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CLINICAL AND LABORATORY STANDARDS INSTITUTE®

December 2009

I/LA33-A

Validation of Automated Systems for Immunohematological Testing Before Implementation; Approved Guideline

This document provides guidance to the end user and laboratory for validation of automated systems used in immunohematological testing before implementation.

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

Clinical and Laboratory Standards Institute

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Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: +1.610.688.0100
F: +1.610.688.0700
www.clsi.org
standard@clsi.org

I/LA33-A
Vol. 29 No. 28
ISBN 1-56238-714-6 Replaces I/LA33-P
ISSN 0273-3099 Vol. 29 No. 12

Validation of Automated Systems for Immunohematological Testing Before Implementation; Approved Guideline

Volume 29 Number 28

Katharine Appleton Downes, MD
Melanie Champion, MBA, MT(ASCP), SBB, HP
Mary Kay Golisano, MPA, MT(ASCP), SBB
Kathie Goodwin, MBA, MT(ASCP)BB
Sheryl A. Kochman, MT(ASCP)
Michael E. Passwater, MT(ASCP)SBB
James W. Piper, PhD
Kathleen E. Puca, MD, MT(ASCP)SBB
Betty-Ann Vesala, MLT(CSMLS), CQM
Candace Williams, MT(ASCP)SBB
Raya D. Zerger, MT(ASCP) SBB

Abstract

Clinical and Laboratory Standards Institute document I/LA33-A—*Validation of Automated Systems for Immunohematological Testing Before Implementation; Approved Guideline* provides guidance to the user and laboratory for validating an automated system for immunohematological testing. Current automated system methodologies are discussed. This document addresses the development of a validation plan and the information required for its creation. It includes guidelines for elements and tasks of the validation process, including installation qualification, operational qualification, and performance qualification. For each of these qualifications, the purpose, prerequisites, responsibilities, considerations for and examples of test cases, and activities performed are included. The Appendix contains templates that may be used by the laboratory for development of test cases related to and for different aspects of installation qualification, operational qualification, and performance qualification.

Clinical and Laboratory Standards Institute (CLSI). *Validation of Automated Systems for Immunohematological Testing Before Implementation; Approved Guideline.* CLSI document I/LA33-A (ISBN 1-56238-714-6). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2009.

Suggested Citation

CLSI. *Validation of Automated Systems for Immunohematological Testing Before Implementation; Approved Guideline.* CLSI document I/LA33-A. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

Previous Edition:
April 2009

Reaffirmed:
March 2014

Archived:
September 2016

ISBN 1-56238-714-6
ISSN 0273-3099

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Foreword

Immunohematological laboratory testing has evolved from test tube–based methods to automated systems that employ a variety of techniques and methods. Automated systems for such testing may bring potential advantages to a laboratory, such as improvements in turnaround time, standardized interpretation of reactions, and positive sample identification using bar-code technology. Increasing use of automated systems in immunohematological testing necessitates the development of a guideline for laboratories for validation of these automated systems.

Before a laboratory can implement an automated system for immunohematological testing, the system should be validated. First, the laboratory should specify the required performance for the automated system. Performance specifications may be defined by local and/or national regulatory requirements and/or medical usefulness requirements. It is the responsibility of the laboratory to determine the applicable requirements. Second, the laboratory should select a system whose vendor's claims meet the required performance specifications. Finally, the laboratory should verify that it can achieve the vendor's claimed results. If the validation steps are successful, the automated system is then introduced into routine use for testing.

The subcommittee had the following principal goals during the development of this guideline:

- To develop a validation protocol that is applicable to all currently available immunohematological automated systems independent of the method employed
- To create a guideline that is simple enough to be applicable in laboratories with a wide variety of experience in automated systems and resources, from the small laboratory to the blood donor center
- To develop a protocol that is sufficiently rigorous to address all elements of validation studies
- To develop simplified templates or worksheets as examples for use in data gathering, statistical calculations, and testing of materials

Key Words

Automated system, immunohematological testing, installation qualification, operational qualification, performance qualification, test case, validation

Validation of Automated Systems for Immunohematological Testing Before Implementation; Approved Guideline

1 Scope

This guideline focuses on the validation of automated systems for immunohematological testing in the laboratory. This document assumes that the vendor of the immunohematological automated system (or systems) developed and validated performance claims using protocols in accordance with regulatory requirements. The elements of this document include immunohematology tests and automated systems, validation process, materials, installation qualification (IQ), operational qualification (OQ), and performance qualification (PQ). The intended audience of this guideline is any laboratory that performs immunohematological testing.

