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1st Edition

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# CLSI EP49™

## Framework for Developing Evidence of Clinical Validity of Medical Laboratory Test Methods

Sample

CLSI EP49 provides a framework for establishing evidence of a medical laboratory test method's clinical validity, with a focus on designing clinical performance studies and key measures of clinical performance.

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A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

# Framework for Developing Evidence of Clinical Validity of Medical Laboratory Test Methods

Michelle R. Campbell, MS, MLS(ASCP)<sup>CM</sup>, MB<sup>CM</sup>, SC<sup>CM</sup>  
Natalya Benina, MS  
Romiyi Barry, PhD  
J. Rex Astles, PhD, FADLM  
Marvin Berman, PhD  
Kate L. DeRosa, PhD, MA  
Mark Kellogg, MLS(ASCP), PhD, DABCC

Marina V. Kondratovich, PhD  
Dana Li, MD, PhD  
Kristen Meier, PhD  
Aimee Tan  
Aleksi Tikhonov, PhD, MS  
Brigit Quinn, MS  
Min Yu, MD, PhD, MBA

## Abstract

CLSI EP49, *Framework for Developing Evidence of Clinical Validity of Medical Laboratory Test Methods* provides test developers (both manufacturers and laboratories that create laboratory-developed tests) with a framework for establishing evidence of clinical validity for a medical laboratory test method. Clinical validation is defined and discussed in the context of clinical utility and analytical validation during the establishment of a test method. CLSI EP49 focuses on evaluating clinical validity through a clinical performance study, comparing a candidate test method with a comparator for assessing a target condition based on the test method's intended use. Purposes and categories of tests are described along with measures of a test method's clinical performance. Considerations are outlined for components of a study protocol and clinical performance study report, as well as for monitoring clinical validity postlaunch.

Additional topics discussed in CLSI EP49 include obtaining samples for clinical performance studies, use of real-world data, potential biases in subject selection, and ethical considerations.

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# Contents

Abstract	i
Committee Membership	iii
Foreword	vii
<b>Chapter 1: Introduction</b>	<b>1</b>
1.1 Scope	2
1.2 Background	2
1.3 Standard Precautions	2
1.4 Terminology	3
<b>Chapter 2: Clinical Validation</b>	<b>9</b>
2.1 Defining Clinical Validation	10
2.2 Clinical Utility Compared With Clinical Validity	12
2.3 Relationship Between Analytical Accuracy and Clinical Validity	13
<b>Chapter 3: Evaluating Clinical Validity</b>	<b>15</b>
3.1 Defining a Target Condition	16
3.2 Intended Use	16
3.3 Design Considerations for the Study Protocol for the Evaluation of Clinical Validity	19
3.4 Categories of Tests	26
3.5 Measures of Clinical Performance	31
3.6 Analyzing the Data	35
3.7 Clinical Performance Study Report	38
3.8 Postlaunch Monitoring of Clinical Validity	40
<b>Chapter 4: Conclusion</b>	<b>41</b>
<b>Chapter 5: Supplemental Information</b>	<b>43</b>
<b>References</b>	<b>44</b>
<b>Appendix A. Uninformative Test Methods</b>	<b>51</b>
<b>Appendix B. Considerations for Specific Categories of Tests</b>	<b>56</b>
<b>Appendix C. Equations for Measures of Clinical Performance</b>	<b>58</b>
<b>Appendix D. Sample Accounting Example</b>	<b>61</b>
<b>The Quality Management System Approach</b>	<b>64</b>

## Foreword

Developers of *in vitro* diagnostic test methods, whether manufacturers or laboratories that create laboratory-developed tests, should evaluate the clinical validity of medical laboratory test methods before they are used in patient care to support clinical decision-making. Clinical performance studies aim to establish evidence that the test method can accurately and reliably identify the presence or absence of a disease or condition according to its intended use. Clinical validation complements analytical validation as an essential component of the Establishment Stage of the Test Life Phases Model (see Figure 1). Expectations for clinical performance should be established based on the intended use of the test method, which stems from the clinical need. See CLSI EP19<sup>1</sup> for additional information on the Test Life Phases Model.

