CLINICAL AND LABORATORY STANDARDS INSTITUTE®

2nd Edition

CLSI EP35™

Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures

CLSI EP35 provides recommendations for assessing clinically equivalent performance for additional similar-matrix specimen types and suitable performance for dissimilar-matrix specimen types, such that the laboratory does not necessarily need to repeat the full measurement procedure validation for each specimen type. The recommendations in CLSI EP35 apply to both quantitative measurement procedures and qualitative examinations.

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

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Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures

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Abstract

Clinical and Laboratory Standards Institute EP35—*Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures* provides information for assessing clinically equivalent performance for additional similar-matrix specimen types and suitable performance for dissimilar-matrix specimen types. During development, medical laboratory measurement procedures are typically validated for the most common specimen type. However, it can be clinically useful to test the measurand in multiple specimen types, including different fluids (eg, serum, plasma, whole blood, urine, cerebrospinal fluid, saliva), anticoagulants, and collection devices. By following the recommendations in CLSI EP35, developers of laboratory measurement procedures do not necessarily need to repeat the full measurement procedure validation for each specimen type. CLSI EP35 applies to both quantitative measurement procedures and qualitative examinations. CLSI EP35 is useful to developers of commercial and laboratory-developed tests and medical laboratory personnel.

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Contents

Foreword

For measurement procedures whose performance characteristics have previously been validated with a primary specimen type, CLSI EP35 provides recommendations for assessing clinically equivalent performance for other similar-matrix specimen types and suitable performance for dissimilar-matrix specimen types. These assessments provide verification options that do not repeat full measurement procedure validation for the additional specimen types, which include different fluids (eg, serum, plasma, whole blood, urine, cerebrospinal fluid, saliva), anticoagulants (eg, EDTA, citrate, oxalate), and collection devices (eg, gel barrier, plain tube). To date, there is no general guidance on requirements or protocols for demonstrating multiple specimen type equivalence or suitability for use on measurement procedure performance. Multiple sources provide guidance (eg, anticoagulant testing in CLSI EP07,[1] discussion of alternate body fluids in CLSI C49,[2] specimen collection tube evaluation in CLSI GP34[3]), but no CLSI documents provide the information as a cohesive whole. CLSI EP35 provides guidance on verifying clinically equivalent or suitable performance for additional specimen types without necessarily having to repeat the full measurement procedure validation for each specimen type. CLSI EP35 applies to both quantitative measurement procedures and qualitative examinations and is useful to developers of commercial and laboratory-developed tests and medical laboratory personnel.

Because measurement procedure performance characteristics can change when specimen types have substantially different matrix characteristics, evaluation of performance often needs to be based on suitability of the observed performance to the clinical requirements for the specific specimen type matrix rather than strict numerical equivalence. Therefore, access to the necessary clinical information is key to establishing equivalent or suitable performance for multiple specimen types, including the expected interval of measurand concentrations, inherent biological variability, medical decision levels, and any other relevant information for each specimen type. These characteristics can vary considerably between specimen types for the same measurand (eg, creatinine in serum vs urine). Once the necessary clinical information is available, the desirable measurement procedure performance attributes can be characterized for each specimen type based on risk assessment. After the performance requirements are established for each specimen type, the protocols described in CLSI EP35 can be used to document clinically equivalent or suitable performance.

Overview of Changes

CLSI EP35 was revised in 2024 under the Limited Revision Process and replaces the first edition of this guideline, which was published in 2019. Several changes were made in this edition, including:

- Reformatting to help improve readability
- Updating and aligning terminology
- Updating one dataset and figures to include the minimum number of 40 samples

NOTE: The content of CLSI EP35 is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

KEY WORDS

candidate specimen type
clinical equivalence
clinical suitability
equivalence
primary specimen type
specimen type
suitable

Chapter 1

Introduction

Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures

1 Introduction

1.1 Scope

CLSI EP35 provides recommendations on establishing clinical equivalence or suitability for multiple specimen types for a single measurement procedure. This guideline provides a protocol for assessing equivalence or suitability for use of a different specimen type compared with the established primary specimen type for a medical laboratory measurement procedure or qualitative examination. CLSI EP35 provides a general framework for studies that establish equivalence among similar-matrix specimen types and clinical suitability among dissimilar-matrix specimen types. It also includes instructions for laboratory verification of alternate specimen types for commercial measurement procedures. This guideline applies to both quantitative measurement procedures and qualitative examinations. The intended users of CLSI EP35 are manufacturers, developers of medical laboratory measurement procedures, and laboratorians verifying alternate specimen types.

CLSI EP35 is intended to be used for specimen types for which the desired measurand has a known clinical indication and for which adequate clinical information is available to establish risk-based clinical performance goals. Establishing clinically based performance goals is beyond the scope of CLSI EP35.

CLSI EP35 focuses on the effect of specimen type on the analytical measurement procedure. There may also be preanalytical factors between specimen types that can affect results. These differences may require additional studies to characterize their effect on the results. Such preanalytical factors are outside of the scope of CLSI EP35.

