
Lab Guidelines & Standards

Setting the Bar for Quality: Improving IgE Antibody Assay Performance and Clinical Utility

Updated CLSI Guideline Valuable for Clinicians, Laboratorians, Regulators, and Manufacturers

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It's Monday morning, the laboratory is buzzing with activity, and a staff member approaches you with three requisitions from three different doctors. One wants a W1 IgE antibody assay, one needs a "common ragweed" test, and a third wants to know about allergy-specific testing for *Ambrosia artemisiifolia*. If you have the new CLSI guideline, you already know these are the same test. In fact, you have the optimal commercial assay set up and running!

The Clinical and Laboratory Standards Institute (CLSI) recently updated the document *Analytical Performance Characteristics and Clinical Utility of Immunological Assays for Human Immunoglobulin E (IgE) Antibodies and Defined Allergen Specificities; Approved Guideline—Second Edition (I/LA20-A2)*.¹ This update will prove useful to several groups, including clinicians who order and interpret the results of human IgE antibodies of defined allergen specificity, laboratory professionals who use commercial kits or design their own procedures for these measurements, laboratory regulators and inspectors, and manufacturers of IgE antibody reagents and assay kits.

This new edition provides updated information about the design, analytical performance, standardization, quality assurance, and clinical application of laboratory assays used in the measurement of human IgE antibodies of defined allergen specificity. "An important aspect of I/LA20-A2 is that it is the second and significantly revised version of the guideline," explained Per N. J. Matsson, PhD, chairholder of the CLSI Subcommittee on Diagnostic Allergy Techniques that revised the original guideline. "This document not only clearly summarizes the clinical value of specific IgE testing but also [shows that] specific IgE testing now can be used in the routine clinical work as a reliable immunoassay test methodology."

Laboratory testing of total IgE and allergen-specific IgE has been performed for more than 40 years, with steady gains seen in analytical sensitivity, quantitation, and reproducibility of assay methods. Automation, together with widely adopted calibration methods traceable to an international IgE reference preparation, has led to enhanced interlaboratory standardization. However, the rapid increase in the number of allergen specificities available in commercial IgE antibody kits has been accompanied by redundant and often conflicting coding schemes for allergen nomenclature.

As a result, you probably have noticed many different ways that clinicians order these tests, and our hypothetical Monday morning query is probably an all-too-common event.

I/LA20 represents a major attempt at harmonization of allergen codes used by manufacturers of allergen-specific IgE antibody assays throughout the world. (Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve uniformity.) CLSI, as a global leader in establishing and promoting laboratory best practices, is firmly committed to achieving global harmonization wherever possible.

I/LA20 defines performance criteria and explains current ways to qualify component reagents and immunoassay systems of total IgE and IgE antibody of defined allergen specificities. The document also explains why different assays may not produce comparable results.

What Makes the new I/LA20 Valuable?

As a laboratory professional, you know how much work is required not only to select and set up optimal IgE antibody assays for allergens but also to maintain a high degree of quality in every assay performed. I/LA20 presents practical information that relates to the specimen, reagent validation, and assay calibration. The document describes interlaboratory proficiency testing requirements and provides practical quality control measures that will help laboratories and manufacturers achieve valid, reproducible results. "The second edition of the I/LA20 guideline is a 'must have' document for clinicians (especially allergists), laboratorians, and regulators who need to know about the quality and reliability of IgE antibody measurements that are performed in diagnostic allergy laboratories," stated Robert G. Hamilton, PhD, D.ABMLI, vice-chairholder of the committee that developed the document. "It serves as a reference guide for available allergen specificities and the assay systems in which they can be measured."

Dr. Matsson emphasized the fact that I/LA20 will help laboratory professionals with the difficult challenge of selecting the right testing methodology from the large number of available reagents and kits. "This guideline is useful in the laboratory [because it] allows the evaluation of different technologies using the same evaluation criteria. This is important because there is a range of different test technologies for specific IgE testing, and the technologies have different prices, measuring ranges, reproducibility, and other features. Using the guideline, it becomes easy to set up the analysis of which technology to select," he explained.

He also pointed out that I/LA20 gives laboratory professionals excellent advice on how to determine if a test is qualitative, semiquantitative, or quantitative, something that is essential for many clinical uses of the test results. "Today, many physicians have realized that the [certain quantitative testing] technologies may guide them [in determining whether] an allergen challenge is required or not. In addition, a patient may be continuously monitored by using a quantitative test," said Dr. Matsson.

