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Ethics in biomonitoring for occupational health

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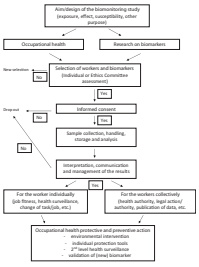
HIGHLIGHTS

- Biomonitoring measures human exposure, effects and susceptibility to chemicals.
- Ethical issues may arise during study design, sampling, and interpretation of data.
- Critical aspects are informed consent, communication, and management of the results.
- The four ethical principles are autonomy, non maleficence, beneficence, and equity.
- Ethical decisions require a balance of the interests of all the parties involved.

GRAPHICAL ABSTRACT

Phases of a biological monitoring program requiring ethical assessment.The decision on whether the priority is purely occupational health or (also) research/validation of new biomarkers is to be taken early and stated clearly in the process. “Yes” and “no” refer to positive and negative ethical outcome, respectively.



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ABSTRACT

Biological monitoring, *i.e.*, the use of biomarkers for the measurement of systemic human exposure, effects and susceptibility to chemicals has increased considerably in recent years. Biomonitoring techniques, originally limited to a few metals and other chemicals in the workplace, are currently applied to a large number of exposure situations and have become a useful tool for occupational and environmental health risk assessment. Almost any biomonitoring program, however, entails a number of relevant ethical issues, which concern all the phases of the entire process, from the selection of the biomarker to the study design, from the collection, storage and analysis of the biological sample to the interpretation, communication and management of the results, from the (truly?) informed consent of the worker to the independence and autonomy of the occupational health professional. These issues require a balanced assessment of the interests and responsibilities of all the parties, the worker primarily, but also the employer, the occupational health professional, the health authorities and, for research studies on new biomarkers, also the scientists involved. Ideally, decisions of ethical relevance concerning biomarkers should be based on, and respectful of the best scientific, legal and ethical evidence available. When, however, a conflict should arise, before any decision is taken a thorough risk-benefit analysis should be done, at the beginning of the process and after listening to the workers and the management involved, by the occupational physician or scientist, based on his/her professional experience, independent judgement and individual responsibility.

1. Introduction

Human biological monitoring or simply biomonitoring (BM) is the measurement of biomarkers in fluids and tissues of subjects

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exposed to chemicals or other risk factors in the workplace or the general environment. This practice has increased dramatically over the last decades, both quantitatively and qualitatively. Various techniques to measure the uptake of occupational chemicals directly in human body fluids were developed early in the 20th century, among which measurements of lead and a few other chemicals or their metabolites (Angerer et al., 2007). Later, larger scale BM was used in exposure and health surveillance programs or as part of regulatory requirements, particularly for workers of the chemical industry and other specific industrial sectors. From the relatively few papers published in the '80s, there are now several thousand papers published in the peer review literature each year, and the trend is still rising.

Initially just a tool for assessing exposure, BM is now used also to assess early biological effects from, and individual susceptibility to a vast array of chemicals. Besides, this technique once used only in the occupational setting is currently also applied to explore exposure conditions in the general environment (Sexton et al., 2004). The application of BM in fact has now expanded significantly beyond the boundaries of occupational and environmental health. BM is not only attracting the scientific interest of occupational health professionals (OHP), as well as public health professionals (PHP) in general, but also the increasing attention of workers, consumers and even members of the general public. Clinicians, researchers, governmental and international agencies, and even environmental health activist groups now employ this tool extensively and for a variety of purposes (Nelson et al., 2009). The most common use of BM is for exposure assessment and for validation of the occupational guidance values recommended by national and international agencies such as ACGIH, DFG, and SCOEL among others. In this context the main ethical issues have already been addressed and biomarkers are routinely used for risk assessment without particular problems. In the UK, the Health and Safety Executive (HSE) has even produced a practical guide to set up a BM program (HSE, 1997).

