CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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EP14

Evaluation of Commutability of Processed Samples

This document provides guidance for evaluating the commutability of processed samples by determining if they behave differently than unprocessed patient samples when two quantitative measurement procedures are compared.

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

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Evaluation of Commutability of Processed Samples

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Abstract

Clinical and Laboratory Standards Institute document EP14—*Evaluation of Commutability of Processed Samples* was developed for manufacturers and providers of proficiency testing or external quality assessment programs, although it is useful to clinical laboratories as well. The document helps users 1) determine whether noncommutability is the source of unexpected results that are sometimes observed with processed samples when two quantitative measurement procedures are compared, 2) display the magnitude of the effects, and 3) ensure that laboratory performance is evaluated fairly if noncommutability is present. The suggested protocol was developed using unprocessed patient samples as the standard of comparison.

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Foreword

The primary goal of manufacturers of *in vitro* diagnostic (IVD) measurement procedures is to accurately report measurand values for patient samples. These measurement procedures may not produce accurate results when processed samples such as external quality assessment (EQA) samples, proficiency testing (PT) samples, or QC samples are measured. Because such processed sample matrixes typically undergo supplementation with additional components, and therefore are altered in some manner, measured results may not reflect the accuracy that would be observed for patient samples. Processed samples that have the same measurement response as that of patient samples that contain the same amount of an analyte are called commutable, while those that do not are called noncommutable. In this document, a matrix effect is defined broadly as differing test result biases in processed samples vs unprocessed patient samples due to unknown causes. The matrix effects that cause biases compared with unprocessed patient samples could be correlated to differences in conditions as encompassing as the entire measurement system or as specific as a reagent lot within a single IVD device.

Biases due to matrix effects in processed samples have the potential to affect the quality of patient care because of an inaccurate estimation of the accuracy of a measurement procedure. Depending on the intended use of the processed sample, the impact can range from negligible to serious. For example, a specific bias in a measuring interval verification sample set may have a different impact on the quality of patient care than the same bias in a QC sample. A measuring interval sample set matrix-related bias can directly affect the measuring interval allowed in patient sample results, whereas a QC matrix-related bias may affect the interpretation of QC results following a reagent lot change.

The objective of EP14 is to provide methods for identifying noncommutability so that improvements in measurement procedure analytical specificity and matrix compatibility may be considered. For example, a beneficial outcome of an evaluation may be a change in the processed sample's matrix or its additives, with an improvement in sample commutability. The techniques described in this guideline are also valid for testing the commutability of other samples, such as patient samples that have been processed (eg, added preservatives or spiking material, diluted, depleted, or frozen). Such samples, designed to substitute for unprocessed patient samples, are referred to as surrogate samples in CLSI document EP39.[1] EP14 will be helpful in exploring differences in test material results between measurement procedures, especially when such material serves as a basis for determining measurement procedure performance.

Overview of Changes

This guideline was revised in 2022 under the Limited Revision Process and replaces the third edition of the guideline, which was published in 2014. Several changes were made in this edition, including:

- Adding content focused on processed samples such as EQA samples, PT samples, QC samples, and altered patient samples
- Adding an option for using preset commutability assessment criteria instead of prediction intervals
- Clarifying that EP14 is not designed for use with IVD manufacturer–specific calibrators and that the assessment methods described in this guideline should not be used in product regulatory submissions from such manufacturers

KEY WORDS

bias **Deming regression** **matrix**

commutability **interference** **matrix effect**

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Chapter 1

Introduction

Evaluation of Commutability of Processed Samples

1 Introduction

This section includes:

- Document scope and applicable exclusions
- Background information pertinent to the document content
- Standard Precautions information, as applicable
- Terms and definitions used in the document
- "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions, where applicable
- Abbreviations and acronyms used in the document

1.1 Scope

This guideline provides protocols for evaluating commutability of processed samples when tested with quantitative measurement procedures. Such processed samples may be those created for proficiency testing/external quality assessment (PT/EQA), measuring interval verification sample sets, or QC samples. Processed samples can also be human specimens that are modified in a way that may change their measurement characteristics. In such cases, only a few processed samples (eg, three to five) should be evaluated to represent the behavior of the modification process being assessed. This restriction is suggested because the underlying analyses in this guideline do not account for the simultaneous assessment of many processed samples. CLSI document EP39[1] mentions the use of surrogate samples for measurement procedure performance testing, sometimes using many such samples, eg, for measurement procedure comparison studies. EP14 does not provide methods to screen a large number of samples in such cases.

This guideline is intended for developers of commercial diagnostic tests as well as laboratory-developed tests. This guideline is also useful for manufacturers of measuring interval sample sets and QC samples, and for PT or EQA providers to determine whether their processed samples are commutable with patient samples when examined with specified measurement procedures. Other options for assessing the commutability of processed samples across multiple measurement procedures are covered in CLSI document EP30[2] and in the literature.[3]

This guideline may also be useful to all clinical laboratory professionals wishing to investigate the commutability of a processed sample analyzed with a specific *in vitro* diagnostic (IVD) device in their laboratory.

EP14 is intended to assist in the education of clinical laboratorians and diagnostic manufacturers about the commutability of processed materials and how a sample's matrix can affect some measurand values and their interpretation (referred to as matrix effects). For example, professionals may not be warned of a matrix effect caused by the interaction of processed PT/EQA material and the measurement procedure, and therefore the data may suggest to them that erroneous patient results are being generated, when in fact the results may be acceptable. Examples of a matrix effect due to the interaction of a processed QC and certain reagent lot(s) exist in the literature.[4] Therefore, these types of effects should not be a surprise to experienced laboratory staff and should not lead to erroneous conclusions about the suitability of results for patient samples. This guideline should assist all interested parties in not only evaluating the presence or absence of a matrix effect, but also by increasing awareness that the intended use of a processed matrix potentially affects patient care.