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ESBIO

Development of a coherent approach to human biomonitoring in Europe

Coordination Action
Priority 8.1

D2.1

Objectives of EU HBM Approach

and of the EU Pilot Project

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[i] See: http://ec.europa.eu/environment/health/index_en.htm

1. Introduction

The overall objective of WP 2 is to define possible objectives of a European-wide human biomonitoring approach and of the EU Pilot Project including proposals for pollutants and appropriate biomarkers and to conceptualize the various elements of the study design.

This entails also the development of guidelines for a harmonised way of participants' recruitment, specimen collection, handling, transport and chemical analyses. Furthermore, the evaluation of data and a protocol for inter-laboratory comparison and efficient collaboration shall be addressed.

WP 2 depends on a large extent on the fruitful in-puts and interactions of all ESBIO WPs, in particular WP 1 ("inventory"), WP 3 ("integration"), WP 4 ("ethics") and WP 6 ("biomarkers").

Since WP 2 forms a central core of the ESBIO work plan, its deliverables will contribute some of the key elements for a European departure towards a coordinated approach on human biomonitoring.

The proposed procedures and guidelines/protocols shall be tested in the common exercise of the EU Pilot Project[ii] at a later stage.

This draft in particular is meant to serve as a contribution for the IG/ESBIO-meeting in Paris, 06-07 September 2006, and is part of objective 2.1 ("to define possible objectives of a European human biomonitoring approach and of the EU Pilot Project") of ESBIO WP 2.

This proposal will built on the results elaborated at the IG/ESBIO-meeting held in Brussels[iii], 27 January 2006 as well as on the objectives as elaborated so far in the 'Second Recommendation from the Implementation Group on Human Biomonitoring'[iv], dated 31 March 2006.

It will further take into account the new developments[v] as resulted from the meeting of the Consultative Forum[vi] in Brussels, 19 April 2006 and the IG/ESBIO-meetings in Berlin, 18-19 May and Paris, 06-07 September 2006.

[ii] See: http://www.eu-humanbiomonitoring.org/sub/epphbm_o.htm
[iii] See: http://www.eu-humanbiomonitoring.org/sub/news_main.htm ('minutes of the Brussels meeting')
[iv] See: http://ec.europa.eu/environment/health/pdf/forum19_04_06/2nd_ig_recommendation.pdf
[v] The Pilot Project has been recommended for the 7th Research Frame Programme 2007-2013.
[vi] See: http://ec.europa.eu/environment/health/19_04_06_consultativegroup_en.htm

2. Objectives of this draft

- Scientific support of ESBIO WP 3, 4, 5 and 8
- Contribution to the IG/ESBIO-meeting scheduled for 06-07 September 2006
- Scientific support of the IG on Human Biomonitoring with regard to the third recommendation
- Provision of possible objectives regarding environmental health-related monitoring activities at the European Union Member State level
- Provision of recommendations regarding the conceptual framework of the intended EU Pilot Project

3. Justification

- Scientific co-operation for the implementation of Action 3 of the European Commission "Environment and Health Action Plan 2004 - 2010"[xii]
- Facilitating the establishment of collaboration networks and the sharing of methodologies as adopted in the general objectives of the ESBIO Project
- Dedication of WP 2 towards Deliverable D2.1 and Milestone 1 of the ESBIO-contract

4. Development of Human Biomonitoring as an integral part of the European Environment and Health Action Plan 2004-2010[vii]

In June 2004 the Commission launched the Environment and Health Action Plan, covering the period of 2004-2010. That was the follow-up of the Commission's European Environment and Health Strategy (referred to as the SCALE initiative[viii]) launched in June 2003.

In the preparation of this «E&H Action Plan 2004-2010[ix]», the European Commission co-operated closely with Member States, Acceding Countries, European Bodies (European Environment Agency, European Food Safety Authority), Networks of Regional and Local Authorities and a broad community of European-wide Stakeholder Organisations like Civil Society, NGO, Research, Industry and the World Health Organisation.

