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.
Clinical and Laboratory Standards Institute

Setting the standard for quality in medical laboratory testing around the world.

The Clinical and Laboratory Standards Institute (CLSI) is a not-for-profit membership organization that brings together the varied perspectives and expertise of the worldwide laboratory community for the advancement of a common cause: to foster excellence in laboratory medicine by developing and implementing medical laboratory standards and guidelines that help laboratories fulfill their responsibilities with efficiency, effectiveness, and global applicability.

Consensus Process

Consensus—the substantial agreement by materially affected, competent, and interested parties—is core to the development of all CLSI documents. It does not always connote unanimous agreement, but does mean that the participants in the development of a consensus document have considered and resolved all relevant objections and accept the resulting agreement.

Commenting on Documents

CLSI documents undergo periodic evaluation and modification to keep pace with advancements in technologies, procedures, methods, and protocols affecting the laboratory or health care.

CLSI’s consensus process depends on experts who volunteer to serve as contributing authors and/or as participants in the reviewing and commenting process. At the end of each comment period, the committee that developed the document is obligated to review all comments, respond in writing to all substantive comments, and revise the draft document as appropriate.

Comments on published CLSI documents are equally essential, and may be submitted by anyone, at any time, on any document. All comments are managed according to the consensus process by a committee of experts.

Appeals Process

When it is believed that an objection has not been adequately considered and responded to, the process for appeals, documented in the CLSI Standards Development Policies and Processes, is followed.

All comments and responses submitted on draft and published documents are retained on file at CLSI and are available upon request.

Get Involved—Volunteer!

Do you use CLSI documents in your workplace? Do you see room for improvement? Would you like to get involved in the revision process? Or maybe you see a need to develop a new document for an emerging technology? CLSI wants to hear from you. We are always looking for volunteers. By donating your time and talents to improve the standards that affect your own work, you will play an active role in improving public health across the globe.

For additional information on committee participation or to submit comments, contact CLSI.

Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: +1.610.688.0100
F: +1.610.688.0700
www.clsi.org
standard@clsi.org
Verification of Comparability of Patient Results Within One Health Care System; Approved Guideline (Interim Revision)

Volume 32 Number 11

Christopher M. Lehman, MD
John Rex Astles, PhD, FACB
Renze Bais, PhD
Sterling Bennett, MD
Ellis Jacobs, PhD, DABCC, FACB
Stan R. Johnson, MA
W. Gregory Miller, PhD

Jeffrey E. Vaks, PhD
Harvey B. Lipman, PhD
Amit Phansalkar, MS
Kenneth A. Sikaris, MD
Dietmar Stöckl, PhD
Greg Cooper, CLS, MHA

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.


The Clinical and Laboratory Standards Institute consensus process, which is the mechanism for moving a document through two or more levels of review by the health care community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of CLSI documents. Current editions are listed in the CLSI catalog and posted on our website at www.clsi.org. If your organization is not a member and would like to become one, and to request a copy of the catalog, contact us at: Telephone: 610.688.0100; Fax: 610.688.0700; E-Mail: customerservice@clsi.org; Website: www.clsi.org.
Contents

Abstract .................................................................................................................................................... i

Interim Revision Changes to C54-A ...................................................................................................... ix

Foreword ................................................................................................................................................ xi

1 Scope .......................................................................................................................................... 1

2 Introduction ................................................................................................................................ 1

3 Standard Precautions .................................................................................................................. 2

4 Terminology ................................................................................................................................ 2

4.1 Definitions ................................................................................................................................ 2

4.2 Abbreviations and Acronyms ............................................................................................... 5

5 Practical Considerations for Designing a Comparability Monitoring Protocol ......................... 5

5.1 Causes of Noncomparability of Results ........................................................................ 5

5.2 Scope of Comparisons .................................................................................................. 6

5.3 Risk Assessment for Noncomparable Results ................................................................ 6

5.4 Frequency and Complexity of Comparability Assessment Protocols ........................... 7

5.5 General Approaches to Comparability Testing ................................................................ 7

5.6 Triggers for Special Cause Comparability Testing ....................................................... 8

6 Samples for Comparability Testing ........................................................................................... 9

