This document addresses performance goals for analytical accuracy and precision for multichannel hematology analyzers; the relationship of these goals to quality control systems and medical decisions; and recommendations for minimum calibrator performance and the detection of measurement errors.
NCCLS...

Serving the World's Medical Science Community Through Voluntary Consensus

NCCLS is an international, interdisciplinary, nonprofit, standards-developing and educational organization that promotes the development and use of voluntary consensus standards and guidelines within the healthcare community. It is recognized worldwide for the application of its unique consensus process in the development of standards and guidelines for patient testing and related healthcare issues. NCCLS is based on the principle that consensus is an effective and cost-effective way to improve patient testing and healthcare services.

In addition to developing and promoting the use of voluntary consensus standards and guidelines, NCCLS provides an open and unbiased forum to address critical issues affecting the quality of patient testing and health care.

PUBLICATIONS

An NCCLS document is published as a standard, guideline, or committee report.

**Standard** A document developed through the consensus process that clearly identifies specific, essential requirements for materials, methods, or practices for use in an unmodified form. A standard may, in addition, contain discretionary elements, which are clearly identified.

**Guideline** A document developed through the consensus process describing criteria for a general operating practice, the procedure, or material for voluntary use. A guideline may be used as written or modified by the user to fit specific needs.

**Report** A document that has not been subjected to consensus review and is released by the Board of Directors.

CONSENSUS PROCESS

The NCCLS voluntary consensus process is a protocol establishing formal criteria for:

- 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 NCCLS 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 (i.e., "tentative") consensus level.

**Proposed** An NCCLS consensus document undergoes the first stage of review by the healthcare 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.

**Tentative** A tentative standard or guideline is made available for review and comment only when a recommended method has a well-defined need for a field evaluation or when a recommended protocol requires that specific data be collected. It should be reviewed to ensure its utility.

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

NCCLS 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 NCCLS’s established consensus procedures. Provisions in NCCLS 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 NCCLS 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 responded to by the committee in an appendix to the document. Readers are strongly encouraged to comment in any form and at any time on any NCCLS document. Address comments to the NCCLS Executive Offices, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

VOLUNTEER PARTICIPATION

Healthcare professionals in all specialities are urged to volunteer for participation in NCCLS projects. Please contact the NCCLS Executive Offices for additional information on committee participation.
Performance Goals for the Internal Quality Control of Multichannel Hematology Analyzers; Approved Standard

Abstract

Performance Goals for the Internal Quality Control of Multichannel Hematology Analyzers; Approved Standard (NCCLS document H26-A) provides recommendations for performance goals for the internal quality control of multichannel hematology analyzers on the basis of the use of physical and chemical standards, accepted reference methods, subcommittee recommendations on what is currently achievable, and the concept of medical usefulness. Critical performance characteristics of quality control systems (i.e., the probabilities of error detection and false rejection) also are considered. A well-designed internal quality control program must achieve the level of error detection specified in this standard; yet it should not be so sensitive as to falsely reject valid results.

Performance Goals for the Internal Quality Control of Multichannel Hematology Analyzers; Approved Standard

Volume 16 Number 12

A. Richardson Jones, M.D.
Joanne Cornbleet, M.D.
Berend Houwen, M.D., Ph.D.
Luc Van Hove, M.D., Ph.D.
John A. Koepke, M.D.
Elkin Simson, M.D., Ch.B., M.Med.
William R. Swaim, M.D.
Onno W. van Assendelft, M.D., Ph.D.
Committee Membership

Area Committee on Hematology

Eugene L. Gottfried, M.D.  
Chairholder  
San Francisco General Hospital  
San Francisco, California

Subcommittee on the Blood Count

A. Richardson Jones, M.D.  
Chairholder  
Coulter Corporation  
Miami, Florida

Joanne Cornbleet, M.D.  
Stanford University Medical Center  
Stanford, California

