



C49

Analysis of Body Fluids in Clinical Chemistry

This guideline provides information for the medical laboratory for evaluating measurement procedures, as well as a strategy to characterize assay performance, when applied to body fluid matrixes. Key concepts that apply to the entire test cycle, including preexamination, examination, and postexamination phases of body fluid testing, are discussed.

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 guideline C49—*Analysis of Body Fluids in Clinical Chemistry* provides guidance to the medical laboratory for evaluating measurement procedures, as well as a strategy to characterize assay performance, when applied to body fluid matrices. Key concepts that apply to the entire test cycle, including preexamination, examination, and postexamination phases of body fluid testing are discussed. This guideline does not consider serum, plasma, whole blood, or fluids for which measurement procedures typically have performance claims in the measurement procedure documentation. Appendix A provides didactic content on the anatomy, physiology, and pathophysiology of fluid accumulation. Appendix B provides the medical rationale for quantifying measurands in body fluids and the interpretation of results in the context of disease. Appendix C provides the user with a quick reference guide to the suggested utility of fluid and measurand combinations.

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Foreword

Since C49's original publication, regulatory requirements for laboratories performing body fluid testing have changed. In addition, the number of publications in peer-reviewed journals as well as single case studies documenting the diagnostic need to test a number of measurands in body fluids has increased substantially. To comply with regulatory requirements when choosing to offer body fluid testing, medical laboratories should determine which fluid types are appropriate to accept for testing through collaborating with the requesting clinical areas, characterizing measurement procedure suitability, and understanding performance limitations of methods not designated for use on body fluids by *in vitro* diagnostics manufacturers. This information is critical to ensure the accuracy of reported results, because physicians use these data for patient management.

Overview of Changes

This guideline replaces the previous edition of the approved guideline, C49-A, published in April 2007. This second edition of C49 provides medical laboratories with a strategy to evaluate method performance, as well as guidance on which measurands have clinical relevance when measured in body fluid matrixes. Several changes were made in this edition, including:

- Providing medical laboratories with a workflow that:
 - Outlines important preexamination conditions to consider when validating and performing body fluid testing (see Chapter 3)
 - Discusses key concepts for body fluid matrix considerations and measurement procedure selection (see Chapter 4)
 - Offers strategies for developing a measurement procedure validation plan to provide meaningful and accurate results for appropriate and timely patient management (see Chapter 5)
 - Offers recommendations for reporting body fluid tests to aid in the diagnostic interpretation of results (see Chapter 6)
 - Covers general laboratory QA activities to support ongoing body fluid testing (see Chapter 7)
- Assisting laboratories in minimizing patient risk and maximizing diagnostic return by:
 - Providing general information related to body fluid composition and pathogenic processes that lead to accumulation of body fluids (see Appendix A)
 - Defining the measurands and their expected concentrations that have diagnostic utility when measured in body fluids (see Appendix B)

NOTE: The content of this guideline is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

Key Words

Body fluid, exudate, matrix effect, measurement procedure validation, organ injury, serous fluid, synovial fluid, transudate

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Chapter 1: Introduction

This chapter includes:

- Guideline's scope and applicable exclusions
- Standard precautions information
- "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions
- Terms and definitions used in the guideline
- Abbreviations and acronyms used in the guideline

1.1 Scope

C49 provides guidance to medical laboratories for the appropriate application of measurement procedures for body fluid testing and for reporting results. This guideline primarily focuses on the recommended practice for verification of measurement procedures for measurands in body fluids and is applicable for laboratory testing requests on body fluids that do not have performance claims in the manufacturer's package insert or an equivalent validated laboratory-developed test. C49 does not cover serum, plasma, whole blood, urine, or fluids (eg, cerebrospinal fluid) for which measurement procedures typically have performance claims in the manufacturer's package insert.

1.2 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 known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of bloodborne pathogens. Published guidelines are available that discuss the daily operations of diagnostic medicine in humans and animals while encouraging a culture of safety in the laboratory.¹ 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 M29.²

1.3 Terminology

1.3.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization whenever 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 different countries and regions and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. CLSI recognizes its important role in these efforts, and its consensus process

focuses on harmonization of terms to facilitate the global application of standards and guidelines. Table 1 is provided to clarify the intended interpretations of the following terms.

