Survey and Human Biomonitoring

Antoni MONTSERRAT MOLINER
European Commission, DG SANCO Health Information Unit

The European Commission Health Directorate is implementing the European Health Examination Survey (EHES). The survey is a coupling of health surveys and Biomonitoring activities. When the Survey was first conceived, it intended to coordinate health policies in Europe with national and regional policies. It needed high-quality support, high-quality indicators, and harmonised methods.

Future legal basis for the developments of Health indicators in the EU Public Health Policy

On 23 October 2007, the European Commission adopted a new Health Strategy, 'Together for Health: A Strategic Approach for the EU 2008-2013'. Building on current work, this Strategy aims to provide, for the first time, an overarching strategic framework spanning core issues in health as well as health in all policies and global health issues. System of European Community Health Indicators with common mechanisms for collection of comparable health data at all levels.

For the period 2008 – 2013, the new Health Program replaces the former Public Health Program. The last phase in the legal architecture should be the adoption of the regulation of the European Council and Parliament creating a framework for data collection on health and safety at work. The Member States decided that the implementation of the surveys is optional.

The Components of the European Health Examination Survey

The European Health Examination Survey is composed of four components:

- The Health Interview Survey (HIS) / Health Examination Survey (HES) database,
- The European Health Interview Survey (HIS) implemented by the Statistical Program:
    - The EHIS annual indicators would cover the prevalence of certain chronic diseases in past twelve months; Body Mass Index (mainly overweight and obesity), hazardous alcohol consumption, physical activity, smoking, consultations of doctors and dentists, medicine use, preventative actions, selected physical and sensory functional limitations, pain and discomfort, SF-12 on mental health
- The mini-European Health Module implemented by the annual EU Statistics on Income and Living Conditions (SILC) under the Community Statistical Program,
    - This is actually used to calculate the Healthy Life Years structural indicator.

- The European Health Examination Survey (HES) implemented by the Health Program and the FP7.

    - HES is a population based survey were the measurements go beyond the questionnaire based data (interview or self-administration), such as blood pressure, blood samples, test of functional capacity etc.

    - HES provides crucial information for health care planning and health promotion that cannot be obtained by other means. There are successful examples of HES in some European countries and in North America.

The Study on the Feasibility of a European Health Examination Survey (FEHES)

To assist in this the Feasibility of a European Health Examination Survey (FEHES) study, led by KTL in Finland http://www.ktl.fi/fehes/ was launched. FEHES defined a roadmap that was adopted by the Member States and includes:

- The FEHES (Feasibility of a European Health Examination Survey) Project, leaded by KTL (Finland), has assessed the feasibility of standardized HESs in European countries and prepared a proposal for their implementation. Project selected in 2006.

- The Work Plan 2008 (February 2008) for the implementation of the Second Health Programme calls for *To implement a pilot European Health Examination Survey in some Member States in order to test the examination modules for this survey defined by the earlier projects, so to contribute to completing the health surveillance and the ECHI indicators in the EU. [Financing mechanism: Call for tender]*

- The International Workshop on Health Examination Surveys (Luxembourg, April 2008) endorses FEHES Recommendations and opens the process for the EHES.

- Call for Tender 2008/S 163-219619 from the European Commission (July 2008): *The development and planning of a pilot European Health Examination Survey in European Union and EFTA Member States in preparation to test examination modules and field procedures for this survey.*

- The Work Plan 2009 (February 2009) for the implementation of the Second Health Programme will call for a *Joint Action for the implementation of the pilot European Health Examination Survey.*

- Creation of the European Union Task Force on Health Examination Surveys in the first semester 2009 as governance body for the process.

- A phase II: Full-scale HES in the 27 Member States, Norway and others is scheduled for 2011-2013 if funding from the FP7 Programme available

Conclusions of the Feasibility of a European Health Examination Survey (FEHES) Project

- In the last 10 years, there have been national HES in 10 countries: Croatia, Czech Republic, Finland, France, Germany, Ireland, Netherlands, Poland, Romania, and the United Kingdom.

- Three counties (Denmark, Luxembourg and Spain) have ongoing surveys.

- Major regional surveys covering several areas (no national HES) in nine countries: Cyprus, Denmark, Iceland, Italy, Lithuania, Norway, Slovakia, Slovenia, and Sweden.

Methodology

- Large questionnaire to collect information on previous and planned health examination surveys (HES) and some key aspects affecting the feasibility of conducting a HES in the European countries.
- Mailed in January 2008 to contact persons in 32 countries
- 32 questionnaires returned by the end of May 2008

Situation in Member States

- **Active plans for a national HES in the adult population in 17 countries (next 5 years)**
  - Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Slovakia, and the United Kingdom

- **4 countries with plans for a specific HES in children and/or the elderly**
  - Finland, Ireland, Luxembourg, and Poland

- **No plans for a national HES in 6 countries**
  - Austria, Estonia, Hungary, Iceland, Latvia, and Macedonia

- Human Biomonitoring (HBM) has been defined in the preparation of the EU Action Plan Environment & Health as "*monitoring activities in human beings, using biomarkers that focus on environmental exposures, diseases and/or disorders and genetic susceptibility, and their potential relationships*".

- ESBIO Project: The ESBIO project aimed to prepare the European Pilot Project to develop a coherent approach to Human Biomonitoring in Europe in close cooperation with the Member States in 2004-2007.

- Several of the ESBIO pilot aims are also relevant for the future EHES as it aims to gain practical knowledge of access to study populations, recruitment procedures and response rates, to test the developed guidelines, protocols and technical procedures for field work, questionnaires, chemical analyses, data handling and processing, to test ethical guidelines and gain experience on ethical rules.

- The study population for the proposed biomonitoring pilot study will be children (aged 6-11years) and their mothers. Scenario 1 (biomarkers: lead, cadmium, methyl-mercury and cotinine) forms the obligatory element and Scenario 2 (a number of organic pollutants) the

optional part of the project. Questionnaires will be used to assess exposure of the individual pollutants, and blood, urine and hair specimens will be collected.

- A questionnaire has been prepared to be used in the EU Human Biomonitoring Pilot Study. It includes questions on children's potential exposure pathways, behaviours and socio-demography.

Future Plans

The joint action will be launched next year to create coordination mechanisms. They will subsequently move towards practice, including the creation of a European Task Force for the European Health Examination Survey. The task force will:

- Correspond to the Member States and the Commission (in the Task Force) to decide on the final modules and protocols of the future full-scale HES in the 27 Member States, Norway and others is scheduled for 2011-2013 if funding from the FP7 Programme is available.

- Be composed by representatives from 27 Member States + Norway + Candidate Countries + European Commission (DG SANCO, ENV and Eurostat) + ECDC + WHO + observers (USA, CDN) + relevant EU projects in the area.

- Make decisions for the full-scale HES to be adopted according to the results of the pilot survey and other additional input (ESBIO or others).

Potential Use of Biomonitoring for REACH

Christiane HEISS
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The new European **REACH** Regulation (**R**egistration, **E**valuation, **A**uthorisation and restriction of **CH**emical substances) is a challenge for the exchange and use of information on chemical risks. This new law entered into force in 2006.

Main Principles of REACH

The Need to Change the Regulatory System in Risk Assessment

The common ground in the risk characterisation of chemicals was the technical guide on risk assessment, last updated in 2003. It started with a hazard assessment based on substance properties with two pillars, exposure assessment and effect assessment. The procedure was dedicated to decision-making. Unfortunately, this approach was very inefficient as the data was inefficient. The industry assumed that "no data" meant "no problem".

REACH: The Response

Ninety per cent of existing chemicals, which were already on the market before 1991, are still without data on risks. We have set up established and highly complex use patterns. Toxic ignorance causes increased public costs. Safe uses and safe products are required by 2020.

