CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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EP14-A3

Evaluation of Commutability of Processed Samples; Approved Guideline—Third Edition

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; Approved Guideline—Third Edition

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Abstract

Clinical and Laboratory Standards Institute document EP14-A3—*Evaluation of Commutability of Processed Samples; Approved Guideline—Third Edition* was developed for manufacturers, regulators, 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 patient samples as the standard of comparison.

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Contents

Foreword

When manufacturers of diagnostic reagents develop measurement procedures, they attempt to design them so that they will report measurand values accurately for the intended patient samples. These measurement procedures may not be designed to produce accurate results when nonpatient samples such as external quality assessment samples, proficiency testing samples, or QC samples are measured. Because such nonpatient sample matrixes typically undergo some processing and spiking of additional components, and therefore are altered in some manner, measurand results may not reflect the accuracy that would be observed for patient samples. Processed samples that recover like patient samples are called commutable, while those that do not are called noncommutable. In this document, as with its previous edition, a matrix effect is defined broadly as differing test result biases in processed samples vs patient samples due to unknown causes. The matrix effects that cause biases compared to 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 measurement system.

Biases due to matrix effects in processed samples have the potential to affect the quality of patient care by giving an incorrect impression 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.

Overview of Changes

As with the previous edition of this document, the objective of EP14 is to provide ways to identify the presence of noncommutability so that improvements in measurement procedure specificity and fluid compatibility may be considered. For example, the beneficial outcome of the evaluation may be a change in the processed sample's matrix or its additives with an improvement in sample commutability. The evaluation is applicable to any type of processed sample, including (but not limited to) common calibrators, trueness controls, and certified reference materials. The techniques described are also valid for testing the commutability of other samples such as measurement procedure–specific calibrators or patient samples that have been altered (eg, added preservatives or spiking material, diluted, depleted, or frozen). This guideline 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.

Key Words

Analytical interference, bias, commutability, Deming regression, matrix, matrix effect

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1 Introduction

This chapter 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 that can evaluate commutability in any nonpatient processed samples when tested using quantitative measurement procedures. Such processed samples may be used for proficiency testing/external quality assessment (PT/EQA), measuring interval verification sample sets, or QC samples.

The guideline is intended to be used by developers of commercial diagnostic tests as well as laboratory-developed tests, manufacturers of measuring interval sample sets and QC samples, and PT or EQA providers. This guideline may also be useful to all clinical laboratory professionals wishing to investigate a processed sample's commutability.

EP14 is intended to assist in the education of clinical laboratorians, regulators, 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.[1] Therefore, these types of effects should not be a surprise to experienced laboratory staff and should not lead to erroneous conclusions about the same effect occurring in patient samples. This guideline should assist all interested parties in not only evaluating the presence or absence of a matrix effect, but also increasing awareness that there may be different levels of risk to the quality of patient care that are dependent on the intended use of a processed matrix.

This guideline can also be used by laboratorians performing quantitative tests for a wide variety of measurands across various disciplines to understand the commutability of processed samples. This guideline does not apply to qualitative tests.