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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.

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



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

Albert Rabinovitch, MD, PhD  
Patrick Barnes  
Krista M. Curcio, MT(ASCP)  
John Dorman, MT(ASCP)  
Albert Huisman, PhD  
Lan Nguyen  
Patrick O'Neil, BS, MLT

### 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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## Committee Membership

### Area Committee on Hematology

**Dorothy M. Adcock, MD**  
**Chairholder**  
**Esoterix Coagulation**  
**Englewood, Colorado, USA**

**Bruce H. Davis, MD**  
**Vice-Chairholder**  
**Eastern Maine Medical Center**  
**Bangor, Maine, USA**

Maria J. Arroz, MD  
 Hospital S. Francisco Xavier  
 Lisbon, Portugal

Josephine M. Bautista, MS,  
 MT(ASCP)  
 FDA Center for Devices and  
 Radiological Health  
 Rockville, Maryland, USA

Rolf D. Hinzmann, MD, PhD  
 Sysmex Europe GmbH  
 Norderstedt, Germany

Hans Hoffmann, PhD  
 Abbott Diagnostics Division  
 Wiesbaden, Germany

Powers Peterson, MD  
 Weill Cornell Medical College  
 in Qatar  
 Education City, Doha, Qatar

Albert Rabinovitch, MD, PhD  
 NovoMetrics, Inc  
 Mountain View, California, USA

Maryalice Stetler-Stevenson, MD,  
 PhD  
 National Institutes of Health  
 Bethesda, Maryland, USA

#### Advisors

David Barnett, PhD  
 UK NEQAS for Leukocyte  
 Immunophenotyping  
 Sheffield, United Kingdom

Larry D. Bowers, PhD, DABCC  
 US Anti-Doping Agency  
 Colorado Springs, Colorado, USA

Donna D. Castellone, MS,  
 MT(ASCP)SH  
 Siemens Healthcare Diagnostics  
 Tarrytown, New York, USA

Douglas J. Christie, PhD, FAHA  
 Siemens Healthcare Diagnostics  
 Newark, Delaware, USA

Naomi B. Culp, DA, MT(ASCP)SH  
 Fishers, Indiana, USA

Charles S. Eby, MD  
 Washington University School of  
 Medicine  
 St. Louis, Missouri, USA

Björn A. Ekberg, BSc, PhD  
 Chempaq A/S  
 Farum, Denmark

Emmanuel Favaloro, PhD  
 Westmond Hospital  
 New South Wales, Australia

Keiji Fujimoto, PhD  
 Sysmex Corporation  
 Kobe, Japan

Ian Giles, MD  
 Sysmex America, Inc.  
 Mundelein, Illinois, USA

Robert C. Gosselin, CLS  
 University of California  
 Sacramento, California, USA

Jan W. Gratama, MD  
 Erasmus University Medical  
 Center-Daniel Den Hoed  
 Rotterdam, Netherlands

Catherine P. M. Hayward, MD,  
 PhD, FRCP(C)  
 McMaster University  
 Hamilton, Ontario, Canada

Mike Keeney, ART, FIMLS  
 London Health Sciences Center  
 London, Ontario, Canada

Stephen Kitchen, FIBMS, PhD  
 Royal Hallamshire Hospital  
 Sheffield, United Kingdom

John A. Koepke, MD  
 Durham, North Carolina, USA

Kandice Kottke-Marchant, MD,  
 PhD  
 Cleveland Clinic  
 Cleveland, Ohio, USA

Samuel J. Machin, MB, ChB,  
 FRCPath  
 The University College London  
 Hospitals  
 London, United Kingdom

Piet Meijer, PhD  
 ECAT Foundation  
 Leiden, Netherlands

Yutaka Nagai, PhD  
 Nihon Kohden Corporation  
 Tokyo, Japan

Oscar G. Segurado, MD, PhD  
 BD Biosciences  
 San Jose, California, USA

Diane I. Szamosi, MA,  
 MT(ASCP)SH  
 Becton Dickinson  
 Franklin Lakes, New Jersey, USA

Andre Valcour, PhD  
 Laboratory Corporation of America  
 Burlington, North Carolina, USA

Elizabeth M. Van Cott, MD  
 Massachusetts General Hospital  
 Boston, Massachusetts, USA

Brent L. Wood, MD, PhD  
 University of Washington Medical  
 Center  
 Seattle, Washington, USA

#### Staff

Clinical and Laboratory Standards  
 Institute  
 Wayne, Pennsylvania, USA

Lois M. Schmidt, DA  
*Vice President, Standards  
 Development*

David E. Sterry, MT(ASCP)  
*Staff Liaison*

Patrice E. Polgar  
*Project Manager*

Melissa A. Lewis, ELS  
*Editorial Manager*

## Acknowledgment

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**Albert Rabinovitch, MD, PhD**  
**Chairholder**  
**NovoMetrics, Inc.**  
**Mountain View, California, USA**

Krista M. Curcio, MT(ASCP)  
Sysmex America, Inc.  
Mundelein, Illinois, USA

John Dorman, MT(ASCP)  
Streck  
Omaha, Nebraska, USA

Albert Huisman, PhD  
University Medical Center Utrecht  
Utrecht, Netherlands

Lan Nguyen  
FDA Center for Devices and Radiological Health  
Rockville, Maryland, USA

Patrick O'Neil, BS, MLT(ASCP)  
Beckman Coulter  
Miami, Florida, USA

### Advisor

Patrick Barnes  
Barnes Jewish Hospital  
St. Louis, Missouri, USA

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## 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



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

### **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,<sup>1</sup> H43,<sup>2</sup> H44,<sup>3</sup> H52,<sup>4</sup> and I/LA24.<sup>5</sup>

### **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.<sup>6</sup> 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.<sup>7</sup>