[vii] See: http://ec.europa.eu/environment/health/index_en.htm
[viii] Communication from the Commission on a European Environment and Health Strategy, COM(2003) 338 final
[ix] See: http://ec.europa.eu/environment/health/pdf/com2004416.pdf ("The European Environment & Health Action Plan 2004-2010", COM(2004)416 final)

For this purpose a number of groups had been established: a "Consultative Group on Environment and Health" and three Technical Working Groups (TWG), divided in several sub-groups. In total about 300 experts were involved in this exercise[x].

Four Technical Working Sub-Groups were focussed on integrated monitoring:

- Integrated monitoring of dioxins & PCBs
- Integrated monitoring of heavy metals
- Integrated monitoring of endocrine disruptors
- Biomonitoring of children[xi].

Principally the work of the latter resulted in the formulation of several recommended options[xii], inter alia

- Develop guidelines for a harmonised EU approach for biomonitoring of children, starting from existing experiences and expertise
- Conduct a EU wide pilot study to test and validate common harmonised approaches in biomonitoring
- Collect information to establish European database on biomonitoring activities
- Establish a European Standard on how social, ethical and legal questions need to be taken into account in biomonitoring surveys and studies

The «E&H Action Plan 2004-2010» served also as the Commission's contribution to the Fourth Ministerial Conference[xiii] on Environment and Health, organised by the WHO in Budapest in June 2004.

The theme of the Conference was "The future for our children" and it placed in the spotlight the measures that Member States can take to address the impacts of a contaminated environment on children's health.

During the Conference it was emphasized again that "Another important area is (bio)-monitoring and research activities (…), as they will continue to provide insight to help improve policy

[x] See: http://ec.europa.eu/environment/health/layers_workinggroups_en.htm
[xi] See: http://ec.europa.eu/environment/health/pdf/twg_biomonitoring.pdf (The Group consisted of HBM experts from several Member States and Croatia. This TWG has been expanded to include more Member States and is now called the Implementation Group (IG) on Human Biomonitoring)
[xii] See: http://ec.europa.eu/environment/health/pdf/merging_options.pdf
[xiii] See: http://www.euro.who.int/budapest2004

development at national and international levels. One area of concern is indoor air quality and, in particular, environmental tobacco smoke."[xiv]

The «E&H Action Plan 2004-2010» proposes an integrated approach involving closer co-operation between the health and environment research areas. Its added value shall be the development of a European System, integrating information on the state of the environment, the ecosystem and human health to render the assessment of the environmental impact on human health more efficient.

To this end, the «E&H Action Plan 2004-2010»[ix] outlines three key elements, whereby the first element reads: "*improving the information chain by developing integrated environment and health information*".

In order "*to understand the links between sources of pollution and health effects*", Action 3 of the Plan reads: "*Develop a coherent approach to biomonitoring in Europe"*

5. Objectives of Human Biomonitoring in the Context of the European Environment and Health Action Plan 2004-2010

Concluding the background information provided in Chapter 4., the overall objective of biomonitoring as outlined in Action 3 of the EU «E&H Action Plan 2004-2010»[ix] and based on the initially elaborated recommendations of the TWG "Biomonitoring of Children" can be termed:

Development of a coordinated approach to human biomonitoring (with focus on children).

In order to tackle this task, the European Commission mandated a multidisciplinary working group of Member States representatives named "**I**mplementation **G**roup" (**IG**) which is technically assisted by an **E**xpert Team to **S**upport **BIO**monitoring (**ESBIO**[xv]).

By addressing the various scientific aspects, political and financial support and appropriate communication with all stakeholders and parties involved, ESBIO/IG is ought to prepare a general concept and particular guidelines for all aspects of biomonitoring of children in Europe.

The ultimate goal is to support environmental policy as well as public health policy by better data comparability and accessibility within and between countries and more effective use of resources through shared development of scientific tools and appropriate strategies.

