European Conference on Human Biomonitoring

From the use of human biomarkers to human biomonitoring

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Conference organised under the auspices of the
French Presidency of the EU Council

Highlights and conclusions of the conference

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The Conference Programme and presentations are available:

http://www.invs.sante.fr/agenda/biosurveillance_2008/programme_2008.pdf
http://www.invs.sante.fr/publications/2008/biosurveillance/index.html

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1. Background information for the conference

The European Commission adopted in **2003 an EU Strategy on Environment and Health**[1] , with the overall aim to reduce diseases caused by environmental factors in Europe. This was followed up by the **European Environment and Health Action Plan 2004-2010**[2] which proposes an **Integrated Information System on Environment and Health** as well as a coordinated approach to **Human Biomonitoring** between Member States to render the assessment of the environmental impact on human health more efficient.

The European Environment and Health Strategy paid particular attention to the potential of Human Biomonitoring (HBM). Human Biomonitoring has been defined in the preparation of the European Environment and Health Action Plan as "***monitoring activities in human beings, using biomarkers, which focus on environmental exposures, diseases and/or disorders and genetic susceptibility, and their potential relationships***". The HBM working group's report shows that while significant resources to collect HBM data, comparison between countries and within each country remains difficult as implemented methodologies differ [3, 4, 5, 6 , 7].

Working towards a more coherent approach, the Expert team to Support BIO Monitoring in Europe(*ESBIO*[8]) has already produced guidelines in the different areas of HBM in view of (1) providing mutual support to countries which have planned to develop national HBM programmes and (2) preparing the European pilot which will lead to more concrete applications of this European work.

As indicated in the mid-term review of the action plan[9], "*since 2004 the Commission has collaborated closely with Member States and experts to prepare an EU pilot project on human biomonitoring (HBM) to test out the feasibility of a coherent HBM approach in Europe. The pilot phase is meant to 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 to embed future HBM activities in an established framework such as the EU Health Examination Survey and will ensure that HBM is linked to the existing regulatory frameworks".*

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[1] COM (2003) 338 final

[2] COM (2004) 416 final, volume I , COM (2004) 416 final, volume II

[3] Baseline report on "Biomonitoring of Children" in the framework of the European Environment and Health Strategy (COM(2003)338 final) produced by the Technical Working Group on Integrated Monitoring subgroup Biomonitoring of Children - 09 January 2004 ; http://europa.eu.int/comm/environment/health/pdf/children_biomonitoring.pdf

[4] 4. Options for Action for "Biomonitoring of Children" in the framework of the European Environment and Health Strategy (COM(2003)338 final) produced by the Technical Working Group on Integrated Monitoring subgroup Biomonitoring of Children - 30 March 2004;
http://europa.eu.int/comm/environment/health/pdf/040330biomonitoring.pdf

[5] Biomonitoring was defined in the baseline report of the TWG as monitoring activities, using biomarkers, that focus on environmental exposures, diseases and/or disorders and genetic susceptibility, and their potential relationships. The term "biomarker" comprises biomarkers of exposure, biomarkers of effects and biomarkers of susceptibility.

[6] See pp 38 - 386 of the Baseline report on "Biomonitoring of Children"

[7] Casteleyn L, Tongelen BV, Fatima Reis M, Polcher A, Joas R. "*Human biomonitoring: Towards more integrated approaches in Europe".* Int J Hyg Environ Health. 2007; 210(3-4):199-200

[8] www.eu-humanbiomonitoring.org

[9] COM(2007) 314 final

The Council of the European Union (Environment) held in Brussels on 20 December 2007 "*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"*.

Thus, step by step, the basis for a coordinated approach to biomonitoring in Europe has grown[10,11].

In this context, sharing experience based on demonstrative examples of existing programmes and activities at national or regional level provides an excellent opportunity, in particular to demonstrate the added value of HBM as a policy tool and as a supporting tool to public health interventions.

