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ISO 15189 ACCREDITATION: NAVIGATION BETWEEN QUALITY MANAGEMENT AND PATIENT SAFETY

ISO 15189 AKREDITACIJA: NAVIGACIJA OD UPRAVLJANJA KVALITETOM DO BEZBEDNOSTI PACIJENATA

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Summary

Accreditation is a valuable resource for clinical laboratories and the development of an International Standard for their accreditation represented a milestone on the path towards improved quality and safety in laboratory medicine. The recent revision of the International Standard, ISO 15189, has further strengthened its value not only for improving the quality system of a clinical laboratory but also for better answering the request for competence, focus on customers' needs and ultimate value of laboratory services. Although in some countries more general standards such as ISO 9001 for quality systems or ISO 17025 for testing laboratories are still used, there is increasing recognition of the value of ISO 15189 as the most appropriate and useful standard for the accreditation of medical laboratories. In fact, only this International Standard recognizes the importance of all steps of the total testing process, namely extra-analytical phases, the need to focus on technical competence in addition to quality systems, and the focus on customers' needs. However, the number of accredited laboratories largely varies between European countries and also major differences affect the approaches to accreditation promoted by the national bodies. In particular, some national accreditation bodies perpetuate the use of fixed scopes, while the European co-operation for accreditation (EA) and the European Federation of Laboratory Medicine (EFLM) Working Group promote the use of flexible scopes. Major issues in clinical laboratory accreditation are the verification of examination procedures for imprecision, trueness and

Kratak sadržaj

Akreditacija je za kliničke laboratorije dragocen resurs i razvoj Međunarodnog standarda za njihovu akreditaciju predstavljao je prekretnicu na putu ka poboljšanju kvaliteta i bezbednosti u laboratorijskoj medicini. Nedavna revizija relevantnog Međunarodnog standarda, ISO 15189, dodatno je povećala njegovu važnost za poboljšanje ne samo sistema kvaliteta u jednoj kliničkoj laboratoriji već i za bolje odgovaranje na zahtev za kompetentnošću, fokus na potrebe klijenata i konačnu vrednost laboratorijskih usluga. Iako se u nekim zemljama još koriste uopšteniji standardi, kao što je ISO 9001 za sisteme kvaliteta ili ISO 17025 za laboratorije za testiranje, sve više se priznaje vrednost ISO 15189 kao najrelevantnijeg i najkorisnijeg standarda za akreditaciju medicinskih laboratorija. Štaviše, samo ovaj Međunarodni standard prepoznaje važnost svakog koraka u ukupnom procesu testiranja, naime ekstranalitičke faze, potrebu da se pored sistema kvaliteta fokusira i na tehničku kompetentnost, kao i fokus na potrebe klijenata. Međutim, broj akreditovanih laboratorija znatno se razlikuje u evropskim zemljama i postoje velike razlike koje utiču na pristupe akreditaciji koje promovišu nacionalna tela. Pre svega, neka nacionalna akreditaciona tela i dalje promovišu upotrebu fiksnih opsega, dok Evropska saradnja za akreditaciju (EA) i Radna grupa Evropske federacije za laboratorijsku medicinu (EFLB) preporučuju upotrebu fleksibilnih opsega. Glavni problemi u akreditaciji kliničkih laboratorija su verifikacija procedura za ispitivanje nepreciznosti, istinitosti i dijagnostičke tačnosti kao i za procenjivanje neizvesnosti merenja. Pored toga, pokaza-

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diagnostic accuracy and for estimating measurement uncertainty. In addition, quality indicators (QIs) are a fundamental requirement of the ISO 15189 International Standard.

Keywords: medical laboratory accreditation, ISO 15189, flexible scope, quality, quality indicators

telji kvaliteta (quality indicators, QI) jedan su od osnovnih zahteva postavljenih u Međunarodnom standardu ISO 15189.

