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GENERAL PAPER

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Occupational and environmental laboratory medicine: A network of EQAS organisers

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Abstract Most people in any community come into contact with chemicals that are potentially harmful to their health. Some elements are essential to health and inadequate amounts in food may also lead to ill health. Measurement of chemicals in blood, urine or other specimens is a fundamental feature of studies undertaken in the field of Occupational and Environmental Laboratory Medicine (OELM). Results are used to assess the risk for either overexposure or deficiency of essential nutrients. External Quality Assessment Schemes (EQAS) aid laboratories to achieve accurate and consistent data and 11 organisers of EQAS in Europe and North America are working to improve the effectiveness of their activities. The aims of the Network of EQAS Organisers in OELM are to stimulate improvements in analytical results, establish equivalence of assessment among Schemes, collaborate to enhance the practice of EQA including whenever possible to warrant traceability of EQAS to primary standards.

Keywords Occupational and environmental laboratory medicine · Equivalence of assessment · Traceability · Uncertainty

Introduction

Undue exposure to agents such as metals, pesticides, organic solvents, etc. can be harmful to health; and some are even carcinogenic. The most likely sources of exposure are within industrial and occupational settings. Harmful chemicals, such as carcinogens and toxic metals, are widely used in the workplace and considerable national and European

legislation exists to minimise occupational exposure and to protect the health of workers.

However, many environmental sources of chemicals are recognised, so that everyone in the community comes into contact with agents that may be harmful. For example,

- contamination of foods and water from natural sources
- contamination of drinking water with agro-chemicals
- airborne dispersion of products from factories, smelters, etc.
- misuse of household products such as paints, solvents, medicines.

Despite the imposition of maximum allowable concentrations for chemicals in water, foods, air, etc. by the World Health Organisation, the European Commission and national authorities, incidents affecting individuals or whole communities leading to severe clinical problems are reported.

In contrast to exposure to harmful chemicals, some are essential for health and well-being. These include vitamins, essential fatty acids, the essential trace elements and other nutrients. Inadequate amounts in foods or other dietary sources may lead to ill health or even death. While recommended daily intakes have been presented for these essential nutrients, many investigations have shown that overt or sub-clinical deficiencies occur both within individuals and in entire communities.

The health and economic implications of undue exposure to harmful agents or the inadequate intake of essential nutrients are recognised by programmes of risk evaluation and reduction. Such programmes may be undertaken at many different levels involving national or even international agencies, single industrial organisations or the relevant trade association, health care professionals, laboratories or even individuals. Measurements of exposure to and absorption of toxic and/or essential agents are achieved by determination of the agent involved (or of a metabolite) in an appropriate specimen (urine, blood, etc.). In November 2005, the European Parliament approved the establishment of a European Chemicals Agency for the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). The evaluation process within REACH requires that Chemical Safety Reports and Safety Data Sheets are provided for substances that are manufactured or imported in excess of 10 tonnes per year [1]. Any new laboratory data used to prepare such reports shall be produced in accordance with Good Laboratory Practice and testing laboratories will be required to follow ISO 17025 [2, 3]. Thus, analyses of biological specimens feature in risk assessments, as obligatory regular programmes of occupational biological monitoring, in specific epidemiological investigations, and in incidents of overt deficiency/toxicity. Occupational and environmental exposure assessment by biological monitoring is undertaken, therefore, because of legal requirements, as in an EU Directive or Resolution, or as part of a considered, planned approach to investigate a specific problem.

The procedures used to analyse biological specimens are often complex; nevertheless, accurate results are crucial. Decisions with far-reaching implications are made and action taken, entirely dependent on the laboratory data. For this reason, there is increasing awareness of the importance of using properly validated methods with each laboratory going through a process of assessing its own uncertainty. Indeed, most laboratories normally have their own systems for analytical quality assurance and many are formally accredited to a particular standard (ISO/IEC 17025, ISO 15189) [2, 3]. It is recognised that truly independent assessments of laboratory performance are provided by properly constructed and managed external quality assessment schemes (EQAS) and participation in EQAS (otherwise known as proficiency-testing scheme) is recommended as one of the methods to assure the quality of the results and to fulfil the requirements for accreditation [2, 3]. Schemes not only measure performance of the participants but also provide a stimulus for improvements in trueness and precision. In some cases, where few certified reference materials are available (for example nickel in urine) participation in EQAS offers the best opportunity to assess the laboratory's performance over the entire range of concentrations and types of matrices. Schemes relating to occupational and/or environmental laboratory medicine are organised from at least ten countries. Most operate on a national basis but some have a wider scope, which allows for formal or semi-formal links and representation from smaller countries. All laboratories involved in this work therefore have access and input to EQAS for occupational and environmental laboratory medicine (OELM).