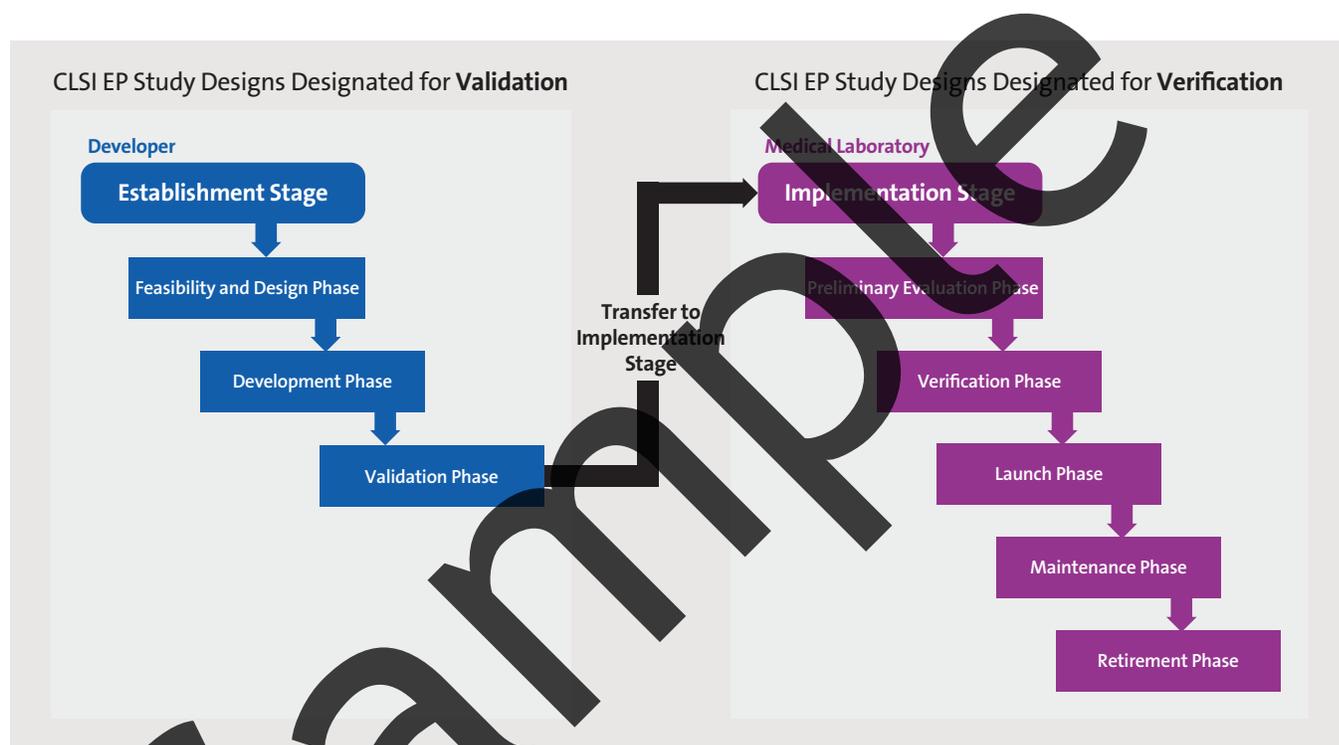


Figure 1. CLSI EP19<sup>1</sup> Test Life Phases Model

**NOTE:** The content of CLSI EP49 is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

### KEY WORDS

clinical performance

clinical sensitivity

clinical specificity

clinical validation

clinical validity

intended use

# Chapter 1

## Introduction

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# Framework for Developing Evidence of Clinical Validity of Medical Laboratory Test Methods

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## 1 Introduction

### 1.1 Scope

CLSI EP49 provides a framework to aid test developers (both manufacturers and laboratories that create laboratory-developed tests [LDTs]) in establishing evidence of clinical validity for medical laboratory test methods using noninterventional clinical performance studies. Examples of measures of clinical performance to support a test method's clinical validity are provided, as well as considerations for the design of clinical performance studies, based on the test's purpose. Categories of tests covered include qualitative, quantitative, semiquantitative, and multianalyte assays with algorithmic analysis. Lastly, general considerations for preparing study protocols and reporting results from clinical performance studies are provided.