Ključne reči: akreditacija medicinskih laboratorija, ISO 15189, fleksibilni opseg, kvalitet, pokazatelji kvaliteta

Introduction

Medical laboratories play an increasingly central role in modern health care systems as laboratory data are an integral part of the physicians' decision-making processes, enabling them to: a) identify risk factors and detect a predisposition to a disease, b) confirm or reject a diagnosis, c) guide patient management, and d) monitor the efficacy of therapy through dose-tailoring (personalized medicine).

To successfully achieve these goals, each medical laboratory should strive to assure quality, namely accuracy of results, safety (quality in the total testing process) and efficiency (cost containment). This, in turn, requires the management of medical, scientific, and technical expertise, by obtaining and properly utilizing resources such as personnel, laboratory equipment, supplies, and facilities. Implementation of ISO 15189 provides a foundation for quality in medical laboratories by linking the quality management system (QMS) to competence in all procedures and processes used in the total testing process (TTP) (1). If QMS should be defined as »a set of interrelated or interacting elements that organizations use to direct and control how quality policies are implemented and quality objectives are achieved«, in the case of medical laboratories the TTP should be viewed as a set of interrelated and interacting processes starting from an appropriate request and sample collection to produce analytical results that have to be transformed in useful clinical information to allow better diagnoses and therapies (2).

In the world of the ISO Standards, the ISO 15189 is the only standard specifically implemented for a health care unit. It represents the achievement of a very important pathway, in which it was recognised that Laboratory Medicine, in the health care system, is an organization with a higher awareness about the importance of quality in the entire TTP and in which the staff competence plays a predominant role as well. The accreditation according to the ISO 15189 guarantees the implementation of processes and procedures that comply with approved international and national guidelines that are the expression of laboratory good practice but, first and foremost, assures the competence of staff about the activities in which they are involved. In order to assure that the ISO 15189 accreditation provides real added value to a laboratory, the basic elements are:

- the training of the staff about the accreditation purpose;
- the achievement of awareness that all processes and procedures have to be implemented on the basis of the test purpose;
- the correct interpretation of each requirement of the ISO 15189;
- the knowledge of the guidelines that can lead the compliance of each requirement;
- the competence and ability to translate into practice what is proposed in the guidelines in order to avoid compliance with the requirements becoming a bureaucratic and useless burden on procedures, in addition to increasing costs;
- the implementation of procedures according to harmonized criteria in order to assure that the risk of Accreditation with flexible scope is prevented (3);
- the performing of audit by assessors with high competence in the laboratory field where the tests in accreditation are involved but, also, in the implementation of quality management systems of the clinical laboratories.

A Quality Management System based only on the management requirements guarantees a system under control in which the efficacy is related to the objectives of the organization. The ISO 15189 accreditation requires compliance with stringent technical and professional requirements, in addition to management requirements. This peculiarity of the ISO 15189 is the fundamental aspect that has a strong impact on patient safety. The assurance of medical laboratories competence, in compliance with the ISO 15189 requirements, depends on the level of laboratory staff competence but, also, on the competence of the assessors during the audit. The assessors play a key role in the release of accreditation. The evaluation of suitable interpretation of a morphologic pattern and the congruity of the interpretation between different operators, for example, can be evaluated only by assessors with high competence in that specific area. Each laboratory activity has to be based on consensus criteria and harmonized procedures complying with technical requirements and structured according to management requirements, but has to be managed by staff with recognised qualification and assessed by assessors with appropriate competence. Only if this aspect is adequately understood and stressed in the implementation of accreditation, the introduction of ISO 15189 should translate into effectiveness for higher quality and patient safety.