2. Logic of the conference

In spite of the extensive debate at the EU level, particularly within the Consultative Forum since 2003, it has become clear during the preparation of the conference that there was still a need:

- to share basic definitions in the HBM area among professionals and with the public as the definitions related to HBM are not totally shared yet, they are not yet commonly accepted (this is also due to a translation issues)
- to clarify issues related to the significance of guidance values, reference values, health-based values
- to understand better the governance of HBM programmes at the national level and in the future at the European level (distribution of tasks and responsibilities)
- to develop criteria to prioritize studies when needed
- to benefit further from the work and practices acquired in occupational health
- to discuss further ethical and communication issues in particular with study subjects, representatives of the public, representatives of the study population and the media
- to have a better appraisal of resources needed at the national, regional or local level to be able to implement long term and sustainable biomonitoring programmes (financial and human resources, mobilisation of scientific competences, infrastructures such as labs and bio banks and access to them, coupling HBM with other health surveillance activities such as health examination surveys, knowledge gaps and research needs)
- To identify trends in human biomonitoring research and their application to environmental health studies

[10] Opinion of the European Economic and Social Committee on the EU Environment and Health Action Plan 2004-2010 (NAT/259 – CESE 1636/2004) adopted on 15 December 2004.
[11] Council Conclusions of 20 December 2007

For this reason, the conference was organised along five major headlines:

- Session 1: **Concepts, history and general use;** the aim of this session was to bring all participants to the same level of understanding with regards to HBM basic definitions and concepts, to share these definitions and concepts, in particular with regards to reference values for a given population and to health-based values. The session also acknowledged the expertise within occupational health.
- Session 2: **Human biomonitoring in Environment health policy**; the aim of this session was to give an overview of activities implemented by different countries (Spain, UK, France, Czech Republic, Ireland, Cyprus, Belgium (Flanders), Sweden, and Germany) for which outcomes of programmes and challenges for the future could be discussed
- Session 3: **Added value of human biomonitoring in environmental health**; some may argue the opportunity of investing in HBM activities while other monitoring activities (environmental monitoring or health surveillance, or surveys) exist. Based on several examples the added value and potential limitations of HBM were discussed. An evaluation of cost benefit of HBM versus environmental monitoring was provided as part of the presentation related to the National Children study, which is being launched in the US. Efforts, perspectives and vision of industry (CEFIC) and NGOs (HEAL and the Commonweal Biomonitoring Resource Center) with regard to HBM added value were also reported in this session.
- Session 4: **Contribution of research to human biomonitoring**; the contribution of research and also how human biomonitoring activities provide information and lead to identify new knowledge gaps were discussed. 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.
- 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.

3. Major outputs of the conference

Session 1: Concepts, history and general use

- 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)**
- importance of **continuous update of the reference values**
- sharing **achievements of the** German **HBM Commission** (set up in 1992) in particular with regards to the development of **health-based values**[12] **that could be used by other countries** (for lead, mercury, PCP, DEHP in blood, urine and human milk). **The mandate of the German Commission** is to support the Federal Environment Agency (UBA) in its work by providing expert opinion, to advice local health authorities, to advice physicians in environmental medicine, to comment HBM related topics in environmental medicine. Its main task is to harmonise assessment of exposure and risks, to look at the sound use of chemical analysis, to derive guidance values (reference and HBM values).
- differences between occupational health and environmental health practices as well as lessons learned from occupational health that could benefit environmental health

Session 2: Human biomonitoring in Environmental Health policy

Spain, UK, France, Czech Republic, Ireland, Cyprus, Belgium (Flanders), Sweden and Germany presented the ongoing HBM activities.

From the presentations of the different countries, one striking outcome is 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 **reduce the opportunity for improved evidence-based regulation using HBM information and cross-border comparisons. Surveillance as well as research activities should be linked with policy measures whenever appropriate.**

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.

[12] In Germany, two types of health-based values are derived HBM1 and HBM2. Above the HBM2 value, damage to health is possible and immediate action to reduce exposure should be taken. Between HBM1 and HBM2 values, damage to health cannot be excluded therefore sources should be identify and exposure reduced.
In 2004, the HBM Commission had published 50 position papers, derived reference values for more than 20 substances, but only 4 HBM values due to the lack of human studies and relevant biological effects. Derivation of HBM values based on tolerable intake doses (TDI, ADI, RfD) is under consideration.

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 allowed to raise 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 Canary Island 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)

Regarding national programmes, some countries have a long-lasting 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 was able to achieve several of the following goals:**

- to generate representative data on exposure to environmental pollution and reference values
- to produce trend analysis
- to warn on emerging risks
- to propose strategies on prevention and reduction of exposure
- to evaluate progress made 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 with regards to 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: Added value of human biomonitoring in environmental health

Based on national programmes and case studies, this session has provided very concrete information with regards to both added value and limitations of human biomonitoring data.

- 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 chemicals '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 thanks to three very concrete examples provided by the city of Frankfurt.
- The **public health perspective** was clearly addressed by **the relationship between exposure data analysis and socio-economic factors** from several German studies among which 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 for 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 have 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. Didactic videos were 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: Contribution of research to human biomonitoring (and vice versa)

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.

