International Journal of Hygiene and Environmental Health 215 (2012) 233–237

Contents lists available at SciVerse ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.de/ijheh

Short communication

Allocation of reliable analytical procedures for human biomonitoring published by the DFG Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area

Thomas Göen[a,b,*], Elisabeth Eckert[a], Anja Schäferhenrich[a], Andrea Hartwig[c]

[a] Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine of the University of Erlangen-Nuremberg, Erlangen, Germany
[b] Working group 'Analyses of Hazardous Substances in Biological Material' of the DFG Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Erlangen, Germany
[c] DFG Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Karlsruhe, Germany

ARTICLE INFO

Keywords:
Analytical reliability
Biological monitoring
Chemical exposure
Hazardous substances
Reliability criteria
Standard operating procedures

ABSTRACT

In 1955 the Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) was founded by the Deutsche Forschungsgemeinschaft (DFG). The Commission is responsible for analysing health risks by chemical exposure at the workplace and for advising public authorities accordingly. Within the Commission, the working group "Analyses of Hazardous Substances in Biological Materials" (AiBM) deals with the development of procedures to analyse chemical substances in biological materials. Most of these detailed, ready-to-use protocols for human biomonitoring, do not only enable the monitoring of occupational exposure, but also the determination of the background exposure in the general population.

The AiBM working group applies a multi-stage process to develop and evaluate human biomonitoring methods. As a matter of special importance, every method is tested by at least one examiner to ensure reproducibility of the analytical procedure and of the reliability data. Submitted methods and examination reports are discussed within the working group. The positively proved methods, if satisfactory, are adopted for publication. Otherwise, they are given back to the author with the demand for revision. In case of fundamental drawbacks, methods are rejected. The adopted methods are published in German and in English at regular intervals.

Since 1985 the working group has published 129 analytical methods (plus 11 methods for markers of susceptibility) in 12 issues of the English edition. The detection limits of eighty methods allow the analyses of background exposure for one or more parameters. About forty methods were specially designed for the application in population studies. Particularly relevant method examples are the determination of the metabolites of organophosphate pesticides, pyrethroides and phthalates in urine as well as the determination of perfluorinated compounds and polychlorinated biphenyls in serum.

Introduction

Both preventive disciplines, the occupational medicine and the public health, have the objective to supervise and evaluate human exposure to chemical substances. In Germany, the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area was founded by the Deutsche Forschungsgemeinschaft (DFG) in 1955 (DFG, 2007). The Commission is responsible for advising the German government and its agencies concerning the health risks caused by substances and materials used at the workplace.

The main tasks of the Commission are the evaluation of MAK values (maximum concentration at the workplace) for volatile chemicals and dusts and BAT values (biological tolerance values). However, within the Commission, it soon became clear that a reliable supervision of exposure is only applicable on the basis of reliable analytical procedures. This is true for both, the determination of the external exposure, e.g. ambient air levels, and the determination of the human internal exposure by human biomonitoring (HBM). Therefore, the working group "Analyses of Hazardous Substances in Biological Materials" (AiBM) was founded within the Commission in 1972 (DFG, 1976–2010). The task of this working group is the development of procedures to analyse

* Corresponding author at: Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Schillerstrasse 25/29, D-91054 Erlangen, Germany. Tel.: +49 9131 8526121; fax: +49 9131 8522317.
E-mail address: Thomas.Goeen@ipasum.med.uni-erlangen.de (T. Göen).

1438-4639/$ – see front matter © 2011 Elsevier GmbH. All rights reserved.
doi:10.1016/j.ijheh.2011.08.013

chemical substances and effect parameters in biological materials. Originally, the HBM methods targeted at the determination of occupational exposure levels. However, many of these methods are not limited to occupational exposure but they also enable the determination of the background exposure in the general population. This diversification was supported by several circumstances. One factor is the innovation and successive improvement of analytical techniques which facilitate the detection of background exposure without great effort (Bader and Göen, 2010). Secondly, it became more and more important to set occupational exposure limits near the background levels to prevent health risks by highly toxic substances. Furthermore, reference values are increasingly used to identify additional exposure at the workplace (Göen et al., 2011a),

The paper demonstrates the work flow in the AiBM working group and presents a useful selection of HBM methods which enable the determination of background levels in the general population.

Methods

The members of the AiBM working group are representatives of national and international universities, research institutions and industry. The group consists of members of the DFG Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, guest members and ad hoc experts. The members of the commission are nominated by the senate of the DFG for three years. Guest members are experts with a general expertise in human biomonitoring and are nominated by the DFG Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area for an indefinite period. Ad hoc experts are selected temporarily by the working group for special methods or to enhance the discussion of special analytical problems. Altogether, the number of the working group members ranges between 20 and 30. All members work in an honorary capacity for the working group. Travel costs for meetings and the duty of the secretary are supported by the DFG.