ISO 15189 Accreditation

The need to comply with quality requirements approved by recognised international bodies was born about twenty years ago. Medical laboratories around the world, in order to satisfy this need, used the available standards and many laboratories were accredited in compliance with the EN 45000, and later ISO 17025, or national standards issued by professional bodies (CCKL, CPA, etc.) or, especially in Italy, were certified in compliance with ISO 9001 (4, 5). The limited value and appropriateness of these norms for medical laboratories promoted the development of a specific standard and, although the first draft was issued in 1997, only in 2003 the first revision of the standard was finally released. The standard has been based on the management requirements proposed in the ISO 9001, technical requirements of the ISO 17025 and specific professional requirements proposed by the European Communities Confederation of Clinical Chemistry (EC4) (6). This standard takes into account all the needs of medical laboratories, namely all the steps of the entire testing process, starting from the appropriate test request to the right notification of laboratory reports and the role of further clinical advice provided by laboratory professionals. It focuses the attention on both the items of the intra-analytical phase (e.g. verification and validation of examination procedures, measurement uncertainty, metrological aspects, etc.), and to the pre- and post-analytical phases (peculiar features of medical laboratories in comparison to testing laboratories), but its limited adoption, particularly in some countries, has been affected by the request acreditate each single test (fixed scope), as typically requested by the ISO 17025 accreditation process. Only in 2008 the accreditation with flexible scope was approved by the European Cooperation for Accreditation (EA) and medical laboratories have started with the ISO 15189 accreditation at an international level (7). Moreover, the identification of a unique national accreditation body has made clear which is the entity that has to manage the accreditation of medical laboratories, promoting its diffusion (8).

Harmonization Needs

The introduction of flexible scopes for ISO 15189 accreditation has called for a definition of the scope of accreditation on the basis of description of coherent groups defined by: the measurand (test), medical field (e.g. clinical chemistry, haematology, etc.), measurand type (e.g. enzymes, biomarkers, hormones, etc.), analytical principles (e.g. direct potentiometry), sample type (e.g. plasma, serum, etc.). All tests are part of a coherent group of associated tests and the accreditation recognises the competence in reference to the features of each group. In the period between audits the laboratory manages the list of accredited tests included in a group and the innovation of accredited tests is possible without asking for scope extension or adding other tests when they achieve compliance with the requirements. The rationale of the flexible scope is the release of accreditation for all tests that can be included in a group that has been accredited (same medical field, same test typology, same analytical principle, same sample type and belong to the same medical area) and are compliant with the requirements (3).

The correct definition of each group and the tests to be included in the group are important for the appropriate management of flexible scopes and to guarantee the assessment of competences during the audit. The accreditation bodies, at the European level, have defined the groups within which the tests should be allocated. However, there is no harmonization in the definition of these groups (formulation too non-specific or too specific in relation to: medical field, test typology, analytical principle), and the same test can be included in a different group depending on its country.

The spread of ISO 15189 accreditation has highlighted the need for harmonization of the list of groups in which tests have to be included. The use of the same list assures a clear understanding of the tests under accreditation for the scientific community from different countries and for patients, and allows distinguishing between laboratories with different quality level of service. Similarly, concerning the check-lists used by assessors during the audits, they should be standardized in order to guarantee a congruent evaluation among different countries.

There is another point to highlight concerning the accreditation with fixed or flexible scopes. In fact, it is possible to require accreditation with flexible scope only for the tests under control with inter-laboratory comparison, such as the External Quality Assessment (EQA)/Proficiency Testing (PT) Programme. However, unfortunately, for rare tests or innovative tests an EQA/PT Programme should be unavailable. The ISO 15189 requires the implementation of alternative approaches to establish the acceptability of EP, when EQA/PT are unavailable, but it does not report what are the approved approaches and if these tests can be included in the flexible scope. The identification of consensus criteria about this matter for the management of these tests is important in order to stimulate the accreditation with flexible scope for the entire service.

Pragmatic Approach In the Application of Requirements

Scientific community promotes accreditation with flexible scope for the complete service, and it is therefore important to define criteria and operative instructions that cover the complete typology of tests.