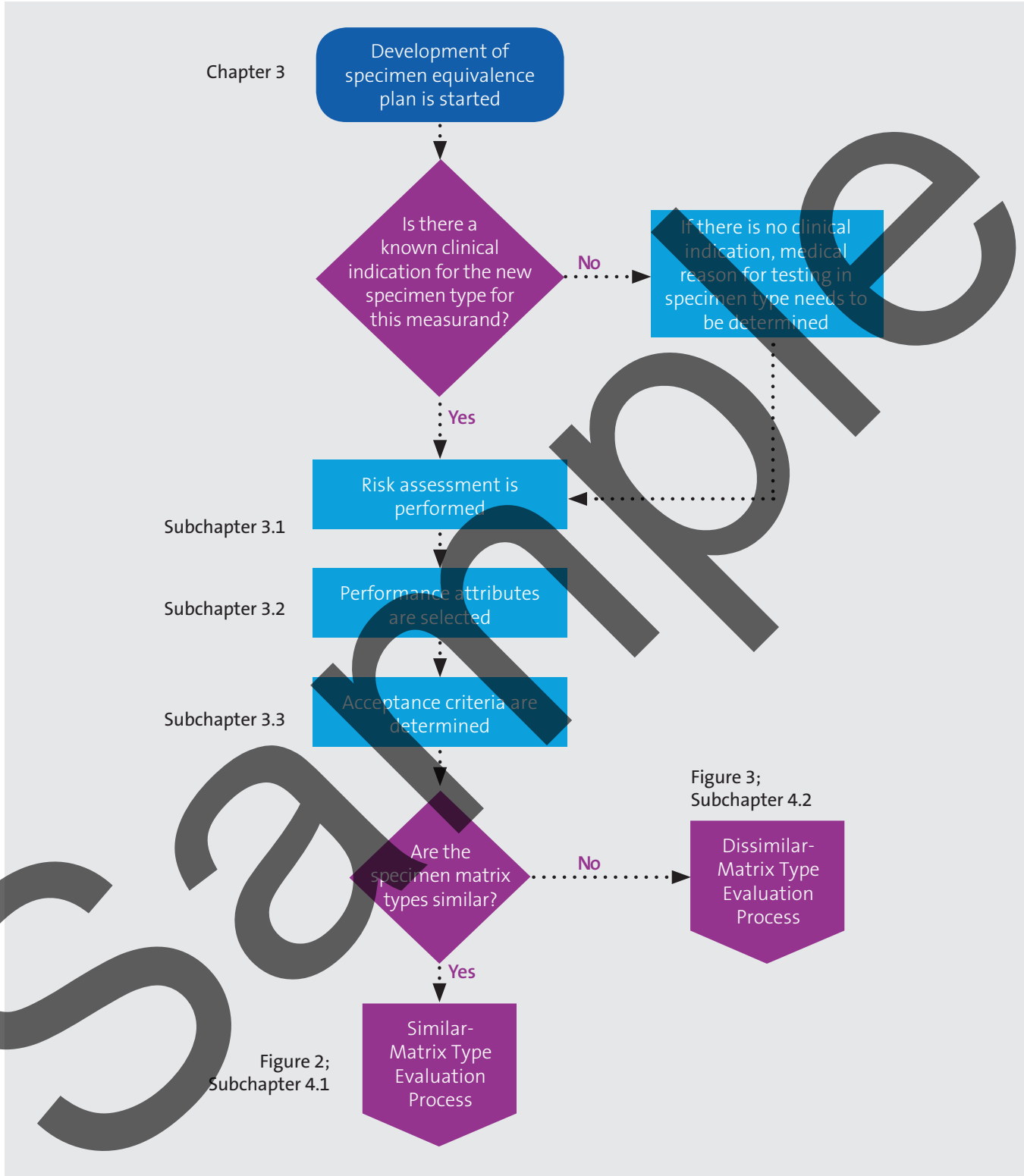
1.2 Background

Medical laboratory measurement procedure performance characteristics are generally established and validated for use for the most commonly used specimen type for the measurand, which is designated as the primary specimen type. However, there is often a clinical need to measure the same measurand in a different specimen type (eg, urine rather than serum). Changing the specimen type can alter both the measurement procedure performance and the performance characteristics desirable for clinical use, so it is important to document that the measurement procedure performance characteristics are clinically acceptable with the candidate specimen type.

For specimen types with a similar matrix (eg, serum and plasma), the measurement procedure's performance can be tested for equivalence among specimen types. When the matrixes are dissimilar (eg, serum and urine), it might not be possible to establish equivalence (eg, because of different measuring intervals), but the new specimen type can still be shown to be clinically acceptable or suitable for use.

To assess specimen type equivalence or suitability, a definition of what constitutes equivalent or suitable performance is needed. Typically, equivalence is defined as the condition of being equal in value, worth, function, etc. In the context of establishing specimen types' equivalence or suitability for a measurement procedure, there are two primary scenarios.

2.2 Establishing Specimen Equivalence or Suitability Process Flow Charts



[a] Five basic symbols are used in process flow charts: oval (signifies the beginning or end of a process), arrow (connects process activities), box (designates process activities), diamond (includes a question with alternative "Yes" and "No" responses), pentagon (signifies another process).

Figure 1. Developing a Specimen Equivalence or Suitability Plan Flow Chart[a]

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