6.1 Commutability .............................................................................................................. 9

6.2 Analyte Concentrations for Testing ............................................................................ 13

6.3 Storage and Transport ................................................................................................. 13

7 Acceptance Criteria for Comparability Testing of Patient Results .......................................... 13

7.1 Evaluation of Comparability Based on Clinical Outcomes ........................................ 14

7.2 Evaluation of Comparability Based on Clinician’s Questionnaire ................................ 14

7.3 Evaluation of Comparability Based on Biological Variability ....................................... 14

7.4 Evaluation of Analytical Performance Based on Published Professional Recommendations .......................................................................................................................... 15

7.5 Evaluation of Analytical Performance Based on Goals Set by Accrediting Agencies 15

7.6 Evaluation of Analytical Performance Based on the General Capability ................... 16

8 Statistical Evaluation of Comparability Data ........................................................................... 16

8.1 Hypothesis Testing ..................................................................................................... 16

8.2 Statistical Analysis of Comparability Data .................................................................................. 17

8.3 Fixed Limit Evaluation ............................................................................................... 19

9 Point-of-Care Testing ............................................................................................................... 19

9.1 Specimen Selection ..................................................................................................... 20

9.2 Specimen Acquisition .................................................................................................. 20

9.3 Range of Specimen Values ........................................................................................... 21

9.4 Multiple Devices of the Same Make and Model ......................................................... 21

9.5 Statistical Considerations for Point-of-Care Comparability Testing ....................... 21

10 Range Test Comparability Protocol .......................................................................................... 22
Contents (Continued)

10.1 Select an Analyte for Comparison ................................................................. 22
10.2 Select the Instruments to Be Compared ....................................................... 22
10.3 Identify an Approximate Analyte Concentration for Comparison Testing ...... 22
10.4 Calculate the Desired Concentration or Activity to Be Used for Comparison Sample Selection .......................................................... 23
10.5 Select a Sample for Comparison Testing ...................................................... 23
10.6 Select the Appropriate Level of Acceptance Criteria That Can Be Applied to the Comparison Test (From Section 7) .............................................. 23
10.7 Calculate the Critical Difference for the Comparability Test ...................... 24
10.8 Determine the Number of Runs and Replicates to Be Run and the Range Rejection Limit ............................................................... 24
10.9 Perform the Comparison ............................................................................. 24
10.10 Evaluate the Clinical Relevance of the Comparison Results ...................... 25
10.11 Troubleshooting Noncomparability ............................................................ 25

References ......................................................................................................... 26

Appendix A. Worked Examples ........................................................................ 28
Appendix B. Tables of Runs, Replicates, and Range Rejection Limits .................. 34
Appendix C. Statistical Concepts ....................................................................... 55
Appendix D. Biological Variation ....................................................................... 60
The Quality Management System Approach .................................................... 62
Related CLSI Reference Materials ................................................................... 63
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. 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. 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 X05 and ISO 17511 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. 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.

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).

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).

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, ISO 3534-1); 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); NOTE 2: The measure of trueness is usually expressed in terms of bias (ISO 3534-1).

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).
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.

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.
Related CLSI Reference Materials*


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.


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.
Explore the Latest Offerings From CLSI!

As we continue to set the global standard for quality in laboratory testing, we are adding products and programs to bring even more value to our members and customers.

By becoming a CLSI member, your laboratory will join 1,600+ other influential organizations all working together to further CLSI's efforts to improve health care outcomes. You can play an active role in raising global laboratory testing standards—in your laboratory, and around the world.

Find out which membership option is best for you at www.clsi.org/membership.

Find what your laboratory needs to succeed! CLSI U provides convenient, cost-effective continuing education and training resources to help you advance your professional development. We have a variety of easy-to-use, online educational resources that make eLearning stress-free and convenient for you and your staff.

See our current educational offerings at www.clsi.org/education.

When laboratory testing quality is critical, standards are needed and there is no time to waste. eCLIPSE™ Ultimate Access, our cloud-based online portal of the complete library of CLSI standards, makes it easy to quickly find the CLSI resources you need.

Learn more and purchase eCLIPSE at clsi.org/eCLIPSE.

For more information, visit www.clsi.org today.