The experience in the field has highlighted some difficulties in applying approved guidelines and recommendations for all tests included in the service because of the different features and test purposes. Moreover, the guidelines and recommendations often do not take into account the costs and the workload needed for their implementation and, therefore, they may represent a type of procedures affected by the level of complexity and not easy to be performed. A pragmatic approach, in line with the approved recommendations and guidelines and using data already available in the laboratory, is needed in order to satisfy the ISO 15189 requirements assuring the reliability of results and promote the introduction of the accreditation process in Medical Laboratories, balancing technological possibilities, risk and personnel and time constraints.

An example concerns the procedures for the estimation of measurement uncertainty (MU), the verification of EP and quality indicators (QIs) management.

Measurement uncertainty

The ISO 15189 does not specify how to estimate the MU and several documents available in the literature propose different theoretical approaches for MU estimation (9–13). However, in most cases a rigorous approach cannot be applied and the laboratories must attempt to identify a procedure that makes a reasonable estimation and does not create a wrong »impression« of the uncertainty. Reasonable estimation must be based on the knowledge of performance of the method and on the test purpose.

Some points in discussion concern: the components that have to be included in calculating MU (the bias, as an estimate of systematic error and imprecision, as an estimate of random error); the need to estimate more than one value of MU in relation to the concentration levels; and the criterion to be used to validate the MU. The correct answer to all points in the discussion requires the identification of a pragmatic approach that could stimulate the implementation in different laboratories, collect and compare these experiences, and formulate a feasible guideline complying with requirements but, also, with the organizational context (14). For example, on the basis of the test purpose and considering different models for calculating MU available in literature (15–17), the bias could not be relevant when the interpretation of the test is made in comparison with the previous result of the same patient. Differently, when the result is interpreted in comparison with a clinical decision level that does not take into account the different diagnostic system used, the inclusion of the bias in the MU formula is important (14).

Verification of examination procedures

The ISO 15189:2012 (5.5.1.2) states that »*the laboratory shall confirm, through obtaining objective evidence (in the form of performance characteristics) that the performance claims for the examination procedure have been met. The performance claims for the examination procedure confirmed during the verification process shall be those relevant to the intended use of the examination results*« (1).

The verification of EP is therefore required for those validated by manufacturers according to the IVD Medical Device Directive 98/79/EC (18). The final aim is to guarantee that the EP validated by a manufacturer, when implemented in a specific laboratory, at least achieve the performances claimed by the manufacturer. The verification of all performance characteristics of EP (e.g. measurement trueness, measurement accuracy, measurement precision; measurement uncertainty, analytical specificity, analytical sensitivity, detection limit and quantitation limit, measuring interval, diagnostic specificity and diagnostic sensitivity), for all tests provided by a laboratory, requires additional work and increased costs (19, 20).

A pragmatic approach reported in literature is based on the awareness that, when a laboratory undertakes the accreditation process, it keeps under control their results using different quality tools (e.g. internal quality control, external quality assessment scheme) for a long time (21). Therefore, two operative flow charts can be identified: one to be applied on the EP just in use (for example, at least since two years) and another for newly introduced EP. Moreover, as the ISO 15189 does not specify what performance characteristics have to be verified and how to do this, they can be chosen on the basis of the intended use of the EP. The verification »at least« of the trueness and precision using CQI and EQA data, for EP used in a laboratory since two years making the theory applicable, satisfies the ISO 15189 requirement.

Differently, the approach for newly introduced EP shall be based on more stringent quality requirements. As there are many manufacturers selling IVD products without declaring all the analytical performances, it is important, from now on, that in the purchasing procedures a laboratory requires the declaration of all analytical performances and metrological traceability of EP. The new introduction of EP has to be provided with accurate information by the manufacturer and the laboratory has to achieve the performances claimed by the manufacturer by a more rigorous verification concerning the number of performance characteristics verified and the procedures used to do it. Open issue concerns what criteria have to be adopted when the manufacturer's performances are not achieved. The comparison of obtained data with the goals based on the hierarchical structure established in the Milan Conference on Performance Specifications and test purpose can be considered a suitable criterion to be applied (22).

