C49-P
Vol. 26 No. 21

Analysis of Body Fluids in Clinical Chemistry; Proposed Guideline

PLEASE

▼▼▼
▼▼
▼

This proposed document is published for wide and thorough review in the new, accelerated Clinical and Laboratory Standards Institute (CLSI) consensus-review process. The document will undergo concurrent consensus review, Board review, and delegate voting (i.e., candidate for advancement) for 90 days.

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

Comment period ends

18 September 2006

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 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

▲
▲▲
▲▲▲

COMMENT

This document provides guidance for the application of widely available measurement procedures for testing body fluids and for reporting and interpreting those results. It emphasizes defining the common clinical situations for this use; acceptable practice for measuring analytes without extended method verification for abnormal body fluid; influence of biologic and analytic variation on interpretation of results; and variability in comparing results between different instrument manufacturers. This document does not consider serum, plasma, whole blood, or fluids for which assays typically have performance claims in the measurement procedure documentation.

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

CLINICAL AND LABORATORY STANDARDS INSTITUTE ™
(Formerly NCCLS)

ifcc International Federation of Clinical Chemistry and Laboratory Medicine

Clinical and Laboratory Standards Institute

Advancing Quality in Healthcare Testing

The 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 the 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.

C49-P
ISBN 1-56238-609-3
Volume 26 Number 21
ISSN 0273-3099

Analysis of Body Fluids in Clinical Chemistry; Proposed Guideline

Richard A. McPherson, MD
Elma Kamari Bidkorpeh
William J. Castellani, MD
Lewis Glasser, MD
Andrea Griesmacher, MD
Alfred E. Hartmann, MD
Kenneth Ingram, Jr., BS, CLT(HHS), CLS(NCA)
Joseph A. Knight, MD
Michael A. Rosen, PhD
Wadid Sadek, PhD
Kenneth A. Slickers, Ph.D., DABCC

Abstract

Clinical and Laboratory Standards Institute document C49-P, *Analysis of Body Fluids in Clinical Chemistry; Proposed Guideline* provides guidance to the clinical laboratory director for the application of widely available measurement procedures for testing body fluids and for reporting and interpreting those results. It emphasizes defining the common clinical situations for this use; acceptable practice for measuring analytes without extended method verification for abnormal body fluids; influence of biologic and analytic variation on interpretation of results; and variability in comparing results between different instrument manufacturers. This document does not consider serum, plasma, whole blood, or fluids for which assays typically have performance claims in the measurement procedure documentation.

Clinical and Laboratory Standards Institute (CLSI). *Analysis of Body Fluids in Clinical Chemistry; Proposed Guideline*. CLSI document C49-P (ISBN 1-56238-609-3). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2006.

(Formerly NCCLS)

Suggested Citation

(Clinical and Laboratory Standards Institute. *Analysis of Body Fluids in Clinical Chemistry; Proposed Guideline.* CLSI document C49-P [ISBN 1-56238-609-3]. Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2006.)

Proposed Guideline
June 2006

ISBN 1-56238-609-3
ISSN 0273-3099

Committee Membership

Area Committee on Clinical Chemistry and Toxicology

David A. Armbruster, PhD, DABCC, FACB
Chairholder
Abbott Laboratories
Abbott Park, Illinois

W. Gregory Miller, PhD
Vice-Chairholder
Virginia Commonwealth University
Richmond, Virginia

John Rex Astles, PhD, FACB
Centers for Disease Control and Prevention
Atlanta, Georgia

David M. Bunk, PhD
National Institute of Standards and Technology
Gaithersburg, Maryland

Neil Greenberg, PhD
Ortho-Clinical Diagnostics, Inc.
Rochester, New York

Christopher M. Lehman, MD
University of Utah Health Sciences Center
Salt Lake City, Utah