Most schemes use similar protocols to monitor performance but each has its own technique to define a satisfactory standard of performance. Often these techniques are complementary to those used by other 'clinical EQAS' within the same country so as to provide for harmonisation within that nation. However, it has been demonstrated that different schemes have the potential to give conflicting conclusions, even from the same raw data [4–6]. In one study, 32 laboratories measured the concentrations of lead in the same five samples of blood. Results were analysed by different EQAS organisers according to their usual procedures and it was seen that an individual laboratory's performance could be evaluated as unsatisfactory by one scheme but acceptable by another [4]. Following from the evidence of possible inconsistencies, discussions among the EQAS organisers identified important topics for closer collaboration with the intention of creating a common quality base for analytical performance in the field of occupational and environmental medicine. This intention is being achieved through the following aims and objectives [7].

1. To develop the scientific integrity of EQAS

1. to apply relevant metrological principles to members' schemes including common measures to warrant traceability to primary standards
2. to elaborate evidence-based quality specifications for assays included in members' schemes
3. to demonstrate equivalence and comparability of assessment among members' schemes

4. to investigate the trends and new developments of laboratory assays in occupational and environmental laboratory medicine

2. To develop the technical and practical features of EQAS

(i) by establishing a web-based programme for (a) reporting results by participants to the organisers, and (b) preparing participants' assessment reports
(ii) by sharing data/specimens among schemes
(iii) by collaborating to help schemes achieve consensus standards (or accreditation)
(iv) by establishing new schemes with shared ownership
(v) by promoting educational and training innovations to the benefit of participants.

This report describes progress towards these objectives and work that is still being undertaken.

An accompanying paper discusses specific projects in greater detail [8]. Within this work, OELM has been limited to the consideration of organic agents such as solvents and to trace elements.

The network membership

The current membership of the OELM EQAS Network is shown in Table 1, which lists the major interests of the scheme and the organising institute. Membership of the network is open to EQAS organisers from other countries and anyone interested may approach the coordinator or any other member to receive further information. Details are also available from the network website at www.occupational-environmental-laboratory.com

Much of the work takes place within individual centres and developments are shared electronically either by email or via the restricted sector of the website. However, members meet together once a year to discuss results, review progress and plan for further projects.

Completed projects

Survey of workloads and needs for quality assurance among testing laboratories

This project sought to characterise laboratories involved in occupational and environmental laboratory medicine using a standardised questionnaire. This requested information concerning factors such as testing repertoire, annual workloads, methodologies, equipment, staffing and accreditation status. Approximately 450 European laboratories were surveyed and the response rate was 44%. The replies showed that 210 organic compounds were listed with annual test numbers of up to 33,435 (t,t-muconic acid), 56,916 (methyl hippuric acid) and (64,351) hippuric acid. Approximately 50 different trace elements were similarly assayed with in excess of 180,000 Pb measurements per year. More than 20,000 tests per year were reported for Zn, Cu, Hg, Al, Cd, and Cr. Equipment used in the laboratories tended to be quite old with more than 50% of the items

Table 1 Membership of the OELM EQAS Network

Country	Schemes for	Organiser/acronym of scheme
Belgium	Trace elements	Scientific Institute of Public Health, Epidemiology Unit/QCB
Canada	Trace elements	Centre de Toxicologie du Quebec
Finland	Organic solvent metabolites	Finnish Institute of Occupational Health, Biomonitoring Laboratory
France[a]	Copper, selenium, zinc in serum	Societe Francaise de Biologie Clinique, Group for Quality Assurance for Trace Elements
France[a]	Aluminium in serum, dialysis fluids	Laboratoire de Biochimie – Toxicologie, Hopital Jean-Bernard, Poitiers
France[a]	Lead in blood	Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) - Unité Contrôle National de Qualité
Germany	Trace elements Organic Solvent Metabolites	German Society of Occupational and Environmental Medicine
Great Britain	Trace elements	University of Surrey/TEQAS
Italy	Trace elements	Istituto Superiore di Sanità/METOS
Netherlands	Trace elements	Stichting Kwaliteitsbewaking Medische Laboratoria
Spain	Lead in blood	Instituto Aragonés de Seguridad y Salud Laboral
Spain	Mercury and Chromium in urine	Centro de Seguridad y Salud en el Trabajo Gobierno de Cantabria
USA	Trace elements	NY State DOH
USA	Trace elements	CDC