Berend Houwen, M.D., Ph.D.  
Loma Linda University  
Loma Linda, California

Luc Van Hove, M.D., Ph.D.  
Abbott Laboratories  
Santa Clara, California

John A. Koepke, M.D.  
Duke University Medical Center  
Durham, North Carolina

Elkin Simson, M.D., Ch.B., M.Med.  
Mount Sinai Medical Center  
New York, New York

William R. Swaim, M.D.  
VA (Minneapolis) Medical Center  
Minneapolis, Minnesota

Onno W. van Assendelft, M.D., Ph.D.  
Centers for Disease Control and Prevention  
Atlanta, Georgia

Advisors

Marti K. Bailey, M.T.(ASCP)  
Milton S. Hershey Medical Center  
Hershey, Pennsylvania

Stuart A. Bentley, M.D.  
University of North Carolina Medical School  
Chapel Hill, North Carolina

J. David Bessman, M.D.  
University of Texas Medical Branch  
Galveston, Texas

William Canfield  
Bayer Corporation  
Tarrytown, New York

Samuel E. Chappell  
National Institute of Standards & Technology  
Gaithersburg, Maryland

Dr. John M. England  
Watford General Hospital  
Watford, England
ACTIVE MEMBERSHIP (as of 1 October 1996)

**Sustaining Members**
- American Association for Clinical Chemistry
- Bayer Corporation
- Beckman Instruments, Inc.
- Becton Dickinson and Company
- Boehringer Mannheim Diagnostics, Inc.
- College of American Pathologists
- Coulter Corporation
- Dade International Inc.
- Johnson & Johnson Clinical Diagnostics
- Ortho Diagnostic Systems Inc.

**Professional Members**
- American Academy of Allergy Asthma & Immunology
- American Academy of Family Physicians
- American Association of Bioanalysts
- American Association of Blood Banks
- American Association for Clinical Chemistry
- American Association for Respiratory Care
- American Chemical Society
- American Medical Technologists
- American Public Health Association
- American Society for Clinical Laboratory Science
- American Society of Hematology
- American Society for Microbiology
- American Society of Parasitologists, Inc.
- American Type Culture Collection, Inc.
- Australasian Association of Clinical Biochemists
- Canadian Society of Laboratory Technologists
- Clinical Laboratory Management Association
- College of American Pathologists
- College of Medical Laboratory Technologists of Ontario
- Commission on Office Laboratory Accreditation
- Corps professionnel des technologistes médicaux du Québec
- Institut für Stand. und Dok. im Med. Lab. (INSTAND)
- International Federation of Clinical Chemistry
- International Society for Analytical Cytology
- Italian Society of Clinical Biochemistry
- Japan Association of Medical Technologists
- Japanese Committee for Clinical Laboratory Standards
- Joint Commission on Accreditation of Healthcare Organizations
- National Academy of Clinical Biochemistry
- National Society for Histotechnology, Inc.
- Ontario Medical Association Laboratory Proficiency Testing Program
- Sociedade Brasileira de Analises Clinicas

**Government Members**
- Armed Forces Institute of Pathology
- Association of State and Territorial Public Health Laboratory Directors
- BC Centre for Disease Control Center for Preventive Medicine (France)
- Centers for Disease Control and Prevention
- China National Centre for the Clinical Laboratory
- Commonwealth of Pennsylvania Bureau of Laboratories
- Connecticut Department of Public Health & Addiction Services
- Department of Veterans Affairs
- Deutsches Institut für Normung (DIN)
- FDA Center for Devices and Radiological Health
- FDA Division of Anti-Infective Drug Products
- Health Care Financing Administration
- INMETRO
- Instituto Scientifico HS. Raffaele (Italy)
- Iowa State Hygienic Laboratory
- Massachusetts Department of Public Health Laboratories
- Michigan Department of Public Health
- National Institute of Standards and Technology
- Ohio Department of Health
- Oklahoma State Department of Health
- Ontario Ministry of Health
- South African Institute for Medical Research
- Swedish Institute for Infectious Disease Control

