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1st Edition

POCT15

Point-of-Care Testing for Infectious Diseases

This report summarizes current knowledge of rapid and point-of-care testing practices used worldwide for infectious diseases.

A CLSI report for global application.

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Point-of-Care Testing for Infectious Diseases

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Abstract

Clinical and Laboratory Standards Institute report POCT15—*Point-of-Care Testing for Infectious Diseases* is intended for use in assessing, implementing, and managing programs for the detection, control, and/or management of infectious diseases using point-of-care testing (POCT) methodologies.

Clinicians rely heavily on laboratory tests for the etiological diagnosis of infectious diseases, which guides both prognostication and management. The clinical importance of these results means that testing must be performed in an optimal manner, and the results must be interpreted with clear knowledge of the methodologies' abilities and limitations. This report summarizes current methods and practice in POCT for infectious diseases.

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Foreword

Infections are responsible for 26% of deaths worldwide and for 30% of worldwide lost disability-adjusted life-years.[1,a] Infectious diseases are the leading killers of children and adolescents and a major cause of adult mortality. Of the top 10 causes of death worldwide, three are infections. In addition, infectious diseases are major causes of illness and are associated with and contribute to poverty. Despite the ability of modern medicine to treat or prevent many infectious diseases, they remain important causes of death and disability.

Effective management of infectious diseases necessitates rapid and accurate diagnosis, and in the case of chronic infections, such as HIV, testing for disease monitoring and support for directed therapies. Because infectious diseases are often characterized by rapid onset and progression, rapid, point-of-care (POC) diagnostics streamline and facilitate effective management. Infectious diseases disproportionately affect poor and marginalized populations. Therefore, delivering diagnostic testing at the point of care has the potential to improve access to care, as well as public and individual health.

This report is intended for use by laboratory professionals, public health professionals, clinicians, and health care managers to guide the selection, implementation, and effective use of POC tests in the diagnosis and management of infectious diseases.

Rapid point-of-care testing (POCT) methodologies for infectious diseases have an enormous spectrum of applications, from routine primary care to nosocomial infections to public health outreach testing to pandemic, disaster, and biopreparedness uses. Widely accepted guidelines for use of such tests would have a broad effect on practice. Guidelines should discuss topics such as appropriate use and interpretation of POCT for infectious diseases; cost-effective practices; and quality promotion both on the analytical and systems levels, promoting appropriate and high-quality testing practices.

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

Key Words

Health care–associated infections, hepatitis, HIV, infectious diseases, influenza, malaria, point-of-care, rapid tests, sexually transmitted infections, tuberculosis

[a] http://www.who.int/healthinfo/statistics/bodgbddeathdalyestimates.xls

Point-of-Care Testing for Infectious Diseases

Chapter 1: Introduction

This chapter includes:

- Report's scope and applicable exclusions
- Background information pertinent to the report's content
- 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 report
- Abbreviations and acronyms used in the report

1.1 Scope

This report provides recommendations for clinicians, laboratories, public health agencies, and policymakers who are responsible for assessing, implementing, performing, and using point-of-care (POC) tests to improve management of infectious diseases. It also provides recommendations for indications, limitations, appropriate use, and reporting and interpretation for the major POC tests available. In addition, this report summarizes potential uses of POC tests in community outreach and public health testing and in resource-limited settings.

The intended users of this report are point-of-care testing (POCT) professionals, including but not limited to POC coordinators, medical directors and laboratory directors of POCT programs, and microbiology laboratory directors. Users may also include public health agencies and public health policymakers.

This report is not intended to provide an overview of QC, QA, or other good laboratory practices as related to these types of POC tests. Nor is it intended to provide a comprehensive review of the emerging technologies in POCT for infectious diseases. For the most part, discussions in this report are confined to commercialized or soon-to-be-commercialized technologies.

1.2 Background

POCT for infectious diseases has enormous scope, ranging from streptococcal pharyngitis testing in routine primary care to outreach HIV testing by community organizations to molecular testing of methicillin-resistant *Staphylococcus aureus* (MRSA) in the inpatient setting. It includes testing for occult *Helicobacter pylori* disease in outpatients with gastroenteritis, testing for sepsis or respiratory pathogens in critically ill inpatients, and HIV screening for persons in developing countries. The complexity of the topic is exceeded only by its potential to improve human health.

POCT15 summarizes available technologies and various tests, as well as describing the diseases in question and the role of diagnostic testing in their management. Laboratory directors, managers, and supervisors are responsible for ensuring POC test methods are only used in situations in which operator competence has been documented. Inexperienced laboratorians should be directly supervised by an experienced laboratorian or use alternate methods until proficiency is achieved.

