

# Quality assurance in medical laboratories

Paths to global competence standards

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**Quality assurance in medical laboratories is of fundamental importance for the process of in vitro diagnosis for many diseases. The ISO 15189 standard ("Medical laboratories — Particular requirements for quality and competence") was developed to address the general dissatisfaction with current standards on the part of those working in the laboratory sector. The present article discusses how the extensive set of requirements presented by the ISO 15189 standard can be fulfilled in practice in the medical laboratory. The article also introduces an initiative designed to standardize and improve quality assurance in medical laboratories worldwide.**

## Importance of in vitro diagnostics

Alongside the medical history, physical exam and imaging techniques, clinical chemistry and laboratory medicine make an important – and frequently, decisive – contribution to the diagnosis of illness and disease [1]. The assessment of clotting parameters before an operation, the detection of bacterial and viral infections or the measurement of hormones and markers for tumors, inflammation or cardiac, renal and hepatic function in blood and serum are just a few examples of modern in vitro diagnostics. The lab findings that result are of fundamental importance for medical diagnostics.

Both diagnostics research and diagnostic device manufacturers are working towards the development of new methods and the improvement of existing techniques. Paired with efficient regulatory oversight, international standards and standardization, these efforts lead to continuous improvements in the precision and accuracy of lab-based diagnostic methods and thus to their diagnostic sensitivity, specificity and predictive value [1].

## Lab accreditation to ISO 15189: a globally-trusted standard

ISO 15189 is a laboratory practice standard that is the result of international cooperation and consensus. Many medical laboratories within Europe have obtained accreditation to this standard. While compliance is (as yet) voluntary in most EU member states, ISO 15189 is now a mandatory standard within some EU countries (such as France).

ISO 15189 was developed because many in the laboratory sector who had argued for a standard for clinical/medical laboratories were of the opinion that this need was not met by the existing standard, ISO 17025 [2]. ISO 17025 is a standard for metrological laboratories. Such laboratories measure the chemical concentration of substances in various media such as water, solutions, etc. The level of accuracy expected from laboratories of this type is not necessary for clinical decision-making or the measurement of biological efficacy, however [2].

In Germany, accreditation to ISO 15189 is voluntary for a laboratory. A minimum requirement, however, is compliance with the Quality Assurance of Medical Laboratory Testing (Rili-BÄK) Guideline issued by the German Medical Association [3].

## Accreditation organizations

Article 4, paragraph 1 of EC Regulation No. 765/2008 has required EU member states to appoint a single national accreditation body from January 1, 2010. In Germany, the German National Accreditation Body (DAkkS) was set up to fulfil this requirement.

An external organization that is given the authority for laboratory accreditation can accredit laboratories that have furnished incontrovertible proof of their competence and compliance with the requirements specified by a particular lab practice standard. As one example, US accreditation organizations must submit proof that their practice standards meet the minimum requirements set out by the CLIA regulations applicable in the USA [4].

Outside the US, laboratories can gain accreditation from an organization whose criteria for accreditation are based on the ISO 17025 or ISO 15189 standards.

The accreditation organizations are free to define their criteria as they see fit, however, so as to ensure a higher standard of quality. This gives accreditation bodies a means of differentiating their services while encouraging laboratories to satisfy higher standards in terms of their quality and output.

## Lab accreditation outside the EU

In non-EU countries, at least one organization is responsible for the accreditation of domestic laboratories. With their introduction of ISO 15189, these countries have adopted a uniform approach to establishing the competence of a medical laboratory. The rollout of this standard also encourages laboratories to adopt (existing) internationally recognized good practice. Laboratories in countries without a recognized accreditation organization can apply for accreditation from established organizations in other countries.