**Industry Members**
- Abbott Laboratories
- ABC Consulting Group, Ltd.
- Advanced Care Products Division (Div. Ortho Diagnostic Systems Inc.)
- aejes
- Bayer Corporation
- Beckman Instruments, Inc.
- Becton Dickinson and Company
- Becton Dickinson Consumer Products
- Becton Dickinson
- Immunocytometry Systems
- Becton Dickinson Microbiology Systems
- Becton Dickinson Primary Care Diagnostics
- Becton Dickinson VACUTAINER Systems
- Behring Diagnostics Inc.
- Behring Diagnostics Inc. - San Jose, CA
- bioMérieux Vitek, Inc.
- Biometry Consultants
- Bio-Rad Laboratories, Inc.
- Biosite Diagnostics
- Boehringer Mannheim Diagnostics, Inc.
- Boehringer Mannheim GmbH
- Bristol-Myers Squibb Company
- CASCO Standards
- ChemTrak
- Cholestech
- Ciba Corning Diagnostics Corp, A Chiron Company
- Ciba Corning Diagnostics Corp, A Chiron Company - Electrophoretic Products
- Ciba Corning Diagnostics Corp,
Associate Active Members

Affinity Health System (WI)
Allegheny University of the Health Sciences (PA)
Allergy Testing Laboratory (TX)
Alton Ochsner Medical Foundation (LA)
American Oncologic Hospital (PA)
Associated Regional & University Pathologists (UT)
Astra Research Center Boston (MA)
Baptist Medical Center - Montclair (AL)
Battelle (OH)
BC Children’s Hospital (Canada)
Bristol Regional Medical Center (TN)
Broward General Medical Center (FL)
Canterbury Health Laboratories (New Zealand)
CENTREX Clinical Laboratories (NY)
Chester County Hospital (PA)
Children’s Hospital Los Angeles (CA)
Children’s Hospital Medical Center (Akron, OH)
Children’s Hospital Medical Center (Cincinnati, OH)
Children’s Hospital - New Orleans (LA)
City of Hope National Medical Center (CA)
City Hospital (WV)
The Cleveland Clinic Foundation (OH)
Coler Memorial Hospital (NY)
Commonwealth of Kentucky
Compunet Clinical Laboratories (OH)
Dean Medical Center (WI)
Dhaahran Health Center (Saudi Arabia)
Diagnostic Systems Laboratories, Inc. (TX)
Dianon Systems, Inc. (CT)
Duke University Medical Center (NC)
Dwight David Eisenhower Army Medical Center (Ft. Benning, GA)
Easton Hospital (PA)
East Texas Medical Center
Ellis Fischel Cancer Center (MO)
Elmhurst Memorial Hospital (IL)
Elyria Memorial Hospital (OH)
Evanston Hospital (IL)
Federal Medical Center (MN)
Fort Leonard Wood Army Community Hospital (MO)
Grady Memorial Hospital (GA)
Great Smokies Diagnostic Laboratory (NC)
Harris Methodist Fort Worth (TX)
Hartford Hospital (CT)
Heritage Hospital (MI)
Hospital Saint Pierre (Belgium)
Hunter Area Pathology Service (Australia)
Incstar Corporation (MN)
Institute for Transfusion Medicine (PA)
Iowa Methodist Medical Center
Japan Association Clinical Reagents Ind. (Tokyo, Japan)
Kaiser Permanente (CA)
Kenora-Rainy River Regional Laboratory Program (Dryden, ON, Canada)
Laboratorio Clinico Borinquen (PR)
Laboratory Corporation of America (NC)
Lahey Hitchcock Medical Center (MA)
Lancaster General Hospital (PA)
Lawrence Memorial Hospital (MA)
Loma Linda University Medical Center (CA)
Maine Medical Center
Malcolm Grow USAF Medical Center (MD)
Martin Army Community Hospital (MD)
Martin Memorial Medical Center (FL)
Maryview Medical Center (VA)
McKennon Hospital (SD)
M.D. Anderson Hospital & Tumor Institute (TX)
MDS Laboratories (Etobicoke, ON, Canada)
The Medical Center of Ocean County (NJ)
Medical College of Virginia Hospital
