I/LA20

Analytical Performance Characteristics, Quality Assurance, and Clinical Utility of Immunological Assays for Human Immunoglobulin E Antibodies of Defined Allergen Specificities

This report provides guidance for the design, analytical performance, standardization, quality assurance, and clinical application of laboratory assays used in the measurement of human immunoglobulin E antibodies of defined allergen specificity.

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Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: +1.610.688.0100
F: +1.610.688.0700
www.clsi.org
standard@clsi.org
Analytical Performance Characteristics, Quality Assurance, and Clinical Utility of Immunological Assays for Human Immunoglobulin E Antibodies of Defined Allergen Specificities

Robert G. Hamilton, PhD, D.ABMLI
Per N. J. Matsson, PhD
Franklin Adkinson, Jr., MD
Sic Chan, PhD
Debra Hovance-Burns, PhD
Jörg Kleine-Tebbe, MD
Carina Magnusson, PhD
Harald Renz, Prof. Dr.
Mark Van Cleve, PhD

Abstract

Clinical and Laboratory Standards Institute report I/LA20—Analytical Performance Characteristics, Quality Assurance, and Clinical Utility of Immunological Assays for Human Immunoglobulin E Antibodies of Defined Allergen Specificities is written for laboratorians, clinicians, manufacturers, and governmental regulators (inspectors, legislators, reviewers). The report summarizes the current state of immunoglobulin E (IgE) antibody assay technology, routinely tested biological specimens, practical methods for the evaluation of human IgE antibody assay-specific reagents, QA methods, and clinical interpretation of total and allergen-specific IgE antibody results.


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Committee Membership

Document Development Committee on Diagnostic Allergy Techniques

Robert G. Hamilton, PhD, D.ABMLI
Co-Chairholder
Johns Hopkins Medical Institutions
USA

Per N. J. Matsson, PhD
Co-Chairholder
Phadia AB
Sweden

Debra Hovanec-Burns, PhD
Siemens Healthcare Diagnostics, Inc.
USA

Sic Chan, PhD
FDA Center for Devices and Radiological Health
USA

Jörg Kleine-Tebbe, MD
Allergy & Asthma Center Westend
Germany

Staff

Clinical and Laboratory Standards Institute
USA

Megan L. Tertel, MA, ELS
Editorial Manager

Laura Martin
Editor

Jennifer K. Adams, MT(ASCP), MSHA
Project Manager

Joanne P. Christopher, MA, ELS
Editor

Michael A. Russell, MA
Editor

Acknowledgment

CLSI and the Document Development Committee on Diagnostic Allergy Techniques gratefully acknowledge the following volunteers for their important contributions to the development of this report:

Mark Van Cleve, PhD
Hycor Biomedical, Inc.
USA

Harald Renz, Prof. Dr.
University Hospital Giessen and Marburg GmbH
Germany

Carina Magnusson, PhD
Phadia AB
Sweden

Franklin Adkinson, Jr., MD
Johns Hopkins University
USA
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Foreword

Allergen molecule–based IgE antibody results supplement allergen extract–based analyses. They lower the allergen-specific immunoglobulin E (IgE) assay’s lower limit of quantitation and increase the analytical specificity (selectivity) and thus permit more effective assessment of cross-reactivity and risk assessment in support of a clinical history–based diagnosis of allergic disease.

This report provides the laboratorian or clinician with practical information on the appropriate specimen type, reagent validation algorithms, assay calibration and QC strategies, intra- and interlaboratory QA plans, and an overview of the clinical utility of IgE antibody measurements. It emphasizes that the presence of IgE antibody is strictly a biomarker for allergic sensitization. Furthermore, allergic sensitization is a risk factor but not equivalent to the definitive diagnosis of allergic disease in humans, which also requires a positive clinical history. I/LA20 also clarifies that in commercially available allergen-containing reagents, the user does not need to repeat the extensive validation testing that includes verification of specificity that has been performed by the manufacturer. An extensive well-documented serum bank is required for frequent repetitive testing of new lots of IgE antibody reagents provided by the manufacturer. Once validated and released to the user, this testing need not be repeated to successfully use the reagent in the user’s IgE antibody autoanalyzer on which the performance of reagents has been evaluated.