As outlined by the National Academy of Sciences, though, the growing information provided by biomonitoring studies in various fields has raised new challenges for scientists, regulators and public health managers. Among these challenges is how to deal with the various ethical issues concerning biomarkers for individual and public health purposes in terms of risk assessment, communication and management (NRC, 2006). A number of high quality review papers on human biological monitoring have also addressed, in general and to different extents, the ethics involved in BM (WHO/IPCS, 2001; NRC, 2006; ACGIH, 2005; IUPAC et al., 2004, 2006, 2007) and international ethical guidelines for human research are available (Council for International Organizations of Medical Sciences (CIOMS), 2002, 2009). Some authors have addressed specific aspects of human biomonitoring for occupational and environmental health, including advantages and limitations (Stokstad, 2004), or specific classes of chemicals (Nordberg et al., 2007; Clarkson et al., 1988). The interacting scientific, ethical and regulatory issues related to BM, and particularly to the use of exposure biomarkers, have been reviewed (Viau, 2005). However, to the best of our knowledge a specific evaluation of the most critical ethical aspects of BM in occupational health (OH), including exposure, effect and susceptibility biomarkers, is not available.

Despite its impressive exploitation, however, or probably because of it, BM is not always correctly used or interpreted, and many related scientific and ethical issues are not firmly established yet. The Code of Ethics of the International Commission on Occupational Health (ICOH) published in 2002 (ICOH, 2002) only provides some general, rather basic recommendations and even the current revision of the Code, approved recently by the ICOH Board and to become public soon, does not seem to have changed the situation. The main ethical questions addressed by the Code are: the general criteria for the selection of biomarkers, their sensitivity and specificity, the risk-benefit dilemma and the issue of the informed consent. According to the Code, "biomarkers must be chosen for their validity and relevance for protection of the health of the worker concerned, with due regard to their sensitivity, specificity and predictive value and should not be used as screening tests or for insurance purposes. Preference must be given, when possible, to non-invasive methods. When invasive tests or tests which involve a risk to the health of the worker are advisable, a risk-benefit analysis for the worker(s) concerned must be done first. In any case biomonitoring is subject to the worker's informed consent and must be performed according to the highest professional standard" (ICOH, 2002). More specific issues, such as sample collection, storage and analysis, interpretation, communication and management of results, are only briefly mentioned in the Code due to space limitation. Other, increasingly relevant aspects, including the ethical issues raised by the new potential biomarkers being developed by molecular biology and "omics" science and technology, their use and limitations and the specific features of biomarkers used for research are not covered by the Code.

The Scientific Committee on Occupational Toxicology (SCOT) of ICOH, whose mission, for twenty years now, has been promoting scientific and professional quality in the exercise of BM, has recently reviewed the use of BM for occupational health risk assessment (Manno et al., 2010). The aim was to provide a basis for an ICOH consensus document on BM by discussing briefly the basic scientific and ethical aspects of BM, among which planning of the study, informed consent, confidentiality and communication issues. In that paper the specificities and potentialities of the three types of biomarkers (exposure, effect and susceptibility) have also been discussed separately.

The aim of the present paper is to address those aspects in a more comprehensive way and in more detail, by expanding, integrating and amending, when necessary, the previous document. Moreover, we will discuss here the practical ethical problems encountered in the application of biological monitoring in OH, by outlining those aspects which have reached a general consensus within the scientific and professional occupational health community and focusing on those which have not, still being a matter for discussion or even conflict. Although most ethical issues apply to both occupational and non occupational contexts, discussion here has been limited to the workplace because of the many differences in the two approaches. These include risk perception and awareness (by the worker *vs*. the citizen), exposure conditions (known *vs*. unknown sources of exposure), risk-benefit assessment (for the same *vs*. different individuals), expected outcome in terms of management of the results (individual *vs*. collective health protection), and professional responsibility (OHP *vs*. PHP or public health authorities).

In order to make the coverage more comprehensive and the reading smoother, we opted to follow the same order usually adopted in the practice of BM, *i.e.*, from study planning and design to sample collection and storage, from laboratory analysis to interpretation, communication and management of results. All articles with the keyword association "biological monitoring" or "biomonitoring" and "ethical issues" or "ethical aspects" in the title/abstract/text from 2004 to 2013 were retrieved from Scopus and PubMed. After reading the abstract, the articles non related to occupational exposure were generally excluded. The other articles were read and those considered to be relevant to the aim of the present review were assessed and quoted, when necessary. Some additional and earlier publications quoted within these articles were also considered and discussed, if relevant.

We hope the present paper may stimulate and help those involved in BM during their scientific and professional activity to