Melbourne Pathology (Australia)
Memorial Medical Center (IL)
Mercy & Baptist Medical Center (LA)
Mercy Hospital (MN)
Methodist Hospital of Indiana
Methodist Hospitals of Memphis (TN)
Mobile Infirmary Association (AL)
Montgomery Regional Medical Center (AL)
Montreal Children’s Hospital (Canada)
Mount Sinai Hospital (NY)
Mount Sinai Hospital (Toronto, ON, Canada)
National Genetics Institute (CA)
National Institutes of Health (MD)
National Naval Medical Center (MD)
Naval Hospital Cherry Point (NC)
New Jersey Department of Health
The New York Blood Center
New York State Department of Health
New York State Library
North Carolina Laboratory of Public Health
North Carolina School of Veterinary Medicine
North Central Bronx Hospital (NY)
North Shore University Hospital (NY)
Northwestern Memorial Hospital (IL)
Ocean County Medical Laboratories (NJ)
Our Lady of Lourdes Hospital (NJ)
Our Lady of the Resurrection Medical Center (IL)
Palo Alto Medical Foundation (CA)
PAPP Clinic P.A. (GA)
Pathogenesis Corp. (WA)
Pathology Associates Laboratories (CA)
Permanente Medical Group (CA)
Polly Ryon Memorial Hospital (TX)
Polyclinic Medical Center (PA)
Puckett Laboratories (MS)
Queens Hospital Center (NY)
The Queen’s Medical Center (HI)
Ravenswood Hospital Medical Center (IL)
Rhode Island Department of Health Laboratories
Riverside Clinical Laboratories (VA)
Riverside-San Bernardino County Indian Health (CA)
St. Anthony’s Hospital (FL)
St. John Hospital and Medical Center (MI)
St. John’s Hospital (IL)
St. Luke’s-Roosevelt Hospital Center (NY)
| St. Mary of the Plains Hospital (TX) | University of Alberta Hospitals (Canada) | University of Virginia Medical Center |
| St. Mary’s Regional Medical Center (NV) | University of California, San Francisco | VA (Albuquerque) Medical Center (NM) |
| St. Paul Medical Center (TX) | University of Cincinnati Medical Center (OH) | VA (Indianapolis) Medical Center (IN) |
| St. Paul Ramsey Medical Center (MN) | University Community Hospital (FL) | VA (Jackson) Medical Center (MS) |
| San Francisco General Hospital (CA) | University of Florida | VA (Miami) Medical Center (FL) |
| Shadyside Hospital (PA) | University of Hawaii at Manoa | VA (Milwaukee) Medical Center (WI) |
| Shanghai Center for the Clinical Laboratory (China) | University Hospital (Gent) (Belgium) | VA (Perry Point) Medical Center (MD) |
| Shore Memorial Hospital (NJ) | University Hospital (London, ON, Canada) | Veterans General Hospital (Republic of China) |
| Sinai Hospital of Detroit (MI) | University Hospital (IN) | Warde Medical Laboratory (MI) |
| SmithKline Beecham Clinical Laboratories (GA) | University Hospital of Cleveland (OH) | Wilford Hall USAF Medical Center (TX) |
| SmithKline Beecham Clinical Laboratories (TX) | The University Hospitals (OK) | William Beaumont Hospital (MI) |
| SmithKline Beecham Clinical Laboratories (WA) | University of Medicine & Dentistry, NJ University Hospital | Wisconsin State Laboratory of Hygiene |
| Specialty Laboratories, Inc. (CA) | University of Michigan | York Hospital (PA) |
| Stanford Health Services (CA) | University of Nebraska Medical Center | Zale Lipshy University Hospital (TX) |
| SUNY @ Stony Brook (NY) | University of Utah Medical Center | |
| Travis Air Force Base (CA) | | |
| Tripler Army Medical Center (HI) | | |
| UNC Hospitals (NC) | | |

