

### Special issue on External Quality Assessment in Laboratory Medicine – current challenges and future trends

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Quality assurance in the modern clinical laboratory is evidenced through the complementary processes of internal quality control and external quality assessment, also known as proficiency testing. By these processes and the achievement of accreditation to international (e.g. ISO) standards, the laboratory is able to demonstrate its competence to the users of its services, i.e. the clinicians and the patients they care for, who have an expectation that the results of diagnostic testing and monitoring of treatment are correct, comparable and fit-for-purpose within the scope of the service, wherever they are performed.

External quality assessment (EQA) was first introduced in the 1950s and 1960s in response to the growing role of laboratory testing as an essential part of disease diagnosis and management and an awareness of the extent of variability in results from one laboratory to another, for example as described by Mitchell Lewis following his initial inter-laboratory trials in the UK (1). The earliest EQA services were developed by committed and enthusiastic individual pathologists and laboratory scientists, often with limited resources and alongside their day-to-day clinical services; at the time, it was thought that harmonisation of performance would be achieved by the operation of a short-term programme of inter-laboratory testing rounds. The aim of this Special issue of *Biochemia Medica* is to provide a comprehensive overview of the latest developments in EQA and keep our readers up-to-date with the role and significance

of EQA in laboratory medicine and its future directions taking into account the changing demands of the profession and the evolution of analytical technology. In this issue we provide a number of outstanding contributions by internationally recognised experts in the field, who have been invited to address various issues and different aspects of EQA in the modern time, almost seven decades after its very origins.

EQA is nowadays available to some degree in all developed healthcare systems and is a means to improving the quality of laboratory performance (2,3). Participation in EQA may be voluntary, although a prerequisite for accreditation, or may be mandatory, for licensing. For example, in the USA, the necessity for EQA (or PT) is enshrined in the Clinical Laboratory Improvement Act of 1988 (CLIA '88) and in Germany, laboratories have to fulfil the RiliBÄK requirements. The provision of contemporary EQA services still relies on the commitment and expertise of individuals; however, the operation of a large, multi-disciplinary EQA programme as a complex, clinical technical service requires a range of skills and expertise including statistics, information technology, batch production procedures, logistics and distribution, in addition to expert subject knowledge.

The World Health Organisation updated and re-issued its manual for the establishment and operation of an EQA programme in 2016, providing comprehensive guidance on the strategies and responsibilities for EQA operation, and the interna-

tional standards ISO17043:2010 Conformity assessment – General requirements for proficiency testing and ISO13528:2015 Statistical methods for use in proficiency testing by interlaboratory comparison give details of the quality standards directly applicable to EQA providers (4). The ISO standards are generic documents, intended for EQA and proficiency testing in all sectors, not just medical laboratories. Although the importance of the role of EQA is recognised by national and international professional laboratory medicine societies, the European Quality Assurance in Laboratory Medicine (EQALM) organisation is the preeminent professional association dedicated solely to EQA provision. EQALM's essential and growing role is reviewed in the article, *"An overview of the European Organization for External Quality Assurance Providers in Laboratory Medicine (EQALM)"* (5). The responsibility for the choice of an appropriate EQA provider organisation lies with the laboratory and diversity in the scope of EQA provision is needed to match the diversity of testing services. Organisations such as EQALM give EQA providers the opportunity to share best practice and learn from the experience of others, with the objective that an appropriate and effective performance standard is applied to laboratory assessment, wherever the test may be undertaken. Harmonisation and standardisation of laboratory medicine practice is not only desirable as part of good patient care but becomes essential when patients' samples may be examined in different locations or by different healthcare providers. Graham Jones reviews the impact and influence of EQA in laboratory medicine harmonisation in his article, *"The role of EQA in harmonisation in laboratory medicine – a global effort"* (6).

EQA of the analytical phase of diagnostic testing entails the EQA provider distributing a sample or other artefact of known but undisclosed content to the participating laboratories or testing sites, which are usually medical laboratories but are increasingly to be found in 'point of care' situations, such as the ward or operating theatre, in clinics or doctors' surgeries and in the community. The sites test the material as if it were a patient's sample and report their results to the EQA provider for

statistical analysis. By comparison with minimum acceptable performance limits, the EQA provider can identify laboratories, methods, kits or reagents with out-of-consensus results and ensure that appropriate corrective action is taken, either by the laboratory or some other regulatory agency. EQA for point-of-care testing (POCT), especially when outside the hospital environment, has different requirements from testing provided by laboratory professionals, although immediate clinical decisions may be made according to the results. EQA for POCT must be robust, easy to operate and fit for the environment in which the testing takes place, as is reviewed by Anne Stavelin in the article, *"Essential aspects of external quality assurance for point-of-care testing"* (7).

