CLINICAL AND LABORATORY STANDARDS INSTITUTE®

1st Edition

# EP34

## Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking



It is often medically necessary to provide results for specimens with concentrations above the analytical measuring interval of an *in vitro* diagnostic measurement procedure. This guideline helps manufacturers and laboratory scientists with establishing, validating, or verifying a dilution scheme that will provide an extended measuring interval for such specimens.

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

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# Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking

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## Abstract

Clinical and Laboratory Standards Institute guideline EP34—*Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking* provides recommendations for establishing a dilution scheme to be used for patient specimens that contain measurand concentrations in the extended measuring interval above a measurement procedure's upper limit of quantitation. Guidance is provided on determining, validating, and verifying the appropriate diluent and dilution ratio to be used for such specimens. This guideline also covers creating spiked samples for use during dilution recovery studies and using spiking to determine the suitability of a sample matrix for dilution recovery studies. The intended users of this guideline are manufacturers of *in vitro* diagnostic tests and medical laboratory scientists, directors, and pathologists.

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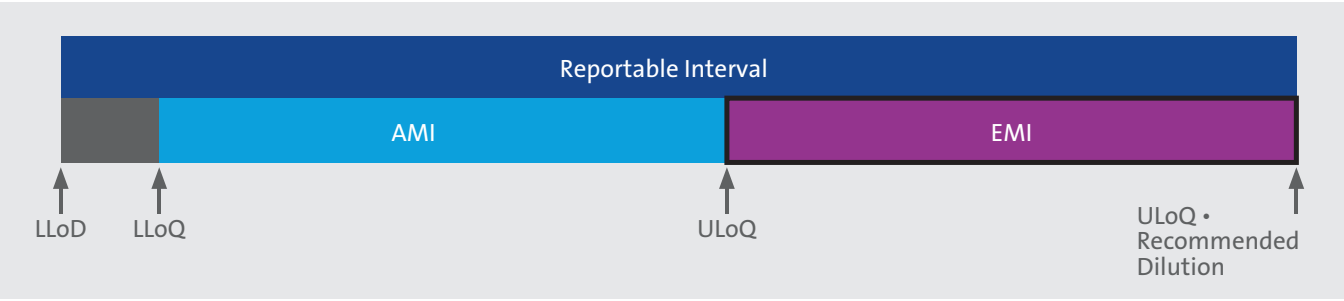
# Contents

# Foreword

Measurement procedures provide measurand results within specified concentration intervals. These intervals are described in Figure 1.




Abbreviations: AMI, analytical measuring interval; EMI, extended measuring interval; LLoD, lower limit of detection; LLoQ, lower limit of quantitation; ULoQ, upper limit of quantitation.

**Figure 1. Concentration Intervals**

The **analytical measuring interval (AMI)** is the interval in which specimen concentrations are measured within the medical and laboratory needs for accuracy with no dilution, concentration, or other pretreatment not part of the standard or routine measurement process. The AMI includes the interval in which linearity, precision, and bias have been deemed acceptable and extends from the LLoQ to the ULoQ. The **extended measuring interval (EMI)** is the interval in which concentrations are measured with appropriate accuracy by diluting the specimen before taking a measurement with the developed measurement process. The upper limit of this interval is defined by the ULoQ multiplied by the dilution factor recommended in the established dilution scheme. The **reportable interval** includes the AMI and EMI but also extends to the LLoD. An example is included in Appendix A.

Guidance on determining the LLoD and LLoQ of the AMI is available in CLSI document EP17.[1] Guidance on determining the linearity interval is available in CLSI document EP06.[2] There is often great clinical need to provide results for specimens with measurand concentration values above the AMI. This guideline aims to assist manufacturers and laboratory scientists with establishing and verifying dilution schemes created to provide an EMI for such specimens.

Manufacturers typically provide recommendations on how to dilute a high-concentration specimen so its resultant concentration value is within the AMI. Thereafter, the measurand concentration value of the specimen before its dilution can be computed. The recommended dilution scheme should include the appropriate diluent and dilution ratio to ensure accurate dilution recovery. Manufacturers are encouraged to follow this guideline in developing measurement procedure– and measurand-specific dilution schemes. When manufacturers do not provide a dilution scheme that meets the laboratory's needs, the laboratory can use the techniques described in this guideline to determine an appropriate dilution scheme.

**NOTE:**

The AMI is the interval in which specimen concentrations are measured with appropriate accuracy with no dilution, concentration, or other pretreatment not part of the routine measurement process.

**NOTE:**

The EMI is the interval in which concentrations are measured with appropriate accuracy by diluting the specimen before taking a measurement.

For some measurement procedures, when a neat specimen is presented, the measuring system uses a process of treatment and conditional dilutions designed to expand the AMI without the need for preexamination dilution commonly used to create an EMI (see Appendix A). For such a measurement procedure, its performance within its AMI should be measured like any standard quantitative procedure. The performance of its internal dilution steps can be tested using some of the procedures provided in this guideline, but the specific testing of an EMI is not necessary unless an examination dilution is also provided as an option.

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


## KEY WORDS

**Analytical measuring interval**
**Diluent**
**Dilution**
**Extended measuring interval**
**Recovery**
**Spiking**
**Upper limit of quantitation**

# Chapter 1

# Introduction

## This chapter includes:

- Guideline's scope and applicable exclusions
- Background information pertinent to the guideline'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 guideline
- Abbreviations and acronyms used in the guideline