Protocol for the Evaluation, Validation, and Implementation of Coagulometers; Approved Guideline

This document provides guidance and procedures to the end user and manufacturer for the selection, evaluation, validation, and implementation of a laboratory coagulometer. 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 H57-A—Protocol for the Evaluation, Validation, and Implementation of Coagulometers; Approved Guideline provides guidance and procedures to the end user and manufacturer for the selection, evaluation, validation, and implementation of a laboratory coagulometer. Guidelines are given on the information that should be sought by the end user and manufacturer before acquisition. Included are guidelines for the procedures, specimens, reagents, and data analysis that may be used in the assessment of a coagulometer. This document addresses the differences in workload and range of tests offered by different laboratories, and this is reflected in the user assessment guidelines. Finally, guidance is given on implementation, including training, education, and interfacing.
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Committee Membership

Area Committee on Hematology

Bruce H. Davis, MD
Chairholder
Eastern Maine Medical Center
Bangor, Maine

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

Dorothy M. Adcock, MD
Esoterix Coagulation
Aurora, Colorado

Frank M. LaDuca, PhD, FAHA
Siemens Medical Solutions Diagnostics
Tarrytown, New York

Ginette Y. Michaud, MD
FDA Center for Devices and Radiological Health
Rockville, Maryland

Albert Rabinovitch, MD, PhD
Abbott Hematology
Santa Clara, California

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

Charles F. Arkin, MD
Lahey Clinic
Burlington, Massachusetts

J. David Bessman, MD
University of Texas Medical Branch
Galveston, Texas

Douglas J. Christie, PhD, FAHA
Dade Behring, Inc.
Newark, Delaware

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

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

Committee Advisors

John A. Koepke, MD
Durham, North Carolina

Francis Lacombe, MD, PhD
Hôpital Haut-Lévêque
Pessac, France

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

Richard A. Marlar, PhD
Oklahoma City VA Medical Center
Oklahoma City, Oklahoma

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

Diane I. Szamosi, MA, MT(ASCP)SH
Greiner Bio-One
North America Preanalytics
Monroe, North Carolina

Subcommittee on Protocol for the Evaluation of Coagulometers

Chris Gardiner, FIBMS, MSc, PhD
Chairholder
University College London Hospitals
London, United Kingdom

Dorothy M. Adcock, MD
Esoterix Coagulation
Aurora, Colorado

Leonthena R. Carrington, MBA, MT (ASCP)
FDA Ctr. for Devices/Rad. Health
Rockville, Maryland

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

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

Charles F. Arkin, MD
Lahey Clinic
Burlington, Massachusetts

J. David Bessman, MD
University of Texas Medical Branch
Galveston, Texas

Douglas J. Christie, PhD, FAHA
Dade Behring, Inc.
Newark, Delaware

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

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

Richard A. Marlar, PhD
Oklahoma City VA Medical Center
Oklahoma City, Oklahoma

David L. McGlasson, MS, CLS/NCA, H(ASCP)
59th Clinical Research Squadron/MSRL
Lackland AFB, Texas

Kathleen Fisher Trumbull, MS, MT(ASCP)
Instrumentation Laboratory
Lexington, Massachusetts

Joseph L. Wheeler, BS
Biotest Diagnostic Corporation
Denville, New Jersey

Staff

Clinical and Laboratory Standards Institute
Wayne, Pennsylvania

Lois M. Schmidt, DA
Vice President, Standards Development and Marketing

David E. Sterry, MT(ASCP)
Staff Liaison

Melissa A. Lewis
Editor
Acknowledgment

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Foreword

Before a coagulometer can be used for testing patient samples, it must receive a thorough evaluation by the purchasing laboratory or an independent expert center. The scope of the evaluation depends upon who is performing the evaluation; the availability of independent evaluation data; the range of tests performed by the laboratory undertaking the evaluation; and the range of samples available to the evaluating laboratory.

Coagulometers used in clinical laboratories have become increasingly complex, and the evaluation of such instruments is complicated and time consuming. In addition to the common screening tests (prothrombin time, activated partial thromboplastin time, thrombin clotting time, and Clauss fibrinogen assay), most coagulometers also perform chromogenic and immunoturbidimetric assays. Some analyzers may also have the capability to perform chemiluminescent assays. Existing evaluation guidelines are generally aimed at clinical chemistry analyzers, in which well-defined analytes, with well-documented reference materials/standards, are assayed and a range of suitable matrices is available. For the majority of coagulation tests, the activity of whole enzyme pathways is assessed; this can only be achieved with citrated plasma samples.

