CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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H02-A5

Procedures for the Erythrocyte Sedimentation Rate Test; Approved Standard—Fifth Edition

This document provides a description of the principle, materials, and procedure for a standardized erythrocyte sedimentation rate (ESR) method; a selected routine method, as well as a procedure to evaluate routine methods; and an outline of quality control programs for the ESR test.

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

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Procedures for the Erythrocyte Sedimentation Rate Test; Approved Standard—Fifth Edition

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Abstract

Clinical and Laboratory Standards Institute document H02-A5—*Procedures for the Erythrocyte Sedimentation Rate Test; Approved Standard—Fifth Edition* is a revision of the fourth edition approved standard (H02-A4) published in December 2000. The document outlines the necessary details for the performance of a standardized (Westergren) method on diluted (1:4) blood specimens for the determination of the erythrocyte sedimentation rate (ESR). Quality assurance and evaluation of other methods to measure the ESR are also described, including procedures for the preparation of a fresh blood reference material for use in the laboratory or manufacturing of ESR devices. This standard provides guidance for the validation, verification, quality assurance, and quality control of ESR measurement devices or related controls. The intended audience includes manufacturers of such devices, end-user clinical laboratories, accrediting organizations, and regulatory bodies.

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Foreword

The erythrocyte sedimentation rate (ESR) test, first described about 70 years ago,[1-3] is one of the most widely performed laboratory tests. The Westergren method[2,3] to measure the ESR has remained essentially unchanged since its inception and was recommended as the method of choice by the International Council (previously Committee) for Standardization in Haematology (ICSH) in 1973[4] and 1977.[5] Subsequently, in 1993, ICSH recommended the use of undiluted blood and adjustment of the hematocrit to 0.35 L/L or lower.[6] Although over the years, other methods to measure the ESR were introduced for routine use (eg, the Wintrobe method[7] and the zeta sedimentation ratio [ZSR] determination),[8] the Westergren method remains the benchmark against which other methods can be, and are, evaluated.

This fifth edition reflects a unifying approach to optimal use of all the current ESR methods. Of particular note is that upon review of the current literature and available expert opinion this edition now recommends a standardized method using diluted blood, thus revising the standardization method for the ESR.

Over the last few years, a number of technical innovations and semiautomated instruments were introduced to eliminate or decrease the risk of exposure of laboratory workers to potentially infectious material, eg, blood. The newer procedures are considered less hazardous, primarily because they are either self-contained or use disposable materials, or both. There is a need to examine these innovations, both for comparability of results to previously employed methods and to ensure, on an ongoing basis, the quality assurance of the results. This document provides standardized methods to address these needs.

Erythrocyte sedimentation is a nonspecific reaction; it is a measure of the presence and severity of pathological processes. In general, the ESR is increased in acute, general infections and in localized, acute, inflammatory conditions. Variations in the ESR depend on the nature and severity of the disease process. The usefulness of ESR is in evaluating patients with unexplained symptoms when inflammation and infectious disease are suspected and a specific diagnosis is not available effectively using other tests. No evidence supports the use of ESR in asymptomatic individuals and the test should not be included in routine investigations aimed to monitor the health status. ESR provides useful information when used as a diagnostic criterion for temporal arteritis, polymyalgia rheumatica, monitoring the activity of giant cell arteritis, and inflammatory arthropathies, as well as following the course of patients with rheumatoid arthritis.[9-17]

On occasion, the ESR may increase where other clinical and laboratory evaluations yield negative results. This should nonetheless be regarded as a sign of disease until such time as the physician is fully satisfied that the patient is perfectly well. However, normal values for the ESR were found in patients with a neoplasm of the liver[18] or with other serious conditions.[19] The ESR was used to differentiate organic disease from functional disorders, or as a guide to the progress of diseases such as rheumatic carditis, rheumatoid arthritis, and certain malignancies, including Hodgkin's disease.

ESR procedures cannot be calibrated. The procedures used to determine the ESR are susceptible to a variety of errors. An inadequately performed ESR that produces an incorrect result may not be detected unless some reference material is available in the laboratory where the ESR procedure is performed. Because the phenomenon of erythrocyte sedimentation is confined to fresh blood and is transient, presently, the only feasible way of providing a control material is for the manufacturer or test developer to specify a method for the production of such material in the laboratory where it will be used. Because of the nature of the human erythrocyte sedimentation reaction, reference or control materials of the usual type are not available for the ESR test.