REACH: Aims and Principles of Governance

REACH aims to provide a very clear and strict framework for industry decisions. The main principles of REACH are:

- Registration: All industrial produced or imported substances have to be registered at the new Chemicals Agency in Helsinki.
- Evaluation: Authorities will focus their work on uncontrollable risks and substances of very high concern (SVHC),
- The Authorisation procedure, the new element in REACH, gives a strong incentive for substitution and for the use of lower-risk chemicals.
- REACH uses market mechanisms for regulatory aims.
- Capacity building for comprehensive risk competence

There will be a new balance of shared responsibility, which includes:

- Governance by information requirements (no data no market)
- Risk assessment for all stages of life cycle
- Obligation for industry to guarantee safe processing and safe products within value chains
- Obligatory communication and cooperation
- Only 5% of substances are evaluated by authorities
- Targeted regulation for substances of very high concern (SVHC)
- Obligatory precaution through authorisation of SVHCs

Industry will be a major player in risk assessment in the future and governance relies mainly on information requirements. There is a requirement for industry to guarantee safe processing and safe products within value chains.

Improved risk information with REACH

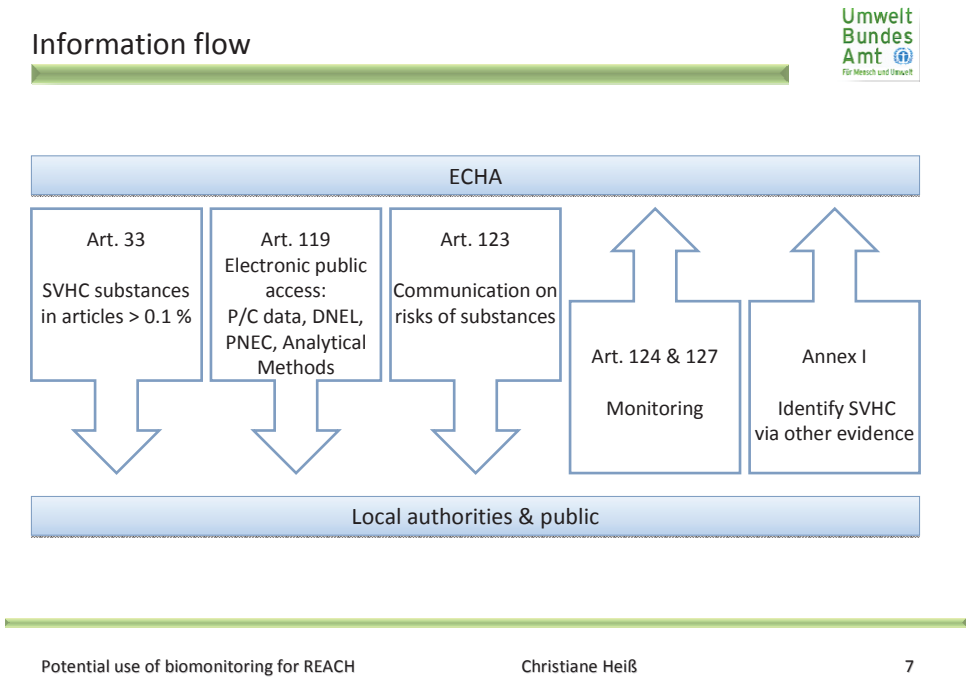
There are three outputs in Reach:

1. Hazardous substance inventory, classification and Labelling. All CMR-substances with harmonized information for authorities and downstream users

2. Recommendations on suitable use conditions, for all professional uses (Safety Data Sheet)

3. Options for risk information, bottom up and top down

Information flow



Exposure Assessment

- Information on chemicals, in particular exposure information, is mostly model-based and submitted by industry.
- There is a great need for quality control. Thresholds for all dangerous substances and impact areas enable risk assessment of measured data.
- Extensive self-responsibility of industry calls for an impact-based monitoring system.
- There is a need for indicators for both humans and the environment.
- Human Biomonitoring data are helpful for success control.

Substances of Very High Concern (SVHC)

To ensure a sufficiently high level of protection for human health and for the environment, SVHCs should, in accordance with the precautionary principle, be subject to careful attention including:

- Identification based on certain substance properties (Art. 57, Annex XIII)
- Priorisation due to wide dispersive use & large production volumes (Art. 58)
- Obligatory Minimisation of emissions by industry (Art. 60, 10)

Preliminary Conclusions

There is a need for human and Biomonitoring data to:

- Identify SVHCs more precisely and review the current criteria of REACH,
- Support decision-making about prioritisation within the authorisation procedure,
- Control the success of precautionary measures over the long term.

The success of the REACH system will depend on the willingness and ability of authorities to cooperate and exchange information.

Overview on European Specimen Banking Activities: Taking the Past into the Future

Andreas GIES
German Federal Environment Agency (UBA)

An environmental specimen bank is an archive of representative environmental and human samples, which are collected at regular intervals. In Europe, specimen banks have existed since the early 1970s and they store biological samples at extremely low temperatures. They were founded for different purposes and under different legislations and proved to be useful tools for retrospective monitoring of chemical pollution levels.

The Purpose of Environmental Specimen Banks

Specimen banking opens the possibility of monitoring retrospectively. Time is on our side if we have archives and we can apply new methods to old samples. The history of a contamination gives us an indication of the sources and makes control strategies more efficient.

History of Environmental Specimen Banks

Sweden

In the early 1960s, scientists in Sweden commenced archiving samples. The Environmental Specimen Bank (ESB) at the Swedish Museum of Natural History, is an integrated part of the National Contaminant Monitoring Program, under the authority of the Swedish Environmental Protection Agency. Samples from terrestrial, freshwater and marine reference sites are collected annually and are prepared and stored in the ESB and ESB has at its disposal samples of tissues and organs from more than 250,000 organisms, mostly from animals but also samples from plants (i.e. moss).

The Nordic Cooperation of Specimen Banks

Generated by the Swedish Environmental Specimen Bank and under the control of the Nordic Council of Ministers, the Nordic countries developed a common approach between their specimen banks. Countries include:

- Norway
- Iceland
- Finland
- Denmark (Greenland)
- Sweden
- Faroe Island

The organisation drew up an inventory of collected species and a manual for specimen collection and storage.

The German Approach

In 1985, the German Environmental Specimen Bank started its systematic work as a control instrument for the new chemicals legislation and was planned as a control instrument for the internal exposure of both environmental and human specimens. Today, there are two pillars: environmental specimens from

representative areas in Germany and human specimens, with samples from students in four German cities to ensure nationwide representation of average contamination levels.

Environmental Specimen Banks in France

Very recently, two Environmental Specimen Banks were set up in France. The first is the *L'Observatoire Pérenne de l'Environnement* focuses on the terrestrial food chain and forest samples, working near an industrial area. The second is the *L'Observatoire de Recherche sur la Qualité de l'Environnement* which archives samples from the Aquitaine region of France.

Conclusion

European cooperation for Environmental Specimen Banks and European cooperation for Biomonitoring specimen banking programs are necessary. REACH requires the independent control of the risk assessments carried out by industry. Environmental Specimen Banks are prepared to carry out this task. Biomonitoring results, rather than chemical risk assessment studies, have often been the driving forces in risk control and risk management.

Biomonitoring of Environmental Chemicals in the Canadian Health Measures Survey

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Biomonitoring Policy Context

Biomonitoring in Canada fits into three essential policy contexts: Regulatory, Public Health, and International and the principle piece of legislation, which governs the actions to manage chemicals in Canada, is the Canadian Environmental Protection Act.

Biomonitoring in the Chemicals Management Plan

In 2006, the Prime Minister launched the Chemicals Management Plan, which radically changed the way Canada manages its environmental chemicals. In the framework of the Information Stream of the Chemicals Management Plan, biomonitoring provides decision-makers with the best possible information and advice so that they can make the appropriate decisions to protect the health of Canadians. The biomonitoring program has three major streams: National Surveys and Studies, Targeted Population Surveys, and Research Support.

The Canadian Health Measures Survey

Overview

The Canadian Health Measures Survey (CHMS) is one of two major projects in the National Surveys and Studies stream of the biomonitoring program. The CHMS is a partner survey between Statistics Canada, Health Canada, and the Public Health Agency of Canada. It is a general health survey of Canadians to provide benchmark data on indicators of environmental exposures, chronic and infectious diseases, fitness, nutritional status, and other risk factor and protective characteristics.