Newer trends in hemostasis testing and reagent/instrument manufacturing necessitate the development of an updated guideline for the evaluation of coagulometers. Early evaluation protocols tended to compare instrument performance to the manual clotting technique; although this remains the international reference method for PT/INR (World Health Organization [WHO] 1983), it has now largely disappeared from routine laboratories. Contemporary reagents are frequently developed exclusively for use with a given instrument and consequently are unsuitable for instruments employing other end-point detection methods. With this trend towards tailored reagent/instrument systems, there is a need for a more holistic outlook to instrument evaluation. This may be achieved by comparison against reference reagents and reference instruments, selected for their suitability to the instrument and reagents under evaluation.

A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization wherever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in the United States, Europe, and elsewhere; that these differences are reflected in CLSI, ISO, and CEN documents; and that legally required use of terms, regional usage, and different consensus timelines are all challenges to harmonization. In light of this, CLSI recognizes that harmonization of terms facilitates the global application of standards and deserves immediate attention. Implementation of this policy must be an evolutionary and educational process that begins with new projects and revisions of existing documents.

In order to align the usage of terminology in this document with that of ISO, the term accuracy, in its metrological sense, refers to the closeness of the agreement between the result of a (single) measurement and a true value of a measurand, and comprises both random and systematic effects. Precision is defined as the “closeness of agreement between independent test/measurement results obtained under stipulated conditions.” As such, it cannot have a numerical value, but may be determined qualitatively as high, medium, or low. For its numerical expression, the term imprecision is used, which is the “dispersion of results of measurements obtained under specified conditions.” In addition, different components of precision are defined in H57-A, primarily repeatability, ie, “the closeness of the agreement between results of successive measurements of the same measurand carried out under the same conditions of measurement”; while reproducibility describes “the closeness of agreement of results of measurements under changed conditions.”
The term *measurand* (a particular quantity subject to measurement) is used in combination with the term *analyte* (component represented in the name of a measurable quantity) when its use relates to a biological fluid/matrix; the term *reportable range* when referring to “a set of values of measurands for which the error of a measuring instrument (test) is intended to lie within specified limits”; and the term *measurement procedure* is combined with *analytical method* for a set of operations used in the performance of particular measurements according to a given method.

All terms and definitions will be reviewed again for consistency with international use, and revised appropriately during the next scheduled revision of this document.

**Key Words**

Coagulation analyzer, coagulometer evaluation, comparability, efficiency assessment, implementation, performance validation, precision
Protocol for the Evaluation, Validation, and Implementation of Coagulometers; Approved Guideline

1 Scope

This guideline specifies recommendations on how to plan and execute the selection, evaluation, validation, and implementation of a laboratory coagulometer. It includes assessment of safety, carryover, precision, bias, linearity, and comparability for coagulometers that perform clotting, chromogenic and/or immunoturbidimetric and/or chemiluminescent testing on plasma. The intended users of this guideline are hospitals, reference laboratories, and manufacturers. It is intended as a guideline for evaluation of commercially available coagulometers that have received prior US Food and Drug Administration 510(k) clearance, CE mark, or other country-specific registration. This guideline is not intended for use by facilities evaluating point of care or manufacturers of point-of-care coagulometers. For information on point-of-care coagulometers, refer to CLSI/NCCLS document H49. It also is not intended to provide guidance for platelet testing or the completion of 510(k) clearance documentation, nor intended to proscribe the level of customer service provided by vendors. This guideline recommends the selection of tests and procedures to validate the performance of coagulometers, but it does not address the process to validate each test method of the device. This guideline is not intended to replace any existing standards or requirements but should be used in addition to existing standards.

2 Introduction

This guideline details several different steps in the evaluation of a coagulometer by the end user and manufacturer. The evaluation of a coagulometer typically progresses from market research, where several desirable instrument platforms are selected, to a preliminary preacquisition evaluation of one or more instruments, to a more detailed postacquisition validation of a single platform, culminating in implementation of the testing system for clinical use. This guideline is intended to guide the end user and manufacturer through the evaluation, validation, and implementation stages of this process. Where applicable, the guideline has addressed separately the level of evaluation considered appropriate for low-volume hospital laboratories vs larger hospital or reference laboratories with a higher test volume and more complex test mix. For information on point-of-care coagulometers, refer to CLSI/NCCLS document H49.

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 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. For specific precautions for preventing the laboratory transmission of all infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all infectious disease, refer to CLSI document M29.

4 Definitions

accuracy (of measurement) – closeness of the agreement between the result of a measurement and a true value of the measurand (VIM93).