CLSI EP49 does not include a step-by-step protocol for studies to establish evidence of clinical validity and is not a substitute for consultation with the test developer's applicable regulatory authority when studies or other methods are designed for demonstrating a test method's clinical validity. CLSI EP49 does not include in-depth discussions of interventional studies related to clinical validation (ie, clinical performance studies in which results from the test method are used for the clinical management of subjects in the clinical study) or provide guidance for establishing a test method's analytical validity (see CLSI EP19<sup>1</sup>), verifying clinical validity or agreement (see CLSI EP12<sup>2</sup>), or developing evidence for clinical utility.

**NOTE:** Studies performed during clinical validation to support regulatory submissions for a test method might be subject to compliance with human subject protection regulations beyond the scientific quality standards for designing, conducting, recording, and reporting clinical performance studies.

### 1.2 Background

Although the activities performed during the establishment of a medical laboratory test method often focus on determining its analytical performance characteristics, its clinical validity should also be evaluated to assess whether results from the test method are useful for patient evaluation. For a test method to reliably inform clinical decisions and improve patient care, it is essential that it be both analytically and clinically valid.<sup>3</sup> Clinical performance studies assess the clinical validity of a test method by evaluating its ability to correctly classify samples (or subjects) according to the presence or absence of a target condition in alignment with its intended use, where the target condition might include a disease or disease stage, health status, or other clinically relevant characteristic.<sup>3-5</sup>

Guidance is important for establishing evidence of clinical validity for medical laboratory test methods in various applications, such as screening, diagnosis, and prognosis, as well as for test methods that report different types of results (eg, quantitative, qualitative). Test developers can benefit from an overview of key concepts related to clinical performance studies as well as general considerations for establishing a test method's clinical validity.

### 1.3 Standard Precautions

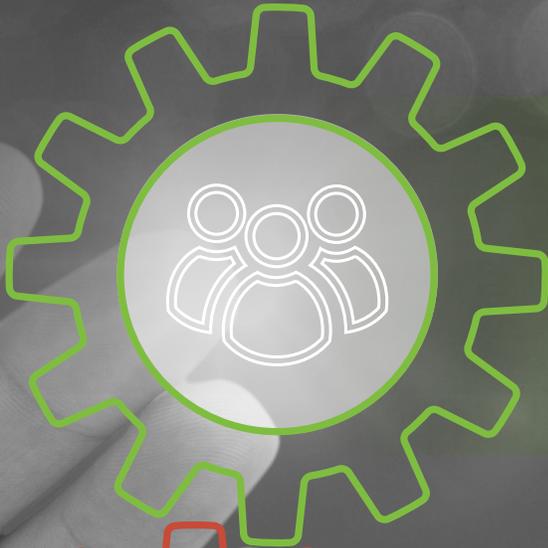
Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are treated as infectious and handled according to "standard precautions." Standard precautions are guidelines that combine the major features of "universal precautions and body substance isolation" practices. Standard precautions cover the transmission of all known infectious agents and thus are more comprehensive

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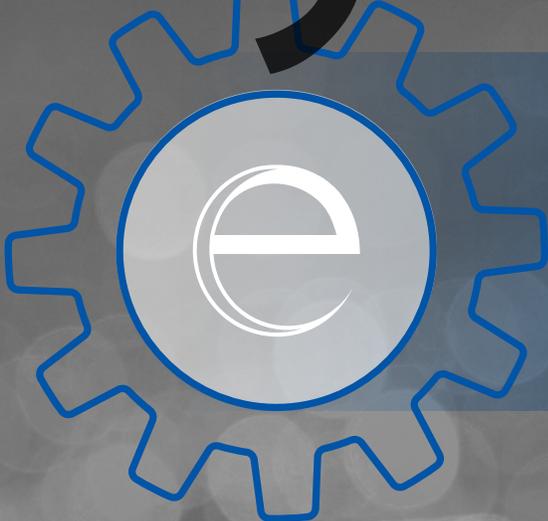
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