Foreword (Continued)

This document describes a standardized procedure for the ESR test, as well as a selected procedure. This standardized method is based on the original methodology of Fåhraeus[1] and Westergren,[3] which used diluted blood in open-ended, Westergren-type glass pipettes of 300-mm length, mounted vertically in a rack or stand. The standardized procedure was verified in studies based on an ICSH procedure.[6] The procedures described in this document are an attempt to measure the ESR in a fashion that is not misleadingly influenced by variations in relative erythrocyte volume. The procedures also permit the preparation of a standardized material for test validation within the laboratory. Such a material, of necessity fresh whole blood, can then be used in the laboratory to ensure the quality of the method(s) routinely in use to determine the ESR.

The document outlines the necessary details for the performance of a standardized (Westergren) method on diluted (1:4) blood specimens for the determination of the ESR. Quality assurance and evaluation of other methods to measure the ESR are also described, including procedures for the preparation of a fresh blood reference material for use in the laboratory. This standard will enable the user of commercial, disposable ESR equipment to ensure that both the test equipment and test procedures are performing adequately.

Key Words

Erythrocyte sedimentation, erythrocyte sedimentation rate (ESR) test, quality control, selected procedure, standardized procedure, Westergren pipette

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1 Scope

This document addresses the methodology and devices for the measurement of the erythrocyte sedimentation rate (ESR) phenomenon. It also provides guidance for validation, verification, quality assurance (QA), and quality control (QC) through standardized approaches to ensure good laboratory science and clinical relevance. The intended audience includes manufacturers of such devices, end-user clinical laboratories, accrediting organizations, and regulatory bodies.

End-user clinical laboratories will also find guidance for establishment of working methods for ESR test validation and for QA of their ESR testing method(s).

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 blood-borne pathogens. Standard and universal precaution guidelines are available from the Centers for Disease Control and Prevention.[20] 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.[21]

3 Terminology

3.1 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, International Organization for Standardization (ISO), and European Committee for Standardization (CEN) documents, as well as in World Health Organization (WHO) publications; and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. In light of this, CLSI's consensus process for development and revision of standards and guidelines focuses on harmonization of terms to facilitate global application of standards and guidelines.

Specifically, in H02, *accuracy* was changed to *trueness* (where appropriate) for consistency with accepted international usage.

3.2 Definitions

accuracy (measurement) – closeness of agreement between a measured quantity value and a true quantity value of a measurand (ISO/IEC Guide 99)[22]; **NOTE 1:** The concept 'measurement accuracy' is not a quantity and is not given a numerical quantity value. A measurement is said to be more accurate when it offers a smaller measurement error (ISO/IEC Guide 99)[22]; **NOTE 2:** The term "measurement accuracy" should not be used for measurement trueness and the term measurement precision should not

be used for 'measurement accuracy,' which, however, is related to both these concepts (ISO/IEC Guide 99)[22]; **NOTE 3:** 'Measurement accuracy' is sometimes understood as closeness of agreement between measured quantity values that are being attributed to the measurand (ISO/IEC Guide 99).[22]

bias (measurement) – estimate of a systematic measurement error (ISO/IEC Guide 99).[22]

measurand – quantity intended to be measured (ISO/IEC Guide 99)[22]; **NOTE 1:** The specification of a measurand requires knowledge of the kind of quantity, description of the state of the phenomenon, body, or substance carrying the quantity, including any relevant component, and the chemical entities involved (ISO/IEC Guide 99)[22]; **NOTE 2:** In the second edition of the VIM and in IEC 60050-300:2001, the measurand is defined as the 'quantity subject to measurement' (ISO/IEC Guide 99)[22]; **NOTE 3:** The measurement, including the measuring system and the conditions under which the measurement is carried out, might change the phenomenon, body, or substance such that the quantity being measured may differ from the measurand as defined. In this case, adequate correction is necessary (ISO/IEC Guide 99)[22]; **NOTE 4:** In chemistry, "analyte," or the name of a substance or compound, is a term sometimes used for 'measurand.' This usage is erroneous because these terms do not refer to quantities (ISO/IEC Guide 99).[22]