Objectives of the CHMS Biomonitoring Component

The CHMS Biomonitoring Component aims to:

- Establish nationally-representative values for a range of environmental chemicals (a first ever for Canada)
- Provide baseline data to track trends over time and allow the comparison of studies of sub-populations in other studies within Canada and with studies in other countries,
- Provide data to explore relationships between environmental chemicals, physical measures, and self-reported information from the questionnaire.

The survey is intended to provide the best scientific information on exposures of Canadian populations in order to assist risk managers in making decisions. Cycle 1 runs from 2005-2007 and is a cross-sectional survey with 257 eligible collection sites. The collection will be stratified in five regions and will cover approximately 96% of the population with a sample size of 5000 of participants aged 6-79.Participants will be interviewed at home and will complete a questionnaire with information on: health status, nutrition and food, medication use, health behaviours, environmental factors and socio-economic information. A mobile clinic is used to collect physical measures such as anthropometry, cardio respiratory and musculoskeletal fitness, physical activity, oral health exam, blood measures (environmental exposures, nutritional status, diabetes, cardiovascular disease, infectious disease, blood

chemistry, DNA sample), and urine measures (environmental exposures, iodine, microalbumin, and creatinine). Below is a list of environmental chemicals that are being measured. At the end of the clinic visits, respondents receive results of their physical tests, and selected laboratory results.

Environmental Chemicals (CHMS Cycle 1)

Measure	Matrix	Sample Size	Age (years)				
			6-11	12-19	20-39	40-59	60-79
Metals (Pb, Cd, Hg, Mn, As, Cu, Mo, Ni, Se, U, Zn, Sb, V)	Blood & Urine	5200	✓	✓	✓	✓	✓
PCB (24 congeners, Arochlor 1260)	Plasma	1500			✓	✓	✓
Organochlorine pesticides (14)	Plasma	1500			✓	✓	✓
Polybrominated compounds (10 congeners)	Plasma	1500			✓	✓	✓
Perfluorinated compounds (PFOS, PFOA, PFHxS)	Plasma	1500			✓	✓	✓
Cotinine	Urine	5200	✓	✓	✓	✓	✓
Bisphenol A	Urine	2400	✓	✓	✓		
Organophosphate pesticides (6 Dialkyl phosphate metabolites)	Urine	2400	✓	✓	✓		
Phenoxy herbicides (2,4-D and 2,4-dichlorophenol)	Urine	2400	✓	✓	✓		
Pyrethroid pesticides (5 metabolites)	Urine	2400	✓	✓	✓		
Phthalates (11 metabolites)	Urine	3000	✓	✓	✓ *		

* 20-49 age group

Conclusions

The Canadian Health Measures Survey (CHMS) is the first comprehensive national biomonitoring study in Canada. It will provide baseline data to track trends and to allow for comparisons with sub-populations in Canada and with other countries and will be a significant resource for future research and monitoring. In addition, there will be multiple uses and applications of the data and results. CHMS Cycle 2 is in the planning phase.

Stockholm Convention and WHO Milk Survey for Persistent Organic Pollutants

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The World Health Organisation (WHO) established the Global Environment Monitoring System/Food contamination monitoring and assessment program (GEMS/Food) in 1976 in collaboration with UNEP and the Food and Agricultural Organisation (FAO). It has been collecting and assessing data on levels and trends of priority chemicals in food. The information is provided by WHO collaborating centres and WHO Member States and gives high priority to organochlorine pesticides.

Why Human Milk?

Human milk is a food and ideally the only food for infants and is a matrix for biomonitoring maternal exposure and an indicator of environmental contamination. Human samples, which may be used as suitable indicators of human exposure to persistent organic pollutants (POPs), include breast milk, blood, and adipose tissues. However, breast milk is the best matrix for measuring POPs due to its high fat content.

What Are POPs?

POP's are chemicals intentionally or unintentionally introduced into environment. They tend to accumulate in many fat-containing foods including human milk. They include organochlorine pesticides such as DDT, Heptachlor, Dieldrin, Hexachlorobenzene and industrial chemicals such as PCB, industrial waste, such as Dioxin and benzofuran. There are 12 Stockholm convention POPs: Aldrin, Chlordane, DDT, Dieldrin, Endrin, Heptachlor, Mirex, Toxaphene, Hexachlorbenzene, PCB, PCDD and PCDF.

Why Worry About POPs?

We worry about POPs because they have toxic properties and some are of special concern due to a variety of effects. Long-term exposure can affect the immune system, the developing nervous system, the endocrine system, and reproductive functions. They do not degrade into less toxic chemicals but rather accumulate into fatty tissues.

WHO Surveys of POPs in Human Milk

From 1997 to 2007, WHO carried out a series of international exposure studies on dioxins and dioxin-like PCBs in human milk in order to determine the health risk to infants exposed to these chemicals through breast-feeding. The WHO/UNEP Global Survey of Human Milk for POPs was launched in December 2007. Its aims are to provide exposure data that could assist in the evaluation of the effectiveness of the Stockholm Convention and to provide additional information on the public health information of POPs. The Survey involves 27 participating countries in four UN regions. According to the research thus far, the benefits of breast-feeding far outweigh the risks. Breast-feeding should be promoted, protected and supported.

Public Health Impact of Biomonitoring Studies in the United States

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The public health impact of the CDC's (Centers for Disease Control and Prevention) biomonitoring Program in the United States was presented by Larry Needham.

Overview

The Program includes the National Health and Nutrition Examination Survey (NHANES), the Arctic Monitoring Assessment Program (AMAP), the ALSPAC program on endocrine disruptors, the North American Commission on Environmental Cooperation. We also assist the State of California and New York City on their HANES programs, and we participate with the NICHD in the National Children's Study. In addition they participate in 60 to 90 epidemiological investigations per year, are involved in emergency response investigations and anti-terrorism activities. They also conduct studies searching for emerging chemicals and undertake analyses of alternative matrices, such as milk, meconium, and saliva.

The NHANES Study

The National Health and Nutrition Examination Survey (NHANES) is administered by the National Center for Health Statistics of the CDC. The measurements for environmental chemicals are done at the National Center for Environmental Health (HCEH) laboratory. The Survey covers approximately 5000 people per year in 15 sites. The estimates of probability are based on the US population as a whole. Information is collected via mobile vans and includes detailed history, physical and laboratory data. The primary focus is on the generation of clinical data. In public health, NHANES studies have been used successfully for policies removing lead from gasoline and reducing exposures to nicotine and to PFCs, showing corresponding reductions in blood levels in the population. The surveys have also provided baseline data for POPs, PBDEs, BPA, triclosan, and phthalates. Due to NHANES activities, there have also been considerable cost savings.

The National Report on Human Exposure to Environmental Chemicals

The CDC's National Report on Human Exposure to Environmental Chemicals is an ongoing biannual biomonitoring assessment of the US population to selected environmental chemicals. In the future, selected modules will be updated every six months. The matrices monitored are blood and its components and urine. http://www.cdc.gov/exposurereport/

Human Biomonitoring in the Slovenian Chemical Act

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National Chemicals Bureau, Ministry of Health, Slovenia and

Milena Horvat
Institute Jožef Stefan, Slovenia

Legislative Basis for Implementation of Biomonitoring

The basic documents for the national biomonitoring program in Slovenia are the European and National laws on the prohibitions, limitations, marketing and use of certain dangerous chemicals, the National Act on Chemicals, the POPs and PICs conventions, and the National Program on Public Health in correlation with the National Program on Chemical Safety. The National Program on Public Health, of particular interest to biomonitoring, defines its goal as the recognition and mastery of environmental risk factors for health. We have also finalised the preparation the Action Plan on Chemical Safety of Children, which will be submitted, to Parliament. Other legislative acts include the European Environmental and Health Strategy Action Plan, WHO guidelines, and national monitoring projects.

Working Group and Financing

The biomonitoring program in Slovenia is financed by the Institute of Health and the National Chemicals Bureau and is coordinated by the JS Institute in cooperation with external experts from regional institutes.

Short-term Objectives

The main short-term aim of the Program is to provide data on the exposure to chemicals and to the related health impacts to inhabitants throughout Slovenia. To do so, they need to establish reference values and to determine spatial differences in exposure.

Long-term Objectives

In the long term, the Program aims to evaluate exposure and to prepare risk assessments for the health of our citizens. They plan to make proposals, and to implement and monitor the measures.

Description of the National Biomonitoring Program

The selected biomarkers include metals PCBs, dioxins, and PCDDs in blood, urine, hair, and breast milk. The inclusion criteria are very strict, based on questionnaires. The target population is 50 nursing women and their male partners in 3 categories of study areas, urban, rural, and contaminated sites.

Vision of Biomonitoring for the Near Future

Slovenia is in the course of the Human Biomonitoring Program for the years 2008–2012, which will cover all of the Slovenian territory. In 2010, they will begin the environmental part.

The 2003 Flemish Parliament Act on Preventive Health Policy

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History of Environment and Health in Flanders

A series of environmental accidents and adverse situations in the 1980s and 1990s resulted in fear and social anxiety on what could be the related health impacts. People living in the polluted areas lost confidence in the central and local authorities and pressed for a solution. In the aftermath of the dioxin crisis in the food chain in 1998, environmental health issues rose to the national level in Belgium.

To address these issues, the first Flemish Pilot Project on Human Biomonitoring was carried out from 1999 to 2001 in an industrial area, an incinerator area, and a rural area. The results of the project shocked the public and showed that it was necessary to embed environmental health into legislation.

In 2001, a Flemish Parliamentary Investigation Committee on environmental health was set up, involving public and stakeholder hearings, scientific experts, and policy decision-makers. The resulting societal policy document was unanimously accepted in the Flemish Parliament.

The Preventive Health Care Decree of 2003

Environmental health became a part of the Preventive Health Care Decree of 2003 and was thereby integrated into preventive public health policy. The concepts in the Decree include the establishment of an Environment and Health Network and Human Biomonitoring. The Decree provides that the Flemish government can take measures to reduce exposure and to protect public health if the established limit values in human beings are exceeded and if the probability of harmful health effects has been demonstrated. The Decree makes it mandatory for the Flemish government to implement a Human Biomonitoring program.

The Flemish Environment and Health Network

Environment and Health is not only about science it is also essential to have good communication, public participation, and respect for ethics. To ensure that all of this was taken into account a consortium of experts and scientists in various fields, including social scientists was put together. The Flemish Environment and Health Network is composed of three levels: Level 1, local environmental health officers; Level 2, the Ministry of Public Health and the Ministry of the Environment; and Level 3, a scientific support group who carry out the Biomonitoring Program. The Flemish also participate in the National Environmental Health Action Plan, based on the European Environmental Health Action Plan, which involves the entire Belgian territory.

Requirements for a European Human Biomonitoring Program for Priority Assessment of Environmental Chemicals

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Department of Environmental Health, Kuopio, Finland

Human Biomonitoring: Advantages and Limitations

Human Biomonitoring integrates the impacts of all exposure media, all pathways and routes of entry, all geographic locations and microenvironments, all activities and consumer products. Nonetheless, HBM has its limitations. It is not applicable for all chemicals or exposures of interest or importance. It reflects exposures differently for different chemicals. Biological Guideline Values (BGV) are available for only a limited set of compounds. Relationships of Human Biomonitoring to results of exposure and health are poorly understood for most chemicals.

What Could We Expect from a European HBM Program?

Technically

A European HBM Program would provide an immense database from which we could extract body burdens (BB) of environmental chemicals, time trends, socio-demographic distributions (geographical, urban/industrial, rural/traffic, proximity to exposure sources, age, gender, ethnicity, occupation, housing, diet, consumer products, etc.).

Public Policy

A European HBM Program could provide early warnings for emerging risks. It could identify vulnerable groups. It could provide guidance for policy targeting and development. Lastly, it could make assessments for policy effectiveness and accountability.

Availability of Analyses

A European HBM Program would provide maps and graphics digestible for decision-makers and for the public. Using factor analysis techniques, it would produce data so as to attribute exposures to sources, products, locations, activities, and target groups. It could also provide data to model past exposures or other exposures outside of the study.

Risk Management

Remarkable benefits of these data and analyses would be acquired through a triad of chemical risks. First, low concern risk chemicals, which would be kept in the HBM program to ensure that the positive trends continue. Second, chemicals of intermediate concern, which would remain under study. Last, chemicals of high concern, to be investigated and acted upon in priority.

What Would Be the Requirements of a European HBM Program?

We need a representative population sample of approximately 10,000 people per year, a continuous sampling and analysis program, blood and urine samples from each individual, a broad range of analyses, and PBPK or other models to estimate body burdens and doses from the measured HBM data.

Cost versus Benefits

The estimated cost of the Program would be between 10-5 million euros per year. The benefits of a European HBM would far outweigh its costs due to the early identification of public health risks and the effective allocation of resources for the development, implementation, and accountability assessment of chemical risk policies. In Europe, what is important is to consider whether you want a country-by-country HBM Program or a European Biomonitoring Program. That is what makes the difference.

Debate: Implementation, and Implementation now!

There are questions that need to be answered. What are the opportunities? Why do we need to act now? What is the interest in harmonising HBM in Europe? What are the possible threats to harmonisation?

Strengths of Human Biomonitoring

If we observe the main strengths of HBM as it stands today, we recognise that it can detect time trends as well as differences in sub-populations with regard to pollutants. It is a powerful tool to raise awareness among populations and politicians. It is also an excellent way of producing policy-relevant outputs and public health actions and is a means of evaluating existing public health policies.

Weaknesses of Human Biomonitoring

Concerning the weaknesses of HBM, we have heard claims of considerable heterogeneity and a lack of actual references or standard values necessary for taking actions. There is a certain amount of confusion with regard to the ongoing activities in European countries. There is also a lack of adequate capacities and of understanding of the possibilities of HBM. Finally, there is insufficient research, in particular with regard to indicators of effects.

Opportunities of Human Biomonitoring

We have seen numerous opportunities, including the fact that a worldwide development of HBM is underway. Within the European Union, we find that policies and new tools have been developed. We heard about the development of European Union policies through the REACH Regulation, and we have had several examples of the use of HBM on the local level. Other opportunities lie in the development of environmental health strategies and plans through WHO, EU, and NEHAPs. Moreover, HBM can be more cost effective than other tools that we are commonly using. If we try to move towards a Europe-wide harmonisation, we can certainly have cost containment on the European level as well as on the Member State level.

Threats of Human Biomonitoring

The threats facing HBM stem from considerable competition for funding. Other major surveillance tools are being set up now. Another threat and challenge is the fact that biomonitoring is a complex issue and requires inter-sectoral and interdisciplinary action and we need to develop the means for processing feedback resulting from biomonitoring.

Summary of the Programs Presented

Firstly, many programs have been in existence since the 1990s, while others are being set up now. The time is ripe for a Europe-wide harmonisation. Secondly, we see that on the level of target populations that there are major differences, which need to be reviewed. We also see that countries are setting up environmental monitoring alongside HBM to back up the information already obtained. Some of the Member States have also set up biobanks in the context of their biomonitoring programs, archiving the samples and obtaining added value from recruiting samples in the population. Lastly, there has been an increasing inclusion of the biomonitoring activities in the US and Canada where there has been an integration of biomonitoring in the health examination surveys.

Taking a look at the pollutants analysed in the programs we have heard about, we see that exposition to POPs has been a priority in all national programs. Right behind POPs, we see metals and other elements, closely followed by phthalates, cotinine, PFCs, various pesticides, BFRs, and PAHs. All have exposure indicators. In several countries, work is increasingly carried out on effect indicators.

