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C49-A

Analysis of Body Fluids in Clinical Chemistry; Approved Guideline

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.

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Analysis of Body Fluids in Clinical Chemistry; Approved Guideline

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Clinical and Laboratory Standards Institute document C49-A—*Analysis of Body Fluids in Clinical Chemistry; Approved 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.

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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.

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-A:

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-A, 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 *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." 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-A 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, synovial fluid, transudate

Acknowledgement

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Analysis of Body Fluids in Clinical Chemistry; Approved 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 US Centers for Disease Control and Prevention.[1] 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 appropriate CLSI document.[2]

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, 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; a subtype is:

> **peritoneal dialysis fluid** – fluid that is instilled into the abdominal cavity and then removed as a form of dialysis in patients with renal failure.

pleural fluid (pleural effusion) – fluid that accumulates in the pleural cavity surrounding the lungs; various subtypes (which may also be applied to other body fluids) are as follows: