International Journal of Hygiene and Environmental Health 215 (2012) 172–175

Contents lists available at SciVerse ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.de/ijheh

Short communication

Harmonised human biomonitoring in Europe: Activities towards an EU HBM framework

Reinhard Joas[a,*], Ludwine Casteleyn[b], Pierre Biot[c], Marike Kolossa-Gehring[d], Argelia Castano[e], Juergen Angerer[f], Greet Schoeters[g], Ovnair Sepai[h], Lisbeth E. Knudsen[i], Anke Joas[a], Milena Horvat[j], Louis Bloemen[k]

[a] *BiPRO GmbH, Research Institute for Integrated Solutions, Grauertstr. 12, 81545 Munich, Germany*
[b] *Katholieke Universiteit Leuven, Center for Human Genetics, Herestraat 49, 3000 Leuven, Belgium*
[c] *FPS Health, Food Chain Safety and Environment, Place Victor Horta, 40 bte 10, 1060 Brussels, Belgium*
[d] *Federal Environment Agency, Department II 1.2 – Corrensplatz 1, 14195 Berlin, Germany*
[e] *Environmental Toxicology, Instituto de Salud Carlos III, 28220 Majadahonda, Spain*
[f] *Institute Prevention and Occupational Medicine (IPA), Ruhr University Bochum, Bürkle-de-la-Camp-Platz 1, 44789 Bochum, Germany*
[g] *Flemish Institute for Technological Research (VITO), Boeretang 200, 2400 Mol, Belgium*
[h] *Health Protection Agency, Centre for Radiation, Chemical and Environmental Hazards (CRCE), OX11 0RQ Chilton, London, United Kingdom*
[i] *University of Copenhagen, Department of Public Health, Oester Farimagsgade 5, DK1353 Copenhagen, Denmark*
[j] *Jožef Stefan Institute, Jamova cesta 39, 1000 Ljubljana, Slovenia*
[k] *Environmental Health Sciences International, Lyceumstraat 2, 4561 HV Hulst, The Netherlands*

ARTICLE INFO

Article history:
Received 19 May 2011
Received in revised form 11 June 2011
Accepted 12 August 2011

Keywords:
Monitoring
Biomarker
Environment and health
Policy tool
Protocol
Pollutants

ABSTRACT

Human biomonitoring (HBM) can be an effective tool to assess human exposure to environmental pollutants and potential health effects and is increasingly seen as an essential element in a strategy when integrating health and environment. HBM can be used (i) to prioritise actions and measures for policy making; (ii) to evaluate policy actions aimed at reducing exposure to potentially hazardous environmental stressors; and (iii) to promote more comprehensive health impact assessments of policy options.

In support of the European Environment and Health Action Plan 2004–2010, European scientists, experts from authorities and other stakeholders joined forces to work towards developing a functional framework and standards for a coherent HBM in Europe.

Within the *European coordination action on human biomonitoring*, 35 partners from 27 European countries in the COPHES consortium aggregated their experiences and expertise and developed harmonized approaches and recommendations for better comparability of HBM data in Europe via the elaboration of a harmonized study protocol. This protocol is the product of discussion and compromises on the selection of environmental exposures, national environmental health concerns, and political and health priorities. The harmonised approach includes sampling recruitment, and analytical procedures, communication strategies and biobanking initiatives. The protocols and the harmonised approach are a means to increase acceptance and policy support and to in the future to enable determination of time trends.

The common pilot study protocol will shortly be tested, adapted and assessed in the framework of the DEMOCOPHES in 17 European countries, including 16 EU Member States.

COPHES and DEMOCOPHES constitute important steps towards establishing human biomonitoring as a tool for EU environmental and health policy and to improve quantification of exposure of the general European population to existing and emerging pollutants.

Introduction

Monitoring activities using biomarkers in human body fluids and tissues that focus on environmental or occupational exposures, diseases and/or disorders and genetic susceptibility, and their potential relationships are called human biomonitoring (HBM). HBM has been used for more than 100 years in occupational health as part of a preventive strategy in the medical surveillance of workers, but more recently has increasingly been recognised as an appropriate means for detection of risks or control of trends in other fields such as public health, environmental health research, public health surveillance and awareness raising, as reported by Casteleyn et al. (2009).

In the field of environment and health policy, HBM can be used as a valuable instrument to verify whether bans on substances or restrictions on their use actually lead to a decrease in exposure in

* Corresponding author. Tel.: +49 89 18979050; fax: +49 89 18979052.
E-mail address: reinhard.joas@bipro.de (R. Joas).

1438-4639/$ – see front matter © 2011 Published by Elsevier GmbH.
doi:10.1016/j.ijheh.2011.08.010

terms of human internal dose. Similarly HBM can be used as an alert system for policy needs when biomarker data reveal elevated body burden and internal exposure. HBM data integrate intake from different exposure routes and take into account toxicokinetics and individual differences in metabolism and life style which may influence the body burden. Via long-term analysis of general contamination trends, this allows also determining whether substances are e.g. persistent or accumulative as highlighted during the international conference on HBM in Berlin 2010 by the German Minister of Environment (see BMU, 2010).

Due to these possibilities, HBM has successfully been used as a tool in policy development at a national level, in particular with regard to control of persistent organic pollutants, or heavy metals. Success stories comprise for example. The dramatic reduction in blood lead levels seen after the ban of lead in petrol, or the reduction of urinary polycyclic aromatic hydrocarbon (PAH) metabolites in the children of the former GDR after the German unification due to a reduction in exposure to environmental pollutants, or the ban of commercial penta- and octa-BDE products following increasing levels of polybrominated flame retardants in blood due to their use in consumer products, or consumer information campaigns related to fish consumption resulting from elevated human dioxin and PCB levels.

Therefore, HBM in some countries or regions in Europe – similar to the United States – has obtained legal standing permitting repeated cycles of measurement and data storage in biobanks.

Exemplary countries and regions which have developed national or regional HBM programmes are Germany (Environmental Specimen Bank for Human Tissues as part of the German Environmental Specimen Bank since 1974, GerES I–IV, 1985–2006), the US (NHANES/CDC, 1971–2008), the Czech Republic, Slovenia, Sweden, Flanders (HBM since 2002 with first regional survey 2006). More recent initiatives have been started in Austria, France (ENNS) as described by Fréry (2010), Italy (PROBE) reported by Alimonti et al., 2010, Spain. Well known global approaches are the WHO survey on dioxins and PCB levels in human milk (see Arendt, 2008) or the envisaged UNEP activity related to mercury.

In total considerable resources are being spent on HBM in scientific research, surveillance and awareness raising activities, but results can generally not be compared easily, due to the fragmentation of results and lack of a coherent approach between countries and studies. To allow evaluations at European scale and a better use of the data obtained, harmonisation and coordination is needed.

Such a coordinated European approach was initiated by Action 3 of the European Environment and Health Action Plan (EHAP) 2004–2010, related to "*the development of a coherent approach to HBM in Europe in close cooperation with the Member States*" (Commission of the European Communities, 2003), which stipulated the need for a pilot study as a first step.

Development and objectives

The development of *a coherent approach to HBM in Europe* was started in 2007 by the ESBIO (Expert team to Support Biomonitoring in Europe) consortium (ESBIO, 2009), providing scientific support to the work of an Implementation Group (IG) consisting of governmental representatives in the national environment and/or health and/or research ministries

In December 2009 the pilot phase started with the COnsortium to Perform Human Biomonitoring on a European Scale (COPHES) funded under 7th Framework Programme, a joint scientific effort of 24 EU Member States, Croatia, Norway and Switzerland. COPHES's major objective is the development and evaluation of a functional framework for a coherent approach towards HBM in Europe.

COPHES aims in particular at:

- developing strategies to harmonise recruitment, sampling, quality control, and data analysis, as well as a strategy for interpretation and use of the data for support to the environmental health policies to improve comparability of HBM data in Europe in a harmonized *European pilot study protocol*.
- elaborating a rationale and strategy for communication and dissemination of information, results and key messages to all stakeholders.
- establishing common ethical standards and a programme for training and capacity building.
- developing a concept for sustainable organisation and structure of an EU HBM network with links to the existing regulatory frameworks and coordinated support to policy needs.
- setting links with research projects dealing with development, validation and use of novel biomarkers including non-invasive markers and effect markers and with similar initiatives in the field of health, in particular with the future European Health Examination Survey (EHES).

The pilot study protocol will be tested from September 2011 in 16 European Union Member States, and Switzerland in the Financial Instrument for the Environment (Life+) supported pilot study "DEMOnstration of a study to Coordinate and Perform Human biomonitoring on a European Scale (DEMOCOPHES). DEMOCOPHES, which can be considered as a twin project to COPHES in the development of *a coherent approach to HBM in Europe*, will feed into the COPHES evaluation with its practical results.

DEMOCOPHES participants are responsible for the national surveys, whereas COPHES continues to provide scientific support. DEMOCOPHES will assess in particular the applicability of the common protocol developed by COPHES, will collect samples and data and will use them to support and evaluate policy, detailing notably the difficulties they encountered in applying common guidelines and procedures at national level.