[a]In France, a compulsory whole blood lead EQAS is organised at the national level whereas for other elements participation in EQAS is voluntary and the schemes are organised by clinical biochemists

having been purchased at least 10 years before. Only 22 laboratories provided any indication of the uncertainty of the measurement result, of which seven stated that they used the ISO procedure to determine uncertainty [9]. It is presumed that the other 15 simply reported their analytical precision. Complete details of the findings from the survey are given in the Network Report [7], while the information reported to the Italian EQAS is separately available [10].

Comparison of procedures to evaluate performance in EQAS

In this project, the protocols used to assess measurements of Pb in blood and Al in serum, were compared. After finding that there were significant differences, a protocol that permits a common approach for performance evaluation was developed [11].

Differences in national legislation for the implementation of lead regulations included in the European Directive for the protection of the health and safety of workers with occupational exposure to chemical agents

When attempting to determine which concentrations of Pb in blood are the more important for EQAS surveillance, it was noted that there are inconsistencies within national legislations with regard to the concentration at which action to protect the health of the worker is implemented. Therefore, a systematic comparison of how the EU Directive 98/24/EC 12] has been put into effect was undertaken. Figure 1 represents the variation in national biological binding limit values compared against the requirements of the directive. Data were collected from countries represented by the European members of the network with some additional information solicited by personal contact with colleagues from other EU member states. While values from all EU countries are not available, there is sufficient information to demonstrate the differences in national legislation that are in place.

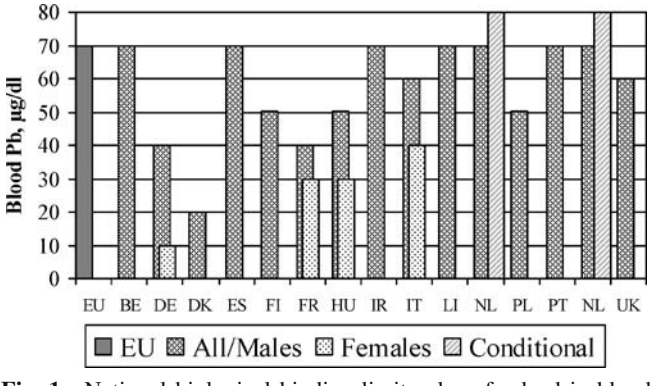

Fig. 1 National biological binding limit values for lead in blood compared to the requirements of the EU Directive 98/24/EU

Projects in progress

Traceability of measurements of Cu, Se and Zn in serum

The accuracy of a laboratory method is demonstrated by the strength of the traceability chain, i.e. the chain of comparisons, each with stated uncertainty, linking a laboratory result to an appropriate representation of the SI unit. The intermediate steps of the chain are represented by measurement procedures and reference materials to which values have been assigned by comparison with CRMs. For many analytical procedures, including the determination of Cu, Se and Zn in plasma and serum, there are no suitable CRMs. However, following the IMEP-17 project, a limited number of vials are available of two serum-based materials with concentrations of Cu, Se and Zn traceable to SI units, assigned using methods of higher metrological order. These materials were certified by the Institute for Reference Materials and Measurements (IRMM) (http://www.irmm.jrc.be/html/interlaboratory_comparisons/) on the basis of measurements performed by reference methods, by IRMM itself and by other metrological institutes and are described as 'certified test samples'. The EQAS organisers for OELM are working to provide traceability for their own EQAS specimens. This is to be achieved via specially prepared secondary reference materials that will be 'certified' by analysis together with IMEP-17 specimens [13]. These secondary reference materials will then be analysed together with samples about to be sent to EQAS participating laboratories thus establishing a traceability chain from the SI unit to the EQAS sample.