Additionally, this report was written to create operationally achievable procedures that can be used by assay manufacturers to validate the quality and test the performance of the allergenic extracts and individual molecular allergens that are used as reagents in the different assay systems. This revision discusses in detail the increasing availability of allergenic molecules as assay reagents and represents a continuing effort by users, manufacturers, and regulators to promote harmonization of allergen codes, QC procedures, and licensing guidelines for allergen-specific IgE antibody assays.

Finally, this report aims to create procedures that can be used by investigators in clinical laboratories to ensure maximal quality of reported IgE antibody results. Regulators are encouraged to view the IgE antibody autoanalyzers in clinical use as single systems into which individual allergen reagents are added as they are identified as clinically important and qualified by evidence-based data.

Overview of Changes

Immunological assays for IgE antibodies of defined specificity continue to manifest improved performance. Previous editions of I/LA20 provided a framework from which IgE assay reagent validation and QC, assay calibration, and QA have been defined. This report has been updated to serve as a more comprehensive resource for laboratorians/clinicians), manufacturers, and governmental regulators (inspectors, legislators, reviewers). The primary goal of this report is to foster harmonization and enhance the quality of IgE antibody measurements that are performed in diagnostic immunology laboratories throughout the world. As such, this report expands upon the technical and clinical utility issues covered in the first two editions. It also includes an examination of allergenic molecules used in molecular-based allergy diagnosis.

Harmonization of definitions, proficiency testing survey protocols, and QA methods have been updated. With this report, diagnostic kit manufacturers are given fundamental benchmark targets that can be used for the validation and performance improvement of IgE antibody assays. Useful strategies for assessing the quality of IgE reagents and the clearance of IgE antibody assays for use in licensed diagnostic allergy laboratories are provided for regulators and inspectors. This report incorporates the most current evidence-based information related to IgE antibody analyses.

NOTE: The content of this report is supported by the CLSI consensus process, and does not necessarily reflect the views of any single individual or organization.
Key Words

Allergen, allergy, assay methods, clinical utility, human IgE, IgE antibody, molecular allergens, molecule-based allergy diagnosis, performance, quality assurance, total IgE, type 1 hypersensitivity
Chapter 1: Introduction

This chapter includes:

- Report’s scope and applicable exclusions
- Background information pertinent to the report’s content
- Standard precautions information
- “Note on Terminology” that highlights particular use and/or variation in use of terms and/or definitions
- Terms and definitions used in the report
- Abbreviations and acronyms used in the report

1.1 Scope

This report defines the current state of reagents and serological assay technology used to measure total immunoglobulin E (IgE) and IgE antibodies of defined allergen specificities in human blood. This report focuses on IgE assay design and calibration, validation methods, QA of assay reagents, QC strategies, and clinical applications.

The report is designed as a general reference for laboratorians, clinicians, manufacturers, and governmental regulators (inspectors, legislators, reviewers). It provides consensus on the current state of assay technology, the appropriate biological specimens that are routinely tested, practical methods for the validation of allergen and immunological reagents, diagnostic allergy laboratory QC strategies, consensus guidelines for clearance of allergen-containing reagents by governmental regulatory agencies, and a brief examination of the clinical interpretation of IgE antibody results. It also emphasizes achievable qualification practices that have been used by manufacturers to validate the quality and test the performance of reagents and configured assay systems. Once validated by the manufacturer, additional new lot specificity testing of allergen-containing reagents purchased by the user for one of the IgE antibody autoanalyzers does not need to be repeated. I/LA20 outlines strategies and procedures that have been successfully used by clinical laboratory workers to supplement manufacturer testing and QC practices with the goal of optimizing the laboratory’s overall QA program. In addition, this report serves as a resource for inspectors and regulators who are involved in qualifying diagnostic reagents and assays and clinical immunology laboratories that perform IgE analyses.

1.2 Background

As early as 1921, investigators showed that local itching and swelling that were surrounded by a zone of erythema occurred when serum from an allergic person was injected intradermally into an unsensitized (nonallergic) person, followed 24 hours later by the injection of specific allergen into the same skin site. This passively transferred allergic or Prausnitz-Küstner reaction maximized within 10 minutes, persisted...