Accordingly, the main objectives of ESBIO/IG are:

[xiv] See: http://www.euro.who.int/document/eehc/ereport.pdf (EUR/04/5046267 /Session 9, page 16)
[xv] See: http://www.eu-humanbiomonitoring.org/ ESBIO -including IG- is funded by the European Commission (Directorate-General Research) under the 6th Framework Programme for Research and Technological Development in close cooperation with Directorate-General Environment, Contract No: 022580 (SSPE)

- Development of a coordinated approach on biomonitoring of children based on existing expertise and experiences gained from surveillance and research programmes in the Member States
- Elaboration how biomonitoring results can be integrated most efficiently with environmental monitoring and registered health data
- Develop strategies to communicate biomonitoring results to stakeholders and the general public including the establishment of websites publicly available and with links to national and international activities resulting in full transparency for all parties thereto
- Elaboration of scenarios for the use of biomonitoring results for policy making

Given the complexity of the issues a STEP-BY-STEP approach has been chosen:

The first step entails the technical preparations of the Pilot Project, which -as the second step- aims to test the developed coordinated approaches and to facilitate the establishment of collaboration networks and sharing of methodologies. The third step will be the performance appraisal at Member State and EU level, as well as an evaluation of quality and results of the Pilot Project. Further steps will be taken subsequently.

6. Potential Objectives of Human Biomonitoring in respect to a European Coordinated Approach

In the following, a compilation of possible objectives for a coherent approach to Human Biomonitoring (HBM) within Europe will be listed. This list represents the common formulation of ESBIO/IG as elaborated preliminary at the Cyprus meeting[xvi], 7 November 2005 and concluded at the meeting in Brussels[xvi], 27 January 2006.

Based on the proposed objectives of the SCALE initiative[viii], those were reviewed and partly adjusted to the scope of the intended EU-wide biomonitoring.

It is noteworthy that the achievement of the individual objectives strongly depends on the conceptual set-up and design of the biomonitoring exercise.

Ultimately, this continuous "work-in-progress" approach by assessing the respective requirements and limitations of the various HBM-study designs should redound to the draft of feasible objectives of the HBM Pilot Project.

[xvi] See: http://www.eu-humanbiomonitoring.org/sub/ighbm_meet.htm (The presentation on the correlation of SCALE objectives relevant for an EU-wide HBM, respectively for the Pilot Project included notes and considerations, which will **not** be addressed within the scope of this deliverable.)

Such applicable objectives will be presented in Chapter 7.

Potential Objectives of EU-wide Biomonitoring:

- To obtain data on the distribution of exposure to a variety of environmental factors among (certain strata/study populations of) the European population
- To obtain data as representative as possible for specific regions with expected different kinds of environmental impacts (urban areas, dense traffic, intensive agriculture, industrial centres)
- To establish HBM reference values on the corporal burden of pollutants that can be utilized to identify people with unusually high exposure, respectively to assess population groups showing elevated exposure levels
- To determine the proportion of the population bearing exposure levels of pollutants (of known toxicity) exceeding those levels associated with (suspected) adverse health effects
- To provide a data base for comparison with other studies (worldwide and in the European Union)
- To assess the effectiveness of public health efforts to reduce the exposures to specific pollutants by monitoring trends over time
- To set priorities for research on adverse effects depending on the magnitude and duration of exposure
- To develop a concept for the integration of HBM with environmental/ambient and health monitoring and for the translation of HBM results into a response system
- To gain insights into the contribution of different compartments (air, water, soil, food) to the integral body-burden and to model the likely exposure pathways
- To improve the coordination activities between research and surveillance projects
- To determine which specific population groups, such as minorities, rural/urban residents, low-income groups and children (of different strata and age groups) bearing elevated risks of exposure
- To design and evaluate precautionary, preventive and interceding actions and control strategies within the framework of policy measures related to health and environment
- To provide a fundament for refined assessments of the relationships between environmental factors (including dietary factors) and health problems
- To establish an "early-warning system" based on biomarker measurements in a representative sample of the population living in different areas that facilitates physicians', scientists' and

health officials' awareness on adverse effects that may result from exposure to environmental factors

7. Proposed Objectives of the EU Biomonitoring Pilot Project

As pointed out previously, the first task of ESBIO/IG can be summarized as the stepwise rectification of development and preparation of comparable protocols and guidelines addressing initiation, design, conduction and follow-up of a harmonized European HBM activity (Step 1).