Quality indicators management

The ISO 15189 requires the use of QIs but it doesn't specify which and how indicators are to be used. Moreover, it requires to:

– establish quality indicators concerning the pre-, intra- and post-analytical phase;

– define goals, method, interpretation, limits, action plans, measurement times in order to assure a monitoring process;

– ensure their continued appropriateness through periodic reviews.

In order to guarantee an effective management system of QIs, complying with the ISO 15189, implementation of an internal assessment system and participation in inter-laboratory comparison have to be included. A well-designed internal assessment system allows the identification of critical activities and their systematic monitoring, guaranteeing appropriate definition and utilization of QIs that successfully raise awareness among the laboratory staff concerning the need to undertake an improvement process. The active participation in inter-laboratory comparison provides information on the performance level of one laboratory compared with that of other participating laboratories. The laboratory can verify how its performance level, measured by its internal assessment system, compares with that of other laboratories using the same QIs (23).

An inter-laboratory comparison for QIs is proposed by the Working Group »Laboratory Errors and Patient Safety« (WG-LEPS) of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) that has been described in numerous papers (24–26). The program of the IFCC WG-LEPS is based on a consensual list of QIs that are used by laboratories at international levels, assuring an ever more significant identification of State-of-the-Art, promoting the reduction of errors and improving laboratory performances.

An effectiveness QIs system assures the reduction of the error rate and patient safety.

Conclusion

The ISO 15189 is the standard of choice for the accreditation of medical laboratories that recognises »world-class quality« and the application of a rigorous process of quality assurance. The ISO 15189 accreditation improves the accountability of the staff and gives the public confidence that the service will catch mistakes before they affect patient care. A pragmatic approach based on the awareness that the staff have achieved a high level of competence is needed in order to promote the use of ISO 15189 in medical laboratories and to define suitable and user-friendly operating procedures.

Conflict of interest statement

The authors stated that they have no conflicts of interest regarding the publication of this article.

References

1. International Organization for Standardization (ISO). Medical laboratories – Particular requirements for quality and competence. ISO 15189:2012.
2. Plebani M, Sciacovelli L, Chiozza ML, Panteghini M. Once upon a time: a tale of ISO 15189 accreditation. Clin Chem Lab Med 2015; 53(8): 1127–9.
3. Thelen MHM, Vanstapel FJLA, Kroupis C, Vukasovic I, Bousier G, Barrett E, et al. Flexible scope for ISO 15189 accreditation: a guidance preparated by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group Accreditation and ISO/CEN standards (WG-A/IAO). Clin Chem Lab Med 2015; 53: 1173–80.
4. International Organization for Standardization (ISO). General requirements for the competence of testing and calibration laboratories. ISO 17025:2005.
5. International Organization for Standardization (ISO). Quality Management System – Requirements. ISO 9001: 2008.
6. Jansen RT, Blaton V, Burnett D, Huisman W, Queralto JM, Allman B. European Communities Confederation of Clinical Chemistry: essential criteria for quality systems of medical laboratories. Working Group on Harmonisation of Quality systems and Accreditation. Eur J Clin Chem Clin Biochem 1997; 35(2): 123–32.
7. European Accreditation. EA Requirements for accreditation of Flexible Scopes. EA-2/15 M:2008.
8. Regulation (EC) No 756/2008 of European Parliament and of Council. 9 July 2008. Setting out requirements for Accreditation and market surveillance relating to the marketing of products and repealing Regulation (EEC) No 339/93. Official Journal of The European Union, 13-08-2008.
9. JCGM 100:2008. Evaluation of measurement data – Guide to the expression of uncertainty in measurement, with minor corrections (GUM). Available at: www.bipm.org. Accessed: Sept 2016.
10. Matar G, Poggi B, Meley R, Bon C, Chardon L, Chikh K, et al. Uncertainty in measurement for 43 biochemistry, immunoassay, and hemostasis routine analytes evaluated by a method using only external quality assessment data. Clin Chem Lab Med 2015; 53: 1725–36.

