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Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard—Second Edition

This document provides guidance for the validation, verification, calibration, quality assurance (QA), and quality control (QC) of automated multichannel hematology analyzers for manufacturers, end-user clinical laboratories, accrediting organizations, and regulatory bodies. In addition, end-user clinical laboratories will find guidance for establishment of clinically reportable intervals and for QA for preexamination and examination aspects of their systems.

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

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- The authorization of a project
- The development and open review of documents
- The revision of documents in response to comments by users
- The acceptance of a document as a consensus standard or guideline

Most documents are subject to two levels of consensus—"proposed" and "approved." Depending on the need for field evaluation or data collection, documents may also be made available for review at an intermediate consensus level.

Proposed A consensus document undergoes the first stage of review by the health care community as a proposed standard or guideline. The document should receive a wide and thorough technical review, including an overall review of its scope, approach, and utility, and a line-by-line review of its technical and editorial content.

Approved An approved standard or guideline has achieved consensus within the health care community. It should be reviewed to assess the utility of the final document, to ensure attainment of consensus (ie, that comments on earlier versions have been satisfactorily addressed), and to identify the need for additional consensus documents.

Our standards and guidelines represent a consensus opinion on good practices and reflect the substantial agreement by materially affected, competent, and interested parties obtained by following CLSI's established consensus procedures. Provisions in CLSI standards and guidelines may be more or less stringent than applicable regulations. Consequently, conformance to this voluntary consensus document does not relieve the user of responsibility for compliance with applicable regulations.

COMMENTS

The comments of users are essential to the consensus process. Anyone may submit a comment, and all comments are addressed, according to the consensus process, by the committee that wrote the document. All comments, including those that result in a change to the document when published at the next consensus level and those that do not result in a change, are addressed by the committee in an appendix to the document. Readers are strongly encouraged to comment in any form and at any time on any document. Address comments to Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

VOLUNTEER PARTICIPATION

Health care professionals in all specialties are urged to volunteer for participation in CLSI projects. Please contact us at customerservice@clsi.org or +610.688.0100 for additional information on committee participation.

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Abstract

Clinical and Laboratory Standards Institute document H26-A2—*Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard—Second Edition* provides guidance for the validation, verification, calibration, quality assurance (QA), and quality control (QC) of automated multichannel hematology analyzers. The intended audience includes manufacturers of such devices, end-user clinical laboratories, accrediting organizations, and regulatory bodies.

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Contents

Contents (Continued)

Foreword

From a medical perspective, the value of an automated hematology analyzer is to provide physicians and other health care providers with reliable hematology data for patient management. From a patient and regulatory perspective, all complete blood count (CBC) results should be statistically and medically comparable on any hematology analyzer.

Reliable data depend on robust system design, which is initially *validated* by the manufacturer using formal study protocols/procedures, and subsequently *verified* by the end-user laboratory. Manufacturers' validations typically include a combination of in-house testing with normal donor blood specimens and evaluations of patient specimens at external practicing clinical laboratories. Verification should focus on the laboratory's specific patient populations.

Because CBC analyses are performed on whole blood, which is a heterogeneous suspension of blood cells, particular attention to various preexamination aspects of specimen collection and handling is critical to success in generating accurate patient results.

With respect to end-user quality control (QC) in the examination phase, the needs of clinical chemistry established the original patterns of internal and external QC methodology and the design of control materials and calibrators. Although automated hematology analyzers share these principles, they also have unique characteristics that require some specialized approaches to QC.

This document replaces and expands on two CLSI hematology documents (H26-A and H38-P) that are no longer in the consensus process. Those documents addressed only calibration and QC of automated analyzers. The present new document adds comprehensive sections for system validation and verification, as well as consideration of preexamination topics. Its approach is more practical than the previous documents, and is focused on specific technical details, with greatly expanded literature references.

Key Words

Analytical measuring interval, automated hematology, carryover, clinically reportable interval, comparability, correlation, imprecision, limit of blank, lower limit of detection, lower limit of quantitation, quality control, reference intervals, repeatability, validation study design, verification study design

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1 Scope

This document covers portions of the life cycle of an automated multichannel hematology system and provides guidance for validation, verification, calibration, quality assurance (QA), and quality control (QC) through standardized approaches to ensure good laboratory science and clinical relevance. The intended audience includes manufacturers of such devices, end-user clinical laboratories, accrediting organizations, and regulatory bodies.

End-user clinical laboratories will also find guidance for establishment of clinically reportable intervals (CRIs) and for QA for preexamination and examination aspects of their systems.

Because current blood cell counters also provide results beyond particle counting and differential separation of cell types, such as expanded platelet and reticulocyte measurements, extended leukocyte differential subtyping, and most recently, proteomic measurements through antigenic identification (ID) using fluorescence measurements, consult the potentially relevant CLSI documents H42,[1] H43,[2] H44,[3] H52,[4] and I/LA24.[5]

2 Introduction

Historically, each complete blood count (CBC) instrument/reagent manufacturer developed its unique approaches to system validation and performance claims. It is hoped that this document will provide better standardization and transparency across manufacturers. Similarly, a uniform approach to end-user laboratory verification was lacking, and this document should assist that audience in developing consistent testing.

Calibration, internal QC, and external quality assessment (EQA) of hematology analyzers are commonly dependent on stabilized blood products that may contain surrogate particles and nonhuman cells in a nonphysiological fluid. When possible, fresh human blood should be part of an overall QC program, to enhance linkage between QC data and reportable patient results.

In addition to the use of stabilized blood, data generated by statistical analyses of patient assays serve as sources of information for QC, as commonly practiced in the hematology section of the clinical laboratory.

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. Standard and universal precaution guidelines are available from the US Centers for Disease Control and Prevention.[6] 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 diseases, refer to CLSI document M29.[7]