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EP25-A

Evaluation of Stability of *In Vitro* Diagnostic Reagents; Approved Guideline

This document provides guidance for establishing shelf-life and in-use stability claims for *in vitro* diagnostic reagents such as reagent kits, calibrators, and control products.

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

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For further information on committee participation or to submit comments, contact CLSI.

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Abstract

Clinical and Laboratory Standards Institute document EP25-A—*Evaluation of Stability of* In Vitro *Diagnostic Reagents; Approved Guideline* provides guidance and regression-based procedures for establishing stability-related claims of *in vitro* diagnostic (IVD) reagents such as reagent kits, calibrators, control products, and sample diluents. This guideline was written primarily for manufacturers and regulatory agencies, but will also be of interest to clinical laboratories. It provides information on the design, implementation, data analysis, and documentation needs for studies to establish and verify shelf life and in-use life of IVD reagents. Additional topics address assessment of product transport conditions on stability and accelerated stability testing.

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Foreword

Stability of an *in vitro diagnostic* (IVD) reagent reflects its ability to maintain consistent performance characteristics over time. Unlike precision, bias, and other common performance attributes, product stability is rarely assessed directly by customer testing. As such, there is increased burden on manufacturers to ensure that stability claims are developed from experimental designs and data analyses that are appropriate for each product's particular requirements and applications.

IVD reagents, in the context of this guideline, represent end-use consumable products sold for the purpose of performing clinical measurements on patient specimens or other samples. Examples of such products are IVD reagent kits and their associated calibrators, controls, sample diluents, and system generic reagents.

Content of this guideline is aligned with European Standard EN 13640:2002—*Stability Testing of* In Vitro *Diagnostics Reagents*,[1] referenced herein as EN 13640. Two other important internationally recognized guidance documents relative to stability study design and analyses are International Conference on Harmonization (ICH) Q1A (R2)[2] and ICH Q1E.[3] Although these were developed for drugs and drug substances, much of their content is directly relevant to IVD reagents.[4]

Key Words

Accelerated stability, allowable drift, calibration interval, expiration dating, in-use life, shelf life, stability monitoring, stability plan, transport simulation

Evaluation of Stability of *In Vitro* Diagnostic Reagents; Approved Guideline

1 Scope

This guidance document provides information on the establishment and verification of shelf-life and in-use stability claims for quantitative and qualitative *in vitro* diagnostic (IVD) reagents. It includes background information and typical content to consider when creating a stability testing plan for a particular product, logistics of performing the studies, recommended data analyses, and documentation of stability claims. Additional topics include assessment of product transport conditions on stability claims, stability monitoring (verification), and uses of accelerated stability testing.

The intended users of this guideline are primarily manufacturers of IVD reagents and regulatory agencies. Clinical laboratorians may find this information useful in interpreting commercial product stability claims, as well as for establishing stability attributes of "laboratory-developed test" methods.

This guideline does not address instrument systems, laboratory equipment, software, or patient samples. Stability testing of raw materials or components of reagent kits or consumables is not addressed explicitly. The principles described in this document could, however, be adapted by manufacturers toward that purpose.

2 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 infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of blood-borne pathogens. Standard and universal precaution guidelines are available from the US Centers for Disease Control and Prevention.[5] For specific precautions for preventing the laboratory transmission of all infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all infectious disease, refer to CLSI document M29.[6]

3 Terminology

3.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization wherever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in the United States, Europe, and elsewhere; that these differences are reflected in CLSI, International Organization of Standardization (ISO), and European Committee for Standardization (CEN) documents; and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. In light of this, CLSI's consensus process for development and revision of standards focuses on harmonization of terms to facilitate the global application of standards.