

EP31-A-IR

Verification of Comparability of Patient Results Within One Health Care System; Approved Guideline (Interim Revision)

This document provides guidance on how to verify comparability of quantitative laboratory results for individual patients within a health care system.

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

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Abstract

Clinical and Laboratory Standards Institute document EP31-A-IR—*Verification of Comparability of Patient Results Within One Health Care System; Approved Guideline (Interim Revision)* provides guidance on how to verify comparability of quantitative laboratory results for individual patients across a health care system. For the purpose of this document, a health care system is defined as a system of physician offices, clinics, hospitals, and reference laboratories, under one administrative entity, where a patient may present for laboratory testing, and whose results may be reviewed by any health care provider within the system for the purpose of providing medical care. This document does not provide guidance on how to correct method noncomparability that may be identified.

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Verification of Comparability of Patient Results Within One Health Care System; Approved Guideline (Interim Revision)

1 Scope

This document provides guidance on how to verify comparability of quantitative laboratory results for individual patients within a health care system. For the purpose of this document, a health care system is defined as a system of physician offices, clinics, hospitals, and reference laboratories, under one administrative entity, where a patient may present for laboratory testing, and whose results may be reviewed by any health care provider within the system for the purpose of providing medical care.

EP31 provides a simple approach to be used for the assessment of patient laboratory result comparability across a maximum of 10 instruments, and assumes that a more comprehensive validation of quantitative measurement system comparability has been undertaken when the measurement systems were initially introduced into the laboratory. A more comprehensive comparison among measurement procedure results can follow a methodology such as that described in CLSI document EP09.¹ Comparability testing is just one facet of a program for assuring quality laboratory performance and is not intended to be a substitute for other quality monitors. This document does not address corrective action should method noncomparability be identified.

The approach described can also be used to verify comparability of patients' results in situations such as those following reagent or calibrator lot changes, instrument component changes or maintenance procedures, alerts from QC or external quality assessment (EQA) (proficiency testing [PT]) events, or other special cause event.

2 Introduction

Out of necessity, or for their own convenience, patients may interface with health care systems for the purpose of laboratory testing in a variety of settings and/or locations. Results of these tests may be compiled and reviewed by providing clinicians at any of the patient care locations. In addition, larger laboratories may have multiple instruments within one location (eg, backup instruments, point-of-care [POC] instruments) that may provide laboratory results for an individual patient during a health care episode. Over time, lots of calibrator and reagents change, calibration and maintenance procedures are performed, and other events may occur that can affect patient test results. The diagnostic value of patient test results is maximized if the measurement systems providing such results are in a state of statistical control (ie, are producing stable and consistent results). Maintaining comparability may involve standardization and calibration of instruments, forced agreement of results among different measurement systems through mathematical transformation, or adoption of different reference intervals and/or therapeutic or diagnostic cutoffs that are clearly indicated in the patient report. Regardless of the approach used to achieve comparable results among different measurement systems, or to accommodate known differences, periodic verification of assay comparability is necessary to provide optimal patient care.

There is no consensus procedure for demonstrating patient laboratory result comparability for patient samples among measurement procedures. A survey of the participants involved in the preparation of this document demonstrated a variety of approaches to testing frequency, number and type of samples tested (eg, random, high and low concentrations, or concentrations spanning the analytical measurement range [AMR]), evaluation and acceptance criteria for the results of comparison testing, and method of dealing with known bias between methods. The intent of this document is to review the salient issues surrounding verification of comparability of patient results among measurement procedures, and to provide a practical, statistically valid approach that laboratories of varying size and resources can use to satisfy this quality

requirement. Other valid procedures for comparability evaluation can be developed by a laboratory, and it is not the intent of this document to exclude their use.

This guideline addresses evaluation and monitoring of comparability of patient results. Recommendations on monitoring stability of the analytical process are provided in CLSI document C24.² Other clinical laboratory procedures are in place to address calibration traceability of routine measurement procedures to reference systems that are intended to ensure long-term consistency of calibration and uniformity of results among providers of *in vitro* diagnostic (IVD) measurement systems (see CLSI document X05³ and ISO 17511⁴ for further information).