He added, “The guideline may also be used for the continuous education of laboratory personnel in order to train individuals in the ‘art’ of specific IgE analysis as well as how to keep the processes and routines up to date.”

Enhancing the Quality and Uniformity of IgE Antibody Measurements Worldwide

Laboratory professionals also want to help ensure that clinicians will get the same result for an analyte no matter where that assay is performed. Through this document, the committee members hope to improve the quality and uniformity of IgE antibody measurements performed in clinical laboratories worldwide. To this end, I/LA20 includes the latest information on an extensive list of common and rare allergens implicated in the development of allergic diseases. Several hundred substances, from both indoor and outdoor environments, have been linked to the induction of allergic responses in previously sensitized persons.

I/LA20 includes a glossary (Appendix A) of all currently available allergen specificities with their Latin and common names and an assignment of whether the allergy specificity is well documented, poorly defined, or totally undefined based on peer-reviewed literature. This glossary also includes an assay descriptor so that readers know which type of analytical system is used; these include thread-based, disc-based, sponge-based, biotin allergen-based, and chip-based systems. Dr. Hamilton indicated why this information is so helpful: “For the laboratorian, Appendix A is invaluable in providing a comprehensive update on which IgE specificities are available with which assay methods. This is used by all laboratory staff to determine if a particular IgE antibody specificity can be tested or even if it is a valid assay. This will save countless hours calling the manufacturers to ask, ‘Do you offer reagents to perform an IgE assay to ABC allergen?’”

I/LA20 also presents extensive guidance on optimal methods of quality control. Dr. Hamilton underscored the usefulness of this information, stating, “[For] the regulator or inspector of laboratories, [I/LA20] provides unique, concise guidance on the important issues in assay design and quality control. It shows the manufacturers what they need to achieve in terms of quality performance. It shows the inspectors who have no direct knowledge of allergy laboratories what they should ask for in an inspection of the laboratory for licensure.”

The revised document also provides the clinical laboratory and all diagnostic kit manufacturers with benchmark targets for the validation and improvement of IgE antibody assays. These include evaluation criteria and minimal performance targets for the assays, as well as additional specific recommendations directed at reagent and assay kit manufacturers. Dr. Hamilton stressed, “The recommendations sections are important in the clinical setting for laboratorians, regulators, and manufacturers.”

Summary

With the hectic pace in today’s laboratories, I/LA20 is an important tool to reduce frustration in deciphering requests for IgE antibody tests. However, this revised guideline offers much

Updates in I/LA20-A2

- ❖ Expanded glossary of harmonized terms related to IgE antibody assays.
- ❖ Discussion of clinical application and quality assurance of IgE antibody assay measurements.
- ❖ Overview of causes for differences in reported IgE antibody levels among the various commercially available assay methods.
- ❖ Glossary of all currently available allergen specificities with
 - their Latin and common names;
 - indication of the assay method that provides that specificity of IgE antibody analysis; and
 - assignment of whether the allergy specificity is well documented, poorly defined, or totally undefined based on peer-reviewed literature.

more information and practical guidance than just a clarification of confusing allergen nomenclature. I/LA20 provides updated information about virtually every aspect of the optimal design and analytical and clinical performance of laboratory assays that measure human IgE antibodies of defined allergen specificity. This guideline also represents an important effort at harmonization of definitions, allergen descriptions and codes, proficiency testing survey protocols, and quality assurance methods used by laboratories, clinicians, manufacturers, and regulators worldwide.

The Experts

Per N. J. Matsson, PhD, chairholder, Subcommittee on Diagnostic Allergy Techniques, and advisor, Area Committee on Immunology and Ligand Assay, Phadia AB, Uppsala, Sweden.

Robert G. Hamilton, PhD, D.ABMLI, vice-chairholder, Subcommittee on Diagnostic Allergy Techniques, Johns Hopkins University School of Medicine, Asthma and Allergy Center, Baltimore, MD.

1. CLSI. *Analytical Performance Characteristics and Clinical Utility of Immunological Assays for Human Immunoglobulin E (IgE) Antibodies and Defined Allergen Specificities; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

Mary E. King, PhD, DABCC, is sole proprietor of Medical & Scientific Communications, a freelance medical writing business based in Boulder, CO.

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