H58-P
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Platelet Function Testing by Aggregometry; Proposed Guideline

PLEASE

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This proposed document is published for wide and thorough review in the new, accelerated Clinical and Laboratory Standards Institute consensus-review process. The document will undergo concurrent consensus review, Board review, and delegate voting (i.e., candidate for advancement) for 60 days.

Please send your comments on scope, approach, and technical and editorial content to CLSI.

Comment period ends

28 August 2007

The subcommittee responsible for this document will assess all comments received by the end of the comment period. Based on this assessment, a new version of the document will be issued. Readers are encouraged to send their comments to the Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA; Fax: +610.688.0700, or to the following e-mail address: customerservice@clsi.org

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COMMENT

This document provides concrete, standard procedures for using aggregometry to assess platelet function in patient specimens with the intent to achieve greater uniformity of results.

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

(Formerly NCCLS)

Clinical and Laboratory Standards Institute

Advancing Quality in Healthcare Testing

Clinical and Laboratory Standards Institute (CLSI, formerly 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. Our process 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, we provide an open and unbiased forum to address critical issues affecting the quality of patient testing and health care.

PUBLICATIONS

A 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, 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 CLSI 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 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 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.

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.

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 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 document. Address comments to Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

VOLUNTEER PARTICIPATION

Healthcare 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 H58-P—*Platelet Function Testing by Aggregometry; Proposed Guideline* provides concrete, standard procedures for using aggregometry to assess platelet function in patient specimens and samples, with the intent to achieve greater uniformity of results by laboratories following these guidelines. Descriptions of light transmission aggregometry, whole blood impedance aggregometry, and shear-flow technologies are provided so both long-time and new users may establish consistent, reproducible platelet function testing programs in their laboratories.

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Foreword

Platelets play a vital role both in hemorrhagic and vascular ischemic disorders. Antiplatelet therapy (APT) is regarded as "the cornerstone of treatment" for various coronary conditions,[1] giving dramatic rise to the introduction of new antiplatelet drugs. This in turn has increased the interest among clinicians and laboratorians to use various tests of platelet function. One such method is platelet aggregometry, a common technology that has been part of clinical laboratory practice for over 40 years. Yet, surprisingly, platelet aggregometry has largely been performed without globally accepted techniques. Consequently, customized procedures and reagents are frequently used, often making it difficult to obtain consistent results.

This guideline provides concrete, standard procedures for using aggregometry to assess platelet function in patient specimens and samples with the intent to achieve greater uniformity of results by laboratories following these guidelines. Descriptions of light transmission aggregometry (LTA), whole blood impedance aggregometry, and shear-flow technologies are provided so both long-time and new users may establish consistent, reproducible platelet function testing programs in their laboratories.

Invitation for Participation in the Consensus Process

An important aspect of the development of this and all CLSI documents should be emphasized, and that is the consensus process. Within the context and operation of CLSI, the term "consensus" means more than agreement. In the context of document development, "consensus" is a process by which CLSI, its members, and interested parties (1) have the opportunity to review and to comment on any CLSI publication; and (2) are assured that their comments will be given serious, competent consideration. Any CLSI document will evolve as will technology affecting laboratory or healthcare procedures, methods, and protocols; and therefore, is expected to undergo cycles of evaluation and modification.

The Subcommittee on Platelet Function Testing has attempted to engage the broadest possible worldwide representation in committee deliberations. Consequently, it is reasonable to expect that issues remain unresolved at the time of publication at the proposed level. The review and comment process is the mechanism for resolving such issues.

The CLSI voluntary consensus process is dependent upon the expertise of worldwide reviewers whose comments add value to the effort. At the end of a 60-day comment period, each subcommittee is obligated to review all comments and to respond in writing to all which are substantive. Where appropriate, modifications will be made to the document, and all comments along with the subcommittee's responses will be included as an appendix to the document when it is published at the next consensus level.

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.

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.

Users of H58-P should understand, however, that the fundamental meanings of the terms are identical in many cases, and to facilitate understanding, terms are defined in the Definitions section of this guideline.

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

Antiplatelet therapy (APT), impedance aggregometry, light transmission aggregometry (LTA), low and high shear, platelet activation, platelet aggregation, platelet function testing

Platelet Function Testing by Aggregometry; Proposed Guideline

1 Scope

This guideline specifies requirements/recommendations for specimen collection, preexamination considerations, patient preparation, sample processing, testing, and quality control in relation to platelet function testing by aggregometry using low and high shear technologies. It covers anticoagulants, specimen storage and transport temperatures, sample selection for various methodologies, establishment of reference intervals, result reporting, result analysis, assay validation, and troubleshooting. The intended users of this guideline are clinicians, hospital and reference laboratorians, manufacturers, and regulatory agencies. This guideline is not intended for use with global hemostasis, platelet counting, flow cytometry, home testing, point-of-care, or research systems. This guideline does not address therapeutic guidance or interpretive guidelines.

2 Introduction

Platelet function testing has been a part of clinical laboratory practice since early in the 20th century. Hundreds of publications have defined healthy and pathologic platelet activity using numerous methodologies, such as the *in vivo* bleeding time, platelet aggregometry techniques, measurement of granular content and release, assessment of membrane surface markers, evaluation of signaling pathways, and *in vivo* platelet survival. Yet, despite this vast wealth of information, no clear standardization exists to guide uniformity among laboratories performing platelet function testing. Establishing such direction is critical, given the role of platelets in both hemorrhagic and thrombotic conditions and the rising significance of antiplatelet therapy (APT) in controlling platelet function across a broad spectrum of vascular disorders. The goal of this guideline is to standardize platelet function testing when using light transmission aggregometry (LTA), whole blood impedance aggregometry, and shear-flow technologies.

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.[2] 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 the related CLSI document.[3]

4 Terminology

4.1 Definitions

accuracy (of measurement) – closeness of the agreement between the result of a measurement and a true value of the measurand (VIM93).[4]

activation – a series of processes and events that change a discoid platelet into a spiny, spiculated entity with extension of pseudopodia that results in the initiation of signal transduction.

adhesion – the process by which platelets attach to surfaces or surface-bound proteins.