Table 1. Common Terms or Phrases With Intended Interpretations

Term or Phrase	Intended Interpretation
“Needs to” or “must”	Explains an action directly related to fulfilling a regulatory and/or accreditation requirement or is indicative of a necessary step to ensure patient safety or proper fulfillment of a procedure
“Require”	Represents a statement that directly reflects a regulatory, accreditation, performance, product, or organizational requirement or a requirement or specification identified in an approved documentary standard
“Should”	Describes a recommendation provided in laboratory literature, a statement of good laboratory practice, or a suggestion for how to meet a requirement

1.3.2 Definitions

1.3.2.1 Body Fluid–Specific Definitions

body fluid testing – measurement of measurand(s) in biological specimens for which no performance claims from the measurement procedure’s manufacturer are available.

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

chylous effusion – fluid resulting from chronic pleural effusion with breakdown of inflammatory cell membranes into cholesterol crystals; **NOTE 1:** This fluid can appear iridescent and is sometimes referred to as “pseudochylous”; **NOTE 2:** The term “chylothorax” indicates the accumulation of fat droplets or chylomicrons in the pleural space due to thoracic (lymphatic) duct disruption or obstruction.

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 (eg, kidney and urinary tract, liver and gall bladder, pancreas, intestine, stomach, esophagus); **NOTE 2:** Quantitation of organ-specific measurands 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, often due to inflammation or malignancy; **NOTE:** The removal of such fluid is performed by pericardiocentesis.

peritoneal 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; also known as ascitic fluid; **NOTE 1:** The pathologic accumulation of fluid in the peritoneal cavity is called ascites and may be identified as ascitic fluid; **NOTE 2:** The removal of such fluid is performed by paracentesis; **NOTE 3:** A subtype is peritoneal dialysis fluid, which is delivered into the abdominal cavity and then removed through dialysis or dialyzed content in patients with renal failure.

Chapter 7: Ongoing Quality Assurance

This chapter includes:

- QC selection
- New reagent lot validation
- Comparison of instruments and methods
- Verification of linearity and reportable interval
- Proficiency testing

Chapter 5 provides laboratories with best practice guidance related to QA for validation of measurement procedure performance in body fluids. Outside of the validation, laboratories must also include necessary elements to comply with ongoing regulatory and accreditation requirements.

7.1 Quality Control Selection

Controls used for QA of measurement procedures in serum, plasma, and urine are usually sufficient, because body fluid-specific controls are not readily available. It is important to include control concentrations with appropriate normal and abnormal levels for the intended use of the body fluid measurement procedure, taking medical decision points into consideration.

7.2 New Reagent Lot Validation: Measurement Procedure Reagents and Calibrators

Evaluation of the acceptability of new reagent lots is good laboratory practice and a requirement for certain regulatory and accreditation agencies. When the laboratory has a protocol in place to evaluate new reagent lots using serum or plasma samples, it might not be necessary to have a separate protocol for body fluid evaluation, as long as similar performance characteristics between the serum and body fluid matrix are demonstrated during the validation phase. Depending on availability, inclusion of three to five body fluid specimens in the reagent lot evaluation protocol should be considered. However, when the reagent is used only for body fluid analysis, a lot-to-lot evaluation protocol should be put in place using the type of body fluids tested for clinical purposes. Refer to CLSI document EP26⁴⁸ as a guide for establishing a protocol.

7.3 Biannual Instrument and Measurement Procedure Comparisons

When body fluid testing is performed on multiple instruments in the same laboratory, it is important to compare results across measuring systems. Biannual interinstrument comparisons using a single specimen type (eg, serum, plasma, urine, or body fluid) ensure delivery of consistent results.

7.4 Biannual Linearity and Reportable Interval Verification

When the testing results of measurands in body fluids are deemed acceptable (see Chapter 5), the routine use of commercially available materials for the semiannual linearity and reportable interval verification of serum, plasma, or urine measurement procedures is sufficient and applicable to body fluid measurement procedures.

Chapter 8: Conclusion

This revised guideline aims to provide medical laboratories with strategies and workflows to evaluate method performance in body fluid matrixes. The step-by-step instructions are intended to support characterization of method performance and clarify the method verification process that is required to comply with regulatory and accreditation standards in the medical laboratory. Once measurement procedure validations (see Chapter 5) are completed, the medical laboratory can offer body fluid testing on a routine basis with assurance that the measurement procedure is acceptable for clinical reporting. Medical laboratories may choose to customize their validation plan to be applicable and scalable based on available clinical body fluid specimens and supported medical service lines.

Chapter 9: Supplemental Information

This chapter includes:

- References
- Appendixes
- The Quality Management System Approach
- Related CLSI Reference Materials

Sample



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