If we try to stand back now and move beyond national programs, into the management of health and environment issues internationally, let us try to find responsibilities for biomonitoring to determine what we can acquire at each of these different levels. Firstly, on the international level, HBM needs to be promoted as a tool for Environment and Health policy-making. Secondly, on the European level, as Matti Jantunen explained so well, responsibility is for harmonisation to make the issue more cost efficient. It should also be a powerful tool to prove the need for implementation of biomonitoring in legislation. The national, regional, and local levels follow quite logically, taking account of the citizen in legislation.

The Stages for an EU Harmonised Approach

Let us try to define the stages we can propose in order to move forward to a harmonised European approach. To succeed, we need Member State and European Union authorities for a decision-making mandate on the environment, health, research, and employment. Support must come from scientists, NGOs, and Industry. The strong basis also lies in legislation.

DEBATE

HARMONISATION AT THE EU LEVEL

Debate: The Use and Added Value of Human Biomonitoring in Environmental Health Policy
How to Create an Effective System at the European and National Levels Producing Comparable Data, Relevant for Policy-Makers:

Pierre BIOT from the Federal Public Service Health, Food Chain Safety and Environment in Belgium moderated this session.

HBM has proven its added value in occupational health as part of a preventive approach, combined with workplace monitoring and hygienic measures. There is general agreement that it is also an important tool in Environmental Health research, surveillance and awareness raising, combined with other - more classical - methods such as environmental/health monitoring and modelling.

As shown by the inventory of HBM programmes in the EU by ESBIO, many programmes are currently running but there is a need for a more coherent approach and for more integration of the different levels of implementation (Local, Regional, National, and European) to increase their usefulness for policy makers.

Within Europe, HBM is used in the environment and health field for scientific research (to study the relationships between certain exposures and the development of disease), surveillance (monitor people's exposure to environmental chemicals over time and space) and awareness raising activities. Different approaches between MS however make results not comparable. Harmonisation (study design, biological and statistical analysis, interpretation of results...) is urgently needed to allow a better use of the data obtained. Examples of experiences presented during the conference show that there is a need now to go beyond a platform for exchanging information and to move towards the implementation or field demonstration of a EU pilot for HBM.

It is acknowledged that differences in environmental exposures and national environmental health concerns, different levels of analytical capacities, differences in political and health priorities, cultural differences, and perhaps also different perceptions of ethics may render a common human biomonitoring survey carried out simultaneously in several European countries a challenge in many respects (political, scientific, organisational and ethical).

HBM national programmes are developing in many countries and over time, they have developed - systematically. From the presentations, one advice is to have a limited number of clear objectives to start with. Care should be given to define objectives that are not overly ambitious so they can be achieved given resource and time constraints.

SWOT analysis for HBM in Europe:

STRENGTHS	WEAKNESSES
• Detection of time trends and exposure differences amongst sub-populations • Strong awareness raising and education tool (politicians and citizens • Examples available of outputs that guided and evaluated Environmental Health policies) • Cost efficiency already demonstrated in specified cases	• Heterogeneity of current actions • Lack of reference and health-based values to take actions • Lack of adequate capacities at national level • Limited understanding of the potential of HBM among stakeholders • Multiple research gaps
OPPORTUNITIES	**THREATS**
• Current development of HBM worldwide • Expected support for EU policies (REACH) • Development of Environment and Health strategies and plans at the level of WHO, EU, and MS* (NEHAPs) • Limitation of resources calls for harmonization and mutualization of tools, avoiding duplication of efforts	• Lack of funding and competition for funding with other surveillance tools • Complexity and need for intersectoral and interdisciplinary work • Separate routes for Health Examination Surveys and HBM at EU or national levels

HBM is not a stand-alone tool and needs to be coupled to other sources of information, thereby increasing its cost efficiency and cost effectiveness. It must be used in targeted situations so that it has a real additional value, sometimes (alone) instead of other tools, sometimes coupled with. Coupling HBM to health interview and/or examination surveys, to house examination survey and/or to environmental biomonitoring and/or to cohort studies could be very beneficial. Difficulties in coupling with other sources of information should nevertheless not be underestimated (the difficulties of data linkage are well known in all Environment and Health Information Systems and are often overcome).

As HBM involves taking samples in humans it raises important ethical and privacy issues so this must be carefully considered.

Good communication and transparency at all stages of the study or programme, not only to study participants, but also to the public and to policymakers, is a key prerequisite in HBM. In the EU, participants have generally the right to know their individual results, but also not to know them if they wish, according to the EU Privacy Directive. On an aggregated basis, results should also be transferred to policy-makers and translated into concrete actions.

Improved communication strategies are not only needed to allow ethically acceptable practices, but also to secure its real relevance/added value. Indeed:

- HBM is known as an important trigger for action at population/policy level but also at personal level: it brings pollution and its effects very close and is real to a person. Knowing what you are being exposed to and how can help make informed decisions to protect health is important to individuals.
- The simple act of measuring in itself already transfers an important message to those involved. The organisation of a programme by a government gives a clear message that the environmental health of the population is of concern to the authorities. The (repeated) measurements are an incentive for prevention at individual level, as shown in occupational health.
- HBM is a strong educational tool as the communication process allows study subjects to learn more about environmental health matters.

Development of some important tools is needed to make use of the full potential of biomarkers such as:

- Kinetic modelling development
- Exposure-dose-response relationship development including identification of the early onset of disease.
- Characterization of biomarkers of exposure and biomarkers of effect
- Optimisation of study design and sample collection

Sustainable organisation of HBM at national and European level needs:

- Legal instruments or national policy or action plans that integrate HBM should be carefully considered
- Capacities, competences and skills, infrastructures (labs, bio banks) should be looked at carefully
- Funding mechanisms providing reasonable future funding for long-lasting programmes, such as those to analyse trends, should be foreseen at a very early stage
- Clear definition of responsibilities and tasks for HBM at national and EU level are needed and are tentatively expressed in the following table.

An Integrated Approach

Level	Responsibilities and tasks
International	• Promote HBM as a tool for environmental health policy making and its use in existing Conventions and Protocols
European	• Develop harmonisation for data comparability and cost efficiency - Guidelines (recruitment, sampling, analysis, communication and ethics) - Reference and HBM values - Pool competences and capacities of MS together when needed (emerging pollutants) • Provide a framework and funding for a HBM integrated with environmental health concerns - Short term: link with European Health Examination Survey - Long term: link with Infrastructure for Spatial Information in the European Community (INSPIRE) to integrate data at global level • Provide a powerful tool for implementation of existing legislation (REACH) with the focus on authorisation • Support and fund research (new biomarkers, kinetic models, internal doses – effects relationships, communication, ethical aspects, public involvement, etc.)
National	• Commit and fund a global integrated approach, using instruments deemed needed at national level including legislative ones. - Define national priorities - Develop programmes in a multidisciplinary team involving Health Environment Research and social specialists • Provide a tool box for effective implementation of HBM or use of biomarkers for investigation at regional and local level
Regional	• Define priorities and develop capacities to - Handle hot spots, socio-economics inequalities and sub-populations - Help decision making at local level - Raise awareness about HBM
Local	• Involve, train and inform stakeholders (health professionals -at school,-at work, teachers, NGO's, local authorities) • Ask for advice and arrange a transparent debriefing

To achieve a long-term vision, more precise key elements are needed including:

- A decision making structure that brings together MS representatives and EU authorities in a HBM Committee. This Committee, which is to be advised by a group of EU Experts, could (1) receive a specific mandate and (2) adopt a transparent decision making strategy with respect to choices of the sample population, biomarkers, representativeness, related policy measures, etc. for the future implementation of HBM, while taking into account information delivered by a group of EU experts and by the pilot study.
- An advisory group of EU experts; this could start from the EU implementation group on human biomonitoring, and provide recommendations to the HBM committee notably regarding some scientific topics, gender issues and ethics.
- A transparent process to define EU LIMIT VALUES; this could build on the process defined for exposure limits for chemicals in the workplace and include a Scientific Committee on Occupational Exposure Limits (SCOEL) that provides scientific advice to the European Commission to underpin regulatory proposals.
- A dedicated BUDGET (see EU Parliament comments). Funding should not be on a competition basis, as this is counter productive for a harmonisation approach and will lead to a decreased fragmentation.
- A coordinating structure in each MS to participate in the debate of the HBM Committee in order to be able to draw conclusions at the EU level and to define the best way for HBM implementation after the pilot project.