## Quality assurance requirements as defined by ISO 15189

The services provided by medical laboratories play a critical role in the provision of healthcare to patients. Accordingly, service provision must ensure that these services cater to both patient needs and to the needs of the clinical personnel responsible for caring for these patients. Examples of such services include: precautions taken for handling test requests; patient preparation; error-free patient identification; the taking of samples; and the transportation, storage, preprocessing and analysis of clinical samples, followed by the provision of validation, evaluation, report writing and consulting services. Service provision must also ensure that safety aspects and ethical issues are adequately accounted for by medical laboratory work [5].

Key aspects of the requirements of ISO 15189 include:

- Specification of quality policy
- Appointment of a quality manager and deputies to cover all key functions
- Establishment of a quality management system (QMS)
- Creation of a quality manual
- Document control

The standard also defines several requirements to be met for the following activities and processes:

- Contract review and performance of tests by contract laboratories
- External services and supplies, consulting services
- Complaints resolution, identification and control of non-conformities
- Corrective and preventive actions, continuous improvement
- Internal audits
- Personnel
- Premises, environmental conditions and laboratory equipment
- Pre-analytical measures, test procedures, post-analytical measures, reports on findings

Only once all of these requirements are addressed, put into practice and satisfied can accreditation be successfully verified by the accreditation organization.

## IQC and EQA: two key elements of controlling quality assurance

Two – essentially distinct – sets of procedures (see tab. 1) are available for performing quality assurance on diagnostic findings:

- Internal quality controls (IQC)
- External quality assessment (EQA, i.e. external quality assurance)

**Table 1** Comparison of internal quality controls/external quality assessment

| Procedure             | Internal quality controls       | External quality assessment  |
|-----------------------|---------------------------------|--|
| Results               | Known                           | Unknown  |
| Results available     | Immediately                     | Only when report issued  |
| Frequency             | Daily, per batch, per shift     | Periodically, e.g. once in four weeks or every two to four weeks or twice yearly, or once annually |
| Analyte concentration | Normal, pathological            | Multiple concentrations, e.g. 6–8  |
| Assessed              | Precision                       | Accuracy and precision   |
| Comparisons           | Only within a single laboratory | Across all laboratories participating in the round robin test                                      |

Internal quality controls are general performed on a daily basis (e.g. every morning, when changing a reagent batch, on changes of shift), and also involve the use of bought-in reagent standards and reagent controls, as well as diagnostic device- and system-specific agents.

Participation in proficiency testing for certain analytes (such testing being mandated in Germany by Rili-BÄK) enables the lab to compare results obtained internally with those from other laboratories. Proficiency testing institutions in Germany include the Düsseldorf-based INSTAND e.V. (Society for Promoting Quality Assurance

in Medical Laboratories) and the Reference Institute for Bioanalytics (RfB), which is based in Bonn.

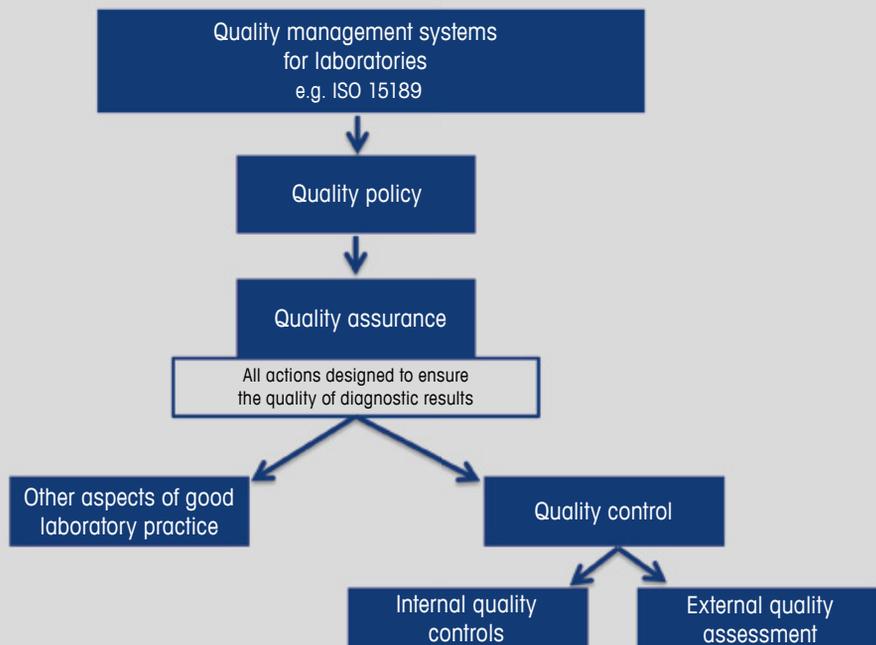
Comparable proficiency testing organizations exist in many other countries within Europe and around the world.