A major challenge for provision of EQA in haematology is the choice of assay material for automated cell counting and the options are reviewed by Barbara De la Salle in her article *"Survey material choices in haematology EQA: a confounding factor in automated counting performance assessment"* (8). There is no ideal assay material for automated cell counting because of the inherent conflict between material commutability and stability and the lack of certified reference materials and methods to which results can be traced. Blood cells are inherently unstable and deteriorate within hours of collection, especially in terms of cell morphology and platelet counting. Methods of cell stabilisation result in changes in the cell membrane, which affect how the cells react in the different cell counting technologies. These technologies are changing rapidly, especially with the introduction of 'black box' technologies in POCT, designed to work with fresh, capillary blood.

The concept of using statistical analysis for quality control as part of the production process was developed in the in the decades between the first and second world wars with the introduction of mass production methods in industry, where control of the quality of the output through the monitoring and sampling of an automated production line rather than the individual attention of a skilled craftsman became standard practice. The application of similar quality control methods were applied in the clinical laboratory alongside the intro-

duction of automated testing, with the development of internal quality control (IQC) and EQA procedures. The standard for methods for statistical analysis in EQA are described in ISO 13528:2015 but the standard can be applied in a number of forms. Although the principles of statistical use in EQA is relatively straightforward, requiring the definition of a target value and statistical performance limits based on distance from the target, there are a number of statistical processes and manipulations involved that require some expert knowledge on the part of the EQA provider and translation into an intelligible format for participants' reports. Wim Coucke's article, "*Demystifying EQA statistics and reports*" reviews the application of the available statistical approaches and these issues are complemented by Kristensen's article, "*Interpretation of EQA results and EQA-based trouble shooting*", which describes a 'diagnostic' approach for identifying the possible causes of an out-of-consensus EQA result, drilling down to separate 'true' performance problems from those relating to, for example, specimen quality or data entry (9,10).

Quality improvement is not static and quality monitoring has now expanded to cover the total testing process, including the pre- and post-analytical stages, where the majority of errors in analytical testing occur (11). There are many points in this pathway, from selection of test, identification of the patient and specimen collection through to timely reporting to the correct physician, where errors that affect the outcome of the testing may occur. The laboratory is required to take responsibility for identifying and controlling these errors and to demonstrate the effectiveness of their procedures for this. Three models for EQA of the pre- and post-analytical phases have been previously described: the external assessment of written procedures (type I), the distribution of specimens with pre-analytical errors, such as labelling errors or haemolysis (type II) and the monitoring of the incidence adverse events in the pre- and post-analytical phases (type III) (12). The Royal College of Pathologists in Australasia Quality Assurance Programme (RCPAQAP) has one of the most well established type III model programmes, reviewed by

Badrick and his colleagues in their article entitled "*External Quality Assessment beyond the analytical phase: an Australian perspective*" (13). The experience of other providers of pre- and post-analytical phase EQA are reviewed by Nikolac and colleagues in their article about the preanalytical external quality assessment organized by the Croatian Society of Medical Biochemistry and Laboratory Medicine and Lenicek Krleza *et al.* in their article on the post-analytical External quality assessment of laboratory testing in medical laboratories in Croatia (14,15).

The transition of EQA theory into practice is a daunting task and EQA provider organisations rely on the sharing of best practice to anticipate and meet the demands of the rapidly changing field of diagnostic testing and the requirement for service harmonisation in modern healthcare. In addition to the review areas of new developments and best practice in EQA, this special edition shares the experiences of establishing and developing effective EQA services in a range of different healthcare systems. The challenge of EQA provision in resource limited countries and the implementation of regional proficiency testing in East Africa, is extensively and comprehensively reviewed by Jane Carter, Stephen Munene and co-workers. Their work represents a truly global summary of the impact and influence of EQA in a challenging environment where allocation of resources to laboratory testing is unfortunately still of very low priority (16,17). Marcos Fleury gives an excellent review of general EQA provision in Brazil in his article, "*Implementation of the External Quality Assessment Program in Brazil*" and Jasna Lenicek Krleza provides a similar insight to the challenges experienced in Croatia in "*External Quality Assessment in Croatia: problems, challenges, and specific circumstances*" (18,19). The experience of providing EQA in specialist areas is highlighted by Zhang *et al.* in the article, "*Proficiency testing of maternal serum prenatal screening in second trimester in China, 2015*", and by Aralica and Lenicek Krleza in the article on sweat-testing EQA in Croatia, "*Evaluating performance in sweat testing in medical biochemistry laboratories in Croatia*" (20,21).

The variety on topics discussed in the special edition shows the relevance of effective EQA as a part of the total quality management of the laboratory. This is relevant not just for medical laboratories but even more relevant for the benefit of the patients they serve. We wish to thank the authors for their efforts in preparing their contributions and for making this Special issue so comprehensive and valuable reading material. It has been an im-

mense privilege for us to work with them and take the advantage of their broad experience and wide knowledge. We hope that you will enjoy reading articles within this issue, as much as we have enjoyed in creating it, from its original concept to the final outcome.

### Potential conflict of interest

None declared.

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