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EP26-A

User Evaluation of Between-Reagent Lot Variation; Approved Guideline

This document provides guidance for laboratories on the evaluation of a new reagent lot, including a protocol using patient samples to detect significant changes from the current lot.

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

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User Evaluation of Between-Reagent Lot Variation; Approved Guideline

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Abstract

Clinical and Laboratory Standards Institute document EP26-A—*User Evaluation of Between-Reagent Lot Variation; Approved Guideline* provides guidance for laboratories on the evaluation of a new reagent lot, including a protocol that uses patient samples to detect significant changes from the current lot. Guidance is provided on establishing what lot-to-lot difference is significant and whether the observed difference is acceptable based on the established criteria. If the initial evaluation indicates a clinically significant difference, then appropriate follow-up studies and actions are also discussed. The protocol attempts to balance the need to reliably detect clinically significant change in reagent performance that may affect patient results with the recognition that reagent lot verification is a relatively frequent task that puts demands on the laboratory's limited resources.

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Foreword

Changes in measurement procedure performance may occur with a change in reagent lot. Possible causes include changes in reagent component materials, instability of a component in a reagent, damage in transportation or storage, or incorrect calibration of the new reagent lot. Consequently, it is good laboratory practice to verify the consistency of patient sample results when introducing a new lot of reagents.

A shift in the results obtained with QC samples may be observed with a new lot of reagents. These changes in QC results are often caused by a difference in the interaction of the QC material being tested with the current and new reagent lots, commonly referred to as a matrix effect, while there is actually no change in the performance of the measurement procedure as measured with patient sample results.[1]

It is also possible that a reagent lot–related change in measurement procedure performance may impact patient sample results with little or no apparent impact on QC sample results. In such instances, an insignificant change in QC material results from one reagent lot to the next could mask a significant change in patient sample results.

This document provides a systematic approach for detecting significant changes in measurement procedure performance for patient samples due to reagent lot changes, and for confirming that patient sample results are consistent between two reagent lots.

Key Words

Commutability, matrix bias, matrix effect, quality control, reagent

User Evaluation of Between-Reagent Lot Variation; Approved Guideline

1 Scope

This guideline provides a simple, practical, and statistically sound protocol to evaluate the consistency of patient sample results when a new analytical reagent lot replaces a reagent lot currently in use. This document is designed primarily for use with quantitative measurement procedures, but the same principles can be applied to measurement procedures that provide a clinically qualitative result based on a supplied quantitative measurement. This guideline is not intended for use with measurement procedures that only provide qualitative results. This guideline is intended for use in the clinical laboratory and is designed to work within the practical limitations that exist in that environment.

This guideline is not intended to provide detailed procedures for reagent manufacturers. The needs of reagent lot-to-lot testing by manufacturers, and the resources available, are different from those of the clinical laboratory. However, reagent manufacturers may use this document to understand the types of verification studies that may be performed in their customers' laboratories.

2 Introduction

The potential for a change in performance with a new reagent lot has been shown for both QC and patient samples[1-23] and is recognized by regulatory and accreditation organizations that have incorporated verification of the performance of a new reagent lot into their recommendations for good laboratory practice.[24-26]

The goal of both reagent manufacturers and clinical laboratories is to provide accurate patient results. Reagent manufacturers use a number of procedures to validate the performance of a new reagent lot during the manufacturing process. Reagents are released only when the performance criteria are met. Manufacturers may have information regarding expected consistency of patient sample results when introducing a new lot of reagents as established internally or at other laboratories.

Even though reagent performance was validated by the manufacturer before release, the laboratory needs to verify that the new reagent lot, as received, meets the laboratory's clinical performance needs. Possible causes of a change in performance with a new reagent lot include:

- Changes in reagent component materials
- Instability of a component in a reagent
- Reagents compromised in transportation or storage
- Incorrect calibration of the new reagent lot

Verifying that these potential changes have not occurred is important to assure the quality of laboratory results.

Between-reagent lot variation can affect results for QC materials, patient samples, or both. For some measurement procedures, reagent lot variation is observed in results for QC products when there has not been a significant change in patient sample results.[1] A systematic change in QC results may not be immediately apparent, but may become recognized only after a number of QC results have been accumulated over a period of time while using a new reagent lot. This variation for QC results is often ascribed to "matrix effects," which suggests that the QC material is not commutable with fresh patient samples. This noncommutability is not surprising because the manufacturing process for QC materials has a significant impact on the matrix of these samples and the reagent manufacturer's first concerns must be accuracy and consistency with patient sample results. However, it cannot be assumed that the absence