In conclusion, one can state that the performance of the necessary internal quality controls in no way replaces the need for external quality assessment (i.e. participation in round robin testing) but that the two sets of quality assurance procedures usefully complement one another.

**A sample general-purpose quality policy**

"The laboratory attached to [name of hospital] undertakes to produce reliable results for patient examinations, and in such a way that ensures the appropriate and timely provision of healthcare to patients. The laboratory will make every effort to produce reliable test results, by combining procedures that work to encourage efficiency, by using technologies suitable for achieving the laboratory's goals, and by providing lab personnel that possess the relevant training and skills to perform their allotted tasks."

**Fig. Monitoring the quality of laboratory results**



## The role of the IFCC in the improvement of quality assurance in medical laboratories

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) is the largest and most important international organization for the field of in vitro diagnostics [6]. Based in Milan, the IFCC is a global umbrella organization, and represents the interests of over 90 national associations working in clinical chemistry and laboratory medicine. Some of the key activities of the IFCC include:

- Development of global standards in cooperation with other international organizations
- Supporting member countries in their research and training activities in clinical chemistry
- Hosting of congresses, conferences and meetings for specialists working in clinical chemistry and laboratory medicine, with the aim of presenting recent findings and exchanging information about best practices

The IFCC's Committee of Analytical Quality (C-AQ) is tasked with active participation in the continuing education of laboratory managers and laboratory personnel. The Committee's work in this respect includes the development and provisioning of appropriate written instructions and manuals for method/instrument validation, and for the standardized performance of internal quality controls and laboratory quality assessments by accredited institutions. Publications and e-learning presentations are authored and made available on the IFCC website.

Workshops and seminars on quality assurance are also offered by local specialists. Past events include those in Nepal (2012), Vietnam (2011) and Sri Lanka (2009). The primary beneficiaries of these programs are thus emerging and developing economies, where quality assurance programs are frequently not yet sufficiently well-established – often to the potential detriment of patients. IFCC member countries are also given the opportunity to invite speakers from abroad, and can also request consultations and help as and when required.

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**Egon Amann** studied biology at the Freie Universität Berlin, majoring in molecular biology, biochemistry and genetics. After obtaining his doctorate from the Max Planck Institute for Molecular Genetics in Berlin-Dahlem, Dr. Amann then spent time working in a DFG-funded research position at Harvard University in the field of biopharmaceutical development. A number of positions in industry then followed, including Behringwerke (Marburg), Hoechst Japan Limited (Tokyo), Behring Diagnostics (Marburg and Boston), Dade Behring, and, lastly, Siemens Healthcare Diagnostics. Egon Amann completed his habilitation in molecular genetics and has been a visiting professor at Marburg's Phillips University since 2005. He has been Professor of Quality Assurance and Product Law at Hamm-Lippstadt University of Applied Sciences since August 2013. The author and holder of numerous publications and patents, he is a highly-regarded speaker at specialist events and conferences in medical diagnostics. He is also a member of several associations within the diagnostics industry, including the European Diagnostic Manufacturers Association (EDMA) and the German Diagnostics Industry Association (VDGH). He chairs the Committee of Analytical Quality within the IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) global umbrella organization [6].