precision (measurement) – closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions (ISO/IEC Guide 99)[22]; **NOTE 1:** Measurement precision is usually expressed numerically by measures of imprecision, such as standard deviation, variance, or coefficient of variation under the specified conditions of measurement (ISO/IEC Guide 99)[22]; **NOTE 2:** The 'specified conditions' can be, for example, repeatability conditions of measurement, intermediate precision conditions of measurement, or reproducibility conditions of measurement (see ISO 5725-3:1994)[23] (ISO/IEC Guide 99)[22]; **NOTE 3:** Measurement precision is used to define measurement repeatability, intermediate measurement precision, and measurement reproducibility (ISO/IEC Guide 99).[22]

reference method (procedure) – an exactly defined technique that is used in association with an internationally agreed reference preparation to provide sufficiently precise and accurate data for assessing the validity of other methods (modified from ICSH)[24]; **NOTE:** The ISO term is *reference measurement procedure* and is defined as a "measurement procedure accepted as providing measurement results fit for their intended use in assessing measurement trueness of measured quantity values obtained from other measurement procedures for quantities of the same kind, in calibration, or in characterizing reference materials (ISO/IEC Guide 99).[22]

reliability – the ability of a system or component to perform its required functions under stated conditions for specified period of time (IEEE 610.12-1990).[25]

reproducibility (measurement) – measurement precision under reproducibility conditions of measurement (ISO/IEC Guide 99)[22]; **NOTE:** See **reproducibility condition.**

reproducibility condition (of measurement) – condition of measurement, out of a set of conditions that includes different locations, operators, measuring systems, and replicate measurements on the same or similar objects (ISO/IEC Guide 99).[22]

sample – one or more parts taken from a system and intended to provide information on the system, often to serve as a basis for decision on the system or its production (ISO 15189)[26]; **NOTE 1:** For example, a volume of serum taken from a larger volume of serum (ISO 15189)[26]; **NOTE 2:** A sample is prepared from the patient specimen and used to obtain information by means of a specific laboratory test.

selected method (procedure) – a method approved by a defined authority as being suitable for routine use, taking account of the limits of its bias and imprecision in the context of its intended (clinical) purpose, economy of materials and labor, ease of performance, and safety; its validity must be verified by

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents. The approach is based on the model presented in the most current edition of CLSI document HS01—*A Quality Management System Model for Health Care.* The quality management system approach applies a core set of "quality system essentials" (QSEs), basic to any organization, to all operations in any health care service's path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager's guide. The QSEs are:

Documents and Records	Equipment	Information Management	Process Improvement
Organization	Purchasing and Inventory	Occurrence Management	Customer Service
Personnel	Process Control	Assessments—External and Internal	Facilities and Safety

H02-A5 addresses the QSEs indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Documents and Records	Organization	Personnel	Equipment	Purchasing and Inventory	Process Control	Information Management	Occurrence Management	Assessments—External and Internal	Process Improvement	Customer Service	Facilities and Safety
				H03	X C28 EP09 H01 H03						H03 M29

Adapted from CLSI document HS01—*A Quality Management System Model for Health Care.*

Path of Workflow

A path of workflow is the description of the necessary steps to deliver the particular product or service that the organization or entity provides. For example, CLSI document GP26—*Application of a Quality Management System Model for Laboratory Services* defines a clinical laboratory path of workflow, which consists of three sequential processes: preexamination, examination, and postexamination. All clinical laboratories follow these processes to deliver the laboratory's services, namely quality laboratory information.

H02-A5 addresses the clinical laboratory path of workflow steps indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Preexamination				**Examination**			**Postexamination**	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
H03	X H01 H03	H03	H03	X H03	X H03	X	X	

Adapted from CLSI document HS01—*A Quality Management System Model for Health Care.*

Related CLSI Reference Materials*

C28-A3c **Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition (2010).** This document contains guidelines for determining reference values and reference intervals for quantitative clinical laboratory tests.

EP09-A2-IR **Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Second Edition (Interim Revision) (2010).** This document addresses procedures for determining the bias between two clinical methods, and the design of a method comparison experiment using split patient samples and data analysis.

H01-A6 **Tubes and Additives for Venous and Capillary Blood Specimen Collection; Approved Standard—Sixth Edition (2010).** This standard contains requirements for the materials, manufacturing, and labeling of venous and capillary blood collection devices.

H03-A6 **Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition (2007).** This document provides procedures for the collection of diagnostic specimens by venipuncture, including line draws, blood culture collection, and venipuncture in children.

M29-A3 **Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Third Edition (2005).** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.

*CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.

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