CONCLUSIONS AND SUMMARY OF THE CONFERENCE

Session 1

This session illustrated:

- The importance of definitions in particular with regards to different types of guidance values for action and methods used to derive these values (either reference values for a given population or health-based values)
- The importance of the continuous update of the reference values
- The achievements of the German HBM Commission (set up in 1992) in particular with regards to the development of health-based values that could be used by other countries (for lead, mercury, PCP, DEHP in blood, urine and human milk).
- The differences between occupational health and environmental health practices as well as lessons learned from occupational health that could benefit environmental health

Session 2

In this session, the ongoing HBM activities in several European countries were presented. The session illustrated:

- The need to reduce fragmentation of studies (even if they have achieved their specifically assigned goals).
- The fragmentation, the lack of a coherent approach and integration between studies carried out at the local, regional, national levels reduces the opportunity for improved evidence-based regulation using HBM information and cross-border comparisons.
- That surveillance as well as research activities should be linked with policy measures whenever appropriate.
- That work at the European level would be a very useful incentive for harmonisation at the country level in particular for those which have not yet developed a national programme.

Nevertheless all studies have already provided useful information for supporting and/or evaluating policy and for awareness raising campaigns, as illustrated by the following examples:

- collecting information to define reference range values for a selection of environmental contaminants (United Kingdom)
- use of children blood lead levels to assess the health impact of an abandoned lead mining area (Ireland)
- cotinine level in preschool children in relation to environmental and tobacco smoke (ETS) before and after an anti-smoking campaign showed that in the Cypriot context children are exposed to ETS regardless of their parents' smoking habits. Most of the exposure occurs outside the home (Cyprus)
- the French study on exposure to dioxin from incinerators has raised awareness of the population living in the vicinity of an old incinerator with regards to the consumption of local products (France)
- The Spanish study on the Canary Islands demonstrate how policy actions can be followed using HBM studies: the DDT/DDE ratio in general population was found to be quite different among the different islands showing a recent use of DDT in agricultural areas (Spain)

With regards to national programmes, many countries have a long experience such as the Czech Republic (since the 1990s), Sweden (since 1993), and Germany (since the mid 80s). In Belgium, the Flemish programme was launched more recently in 2001. Each of these programmes were able to achieve several goals including:

- generating representative data on exposure to environmental pollution and reference values
- producing trend analysis
- warning of emerging risks
- proposing strategies on prevention and reduction of exposure
- evaluating progress to allow further to policy actions

The innovative Flemish approach of the participation of stakeholders including the public in the selection of hot spots studies has provided food for thought to the participants. It offers a formal framework for such studies that involves stakeholders in a transparent manner. In addition to the work presented in session 1 concerning the achievements of the German HBM commission, the German programme (GerES) appears to be very comprehensive and able to produce very useful information for policy action.

Session 3

Based on several concrete examples the added value and potential limitations of HBM were discussed including:

- The Flemish programme (2001-2006), covering 8 study areas and concerning 3 age groups, which investigated several pollutants and health effects has produced a very complex mixture of results (comparison of study areas values with Flemish calculated reference values). The relevance of biomarkers anomalies for environment and health policies was looked for as well as causes for such anomalies and policy measures to be considered. The very innovative process to derive a phased action plan was debated with the participants. The participatory approach that involves expert and a stakeholders' jury was presented and could be inspiring for other countries even though its complexity should not be underestimated. The Flemish programme shows also the importance of an open communication of HBM results and resulting policy answers to broaden the social basis for a broad environmental health policy and awareness raising.
- The case study on mercury and pesticides exposure in New York City (NYC) has led to several policy actions taken by the City of New York such as: embargoing and seizure of imported products containing inorganic mercury, increase of sampling of fish of NYC wholesales markets as a result of high level of organic mercury for high fish consumers; restriction of the governmental use of pesticides by a local law. This cases study has led to education campaigns targeted to the populations at stake for mercury and pesticides.
- The presentation of the National Children Study in the United States (US) has provided interesting considerations with regards to the cost of human biomonitoring versus the cost of environmental monitoring showing that biomarkers can be used at a reasonable costs compared to environmental measurements to estimate a wide range of chemical exposures. Collection, storage and analysis of HBM and environmental samples (indoor and outdoor, drinking water, house dust, soil and food sampling) were taken into account. It was also considered that taking HBM sampling could fit better

to the on-site visit than environmental monitoring (time for sampling technicians and burden for participants).

- The power of biomonitoring to explore exposure pathways was also demonstrated by three very concrete examples provided by the city of Frankfurt.
- The public health perspective was addressed by the relationship between exposure data analysis and socio-economic factors from several German studies among them GerES IV. Based on these studies, there was some evidence of current environmental injustice across Germany. Such findings impact preventive measures, public health promotion and recommendations for policy including setting up priorities for surveillance and exposure reduction and help to understand social differences in vulnerability and susceptibility characteristics.

CEFIC reminded us that human biomonitoring is a tool used by industry for many years for occupational safety and in occupational medicine.

- Progress made in analytical methods to detect trace amounts of chemicals, decreasing costs of biomonitoring and generation of more exposure data to be used in exposure assessment have created great expectations as well as concerns among all stakeholders in particular the public. There is therefore a crucial need to improve interpretation of human biomonitoring information.
- The chemical industry's research programme, LRI – Long Range Initiative, focuses particularly on issues regarding (1) basic understanding (sound interpretation of data and baselines levels of biomarkers), (2) use of biomarkers and analytical exposure methods for assessing and managing occupational and environmental health risk, (3) understanding mechanisms and the selection of appropriate biomarkers for use in risk assessment, health significance of DNA adducts.

- The two non governmental organisations (NGOs), the Health and Environment Alliance (HEAL, based in Brussels) and the Commonweal Biomonitoring Resource Center from the United States explained why such organisations use human biomonitoring. Their main objectives are to help consumer choices and improve product design, to raise awareness of the population about the use of products that contain toxicants, the current risks in view of changing values, policies and standards, to trigger or speed up policy changes and promote prevention interventions and new tools (biomonitoring).

- Ethics and communication are very critical when conducting human biomonitoring. A didactic video was shown to the participants in order to raise their awareness with regards to the conditions to obtain an authentic informed consent from the volunteered study participants and the importance of good quality information delivered by the researchers or physicians. Communication is crucial both to obtain informed consent but also when results are delivered to the study participants. The social acceptance of HBM practices relies on good information and communication.

Session 4

The contribution of research and how human biomonitoring activities provide information and lead to identify new knowledge gaps were discussed in this session. Several areas of research were covered: from the use and limitations of biomarkers of exposure and effects in population studies to advanced risk assessment modelling techniques. Research needs were highlighted through their challenging and stimulating potential contribution to HBM.

Projects presented in this sessions are examples of current research projects funded by EU Member States or the European Commission's Research Directorate-General, which has been an important funding source for HBM projects for many years through the framework programmes of research. A large number of EU-wide projects including cohort studies are ongoing, focused on the development of exposure and effect biomarkers to a multitude of environmental contaminants.

Preliminary results of the Pelagie cohort study in Brittany, France (a mother-child cohort, 2002-2005) on exposure of pregnant women to pesticides (atrazine banned in 2003 and organophosphorous insecticides) were presented. The aim of this cohort study is to assess the impact of prenatal exposure to pesticides on intrauterine growth. The first results revealed:

- a slight decrease in birth weight, birth length and in head circumferences among babies of mothers with high urinary level of atrazine mercapturate
- a decreasing birth weight and birth lengths with increasing levels of organophosphorus insecticides
- a slight increase in birth weight among babies of mothers having urinary levels of a specific metabolite of chlorpyrifos above detection levels.