Major achievements and remaining challenges

The major provisions of the standardised European pilot study protocol

The harmonised pilot study protocol contains detailed provisions and procedures for selection of study participants, recruitment and fieldwork; biological sample handling in terms of collection, transport, and analysis; data management and evaluation and data interpretation.

The target population are children aged 6–11 years, and their mothers in childbearing age (aged up to 45 years). The sample size requested is 120 mother–child pairs (i.e. 240 samples) balanced by living surrounding, age and gender as a general rule. Information collection comprises biological samples and a detailed questionnaire. The protocol contains SOPs and harmonised procedures for urinary cadmium, urinary cotinine, and urinary levels of phthalate metabolites as well as total mercury in hair that will be analysed as standard set of biomarkers in all participating countries. In addition harmonised procedures are offered for Bisphenol A (BPA) on an optional basis. Storage of biological material for 10 years is foreseen and allows for the inclusion of additional substances of interest at a later stage.

The protocol establishes precise internal and external quality assurance schemes for data analysis and management. These are particularly detailed for biological sample analysis, for which a central Quality Assessment Unit (QAU), External Quality Assessment Schemes (EQUAS) and Inter-laboratory Comparison Investigations

(ICIs) are established to assure accuracy and comparability of analytical results.

For communication purposes the protocol contains provisions and recommendations for strategic approaches and practical information material in terms of information leaflets, fact sheets, invitation letters, etc.

Ethics and data protection guidelines aim at an optimal protection of the rights and dignity of all study subjects, in line with the Oviedo Convention (Council of Europe, 1997) and its Additional Protocol concerning biomedical research and with the European Union Data Protection Directive 95/46/EC (Commission of the European Communities, 1995). Practical recommendations on how to submit for approval to the ethics committee and to notify to the data protection authority are added to facilitate the formal procedures.

Training recommendations include information on general approaches and training material for participating countries, decision making structures and conversion/translation into national protocols.

The implementation of the pilot study on national level is under the responsibility of a *National Management Units* (NMU). NMU are preferentially embedded in the already existing system, such as environment or health authorities and public health research centres, respectively.

Challenges

For a proper interpretation and use of HBM data for policy making initiatives, there is a need to integrate HBM information with information from environmental monitoring and health surveillance and modelling work for external and internal exposure. The challenges for HBM as a policy tool and its potential for public health actions was further discussed and highlighted in 2010 at various occasions such as the Fifth Ministerial Conference on Environment and Health "Protecting children's health in a changing environment" resulting in the Parma Declaration on Environment and Health (WHO Europe, 2010), the International Conference on Human Biomonitoring – Political benefits – scientific challenges, organized by the German Ministry of Environment (BMU) and the Federal Environment Agency (UBA) in Berlin (BMU, 2010), and the European Conference "From human biomonitoring to policy: a sustainable 'marriage' between health and environment" organised by the Environment, Nature Energy Department of the Flemish government under the Belgian Presidency of the European Union in October 2010 as compiled by Van Campenhout (2010).

Conclusions on status achieved and outlook to future developments

Incorporation of HBM as a scientific and policy tool at a European level requires the availability of European-wide structures for gathering, storing and analyzing biomarker, data from environment and health monitoring and a consistent interpretation framework.

COPHES – bringing together most European Member States – and DEMOCOPHES – testing a harmonized approach in 17 European countries – take a first and important concrete step in a process towards harmonisation of HBM in Europe, and towards a fully operational, sustainable and scientifically sound EU HBM programme, that can be exploited at the same level as for example its counterparts in the United States, the National Health and Nutrition Examination Survey (NHANES), or as the German Environmental Survey (GerES), and can run in parallel with a European harmonisation approach for Health Examination Surveys (EHES).

COPHES/DEMOCOPHES will provide first comparable European level data on distributions of chemicals in humans by areas (countries, urban/rural), and socio-demographic background (age, gender, socioeconomic status, ethnicity).

It is hoped that the process continues and is expanded to more substances and includes all countries so to allow generating better exposure maps and graphics for the interests of the public and of decision makers. After some years time trends could be analysed. Such results could lead to new and better targeted risk assessments and risk management actions. Key elements for future and long-term success include appropriate decision-making structures at European level, a transparent determination of EU HBM reference and health based values, long-term funding schemes, legal instruments or policies that allow to integrate capacities, competences, skills, and infrastructures (laboratories, biobanks), as well as a clear definition of the responsibilities and tasks at national and European level as stressed by Casteleyn et al. (2009).