**OFFICERS**

| A. Samuel Koenig, III, M.D., President Family Medical Care | Carl H. Blank, Dr.P.H. Wyoming Department of Health | Robert F. Moran, Ph.D., FCCM, FAIC Chiron Diagnostics Corporation |
| William F. Koch, Ph.D., President Elect National Institute of Standards and Technology | Carl A. Burtis, Ph.D. Oak Ridge National Laboratory | David E. Nevalainen, Ph.D. Abbott Laboratories |
| F. Alan Andersen, Ph.D., Secretary Cosmetic Ingredient Review | Sharon S. Ehrmeyer, Ph.D. University of Wisconsin | Donald M. Powers, Ph.D. Johnson & Johnson Clinical Diagnostics |
| Donna M. Meyer, Ph.D., Treasurer St. Joseph Hospital | Helen M. Free, D.Sc. Bayer Corporation | Eric J. Sampson, Ph.D. Centers for Disease Control and Prevention |
| Charles F. Galanaugh, Past President Becton Dickinson and Company | Elizabeth D. Jacobson, Ph.D. FDA Center for Devices and Radiological Health | Marianne C. Watters, M.T.(ASCP) Parkland Memorial Hospital |
| John V. Bergen, Ph.D., Executive Director | Kenneth D. McClatchey, M.D., D.D.S. Loyola University Medical Center | Ann M. Willey, Ph.D. New York State Department of Health |
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract</td>
<td>i</td>
</tr>
<tr>
<td>Committee Membership</td>
<td>iv</td>
</tr>
<tr>
<td>Active Membership</td>
<td>vi</td>
</tr>
<tr>
<td>Foreword</td>
<td>xi</td>
</tr>
<tr>
<td>1. Introduction</td>
<td>1</td>
</tr>
<tr>
<td>2. Scope</td>
<td>1</td>
</tr>
<tr>
<td>3. Definitions</td>
<td>1</td>
</tr>
<tr>
<td>4. Performance Goals</td>
<td>4</td>
</tr>
<tr>
<td>4.1. Analytical Error: Inaccuracy</td>
<td>4</td>
</tr>
<tr>
<td>4.2. Analytical Error: Calibrator Bias</td>
<td>5</td>
</tr>
<tr>
<td>4.3. Analytical Error: Calibrator Use</td>
<td>5</td>
</tr>
<tr>
<td>4.4. Analytical Error: Nonlinearity</td>
<td>6</td>
</tr>
<tr>
<td>4.5. Analytical Error: Imprecision</td>
<td>6</td>
</tr>
<tr>
<td>4.6. Analytical Error: Interferences</td>
<td>7</td>
</tr>
<tr>
<td>4.7. Analytical Error: Drift</td>
<td>8</td>
</tr>
<tr>
<td>5. Relating Performance Goals to Medical Decisions</td>
<td>8</td>
</tr>
<tr>
<td>5.1. Effect of Assay Bias</td>
<td>9</td>
</tr>
<tr>
<td>5.2. Effect of Assay Imprecision</td>
<td>13</td>
</tr>
<tr>
<td>Appendix</td>
<td>16</td>
</tr>
<tr>
<td>References</td>
<td>17</td>
</tr>
<tr>
<td>Additional Bibliography</td>
<td>18</td>
</tr>
<tr>
<td>Summary of Comments and Subcommittee Responses</td>
<td>19</td>
</tr>
<tr>
<td>Related NCCLS Documents</td>
<td>25</td>
</tr>
</tbody>
</table>
Foreword

The primary objective of quality control in the clinical laboratory is to ensure that the analytical values are sufficiently reliable to be used in the care of patients. Once quality goals are established for an assay, their results can be evaluated in terms of clinical usefulness. This approach can have distinct advantages in the quality control of multichannel hematology analyzers.

This standard examines the effects of the following variables on performance goals:

- Calibration of the instruments
- Imprecision of the analytical measurements
- Analyte variations within an individual
- Inherent differences in values among persons.

