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Introduction

Biomonitoring for occupational health risk assessment (BOHRA)☆

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ABSTRACT

Biological monitoring (BM or biomonitoring) deals with the assessment of individual human exposure, effect and susceptibility to occupational risk factors. It is a fundamental tool in occupational health risk assessment (OHRA) and occupational health practice (OHP) and it has become one of the most, if not the most active area in occupational health (OH) research today. From the few hundred BM papers published in the 80s, there are now several tens of thousand papers published in the peer review literature each year, and the trend is still rising exponentially. As a result, BM has become a priority for the Scientific Committee on Occupational Toxicology (SCOT) of the International Commission on Occupational Health (ICOH). Moreover, there has been a long-term interest in biological monitoring by other SCs of ICOH such as the Scientific Committees on Toxicology of Metals (SCTM) and on Rural Health (SCRH).

Despite its current popularity, though, BM is not always correctly used or interpreted by those involved in OHRA or OHP. The present review has been prepared to fill this gap and to help preventing misuse and misinterpretation of data. Although the document is meant to be a reference primarily for those involved in OH research and/or practice, it might become of interest for a wider audience within and outside ICOH, including scientists, occupational physicians, industrial hygienists and occupational or public health professionals in general, involved in chemical risk assessment for occupational health. The mission of SCOT and also of other SCs of ICOH, such as SCTM and SCRH, is indeed to promote the advancement and diffusion of knowledge on biological monitoring and other relevant occupational toxicology aspects and to make them available and useful to the entire OH scientific community.

All articles retrieved as of 3 January, 2007 as "Review" with the combined key words "biological monitoring" in PubMed from 2000 to 2007 have been scanned individually. This yielded a total of 1400 articles from a grand total of 2486 (excluding limitation on year of publication). When the title was related to human occupational biological monitoring, the abstract was read and its content was included. Articles outside the 2000–2007 time frame or that are not classified as "Review" in PubMed have also been included, when relevant.

The review is in four parts: (a) the introduction, containing the basic principles and definitions of BM and the different types of biomarkers (BMK), their toxicological significance, practical use and limitations, (b) the methodological and analytical aspects of BM in exposed workers, (c) the interpretation and management of BM data, including a number of recommendations to be considered when planning, performing and interpreting BM results and, finally, (d) the ethical aspects of BM. A list of key references to relevant papers or documents has been included. The BM of specific chemicals or groups of chemicals is outside the purpose of the review.

The document is aimed to represent the state of the art on biological monitoring in occupational risk assessment. We expect that reference to its content will be made, whenever appropriate, by those involved in occupational health practice and research when dealing with BM issues. The document is not meant, though, to represent a rigid nor a permanent set of rules and it will be periodically updated according to new developments and any significant advance in BM science. Any part of the document, therefore, is open to suggestions by scientifically qualified persons or institutions officially involved in BM and comments should be sent directly to the authors. A preliminary draft of the document has been presented at the 7th International Symposium on Biological Monitoring, Beijing, 10–12 September, 2007.

Notes on the literature survey for the preparation of this review

All articles retrieved as of January 3, 2007 as "Review" with the key words "biological monitoring" (no operator, just the two words side by side) in PubMed from 2000 to 2007 have been scanned individually. This yielded a total of 1400 articles from a grand total of 2486 (excluding limitation on year of publication).

When the title was related to human occupational biological monitoring, the abstract was read and, when appropriate for the purpose of the current review, the article was retrieved in EndNote. Four key documents are also cited: the National Academy of Sciences

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report on biomonitoring (Committee on Human Biomonitoring for Environmental Toxicants, 2006), the WHO document on validation of biomarkers (WHO, 2001), the ACGIH Introduction to BEI®s (ACGIH, 2005) and its German counterpart on BATs (Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, 2005).

Contributors of this document also added references from their own knowledge of the field and own bibliographic search. These references have extended sometimes outside the 2000–2007 time frame retained here as a starting point. They have also included articles that are not classified as "Review" in PubMed. Finally, further discussion within the scientific community should occur on the proposed outline (e.g. introduction, methods in BM, interpretation and management of BM data, ethical considerations) before this review is submitted to ICOH for approval. The current review is the authors' responsibility and it is only meant to be a starting point or a teaser for the proposed consensus document to be possibly approved officially by ICOH.

