CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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EP39

A Hierarchical Approach to Selecting Surrogate Samples for the Evaluation of *In Vitro* Medical Laboratory Tests

This guideline establishes a definition of a surrogate sample, provides recommendations for determining when to use surrogate samples, and describes a process for selecting the most appropriate surrogate sample.

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

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Abstract

Clinical and Laboratory Standards Institute guideline EP39—*A Hierarchical Approach to Selecting Surrogate Samples for the Evaluation of* In Vitro *Medical Laboratory Tests* establishes a standard definition for a surrogate sample. It presents a hierarchical approach for determining when to use surrogate samples and selecting an appropriate one. It also describes elements of a surrogate sample plan and includes technical preparation guidance for the characteristic to be measured or detected and for artificial matrix compositions. This guideline provides examples for specific performance study types.

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Foreword

Terms such as “contrived,” “altered,” “processed,” “diluted,” “supplemented,” and “simulated” have been used interchangeably to describe substitutions for patient samples. This guideline establishes a uniform term, “surrogate sample,” and definition to describe material(s) that is used as a substitute for body fluid or tissue from a single human individual.

When appropriately characterized patient samples are unavailable, surrogate samples serve an important role in the development, validation, and verification of laboratory tests. Surrogate samples may be needed for many reasons including limited sample volume or inadequate numbers of patient samples with concentrations at medical decision levels or at the extremes of the analytical measuring interval. A lack of available patient samples may be due to low disease prevalence, invasive sampling methods, or other reasons.

This guideline establishes an approach for selecting, preparing, and using surrogate samples. It describes the principles for creating a surrogate sample plan and presents a hierarchy, by performance study type, for selecting an appropriate surrogate sample. The hierarchical approach is demonstrated through product- and performance-specific examples.

KEY WORDS

Artificial analyte
Artificial matrix
Hierarchy
Pooled
Sample plan
Simulated
Supplemented
Surrogate sample

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Chapter 1

Introduction

This chapter includes:

- Guideline's scope and applicable exclusions
- Background information pertinent to the guideline's content
- Standard precautions information
- Terminology information, including:
  - Terms and definitions used in the guideline
  - Abbreviations and acronyms used in the guideline

A Hierarchical Approach to Selecting Surrogate Samples for the Evaluation of *In Vitro* Medical Laboratory Tests

1 Introduction

1.1 Scope

This guideline establishes a definition of "surrogate sample" and an approach for selecting, preparing, and using these samples. It discusses surrogate sample:

- Composition
- Technical preparation
- Selection criteria
- Documentation and planning
- Use in specific performance study types

The intended users of this guideline are *in vitro* diagnostic (IVD) device developers, laboratorians, and regulators. This guideline does not describe performance study design, which is covered in other standards and guidelines (see CLSI document EP19[1]).

1.2 Background

Development, validation, and verification of laboratory tests depends on the availability of patient samples for testing. When appropriate patient samples are unavailable to validate test performance, using surrogate samples enables more efficient use of biological materials, improves testing efficiency, and facilitates the development of tests for new biomarkers. Patient samples for test development and other uses may be unavailable for several reasons.

Reasons that patient samples cannot be used include:

- Logistical constraints
- Insufficient sample volumes
- Inadequate numbers of samples, such as those with concentrations at medical decision levels (MDLs) or at the extremes of the analytical measuring interval (AMI)
- Technical constraints
- Unsatisfactory samples (ie, that lack the necessary characteristics for a performance study)
- Instability of samples
- Unavailability of blank or negative samples