The first two of these sources of variation define opportunities for improvement in analyzer design. The second two define irreducible biological variables.

In this document, the Subcommittee on the Blood Count provides goals for standards of performance that are useful for diagnosis, patient monitoring and control of therapeutic regimens. These performance goals set the stage for a review of quality control options that are intended to provide a framework for ensuring that patients’ assays are made as precisely and accurately as the analyzer allows. To this end, the production of a companion document is planned that will address the principles and methods of quality control that will help users and makers of automated hematology analyzers achieve these goals. This approach should stimulate improvements in analyzer design and interpretation of assay results. One goal is that manufacturers will recognize the need to coordinate the performance of different analytical methods so that assay results from different analyzers will have a reasonable degree of interchangeability. A further goal in this context is for designers to strive to minimize some of the existing disparities between analyzer and reference assays.

Universal Precautions

Because it is often impossible to know which might be infectious, all patient blood specimens are to be treated with universal precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention [MMWR 1987; 36 (Suppl 2S) 2S–18S]. NCCLS document M29-T2, Protection of Laboratory Workers from Infectious Disease Transmitted by Blood, Body Fluids and Tissue—Second Edition; Tentative Guideline, deals specifically with this issue.

Key Words

Accuracy, analytical bias, calibration, calibrator, imprecision, linearity, quality control, sensitivity, specificity, value.
Performance Goals for the Internal Quality Control of Multichannel Hematology Analyzers; Approved Standard

1 Introduction

The elements of the complete blood cell count (CBC) included in this standard are the measurement of hemoglobin concentration (Hb), hematocrit (Hct), erythrocyte count (RBC), mean cell volume (MCV), leukocyte count (WBC), and platelet count (Plt). Goals for the derived red cell indices, mean cell hemoglobin (MCH), and mean cell hemoglobin concentration (MCHC) are not included.

The widespread acceptance of automated whole blood analyzers and concomitant improvements in calibrators and control materials has had a major effect on the efficiency of laboratory operation. Also, a marked improvement in intralaboratory and interlaboratory precision and accuracy has occurred. For values in the adult reference range, within-laboratory coefficients of variation (CV) of less than 1.0% for RBC, Hb and MCV are readily achieved on the newest generation of analyzers, while WBC counts show CVs less than 2% and Plt counts CVs less than 3%. However, maintaining accuracy by preventing or predicting drift during routine operation remains a problem with some types of analyzers.

2 Scope

This document presents performance goals for analytical accuracy and precision of multichannel hematology analyzers capable of being calibrated. These clinical performance goals relate the majority of routinely produced analytical values to reference populations and to action limits established by the laboratory.

Goals for standards for specimen handling, equipment operation, electronic checking, preventive maintenance, and reagent quality are not included in this document, but their effect on performance is discussed where relevant.

This standard will be useful to laboratory directors, supervisors, quality control officers, and others who have responsibilities for ongoing quality control in hematology laboratories, particularly in the light of current regulatory pressures. It is a starting point for national and international discussion of the issues surrounding the design of quality control systems for multichannel hematology analyzers and as an aid to manufacturers who seek to improve the performance of their products.

3 Definitions

Within this document, terms are defined as follows:

Accuracy: A measure of agreement between the estimate of a value and a "true" value; quantifiable in terms of departure from accuracy; expressed as systematic error or bias.

- Accuracy, of an analytic process: Expressed as the difference between the average result obtainable by a method under specified conditions and the result accepted as true or standard; expressed in the same units as the result, or as a percentage of the standard result (relative accuracy).

NOTE: The lower the difference, the higher the accuracy (the lower the inaccuracy). Conventionally, this difference includes only process inaccuracy (process bias or systematic error) because the contribution of process imprecision (random error) is minimized by the averaging of multiple determinations.

- Accuracy, of a result: Expressed as the difference between a result and the "true" value.


---

This is a preview of "H26-A". Click here to purchase the full version from the ANSI store.