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 can be summarised as follows: 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 could be summarised as follows: 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 more 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 bioaccumulative 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.

Although research remains essential to improving the quality and interpretation of HBM results (Session 4) , the conference illustrated that efficient policy measures can already be taken (Sessions 2 and 3).

Session 5: Sustainable organisation of human biomonitoring

The different approaches in EU HBM surveillance and research projects hamper the usefulness of the results for policy making. Therefore, the European Environment and Health Strategy and Action focused on a more coherent EU approach. The political support from the Environment Council (20 December 2007) and from the European Parliament (September 2008) 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 know-how.

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 5 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 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 is very much linked to the Stockholm convention and other international agreements and provisions dealing with the 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[13]. 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 principle 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

[13] 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.

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 the HBM programme is financed by different Ministries. 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). The 4th National report on human exposure to environmental chemicals (1999-2004) is due to be released in early 2009. **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.**

As it was mentioned at the beginning of the conference by the United Kingdom, HBM 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 saving money** (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

Health Canada provided an overview of a well planned HBM strategy: 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 3**:

- 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; 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.

4. Concluding remarks based on presentations and debates

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. They **have expanded step by step with time**. From the presentations, one advice is to have a **limited number of clear objectives** to start with. Care should be given to define not too ambitious objectives so they can be achieved given resource and time constraints.

Given the information presented at the conference **a SWOT analysis for HBM in Europe** can be drawn as below:

STRENGTHS	WEAKNESSES
• Detection of time trends • Detection of differences in sub-populations for pollutants • Awareness raising and education (politicians and citizens) • Existing examples of policy-relevant outputs and public health actions • Evaluation of public policies	• Heterogeneity of methodologies and lack of guidance values : lack of reference and health-based values to take actions • Puzzle of on-going activities • Lack of adequate capacities at national level • Still a limited understanding of the potential of HBM among stakeholders • Still many research gaps • Knowledge in many different areas is needed: analytical chemistry, environmental chemistry, biology, ecology, biostatistics, biomathematics, toxicology and medicine, ethics and communication, stakeholders' involvement.
OPPORTUNITIES	**THREATS**
• On-going development of HBM worldwide and in the EU • Interest on the part of Member States • Development of HBM can support EU policies (REACH) and answer to local or national policy questions • Development of EH strategies and plans (WHO, EU, NEHAPs) • Cost efficiency of HBM has already been demonstrated in some cases • Limited resources at EU and national levels may lead to speed up harmonisation and mutualisation of tools, and search to avoid duplicating efforts (e.g. Derivation of health-based values)	• Competition for funding for other surveillance activities • Complexity and need for intersectoral and interdisciplinary work • Separate routes for Health Examination Survey and HBM at EU or national levels

HBM is not a stand alone tool and needs to be coupled to other sources of information, increasing its cost efficiency and cost effectiveness. It must be used in the situations targeted so that it has a real additional value, sometimes (alone) in state 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 (these 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.**

Good communication and transparency at all stages of the study or programme, not only to study participants, but also to the general 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 real to a person. Knowing what you are being exposed to and how can help make informed decisions to protect health.
- The simple act of measurement on itself already transfers an important message to all 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 and that they take their responsibility. **The (repeated) measurements are an incentive for prevention at individual level, as shown in occupational health.**
- HBM is a strong **educational tool** as the whole communication process allows study subjects to learn more on environmental health matters.

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

- Kinetic modelling development
- Exposure-dose-response relationships development including identification of the early onset of disease.
- Characterization of biomarkers of exposure/biomarkers of effects
- Optimisation of study design and sample collection (also refers to the participant's burden)

A review of the chemical compounds investigated by the different programmes presented during the Conference shows that there is already a long tradition in measuring heavy metals and POPs and that new chemicals are increasingly added such as phthalates, cotinine, PFCs, BFRs, and insecticides, bisphenol A, and biomarkers of effects.

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 for long-lasting programmes to analyse trends for example should be foreseen at a very early stage
- **Clear definition of responsibilities and tasks for HBM at national and EU level** as tentatively expressed in the following table.

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[14] were shortly highlighted. They relate to decision-making structures at EU level, scientific support, a transparent determination of EU HBM limit

[14] 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 (see below), 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.

values, and funding. Their implementation should be discussed in the coming months at the Consultative forum.

5. Conclusions 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.

- 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.

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