A second EU Environment and Health Action Plan (EHAP) covering the time period from 2011 to 2015, as strongly promoted under the Belgian Presidency would be an additional political driver. Envisaged policy options for integration of EU HBM could be the Community Strategy concerning Mercury and its review (Commission of the European Communities, 2005 and Council Conclusions, 2011) or the European Health Examination Survey (EHES). Sustainable operational funding mechanisms could be LIFE+ the EU's financial instrument supporting environmental and nature conservation projects (Commission of the European Communities, 2007a,b) or the European Environment Agency (EEA).

Acknowledgements

We wish to thank the European Commission, DG for Research and Innovation (RTD), who is funding COPHES in the 7th Framework Programme and DG Environment, who is co-funding DEMOCOPHES under the LIFE+ Programme. We also would like to thank all project partners and all Ministries and Institutions, and other research projects in the European Member States, other European countries and countries worldwide that supported the project with information and experience. Updated information on the projects and progress made can be derived from the project website http://www.eu-hbm.info/.

References

Alimonti et al, 2010. Italian biomonitoring survey for metals in adults and children. Human Biomonitoring Nutzen für die Politik – Herausforderung für die Wissenschaft. Political Benefits – Scientific Challenges, 26–28 September 2010, Berlin, Book of Abstracts, 108 p.

Arendt, M., 2008. Communicating human biomonitoring results to ensure policy coherence with public health recommendations: analysing breastmilk whilst protecting, promoting and supporting breastfeeding. Environmental Health 7 (Suppl. 1 (June)).

Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit und Umweltbundesamt (BMU), 2010. Human Biomonitoring Nutzen für die Politik – Herausforderung für die Wissenschaft. Political Benefits – Scientific Challenges, 26–28 September 2010. Ludwig Erhard Haus, Berlin. http://www.fbuberlin.de/HBM_conference_Berlin_2010/assets/files/HBM-Conference-Berlin-2010_transcript_en.pdf.

Casteleyn, L., Biot, P., Viso, A.C., 2009. From human biomarkers to human biomonitoring in environmental health in Europe. Highlights of the Conference held in Paris on November 4–5, 2008. Bulletin épidémiologique hebdomadaire, 16 June 2009. Special edition. http://www.invs.sante.fr/publications/2008/biosurveillance/conference_report.pdf; http://www.invs.sante.fr/publications/2008/biosurveillance/annex_conference_report.pdf.

Council of Europe, 1997. Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine. Convention on Human Rights and Biomedicine.

Commission of the European Communities, 1995. Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. Official Journal L 281, 0031–0050. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31995L0046:en:HTML.

Commission of the European Communities, 2003. A European Environment and Health Strategy, Communication from the Commission to the Council, the Euro-

pean Parliament and the European Economic and Social Committee Brussels, 11.6.2003, COM (2003) 338 final.
Commission of the European Communities, 2007. Regulation (EC) No 614/2007 of the European Parliament and of the Council of 23 May 2007 concerning the Financial Instrument for the Environment (LIFE+) – Commission Statement OJ L 149, 2007. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32007R0614:EN:NOT.
Commission of the European Communities, 2005. Communication from the Commission of 28 January 2005. Community Strategy concerning Mercury. COM, 2005, 20 Final – Official Journal C 52 of 2 March 2005.
Council conclusions, 2011. Review of the Community Strategy Concerning Mercury, 14 March 2011. http://ec.europa.eu/environment/chemicals/mercury/.
Commission of the European Communities, 2007. Mid Term Review of the European Environment and Health Action Plan 2004–2010. Communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee, Brussels, 11.6.2007, COM (2007) 314 final.
ESBIO, 2009. Development of a coherent approach to human biomonitoring in Europe. Coordination Action, Final Activity Report. http://ec.europa.eu/research/endocrine/pdf/esbio_en.pdf 2; www.eu-humanbiomonitoring.org.
Fréry, N., 2010. News and perspectives of the French HBM programmes. Human Biomonitoring Nutzen für die Politik – Herausforderung für die Wissenschaft. Political Benefits – Scientific Challenges, September 2010, Berlin, Book of Abstracts, 20 p.
Van Campenhout, K., 2010. From human biomonitoring to policy: a sustainable 'marriage' between health and environment. Book of Abstracts, 27–28 October 2010. http://www.lne.be/en/2010-eu-presidency/events/human-biomonitoring-conference/abstracts_posters/book-of-abstracts.
WHO Europe, 2010. Parma Declaration on Environment and Health, Fifth Ministerial Conference on Environment and Health "Protecting children's health in a changing environment" , 10–12 March, Parma, Italy, WHO EUR/55934/5. 1 Rev. 2 11 March 2010, 100604 http://www.euro.who.int/_data/assets/pdf_file/0011/78608/E93618.pdf.