Richard R. Miller, Jr.
Dade Behring Inc.
Newark, Delaware

Linda Thienpont, PhD
University of Ghent
Ghent, Belgium

Hubert Vesper, PhD
Centers for Disease Control and Prevention
Atlanta, Georgia

Advisors

Mary F. Burritt, PhD
Mayo Clinic
Rochester, Minnesota

Paul D'Orazio, PhD
Instrumentation Laboratory
Lexington, Massachusetts

Carl C. Garber, PhD, FACB
Quest Diagnostics, Incorporated
Lyndhurst, New Jersey

Uttam Garg, PhD, DABCC
The Children's Mercy Hospital
Kansas City, Missouri

Harvey W. Kaufman, PhD
Quest Diagnostics, Incorporated
Lyndhurst, New Jersey

Gary L. Myers, PhD
Centers for Disease Control and Prevention
Atlanta, Georgia

David Sacks, MD
Brigham and Women's Hospital and Harvard Medical School
Boston, Massachusetts

Bette Seamonds, PhD
Mercy Health Laboratory
Swarthmore, Pennsylvania

Dietmar Stöckl, PhD
STT Consulting
Horebeke, Belgium

Thomas L. Williams, MD
Nebraska Methodist Hospital
Omaha, Nebraska

Jack Zakowski, PhD, FACB
Beckman Coulter, Inc.
Brea, California

Subcommittee on Analysis of Body Fluids in Clinical Chemistry

Richard A. McPherson, MD
Chairholder
Virginia Commonwealth University
Richmond, Virginia

William J. Castellani, MD
Penn State Hershey Medical Center
Hershey, Pennsylvania

Kenneth Ingram, Jr., CLT(HHS), CLS (NCA)
FDA Ctr. for Devices/Rad. Health
Rockville, Maryland

Andrea Griesmacher, MD
University Hospital of Innsbruck
Innsbruck, Austria

Alfred E. Hartmann, MD
Avera McKennan Hospital
Sioux Falls, South Dakota

Kevin Jones, B.Sc, PhD, MRSC Cchem
Whatman International LTD.
Clifton, New Jersey

Joseph A. Knight, MD
University of Utah School of Medicine
Salt Lake City, Utah

Michael A. Rosen, PhD
Dade Behring Inc.- Glasgow
Newark, Delaware

Kenneth A. Slickers, PhD, DABCC
Roche Diagnostics Corporation
Indianapolis, Indiana

Advisor

Jack Zakowski, PhD, FACB
Beckman Coulter, Inc.
Brea, California

Staff

Clinical and Laboratory Standards Institute
Wayne, Pennsylvania

John J. Zlockie, MBA
Vice President, Standards

Tracy A. Dooley, MLT(ASCP)
Staff Liaison

Patrice E. Polgar
Project Manager

Donna M. Wilhelm
Editor

Melissa A. Lewis
Assistant Editor

Contents

Foreword

Measurements of analytes in body fluids other than plasma or serum almost never have performance claims from a method provider, despite occasional clinical need to perform these analyses in abnormal body fluids (e.g., peritoneal, pleural, drainage) to detect specific organ involvement or injury that caused the fluid formation. Such measurements for a number of analytes are widely available, automated, and reasonably inexpensive. Furthermore, the information they provide is unique, frequently definitive, and may not be available from any other noninvasive procedure.

Strict interpretation of laboratory regulations would rule out the performance of analyses on these abnormal body fluids, because:

- manufacturers usually do not have performance claims for measurements in fluids other than serum, plasma, or urine;
- clinical laboratories do not generally have the resources to perform complete method verifications for such samples; and consequently,
- clinical laboratories have not established reference ranges for analytes in those fluids.

Furthermore, matrix effects from proteins and other constituents in serum or plasma and body fluids can be expected to alter measurement of analytes. Because concentrations of these constituents can vary several-fold in body fluids, the matrix effects may be unpredictable in any given fluid. Accordingly, a comparison between measured values from a body fluid and serum or plasma has inherent uncertainty due to this influence on analytic variability.