3 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 known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of blood-borne pathogens. The Centers for Disease Control and Prevention address this topic in published guidelines that focus on the daily operations of diagnostic medicine in human and animal medicine while encouraging a culture of safety in the laboratory.⁵ For specific precautions for preventing the laboratory transmission of all known infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all known infectious disease, refer to CLSI document M29.⁶

4 Terminology

4.1 Definitions

accuracy (measurement) – closeness of agreement between a measured quantity value and a true quantity value of a measurand (JCGM 200:2012).⁷

alpha error – probability of falsely rejecting the null hypothesis when it is true.

analyte – component represented in the name of a measurable quantity (ISO 17511).⁴

analytical measurement range (AMR) – the range of analyte values that a method can directly measure on the sample without any dilution, concentration, or other pretreatment that is not part of the typical assay process.

beta error – probability of falsely rejecting the alternative hypothesis when it is true.

bias – difference between the expectation of the test results and an accepted reference value (ISO 5725-1,⁸ ISO 3534-1⁹); **NOTE 1:** Bias is the total systematic error, as contrasted to random error. There may be one or more systematic error components contributing to the bias. A larger systematic difference from the accepted reference value is reflected by a larger bias value (ISO 5725-1)⁸; **NOTE 2:** The measure of trueness is usually expressed in terms of bias (ISO 3534-1).⁹

calibration – operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication (JCGM 200:2012).⁷

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents. The quality management system approach applies a core set of “quality system essentials” (QSEs), basic to any organization, to all operations in any health care service’s path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager’s guide. The QSEs are as follows:

Organization	Personnel	Process Management	Nonconforming Event Management
Customer Focus	Purchasing and Inventory	Documents and Records	Assessments
Facilities and Safety	Equipment	Information Management	Continual Improvement

EP31-A-IR addresses the QSE indicated by an “X.” For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
			C30			X C24 C30 C37 EP05 EP09 EP15 X05	C30				

Path of Workflow

A path of workflow is the description of the necessary processes to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver the laboratory’s services, namely quality laboratory information.

EP31-A-IR addresses the clinical laboratory path of workflow steps indicated by an “X.” For a description of the other document listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Preexamination				Examination			Postexamination	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
X	C30	X			X C30		C30	

Related CLSI Reference Materials*

- C24-A3** **Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline—Third Edition (2006).** This guideline provides definitions of analytical intervals, planning of quality control procedures, and guidance for quality control applications.
- C30-A2** **Point-of-Care Blood Glucose Testing in Acute and Chronic Care Facilities; Approved Guideline—Second Edition (2002).** This document contains guidelines for performance of point-of-care (POC) blood glucose testing that stress quality control, training, and administrative responsibility.
- C37-A** **Preparation and Validation of Commutable Frozen Human Serum Pools as Secondary Reference Materials for Cholesterol Measurement Procedures; Approved Guideline (1999).** This guideline details procedures for the manufacture and evaluation of human serum pools for cholesterol measurement.
- EP05-A2** **Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition (2004).** This document provides guidance for designing an experiment to evaluate the precision performance of quantitative measurement methods; recommendations on comparing the resulting precision estimates with manufacturers' precision performance claims and determining when such comparisons are valid; as well as manufacturers' guidelines for establishing claims.
- EP09-A2** **Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Second Edition (Interim Revision) (2010).** This document addresses procedures for determining the bias between two clinical methods, and the design of a method comparison experiment using split patient samples and data analysis.
- EP15-A2** **User Verification of Performance for Precision and Trueness; Approved Guideline—Second Edition (2006).** This document describes the demonstration of method precision and trueness for clinical laboratory quantitative methods utilizing a protocol designed to be completed within five working days or less.
- M29-A3** **Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Third Edition (2005).** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.
- X05-R** **Metrological Traceability and Its Implementation; A Report (2006).** This document provides guidance to manufacturers for establishing and reporting metrological traceability. A CLSI-IFCC joint project.

* CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.

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