1.3 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.[2] 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.[3]

1.4 Terminology

1.4.1 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

1.4.2 Definitions

accuracy – closeness of agreement between a test result and the accepted reference value.[4]

amplicon – the product of polymerase chain reaction; a fragment of nucleic acid that has been synthesized using amplification techniques.

amplification – the process of producing multiple copies of a specific segment of DNA, usually a gene, to obtain enough material for additional study; **NOTE:** Polymerase chain reaction is a commonly used method of amplification.

analyte – substance being measured or detected.

bias (of measurement) – difference between the expectation of a test result or measurement result and a true value.[5]

Chapter 3: Indications, Issues, and Guidance by Pathogen

This chapter includes:

- Information on the clinical role, technical complexities, sensitivity, specificity, and time to results for various POC test methods and systems for infectious diseases

3.1 Respiratory Pathogens

3.1.1 Group A *Streptococcus*

Clinical criteria alone are not sufficient to accurately diagnose group A streptococcal pharyngitis, because symptoms may result from various infectious etiologies other than *Streptococcus pyogenes* infection. Prevention of rheumatic fever is one of the main rationales for early detection and treatment of streptococcal pharyngitis. Early antimicrobial treatment is beneficial for decreasing transmission, symptom duration, and other suppurative complications.[28] The standard test method for group A *Streptococcus* (GAS) detection is culture of a throat swab.[29] POCT for GAS has proven to be an important development in the office management of patients with pharyngitis. GAS accounts for 15% to 30% of sore throats in children and is the most common bacterial cause of acute pharyngitis. The rapid antigen test (RAT) provides detection of GAS directly from throat swabs. RATs have many variations in test methods, such as latex agglutination, ICT, and EIA. Older first-generation RATs, which used latex agglutination technology, had a much lower sensitivity than second-generation RATs that use EIA technologies. Chemiluminescent DNA probe assays use nucleic acid hybridization to detect GAS from throat swabs, resulting in a measured numerical result, thereby eliminating subjective interpretation of visual end points. Real-time molecular testing is the most sensitive of the nonculture-based technologies.[30,31] Table 2 summarizes the performance characteristics of GAS POC tests.

Table 2. Performance of GAS Tests

Test	Sensitivity	Specificity	Approximate Time to Result
Throat culture[30]	80% to 99%	100%	24–48 hours
EIA-based rapid tests[30]	64% to 85%	>95%	10–20 minutes
RATs[32-34]	70% to 96%	91% to 100%	5–15 minutes
Chemiluminescent DNA probes[30,35]	>95%	>95%	2–4 hours
Amplified molecular tests[30,31,36]	93% to 99%	98% to 100%	5 minutes–3 hours

Abbreviations: DNA, deoxyribonucleic acid; EIA, enzyme immunoassay; GAS, group A *Streptococcus;* RAT, rapid antigen test.

The sensitivities of RATs for GAS pharyngitis are variable and depend on the clinical presentation of the tested patient and the quality of the specimen collected.[33] The tonsils should be swabbed vigorously while avoiding the cheek and saliva. The test manufacturer's instructions for proper specimen collection must be followed. The performance of RATs can also vary according to the skill level of the personnel performing the test.[37]

Current pediatric practice guidelines recommend follow-up testing of patients with supportive clinical symptoms whose samples yielded negative RAT results.[32,37,38] Culture or molecular assays can be used to confirm negative RAT results in children and adolescents.[39] Adults with GAS are at lower risk for rheumatic complications, meaning that confirmatory testing in adults with negative RAT results is probably unnecessary.[38] However, serious complications have recently been described in adults with positive cultures but negative RATs.[40]

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system (QMS) approach in the development of standards and guidelines that facilitates project management, defines a document structure using a template, and provides a process to identify needed documents. The QMS 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:

• Organization and Leadership • Customer Focus • Facilities and Safety Management • Personnel Management	• Supplier and Inventory Management • Equipment Management • Process Management • Documents and Records Management	• Information Management • Nonconforming Event Management • Assessments • Continual Improvement

POCT15 covers the QSE indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section.

Organization and Leadership	Customer Focus	Facilities and Safety Management	Personnel Management	Supplier and Inventory Management	Equipment Management	Process Management	Documents and Records Management	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
		M29				X M53 MM03					

Path of Workflow

A path of workflow is the description of the necessary processes to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver their services, namely quality laboratory information.

POCT15 covers the medical laboratory path of workflow processes indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section.

Preexamination				Examination				Postexamination		
Examination ordering	Specimen collection	Specimen transport	Specimen receipt, accessioning, and processing	Examination method selection	Examination performance	Results review and follow-up	Laboratory results interpretation	Communication of alert values and issuance of preliminary reports	Release of final reports	Specimen management
	MM03	MM03	MM03	X MM03	X MM03	M53 MM03	M53	M53 MM03	M53 MM03	M53

Related CLSI Reference Materials*

M29 **Protection of Laboratory Workers From Occupationally Acquired Infections. 4th ed., 2014.** 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.

M53 **Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection. 1st ed., 2011.** This document provides guidance for laboratorians performing human immunodeficiency virus testing and for the interpretation of results by health care providers in advanced diagnostic laboratories.

MM03 **Molecular Diagnostic Methods for Infectious Diseases. 3rd ed., 2015.** This report addresses topics relating to clinical applications, amplified and nonamplified nucleic acid methods, selection and qualification of nucleic acid sequences, establishment and evaluation of test performance characteristics, inhibitors, and interfering substances, controlling false-positive reactions, reporting and interpretation of results, quality assurance, regulatory issues, and recommendations for manufacturers and clinical laboratories.

* 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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