Nevertheless, clinicians can successfully use the results from fluids in direct comparison with concurrent results in serum or plasma to establish whether the fluid has a very high concentration of the analyte or a very low one (i.e., similar to that in serum or plasma). A high concentration of the analyte in a body fluid suggests direct involvement of the suspect organ; a concentration in the fluid similar to that in serum or plasma indicates no involvement of the organ.

This document provides guidance to clinical diagnostic laboratories for applying widely available measurement procedures to body fluids and for reporting and interpreting those results. Emphasis is placed on:

- the common clinical situations for this use;
- acceptable practice for measuring analytes without extended method verification for abnormal body fluids;
- influence of biologic and analytic variation on interpretation of results;
- variability in comparing results between different instrument manufacturers; and
- recommended reporting format.

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 Area Committee on Clinical Chemistry and Toxicology 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 90-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 following terms are used in C49-P:

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. *Trueness* is used in this document when referring to the "closeness of the agreement between the average value from a large series of measurements and a true value of a measurand"; the measurement of trueness is usually expressed in terms of *bias. 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, a different component of precision is defined in C49-P, namely, *reproducibility,* i.e., "the closeness of the agreement between the results of measurements of the same measurand carried out under changed conditions of measurement."

The term *measuring range* has replaced r*eportable 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." The term *diagnostic sensitivity* has replaced the term *clinical sensitivity* because in Europe, the term "clinical" often refers to clinical studies of drugs under stringent conditions.

Users of C49-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

body fluid, exudate, matrix effect, method validation, organ injury, serous fluid, transudate, synovial fluid

Acknowledgement

This guideline was prepared by CLSI, as part of a cooperative effort with IFCC to work toward the advancement and dissemination of laboratory standards on a worldwide basis. CLSI gratefully acknowledges the participation of IFCC in this project. The IFCC expert for this project is Andrea Griesmacher, MD, University Hospital of Innsbruck, Austria.

Analysis of Body Fluids in Clinical Chemistry; Proposed Guideline

1 Scope

CLSI document C49 provides guidance to the clinical laboratory director for the application of measurement procedures for testing body fluids, and for reporting and interpreting those results. The document emphasizes: the most common clinical situations; acceptable practice for measuring analytes without extended method verification for abnormal body fluids; the influence of biologic and analytic variation on interpretation of results; and the variability in comparing results between different instrument manufacturers.

This document does not consider serum, plasma, whole blood, or fluids for which assays typically have performance claims in the measurement procedure documentation.

2 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 U.S. Centers for Disease Control and Prevention (Garner JS, Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. *Infect Control Hosp Epidemiol*. 1996;17:53-80). 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 most current edition of CLSI document M29—*Protection of Laboratory Workers From Occupationally Acquired Infections*.

3 Terminology

3.1 Glossary of Body Fluids

cerebrospinal fluid (CSF) – the fluid in the ventricles of the brain, between the arachnoid and the pia mater, and surrounding the spinal cord.

drainage fluid – fluid that drains through the skin from a surgical site, wound, or other penetrating injury; **NOTE 1:** The medical need is typically to determine whether the fluid is produced locally at the cutaneous site or whether it derives from deeper organ injury (e.g., kidney and urinary tract, liver and gall bladder, pancreas, intestine, stomach, esophagus, etc.); **NOTE 2:** Quantitation of organ-specific analytes in a drainage fluid can often provide unique diagnostic information to indicate what organs might need surgical repair.

pericardial fluid – fluid that accumulates in the pericardium, a closed sac of tissue surrounding the heart, most often due to inflammation or malignancy.

peritoneal fluid (ascites, ascitic fluid) – fluid that accumulates in the peritoneal cavity of the abdomen, often due to hepatic cirrhosis and less frequently due to malignancy or cardiac failure; **NOTE:** A subtype is peritoneal dialysis fluid that is instilled into the abdominal cavity and then removed as a form of dialysis in patients with renal failure.