Pros and cons of using mother-child cohorts for HBM were highlighted.

- Pros: provide essential data for perinatal epidemiological studies including studies on environment-life-style-gene interactions, potential for follow up and nested case-control study as well as evidence for future prevention of adverse environment exposure early in the life and optimisation of health recommendations.
- Cons: large sample size is required, data and samples are not always available, ethical issues of future use may not be foreseen at the time of informed consent.

Most of the surveillance activities focus on exposure biomarkers. The research projects presented results related to health effects and genetic biomarkers. For this reason, there was a plea for considering biomarkers of genetic damage in European HBM activities in view of ensuring prevention of human cancers and damage of genetic materials. It was reported that air pollution affected DNA adducts in children. In another Czech study, DNA adducts of police officers and bus drivers in Prague were found to be affected by exposure to PM2.5 and to carcinogenic polycyclic aromatic hydrocarbons (PAHs). Often these results did not adequately lead to environmental policy measures.

A wise selection of biomarkers and a complete (analytical) validation of biomarkers are crucial steps for any HBM programme or study. External quality assessment schemes ensure comparability of biomonitoring results (e.g. the German External Quality assessment scheme for biological monitoring in occupational and environmental medicine). So far, 137 SOPs (Standards Operating Procedures) for hazardous substances in biological materials have been published between 1985 and 2008. New biomarkers should be identified and validated for new/emerging chemicals, High Production Volume (HPV) chemicals and for carcinogenic, mutagenic and reproductive toxicants (CMR)

The need for markers for combined effects of mixtures of chemicals was demonstrated by case-control studies in breast cancer in Southern Spain. To address the impact of low-level exposure to a large number of chemicals, a standardised biomarker for human exposure to bio accumulative xenoestrogens was used. No individual chemical present in an extracted sample could be associated with the hormonal activity depicted in the bioassay, suggesting that the combined effect is ultimately responsible for the biological activity of the samples.

A very challenging issue is the use of HBM data to improve advanced risk assessment models. In fact, a complete usage of HBM data regarding public health decisions, regulatory purposes or individual interventions relates to models able to join internal doses or body burden of a chemical or its metabolites (i.e. biomarkers of exposure) with health effects or even better with early indicators of health effects (i.e. biomarkers of effects). To do so, pharmacokinetic models (compartmental or PBPK) have to be developed and made available, but they also have to be put in front of effects data. This is what advanced risk assessment models propose by integrating both aspects and all individual data (i.e. multilevel modelling). All that area of research is a key issue in order to use fully HBM data, and to understand their limitations, variability and sources of uncertainty.

Session 5

If countries are willing to implement programmes, they will need to design resources, programmes and funding in a coherent way. This will mean, among others, exchanging and harmonising practices between countries in order to avoid duplication. This session helped to understand in which context the national programmes were planned, the role of regulatory instruments and the underlying national policies as well as the importance of ensuring comparability across Europe.

The different approaches in EU HBM surveillance and research projects hamper the usefulness of the results for policymaking. Therefore, the European Environment and Health Strategy and Action focused on a more coherent EU approach. The political support from the Environment Council and from the European Parliament further to the mid-term review of the Environment and Health Action Plan was highlighted by the coordinator of ESBIO.

The achievements of the Expert team to Support Biomonitoring in Europe (ESBIO) were described as a first technical step to prepare such harmonised EU approach.

The development of a coherent approach of HBM at EU level is very challenging as not all MS have the same needs, capacities (incl. financial resources) and expertise.

Definition of pollutants of common interest, representativeness of data, ethical considerations, and modalities to involve stakeholders are issues to be solved. With regards to the selection of pollutants, scenarios were defined to facilitate the participation of most of the Member States. Advantages of a coordinated European HBM pilot project were described.

European Commission's Joint Research Centre (JRC)-Institute for Health and Consumer Protection presented its work plan to support the preparation of EU human biomonitoring Pilot Project based on the results of ESBIO and on the recommendations of the HBM Implementation Group. JRC identified five tasks for this work plan, which is developed as part of an administrative arrangement with DG ENV to fill the gaps between ESBIO and the EU HBM pilot and allow a swift implementation of the pilot.

The Environment and Health Action plan involves several Directorates-General (DGs) (Environment, JRC, Research and Health and Consumers [SANCO]).

All actors concerned stressed the need to develop closer links between the preparatory work of the HBM pilot study and the European Health Examination Survey (EHES). DG SANCO presented a road map for EHES and main conclusions of the feasibility study. Several of the HBM pilot project's aims are relevant for the future EHES. The creation of the EU Task Force on Health Examination Survey in the first semester of 2009 as a governance body for the whole process was announced.

The participation of a representative of the HBM pilot project so that activities could be streamlined in a later phase is to be considered.

Legal instruments that could be considered to support a sustainable programmes where also presented in this session.

The WHO presented the rationale of the human breast milk surveys for persistent organic pollutants (POPs) coordinated by WHO in cooperation with United Nations Environment Programme (UNEP) in the context of the Stockholm convention. From 1997 to 2007, WHO carried out a series of international exposure studies on dioxins and PCBs in order to determine the health risk to infants exposed to these chemicals through breast-feeding. The WHO/UNEP Global Survey of human milk for POPs was launched in 2007. The aims of this survey are to provide exposure data that could assist in the evaluation of the effectiveness of the Stockholm Convention and additional information on the public health implications of POPs. Harmonisation of protocols between countries (27) for the national surveys in order to compare results, consideration of limited resources to carry out the surveys, ethical issues for the donors and the credibility and reliability of results are of key importance. The benefits of breastfeeding far outweigh the risks according to WHO surveys.

The HBM public interest campaigns by several NGOs were launched in the context of the adoption of REACH (Registration, Evaluation, Authorisation and Restriction of Chemical substances) directive. The potential use of biomonitoring information for REACH was discussed at the conference and related in particular to the more precise identification of substances of very high concern (SVHC), to the support for decision making about need for action, to the evaluation of effects of precautionary measures on the long term.

Slovenia and Belgium (Flanders) provided information on their own legal instruments.

The Slovenian biomonitoring (for humans and organisms) programme is embedded in the Slovenian Chemical Act in Article 51 and is very much linked to the Stockholm convention and other international agreements and provisions dealing with restricted or prohibited chemicals.

This article lays down clearly aims of the biomonitoring programmes and defines the different responsibilities distinguishing the competent authorities from the scientists carrying out the programme:

> " *For the purpose of preparing and monitoring of measures to limit the risk of chemicals to people and the environment, monitoring of presence of chemicals and their breakdown products in people and organisms (hereinafter: biomonitoring) shall be conducted in professionally justified intervals of time*[1]*. Biomonitoring is coordinated by the competent authority for chemicals and carried out by health and other public institutes authorised by the Minister, for people and organisms together or separately (hereinafter: biomonitoring performers). Biomonitoring performers shall cooperate with the competent authority for chemicals and among themselves on: preparing a short- and long-term*

biomonitoring programme, its intersectoral coordination, monitoring of its implementation, performing expert evaluation and proposals for measures. Conditions regarding the professional and technical competence of public institutes for performing the biomonitoring from the preceding paragraph shall be set out by the Minister. Provisions for biomonitoring from this article do not infringe upon provisions for biological monitoring at the workplace which are governed by regulations on occupational safety and health"

A 5-year programme of environment and human biomonitoring (2008-2012) is planned to cover all the Slovenia systematically. Short-term objectives are to provide data on exposure of the inhabitants to chemicals and related health impact throughout Slovenia, to provide reference (background) values, to identify spatial differences in exposure. The long-term objectives are to make proposals, implement and evaluate appropriate measures.