These elaborated protocols and guidelines shall be applied in the EU Pilot Project (Step 2), which is regarded as a "learning-by-doing tool". It aims to test and evaluate the developed coordinated approaches and to facilitate the establishment of collaboration networks and shared methodologies.

Clearly, the Pilot Project focuses mainly on the organisational, technical, logistical and infrastructural feasibility of a pan-European biomonitoring, in place of immediately utilizable scientific research or survey results, generated from a large-scale experiment.

However, given the unique opportunity of a coordinated HBM-activity of Member States with all sorts of capacities and experience, flexibility of the study design and objectives at national level is regarded an extra-added value.

Therefore, the overall objective of the Pilot Project can be outlined:

To test the hypothesis that HBM can be performed in a coherent and harmonised approach throughout Europe by means of commonly developed protocols, strategies and scientific tools ensuring reliable and comparable data, whilst also leading to a more effective use of resources involved.

Specific objectives of the Pilot Project deduced thereof:

- To gain practical knowledge of access to study populations, recruitment procedures and response rates, particularly in regard to children
- 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, within the frame of social and legal aspects of the different Member States
- To receive practical information on overall performance of participating Member State units including the laboratories involved via an inter-laboratory comparison
- To collect biomonitoring data from different European countries
- To obtain preliminary reference values of selected biomarkers from all participating Member States
- To obtain basic data on the distribution of biomarkers X, Y and Z among the proposed study populations (children and their mothers)
- To assess the costs of the applied HBM-programme, preferably including a concept to improve time and cost efficiency
- To collect basic data for the development of initial scenarios for the translation of biomonitoring results into risk management and environment and health policy

The decisions on fundamental parameters of a HBM study design (such as: population under study, criteria for exclusion, sampling rates and required number of participants, spatial distribution of sampling locations, type and amount of specimen-material required, number and characteristics of biomarkers under investigation, questionnaires, etc) have a major impact onto the depth, quality and degree of utilization of the data generated.

In that regard -and keeping the overall objective of the Pilot Project in mind- this very first attempt of an EU-wide Biomonitoring programme is characterized mainly by the scrutiny of the technical and operational feasibility, aiming at the development of a European framework for surveillance. Such development is however seen as a research effort in itself.

Moreover, experienced Member States are supposed to add further HBM-elements according to their national priorities in policy and research. HBM is embedded in a field that is evolving rapidly and depends scientifically on continuous research activities.

8. Recommended Priorities of the Pilot Project and Justifications

On the basis of the "Second Recommendation from the IG on HBM"[xvii] the study population, a number of biomarkers of exposure and several organizational and conceptual matters of the Pilot Project have been proposed so far.

Study Population: children and their related mothers (one-to-one dependent samples)

Since the Environment and Health Action Plan 2004-2010 threw a focus on children the study population of the Pilot Project should reflect this emphasis.

In that regard, children represent the prime target group and ought to be sampled as representative as possible.

In order to arouse public interest, to gain access to and acceptability for future surveys on children it is recommended to include their respective mothers into the scope of the Pilot Project. Though the proposed biomarkers of Scenario 1 (see below) are of lesser concern regarding a pre-natal mother to child transfer, the facultative pollutants of Scenario 2 (in particular phthalates) bear health relevance for the future offspring.

Communication and Recruitment:

In terms of population acceptance and the favoured sensitisation on children's health, the involvement of media campaigns is recommended to convey the value of HBM surveys. Additionally, the option of reporting personal results to the participants as well as the use of study incentives should be considered in regard to the Pilot Project in order to enhance the benefits for study participants and to raise response and commitment in return.

Biomarkers:

The lengthy review and discussion of currently known biomarkers revealed that only biomarkers of exposure can be recommended for the Pilot Project.

Only biomarkers which are covered by sufficient analytical experience in terms of validated analytical methods of adequate sensitivity, specificity and precision are regarded as suitable. The availability of appropriate reference materials allows for the recommended external quality assurance like round-robin-tests and parallel sample measurements to be carried out by selected reference laboratories.