The decisive factor for the appointment of experts to the working group is their ability to develop and examine analytical procedures in their own laboratories. These scientific experts develop and examine HBM methods in a multi-stage process (Fig. 1).

Generally, a member of the working group or an external expert ('author') submits a human biomonitoring method to the group, which was developed or established in his/her laboratory. The author submits a detailed, ready-to-use analytical procedure containing all relevant reliability data (see below). After a first discussion about the submitted method, the AiBM group appoints at least one examiner (stage 1), who tries to reproduce the method and to verify the given reliability data. The examiner's report is then discussed within the group (stage 2). If approved, the method is adopted for publication. Otherwise, the method is given back to the author with demand for revision. In that case, the revised method is reviewed by the examiner, again. In case of fundamental drawbacks, the method is rejected. The adopted methods are published in German and English at regular intervals (DFG, 1976–2010, 1985–2004, 2005–2010).

The AiBM working group also discusses new human biomonitoring parameters, if there is no appropriate method in the collection of the working group, yet. If a suitable method is not available, neither from a member of the group nor from an external expert, a member of the group is asked to develop such a method (stage 0). After successful development, the examination of the method runs through stage 1 and 2.

The adopted and published HBM methods are prepared as ready-to-use standard operating procedures (SOP). The SOPs list the equipment, consumables and chemicals which are necessary

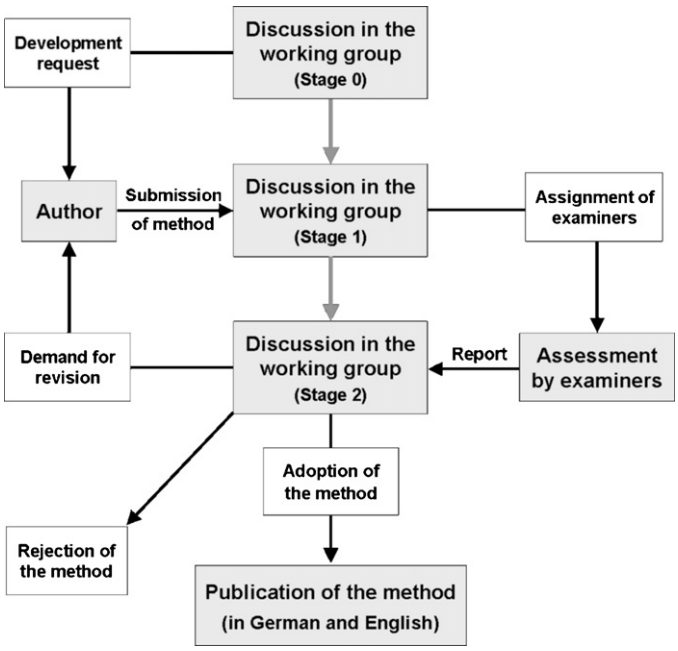

Fig. 1. Schematic diagram of the work flow in the DFG working group "Analyses of Hazardous Substances in Biological Materials".

for the execution of the procedure. The preparation and storage conditions of the solutions, used during analysis, are also described in detail. A detailed description of the sample preparation is given as well as information on the pre-analytical phase. Additionally, operational parameters of the analytical instruments and the estimated characteristics of the analytes, like detectable fragments, decomposition reactions and retention times are listed. The calibration process and the calculation of the analytical results are described, too.

Finally, every method contains a detailed description of the reliability data, which are achievable. The reliability criteria, which have to be tested and documented by authors and examiners, are at least:

- Repeatability: contains data for the precision in series and the precision from day to day.
- Accuracy: information on relative and absolute recovery; if available: results for certified reference materials (CRM) or intercomparison studies.
- Sensitivity: demonstrated by the limit of detection (LOD) and the limit of quantification (LOQ).

Moreover, information on working range, linearity, robustness and interferences are documented and discussed.

As a special feature, every method includes a preface which gives information on the chemical compounds which are monitored and, if available, on average levels of the biomarker in occupational and population studies.

Results and discussion

Since 1985 the working group has published 129 analytical methods for biological exposure and effect monitoring in 12 issues of the English MAK collection Part IV. Furthermore, 11 HBM methods for markers of susceptibility were published. The detection limits of eighty methods allow the analyses of background exposure for one or more parameters. About forty methods were especially designed for the application in population studies.