This document addresses the validation of automated systems for immunohematological testing before implementation. It is applicable to situations in which validation should be performed before implementation; for example, when changing from a manual platform for immunohematological testing to an automated system, adding an automated system, or changing from one automated system to another automated system. Although this guideline focuses on preimplementation validation, it may also provide useful information for validation postimplementation, such as when adding new intended uses or tests, relocating equipment, or changing reagents and critical materials; when upgrading an existing automated system (eg, new software, hardware, firmware); when a component is modified; when new quality control (QC) material or new or revised software is implemented; or when the laboratory acquires a new laboratory information system (LIS) or Blood Establishment Computer Software (BECS).

The exclusions and limitations of this document include selection of automated systems, prevalidation, manual immunohematological testing, validation of LIS or BECS (refer to CLSI document AUTO08),[1] implementation or postimplementation of automated systems, validation of off-label usage, and validation of a bar-code system (refer to CLSI document AUTO02).[2]

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.[3] 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 diseases, refer to CLSI document M29.[4]

3 Terminology

3.1 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 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; 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 focuses on harmonization of terms to facilitate the global application of standards and guidelines.

In order to align the usage of terminology in this document with that of ISO, the term *validation* in its metrological sense refers to provision of objective evidence that a given item fulfills specified requirements when the specified requirements are adequate for an intended use; whereas *verification* refers to the provision of objective evidence that a given item fulfills specified requirements (see ISO/IEC Guide 99).[5]

However, for the purpose of this guideline, *validation* is further defined as "establishing recorded evidence that provides a high degree of assurance that a specified process will consistently produce an outcome meeting its predetermined specifications and quality attributes,"[6] whereas *verification* is further defined as the "confirmation by examination and provision of objective evidence that specified requirements have been met."[6] These definitions were based on the technical manual (ie, AABB Standards for Blood Banks and Transfusion Services) used as the main reference of this guideline's target audience.

3.2 Definitions

agreement – the proportion of specimens where results obtained using a new test and those obtained using an imperfect standard agree; overall percent agreement, agreement of new test with imperfect standard-positive, and/or agreement of new test with imperfect standard-negative.

The following terms relate to the term "agreement" in the context of this document:

- **negative percent agreement (NPA) –** the proportion of nonreference standard negative samples in which the new test is negative.
- **positive percent agreement (PPA) –** the proportion of nonreference standard positive samples in which the new test is positive.[7]
- **overall percent agreement –** the proportion of samples in which the new test and the nonreference standard give the same outcome.

AHG (antihuman globulin) phase – testing step where the use of a secondary antibody, typically directed against human immunoglobulin G (IgG) or C3 molecules, detects bound IgG or C3 on red blood cells (patient, donor, or reagent); the secondary antibody binds to the cell-bound IgG or C3 that has attached to the red cell either *in vivo* or *in vitro.*

antibody identification – the testing of serum or plasma against a panel of different materials that express red blood cell (RBC) antigens to identify the antibody or antibodies.

antibody screen//antibody detection – the testing of serum or plasma with material expressing RBC antigens for detection of unexpected antibodies.

antihuman globulin (AHG) – an antibody directed against human immunoglobulin and/or complement; **NOTE:** It is used to perform the antihuman globulin test (previously known as Coombs test). The preparation may be either polyspecific (anti-IgG plus anticomplement) or monospecific (anti-IgG or anticomplement).[8]

assay – a quantitative determination or measurement of the amount, activity, or potency of a constituent or characteristic; **NOTE 1:** For the purpose of this document, assay is also known as the **measurement**

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/NCCLS 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

I/LA33-A 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
X GP02		 GP21	X AUTO02 H57		X AUTO02 AUTO08 EP07 EP14 EP18 H57 M29	 GP02	 EP18	 EP18 H57	 EP07 EP18		 M29

Adapted from CLSI/NCCLS 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/NCCLS 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.

I/LA33-A 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
AUTO08					H57		AUTO08	

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

Related CLSI Reference Materials*

AUTO02-A2 **Laboratory Automation: Bar Codes for Specimen Container Identification; Approved Standard—Second Edition (2005).** This document provides specifications for use of linear bar codes on specimen container tubes in the clinical laboratory and for use on laboratory automation systems.

AUTO08-A **Managing and Validating Laboratory Information Systems; Approved Guideline (2006).** This document provides guidance for developing a protocol for validation of the laboratory information system (LIS), as well as protocols for assessing the dependability of the LIS when storing, retrieving, and transmitting data.

EP07-A2 **Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition (2005).** This document provides background information, guidance, and experimental procedures for investigating, identifying, and characterizing the effects of interfering substances on clinical chemistry test results.

EP14-A2 **Evaluation of Matrix Effects; Approved Guideline—Second Edition (2005).** This document provides guidance for evaluating the bias in analyte measurements that is due to the sample matrix (physiological or artificial) when two measurement procedures are compared.

EP18-A2 **Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline—Second Edition (2009).** This guideline describes risk management techniques that will aid in identifying, understanding, and managing sources of failure (potential failure modes) and help to ensure correct results. Although intended primarily for *in vitro* diagnostics, this document will also serve as a reference for clinical laboratory managers and supervisors who wish to learn about risk management techniques and processes.