In Flanders (Belgium), in the last decade environment and health has been put on the political agenda further to a series of environmental health problems and the results of the Flemish HBM pilot project in 2001. As a result, environmental health, HBM, preventive action, the polluter pays principle and the precautionary principles were embedded in the Flemish Decree of preventive health care in 2003. Subsequently, the Flemish government can establish limit values in human beings, can take measures to reduce exposure and to protect public health if the limit values in human beings are exceeded, can establish a network for surveillance of exposure measured in human beings and/or effects of physical and chemical factors on the population with the aim to be able to take measures to protect public health, takes at least measures for development and implementation of a HBM programme. The Decree defines legal modalities for funding. The Flemish government can establish a fund and determine the functioning, the extend and the procedure of financing it, and establish obligatory contribution of the polluters (industry, citizen, car owners..). Until now, different Ministries finance the HBM programme. The decree makes the implementation of HBM mandatory in the Flemish region.

Taking into account their own institutional arrangements, some countries could be inspired by the Slovenian and Flemish experiences.

The public health implications of biomonitoring studies in the US were discussed. US studies are often referred to in the debate regarding the usefulness of HBM, in particular the National Health and Nutrition Examination Survey (NHANES) administered by the National Center of Health Statistics of the Centers for Disease Control (CDC), the environmental measurements being done by the National Center for Environmental Health (NCEH) laboratory of the CDC. Looking at the history of NHANES (1971 to 2004), the environmental chemicals part has developed drastically and in 2004, 250 environmental chemicals were measured (5000 people, 15 sites). NHANES was used among other things for tracking reduction in exposure to nicotine (ETS), changes in exposure to organophosphate pesticides after the Food Quality Protection Act of 1996, and reduction in exposure to PFCs. NHANES has provided baseline data for POPs and PBDEs, triclosan and phthalates.

It was also illustrated that the example and experience of the United Kingdom can be used for emergency response investigations. One example was provided by CDC; i.e., misuse of application of methyl parathion in 1800 homes. In this example, it was shown that the biological testing (methyl parathion metabolite in urine) was critical in directing intervention efforts and in cost savings (estimated to 70 millions dollars) in the decontamination of houses.

During the conference, examples of coupling HBM component to health surveys were given by several countries in particular by Germany and the US.

The Canadian Health Measures Survey (CHMS) and its biomonitoring component was also presented and includes national surveys and studies, targeted population studies and research projects. The Canadian Health Measures Survey (CHMS) and its biomonitoring component were presented, including the organisation set up between Statistics Canada and Heath Canada. Health Canada limited the objectives for the CHMS biomonitoring component (5000 individuals, age 6-79) to the following three:

- establish nationally representative values for a range of environmental chemicals (first ever for Canada)
- provide baseline data to track trends and to allow for comparisons with subpopulations in Canada and other countries
- provide data to explore relationships between environmental chemical, other physical measures and self-reported information

The criteria for the selection of chemicals for the first cycle (2007 -2009) were presented (public health considerations (known or suspected health risks or effects, need for public health action, public concerns); evidence of population exposure; feasibility of filed collection of bio specimens and respondent's burden; availability and efficiency of lab analytical methods; consistency with other surveys; and cost.

A last presentation highlighted the possible requirements for a European Human Biomonitoring programme and introduced the debate. Pros and cons, content, requirements to be successful and cost effectiveness of such a programme were detailed summarising the main messages from the Conference.

- German Environmental Survey (1985…2006) and CDC/NHANES National Reports on Human Exposure to Environmental Chemicals (2000…2008) were presented as examples.
- Linking the European Biomonitoring Programme with the European Health Examination Survey (as proposed by the Feasibility of a European Health Examination Survey (FEHES) was recommended).
- The suggested requirements for a successful programme included full European coverage, continuous sampling and analysis programme, and sufficiently large population sample and chemical palette to allow for statistical analyses of time trends, area, social and cultural exposure distributions, and attribution of exposures to sources/causes.
- Cost effectiveness of such European HBM Programme would be acquired via the public health benefits from better-targeted risk assessment and risk management actions, e.g. focusing on increasing exposure trends, identifying highly exposed population subgroups and sources for the exposures at the high end of the distributions.

CLOSURE OF THE CONFERENCE

by the Ministry of Health, Youth, Sport, and the Voluntary sector (based on the translation of Ms Sophie Delaporte's closing speech, Deputy to the Director General for Health)

There is a need to develop HBM tools that provide a real added value for Public Health and that support operational corrective measures when needed to protect the population from health effects of environmental contaminants. Ethics and communication are essential to guarantee the involvement of all stakeholders and the quality of results in terms of public health. The presentations demonstrate the importance of pursuing and strengthening the development and validation of biomarkers. This leads to a more general need to improve our research capacities in the area of environment and health.

At present, it is essential to create the conditions for a long-lasting support to HBM in making sustainable infrastructures available. In the future, HBM studies should be able to produce relevant results regarding long-term health effects of environmental contaminants as well as trend analysis with regards to the exposure of the population to some environmental contaminants to evaluate the efficiency of implemented corrective measures. Nowadays, MS have put in place national programmes, which are far from identical. Nevertheless, they have to face common challenges and our destinies are united within one single political community, which implies a better coordination in view of producing comparable data. The Europe of human biomonitoring should be a Europe of the coordination and of the harmonisation in view of producing operational tools for the future.

Our will is to make progress in the following areas:

- To improve European harmonisation to increase the significance of our national and local results in particular by the implementation of a EU HBM pilot study
- To consider the setting-up of guidance values that can support public health decision and environmental risk reduction
- To share the burden of tasks between MS with the support of the European Commission taking into account MS specificities and respective priorities as efficiency should be a concern.
- To consider coupling HBM approach with other surveillance systems, environmental surveillance or health surveillance system such as repeated health examination surveys at national and EU level.
- To develop an integrated vision of the different levels of implementation of HBM activities (European, national, regional, local). Such integration would allow more informed decisions.

To develop such a European Biomonitoring programme, there is a need to set up a European technical platform with sufficient resources under the auspices of the European Commission. This platform would first allow mutualising tools and resources and would further be in charge of the exploitation of the results produced.

LIST OF ACRONYMS

BFRs:	Brominated flame-retardants
CDC:	Centers for Disesae Control and Prevention
CEFIC:	European Chemical Industry Council
CHMS:	Canadian Health Measures Survey
CMR:	Carcinogenic, mutagenic and reproductive toxicants
DDT:	Dichlorodiphenyltrichloroethane
DDE:	Dichlorodiphenyldichloroethylene
DEHP:	Di (2-ethylhexyl) phthalate
DG ENV:	Directorates-General Environment
DNA:	Deoxyribonucleic acid
EHES:	European Health Examination Survey
ESBIO:	Expert team to Support BIO Monitoring in Europe
ETS:	Environmental Tobacco Smoke
EU:	European Union
FEHES:	Feasibility of a European Health Examination Survey
GerES:	German Environmental Survey
HBM:	Human Biomonitoring
HEAL:	Health and Environment Alliance
HES:	Health Examination Survey
HPV:	High Production Volume
INSPIRE:	Infrastructure for Spatial Information in the European Community
InVS:	Institut de veille sanitaire
JRC:	Joint Research Centre, European Commission
LRI:	Long Range Initiative
MS:	Member States
NCEH:	National Center for Environmental Health
NCHS:	National Center of Health Statistics
NCS:	National Children's Study
NEHAPs:	National environmental health action plans
NGO:	Non-governmental organisation
NHANES:	National Health and Nutrition Examination Survey
NIH:	National Institute of Health
NYC:	New York City
PAH:	Polycyclic aromatic hydrocarbons
PBDEs:	Polybrominated diphenyl ethers
PBPK:	Physiologically-based pharmacokinetic
PCBs:	Polychlorinated biphenyls
PFCs:	Perfluorocarbons
POPs:	Persistent organic pollutants
REACH:	Registration, Evaluation, Authorisation and Restriction of Chemical substances
SANCO:	Directorates-General Health and Consumers
SOPs:	Standards Operating Procedures
SVHC:	Substances of very high concern
SWOT:	Strengths, Weaknesses, Opportunities, and Threats
UBA:	Umweltbundesamt (German Federal Environment Agency)
UNEP:	United Nations Environment Programme
WHO:	World Health Organisation

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