Development of common EQAS facilitated by shared samples and a common database

Within an analytical sector such as OELM there are usually several national EQAS. Most schemes use their own procedures to define a satisfactory standard of performance that is often complementary to those used by other "clinical EQASs" within the same country to provide for harmonisation within that nation. This diversity of nationally focused schemes acts as a barrier to new developments. A concept has been developed that prevents loss of national identity and provides options to meet national technical desires. This involves the use of shared specimens by all organisers and having a website as a 'hub', linking schemes and the participants. Initially it is likely that this will apply to new or infrequently measured analytes although the concept could be extended further. The 'single-source' specimens will be sent by organisers to their participants. Results from all the schemes will be directly reported back to the website for collation. At this point statistical analysis and report generation can take place but it is possible for all the results to be redirected to all of the national scheme organisers for preparation of reports in their preferred formats. Thus the

advantages of larger numbers of participants are realized with the maintenance of national identity.

Development of quality specifications for the total allowable error of assays for Cu, Se and Zn in serum

This work is described in more detail in an accompanying paper [8].

Conclusion

Reliable measurements of chemical agents are necessary for the protection of the population. In addition, new methods and new biological indices must be evaluated with respect to analytical performance and clinical utility. Organisers of external quality assessment schemes are responsible for ensuring that reports to participants are informative, useful and offer a stimulus for improvement. In the field of occupational and environmental laboratory medicine, scheme organisers have collaborated to devise procedures that allow for equivalent monitoring of laboratories at clinically relevant concentrations and with regard to fitness for the clinical purpose for which the assay is required. Projects include demonstration of traceability, the development of clinically based quality specifications, and procedures to establish the equivalence of assessment of laboratory performance necessary to establish mutual recognition agreements.

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References

1. European Union (2005) Proposal for a Regulation of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency and amending Directive 1999/45/EC and Regulation (EC) {on Persistent Organic Pollutants} Proposal for a Directive of the European Parliament and of the Council amending Council Directive 67/548/EEC in order to adapt it to Regulation (EC) of the European Parliament and of the Council concerning the registration, evaluation, authorisation and restriction of chemicals. (COM 2003 0644 (03)) http://europa.eu.int/comm/enterprise/reach/index_en.htm
2. ISO/IEC 17025 (2005) General requirements for the competence of testing and calibration laboratories, ISO, Geneva
3. ISO 15189 (2003) Medical laboratories – Particular requirements for quality and competence. ISO, Geneva
4. Christensen JM, Olsen E (1996) Ann Ist Super Sanità 32:285–294
5. Van Blerk M, Libeer J-C (2003) EQANews 14:62–66
6. Boley N (2006) Comparability of PT schemes – what did we learn from COEPT? Eurachem 5th Workshop Proficiency Testing in Analytical Chemistry, Microbiology and Laboratory Medicine, Portoroz, Slovenia 26–27 September 2005. Accred Qual Assur 2006 (this issue) DOI 10.1007/s00769-006-0106-z
7. Project Report SMT4-CT98-7522 to the European Commission, 2002
8. Taylor A, Angerer J, Arnaud J, Claeys F, Jones RL, Mazarrasa O, Menditto A, Parsons PJ, Patriarca M, Pineau A, Valkonen S, Weber J-P, Weykamp C (2006) Quality specifications for evaluation and comparison of performance among external quality assessment schemes in occupational and environmental laboratory medicine. Eurachem 5th Workshop Proficiency Testing in Analytical Chemistry, Microbiology and Laboratory Medicine, Portoroz, Slovenia 26–27 September 2005. Accred Qual Assur 2006 (this issue) DOI 10.1007/s00769-006-0118-8
9. BIPM, IEC, IFCC, ISO, IUPAC, IUPAP, OIML (1993) Guide to the expression of uncertainty in measurement. ISO, Geneva (corrected and reprinted in 1995)
10. Chiodo F, Patriarca M, Menditto A (2005) Microchem J 79:341–347
11. Taylor A, Angerer J, Claeys F, Kristiansen J, Mazarrasa O, Menditto A, Patriarca M, Pineau A, Schoeters I, Sykes C, Valkonen S, Weykamp C (2002) Clin Chem 48:2000–2007
12. European Union (1998) Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC) Official Journal L 131:11–23
13. Van Nevel L, Örnemark U, Smeyers P, Harper C, Taylor P (2003) IMEP-17 Trace and minor constituents in human serum. Report to participants GE/R/IM/42/02, IRMM, Geel, Belgium, June 2003