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Review

Accreditation in autoimmune diagnostic laboratories. A position paper of the European Autoimmunity Standardisation Initiative (EASI)

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ABSTRACT

Reliable autoantibody detection is important for early diagnosis and appropriate treatment of autoimmune disorders. However, in contrast to testing for classical clinical chemistry analytes, autoantibody testing is complex and evolving. Moreover, there is a lack of standardization. Nevertheless, it is important that laboratories that provide autoimmune tests comply with the requirements set forward by general international accreditation bodies. In the present manuscript, an ad hoc committee of the European Autoimmunity Standardisation Initiative (EASI) group provides background information on accreditation and identifies the minimum requirements needed to set up an accredited autoimmunity lab and to ensure that high-quality results are provided (in terms of personnel, procedures, validation, quality control, and reporting). Areas in which additional work needs to be done are identified.

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1. Introduction

Detection of autoantibodies is a well-established part of the routine repertoire in most clinical diagnostic laboratories. However, in contrast to many other laboratory methods, autoantibody diagnostics, due to its high complexity, has not yet been standardized to the same level as many other laboratory procedures. In recent years, several ISO standards have been introduced. ISO 15189 [developed for medical laboratories from the ISO/IEC 17025 standard] and ISO/IEC 17043 [developed for providers of external quality assessment (EQA or proficiency testing (PT)) programmes] aim to facilitate parity in accreditation processes, and thus ensure that accredited laboratories in different geographical regions operate in a similar manner and provide similar levels of service. However, passing an accreditation process is

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still a real challenge and involves an enormous amount of work and effort by all staff involved.

The present document, prepared by an ad hoc committee of the European Autoimmunity Standardisation Initiative (EASI) group, provides background information on accreditation and identifies the minimum requirements needed to set up an accredited autoimmunity lab, either dedicated only to autoimmune diagnostics or integrated in a general clinical lab. The objective of this document is to define the organizational model and the resources and expertise required for a specialized autoimmunity lab in order to ensure that high-quality results are provided. It also identifies the areas in which additional work needs to be done to further enhance the overall quality of autoimmune testing.

2. What is accreditation?

Accreditation, "a third-party recognition of competence to perform specific tasks", attests that a laboratory has been successful in meeting the requirements of international accreditation standards [1]. For medical laboratories, it confirms the successful implementation of elements of a comprehensive quality management system according to ISO 15189:2012 [2]. The standard ISO 15189 "Medical laboratories—Requirements for quality and competence" was first published in 2003 by the International Organization of Standardization and is the first internationally accepted set of requirements specifically designed for the medical laboratory [2,3].

Autoimmune diagnostics is usually placed within an accredited clinical sector, commonly immunology. However, ISO 15189 does not include any specific standards or criteria for autoantibody testing.

Quality should cover all aspects for clinical laboratory service. Accreditation should demonstrate that the methods and techniques employed are used in the proper application, respond to the requirements for patient care, and that the laboratory is fully competent in the specific methods. Besides, accreditation also helps to improve laboratory management by providing a better understanding of the laboratory structures and processes in order to achieve a consistently high level of quality. It helps to reduce the risk of failure and enhances confidence from patients, physicians, hospitals, and contract partners. It is assumed that accredited laboratories produce accurate and reproducible results. Furthermore, by clarifying and formalizing its procedures, the laboratory will also improve its governance, process transparency, diagnostic support and, importantly, overall diagnostic quality [3]. So, risks and incertitude due to the daily practice of a diagnostic laboratory can be better controlled and routine can be improved by the accreditation process. Accreditation impels the tracking of samples, reagents, and processes, and keeps records allowing retrospective enquiry from the pre-analytical to the post-analytical phases.

ISO 15189 requirements go far beyond the typical quality assessment (QA) measures in the analytical phase of medical laboratory analysis. The standard includes criteria for the examination of management competence and impartiality, review of contracts, competency of personnel as result of qualification, training, compliance evaluation, advisory services, competency assessment and professional development, environmental conditions, laboratory equipment, the pre-examination phase, examination procedures, and the post-examination phase including reporting of results. The aim of accreditation according to ISO 15189 is to provide assurance, reliability, and reproducibility of test results for patients and laboratory staff independent of location. It is a generic standard designed to be applied to any clinical laboratory irrespective of the offered medical laboratory disciplines or tests.

Essentially, ISO 15189 is divided into two distinct areas: management and technical. The former explains the general principles that need to be applied by laboratory management with specific emphasis on the quality management system, education, and training. The technical section covers every stage of laboratory work ranging from system implementation and selection to participation in external quality assessment (EQA) programmes; particularly emphasizing that participation in ISO/IEC 17043-accredited EQA programmes is recommended.

For each test undertaken, the laboratory should have a written policy to identify and define potential errors and risks so that these are dealt with in an appropriate and timely fashion. Therefore, these standards are designed to ensure that every clinical laboratory, irrespective of geographical location, has a prescribed and agreed set of protocols. Exactly how these standards are implemented is the responsibility of each laboratory, provided that there is documented and auditable evidence for standard compliance. For example, ISO 15189 does not state how to implement or write a quality management system (QMS) or standard operating procedures (SOP), but it does define the minimum criteria expected for such documents and that they must be in place to achieve accreditation: in essence, write down exactly what you do, do what is written, and document that you have done it. The accreditation procedure therefore helps formalize the process.

3. National implementation

Whilst ISO 15189 is not compulsory across the EU, countries such as France, Germany, Italy, Spain, and the United Kingdom have driven the adoption of accreditation via professional bodies, societies, and customers. Overall, the ISO 15189 accreditation project has been widely accepted in Europe [4]. As stated earlier, ISO 15189 is not test- or technique-specific and therefore autoimmune diagnostics is usually accredited within the process of the department where it resides. Today, more and more laboratories analysing autoantibodies are in the process of accreditation.

4. Further guidelines

Besides accreditation, various systems have been established with the same purpose, but under different basic conditions. These approaches do not replace accreditation and are independent of it, despite parallels in the underlying quality management approaches.

Some pathology disciplines have established expert groups to identify areas where guidelines are required and recommend the application of relevant national/international guidelines. There are also many peer-reviewed guidelines and professional development courses in this field. They help laboratory scientists by giving advice, explaining guidelines, and offering blueprints. This will contribute to harmonization and quality improvement of autoantibody laboratories [5–14].

The College of American Pathologists (CAP) accreditation programme (http://www.cap.org) differs from ISO 15189 requirements. Laboratories that achieved ISO 15189 accreditation fulfill the requirements to participate in US-driven clinical trials applying for FDA approval. A comparison between ISO 15189 accreditation and FDA rules is described by Kramer et al. [15].

5. Steps to follow when undergoing accreditation

Accreditation is a continuous process, starting after adequate structures and processes have been established and ongoing after the first assessment. Accreditation bodies offer support and information, such as interview forms, checklists, or recommendations to smooth the process. Besides, consensus documents and guidelines do exist specifically for autoantibody analysis, such as the international recommendations for anti-nuclear antibody testing from EASI [6] and from the American College of Rheumatologists (ACR) [7].

Organization requirements for autoimmunity laboratories do not differ from those required of any clinical laboratory service, and include arrangements for patient identification, collection of samples, transportation, storage, processing and examination of clinical samples with subsequent validation, interpretation, reporting, and advice, as well as