Therefore, the proposed biomarkers have been divided into two scenarios, whereby Scenario 1 forms the obligatory element and Scenario 2 the facultative part of the Pilot Project.

[xvii] See: http://ec.europa.eu/environment/health/pdf/forum19_04_06/2nd_ig_recommendation.pdf

Scenario 1 biomarkers: Lead, Cadmium, Methyl-Mercury and Cotinine

Scenario 1 contains three heavy metal pollutants and one biomarker of ETS-exposure, all of which are of public health concern due to their largely recognized toxicity and toxicological assessments available (e.g. threshold/HBM-values, PTWI). On top of this, validated analytical methodologies for sufficiently sensitive determination are readily available and assumed to be established in the Member States. Cost efficiency of the chemical analyses has been considered.

Out of the four proposed biomarkers, at least one of those shall find general approval in order to be measured in **all** Member States participating in the EU Pilot Project.

Scenario 2 biomarkers: a number of organic (emerging) pollutants

Scenario 2 does comprise additional biomarkers of exposure which do not fulfil all the criteria defined for Scenario 1. However, Scenario 2 offers the eligible opportunity to include current pollutants of concern into the framework of the Pilot Project at Member State level.

A list of potential compounds, e.g. PAHs, Phthalates, per-fluorinated or poly-brominated chemicals and certain pesticides has been compiled for Scenario 2.

Keeping the objective of comparability in mind, the suggestion that at least 5 Member States should address the same biomarker(s) of Scenario 2 is a scientific recommendation but not an operational condition for the Pilot Project.

Specimen material:

With regard to the type of specimen material, urine is regarded superior in ranking to blood (invasive, more critical to collect, ethical concerns, particularly in respect to smaller children) and to hair (limited to only a few -widely accepted- biomarkers; here Methyl-Mercury).

Questionnaires:

Questionnaires are an essential tool for exposure assessments of the individual pollutants addressed. Tailor-made questionnaires will therefore comprise all sources and pathways identified up to the present and of potential relevance for the population under study.

The questions placed and associated categorized answers shall be easy to comprehend without sacrificing the required accuracy of information. The master-questionnaires elaborated in English will be subjected to one-to-one translations in languages of participating Member States, ensuring a unified content and appearance. By providing sufficient explanatory information on the meanings of questions and answers, the involvement of guiding interviewers (and therefore additional resources) might render unnecessary. A small-scale validation of the translated versions prior to the Pilot Project is recommended.

Field work:

In terms of population sampling strategy, recruitment, specimen/data collection and handling, etc., national study management units at Member State level are recommended. These national units shall be responsible for the implementation of guidelines and protocols delivered for the harmonized conduction of the Pilot Project.

Due to the differences in registration, governance, culture and ethics, a rigid scheme of mandatory operational procedures (*protocols*) to fit for all Member States does not seem purposive. Instead, the individual Member States should be allowed some flexibility to adopt certain study elements (following *guidelines*) according to the country's realities, in order to use existing resources but to ensure the quality of adequate procedures and validity of data alike. Deviations from the described guidelines need to be intelligibly disclosed and explained in a verbatim study management report.

These national units shall supervise and coordinate the various HBM activities within the Member States, as well as establish and maintain close communication to all stakeholders and to the central EU study management unit, respectively.

Principal organisational requirement:

Addressing the Member State level, it is regarded as essential to build up a network of legal, registration/administration, research and health authorities, including partly private enterprises and the media if applicable. Such networks will proof vital for the proper conduction of further and large-scale EU-Biomonitoring surveys.

In particular for the planning and set-up of HBM surveys, an established co-operation among health and environment authorities, registration/population database offices, national ethics councils and involved political/governmental institutions will greatly facilitate the effective management of surveys.

In that regard, the mutual exchange of concerned staff and the conduction of national training and management workshops is recommended.

Member States lacking established resources in HBM could also be assisted by qualified consultants/supervisors experienced in the various aspects of surveys, in order to implement the guidelines and to apply the protocols.