1. Introduction

A number of extensive and detailed high quality review papers have already been published on various aspects of human biological monitoring (BM or biomonitoring). These publications have been the result of the collaborative effort of several groups of experts, and provide an invaluable contribution to harmonize the scientific approach to BM and facilitate the practical work of those involved in BM in different areas of the world. Within ICOH the SCTM has long recognized the importance of BM and published several consensus documents related to BM, e.g. TGMA (1973), Clarkson et al. (1988) where risk assessment is specifically addressed, and, recently, the 3rd edition of the Handbook on the Toxicology of Metals (Nordberg et al., 2007) where risk assessment is specifically addressed (Nordberg and Fowler, 2007). These publications reflect the background of the authors, the scientific context in which the reviews were prepared and, of course, their specific purpose. The Environmental Health Criteria 222 on Biomarkers in Risk Assessment: Validity and Validation (WHO, 2001), for example, is focused on methodological issues, whereas the more recent publication Human Biomonitoring for Environmental Chemicals prepared by the Committee on Human Biomonitoring for Environmental Toxicants (NRC-USA, 2006) is focused on the role of biomonitoring as an exposure assessment tool finalized to public health efforts. In the widely known Introduction to Biological Exposure Indices (BEI®), a classic reference text for industrial hygienists and professional BM operators updated yearly by the ACGIH, discussion is focused on exposure biomarkers (ACGIH, 2005). Moreover, a number of publications have addressed important aspects of BM, including terminology, related to specific risk factors such as toxic metals and pesticides (IUPAC, 2003, 2006, 2007).

The Scientific Committee on Occupational Toxicology (SCOT) has noticed that none of these efforts has specifically addressed, in a comprehensive and exhaustive way, all the general issues related to the design, use and interpretation of biomonitoring in occupational health (OH). Considering the increasing role, in recent years, of BM in occupational health practice and, also, the difficulties and limitations still existing in the correct use and interpretation of different biomarkers, particularly of newly developed and validated biomarkers, SCOT has considered it was the time to take the challenge of publishing a document which may represent the consensus currently existing on BM within the OH community. The difficulty has been, therefore, to extract from the exploding BM arena those concepts which are on the one hand most relevant for their use by OH professionals (OHPs) and on the other a common basis for improving harmonization and quality in BM protocols.

The focus of this document is to address, in a concise and synthetic form, the most relevant areas of interest for the OHP, i.e. planning, implementing, interpreting and communicating the results of BM studies and protocols. Attention has been made to highlight advantages and limitations of BM versus other tools used for risk assessment such as environmental monitoring, health surveillance, animal experimentation and modelling. A clear distinction has to be made between biomarkers for use in research, i.e. those tests which have not been yet fully validated for a routine application, and biomarkers commonly used in OH practice, i.e. those tests which have already been interpreted and validated in the scientific literature and can, therefore, be routinely used for occupational health purposes. This distinction is particularly important in relation with susceptibility biomarkers, many of which have not yet been sufficiently validated in the workplace.

1.1. Definition and significance of biological monitoring (BM)

A number of similar, although not identical, definitions of biological monitoring exist (Zielhuis and Henderson, 1986). For the purpose of the present document BM is defined as the repeated, controlled measurement of chemical or biochemical markers in fluids, tissues or other accessible samples from subjects exposed or exposed in the past or to be exposed to chemical, physical or biological risk factors in the workplace and/or the general environment. This document will focus on biomonitoring for chemical risks. BM of workers has three main aims: the primary is individual or collective exposure assessment, the second is health protection and the ultimate objective is occupational health risk assessment. BM consists of standardized protocols aiming to the periodic detection of early, preferably reversible, biological signs which are indicative, if compared with adequate reference values, of an actual or potential condition of exposure, effect or susceptibility possibly resulting in health damage or disease. These signs are referred to as biomarkers. The periodicity of measurement is important to ensure that any early change is timely detected. The validity (sensitivity and specificity) of a biomarker is, however, the single most important aspect to be considered. Sensitivity, i.e. the ability to avoid false negative results, is fundamental for preventive purposes, whereas specificity, i.e. the capacity to avoid false positive results, is usually more important for diagnostic purposes.

1.2. Role of BM in exposure assessment

The term BM has come into use as a natural adaptation of the term environmental monitoring (EM), i.e. the periodic measurement of the level or concentration of a chemical, physical or biological risk factor in the workplace environment, which is traditionally used as an indirect measure of human exposure. Indeed, the most frequent use of biological monitoring is for assessing individual exposure to chemicals by different routes (inhalation, dermal and ingestion). Measurements of the concentration of substances or their metabolites in urine, for example, can provide useful information to assess inadvertent ingestion, but only in conjunction with measurements of exposure by other relevant routes such as inhalation and/or dermal (Cherrie et al., 2006). On the other hand, biomarkers of exposure should be used with care when single routes of absorption have to be assessed. For example, while biomonitoring can provide valuable information on dermal uptake in controlled conditions, it must be used with care in assessing the amount of dermal exposure in workplaces where the chemical may be additionally absorbed by inhalation or ingestion (Semple, 2004).

When compared to EM, BM provides additional information which can be effective in improving occupational risk assessment at the individual and/or group level. This information includes the assessment of the integrated total uptake of the chemical by dif-