11. Nordic Innovation. Handbook for calculation of Measurement Uncertainty in Environmental Laboratories. NT TR 537 – Edition 3.1, 2012. Available at: www.nordtest.info. Accessed: Sept 2016.

12. Guide to the evaluation of measurement uncertainty for quantitative test results. Technical Committee for Quality Assurance in Testing (TCQA). EUROLAB Technical Report No. 1/2006.

13. Quantifying Uncertainty in Analytical Measurement. Eurachem/CITAC Guide CG 4. Third Edition. Available at: www.eurachem.org. Accessed: Nov 2016.

14. Padoan A, Antonelli G, Aita A, Sciacovelli L, Plebani M. An approach for estimating measurement uncertainty in medical laboratories using data from long-term quality control and external quality assessment schemes. Clin Chem Lab Med. 2017 Feb 28. pii: /j/cclm.ahead-of-print/cclm-2016-0896/cclm-2016-0896.xml. doi: 10.1515/cclm-2016-0896. [Epub ahead of print] PubMed PMID: 28245184.

15. Jones DGR. Measurement uncertainty for clinical laboratories – a revision of the concept. Clin Chem Lab Med 2016; 54: 1303–7.

16. Farrance I, Badrick T, Sikaris KA. Uncertainty in measurement and total error – are they so incompatible? Clin Chem Lab Med 2016; 54: 1309–11.

17. Tate JR, Plebani M. Measurement uncertainty – a revised understanding of its calculation and use. Clin Chem Lab Med 2016; 54: 1277–9.

18. EU Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices (1998). www.europa.eu/legislation_summaries/ internal_market/single_market_for_goods/ technical_harmonisation/l21010c_en.htm.

19. Theodorson E. Quality assurance in clinical chemistry: a touch of statistics and a lot of common sense. J Med Biochem 2016; 35: 103–12.

20. Braga F, Infusino I, Panteghini M. Role and responsibilities of laboratory medicine specialists in the verification of metrological traceability of in vitro medical diagnostics. J Med Biochem 2015; 34: 282–7.

21. Antonelli G, Padoan A, Aita A, Sciacovelli L, Plebani M. Verification of examination procedures in clinical laboratory for imprecision, trueness and diagnostic accuracy according to ISO 15189:2012: a pragmatic approach. Clin Chem Lab Med. 2017 Feb 21. pii:/j/cclm.ahead-of-print/cclm-2016-0894/cclm-2016-0894.xml. doi: 10.1515cclm-2016-0894. [Epub ahead of print].

22. Sandberg S, Fraser CG, Horvath AR, Jansen R, Jones G, Oosterhuis W, et al. Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine. Clin Chem Lab Med 2015; 53: 833–5.

23. Sciacovelli L, Aita A, Plebani M. Extra-analytical quality indicators and laboratory performances. Clin Biochem 2017; 50: 632–7.

24. Plebani M, Astion ML, Barth JH, Chen W, de Oliveira Galoro CA, Escuer MI, Ivanov A, Miller WG, Petinos P, Sciacovelli Shcolnik LW, Simundic AM, Sumarac Z. Harmonization of quality indicators in laboratory medicine. A preliminary consensus. Clin Chem Lab Med 2014; 52: 951–8.

25. Plebani M, Aita A, Sciacovelli L. Quality Indicators for the Total Testing Process. Clin Lab Med 2017; 37: 187–205.

26. Sciacovelli L, Lippi G, Sumarac Z, West J, Garcia Del Pino Castro I, Furtado Vieira K, Ivanov A, Plebani M; Working Group »Laboratory Errors and Patient Safety« of International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). Quality Indicators in Laboratory Medicine: the status of the progress of IFCC Working Group »Laboratory Errors and Patient Safety« project. Clin Chem Lab Med 2017; 55: 348–57.

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