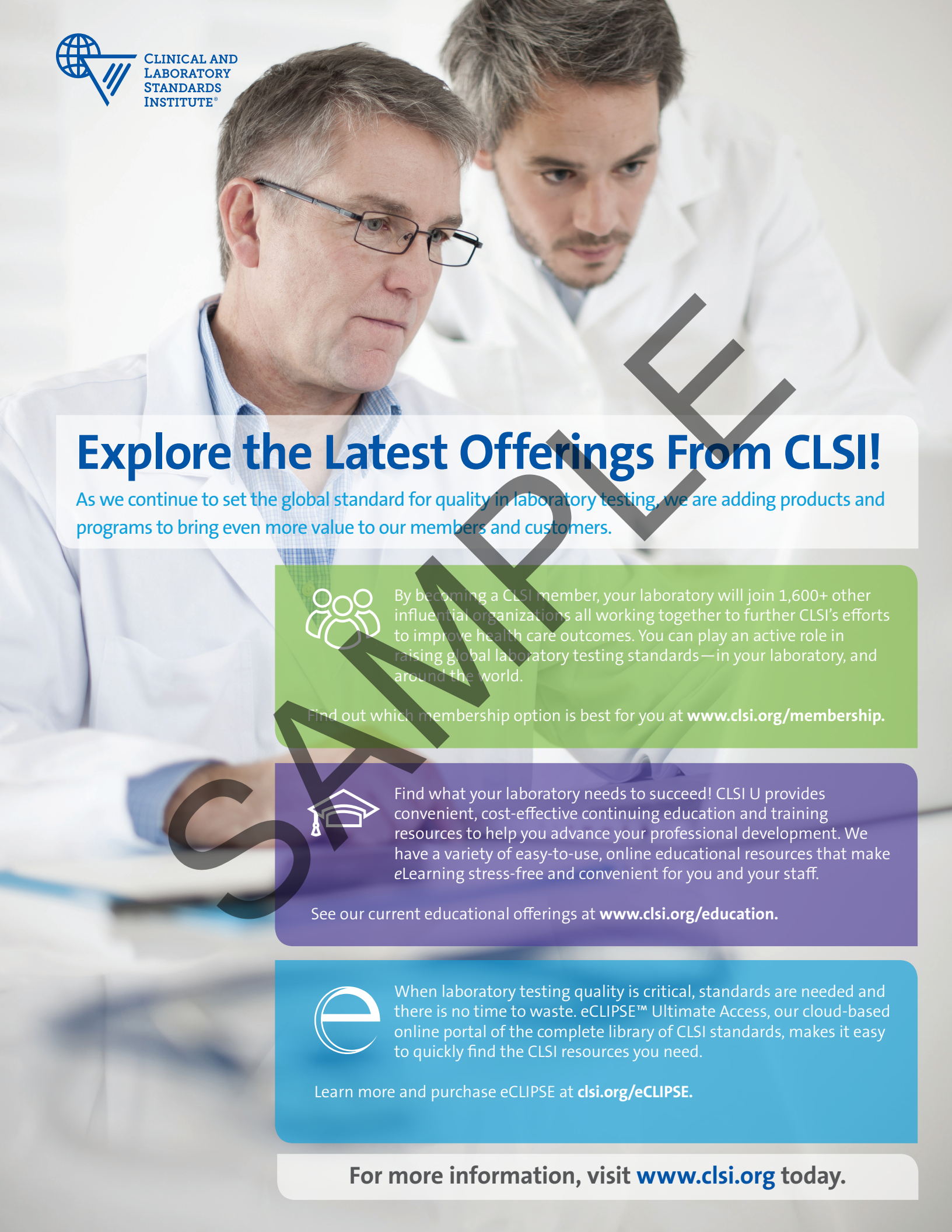
GP02-A5 **Laboratory Documents: Development and Control; Approved Guideline—Fifth Edition (2006).** This document provides guidance on development, review, approval, management, and use of policy, process, and procedure documents in the medical laboratory community.

GP21-A3 **Training and Competence Assessment; Approved Guideline—Third Edition (2009).** This document provides background information and recommended processes for the development of training and competence assessment programs that meet quality and regulatory objectives.

H57-A **Protocol for the Evaluation, Validation, and Implementation of Coagulometers; Approved Guideline (2008).** This document provides guidance and procedures to the end user and manufacturer for the selection, evaluation, validation, and implementation of a laboratory coagulometer.

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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950 West Valley Road, Suite 2500, Wayne, PA 19087 USA

P: +1.610.688.0100 **Toll Free (US):** 877.447.1888 **F:** +1.610.688.0700

E: customerservice@clsi.org **www.clsi.org**

ISBN 1-56238-714-6