CLINICAL AND LABORATORY STANDARDS INSTITUTE®

June 2014

# M40-A2

## Quality Control of Microbiological Transport Systems; Approved Standard—Second Edition



This document provides criteria to assist manufacturers and end users of transport devices in providing and selecting dependable products for the transport of microbiological clinical specimens.

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

# Clinical and Laboratory Standards Institute

*Setting the standard for quality in clinical laboratory testing around the world.*

The Clinical and Laboratory Standards Institute (CLSI) is a not-for-profit membership organization that brings together the varied perspectives and expertise of the worldwide laboratory community for the advancement of a common cause: to foster excellence in laboratory medicine by developing and implementing clinical laboratory standards and guidelines that help laboratories fulfill their responsibilities with efficiency, effectiveness, and global applicability.

**Consensus Process**

Consensus—the substantial agreement by materially affected, competent, and interested parties—is core to the development of all CLSI documents. It does not always connote unanimous agreement, but does mean that the participants in the development of a consensus document have considered and resolved all relevant objections and accept the resulting agreement.

**Commenting on Documents**

CLSI documents undergo periodic evaluation and modification to keep pace with advancements in technologies, procedures, methods, and protocols affecting the laboratory or health care.

CLSI's consensus process depends on experts who volunteer to serve as contributing authors and/or as participants in the reviewing and commenting process. At the end of each comment period, the committee that developed the document is obligated to review all comments, respond in writing to all substantive comments, and revise the draft document as appropriate.

Comments on published CLSI documents are equally essential, and may be submitted by anyone, at any time, on any document. All comments are addressed according to the consensus process by a committee of experts.

**Appeals Process**

If it is believed that an objection has not been adequately addressed, the process for appeals is documented in the CLSI Standards Development Policies and Process document.

All comments and responses submitted on draft and published documents are retained on file at CLSI and are available upon request.

**Get Involved—Volunteer!**

Do you use CLSI documents in your workplace? Do you see room for improvement? Would you like to get involved in the revision process? Or maybe you see a need to develop a new document for an emerging technology? CLSI wants to hear from you. We are always looking for volunteers. By donating your time and talents to improve the standards that affect your own work, you will play an active role in improving public health across the globe.

For further information on committee participation or to submit comments, contact CLSI.

Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: 610.688.0100
F: 610.688.0700
www.clsi.org
standard@clsi.org

ISBN 1-56238-963-7 (Print)
ISBN 1-56238-964-5 (Electronic)
ISSN 1558-6502 (Print) M40-A2
ISSN 2162-2914 (Electronic) Vol. 34 No. 9

# Quality Control of Microbiological Transport Systems; Approved Standard—Second Edition

Volume 34 Number 9

Paul Bourbeau, PhD, D(ABMM)
Paul L. Cerwinka, MSc, RM(AAM)
Jerry Abramson, PhD, F(AAM), SM(AAM)
Susan Finn, MLT
Musa Y. Hindiyeh, PhD, D(ABMM)
Michael J. Loeffelholz, PhD, D(ABMM)
Elaine Seavey Maliff
Charles Thomas Nugent IV, PhD
CDR Raquel Peat, PhD, MPH
Norman Sharples
Douglas J. Shedden
Kenneth Van Horn, PhD, D(ABMM)



## Abstract

Clinical and Laboratory Standards Institute document M40-A2—*Quality Control of Microbiological Transport Systems; Approved Standard—Second Edition* presents the criteria that shall be considered when choosing a microbiological transport device to facilitate sample preservation. QC considerations for the manufacturer and testing laboratory are presented, as well as techniques, control microorganisms, and acceptability criteria. This document provides a consistent protocol for initial testing of microbiological transport devices by manufacturers and a method by which laboratories can validate manufacturer claims and compare devices.

Clinical and Laboratory Standards Institute (CLSI). *Quality Control of Microbiological Transport Systems; Approved Standard—Second Edition*. CLSI document M40-A2 (ISBN 1-56238-963-7 [Print]; ISBN 1-56238-964-5 [Electronic]). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2014.



CLINICAL AND LABORATORY STANDARDS INSTITUTE®

**Suggested Citation**

CLSI. *Quality Control of Microbiological Transport Systems; Approved Standard—Second Edition.* CLSI document M40-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

**Proposed Standard**
August 2002

**Approved Standard**
December 2003

**Approved Standard—Second Edition**
June 2014



ISBN 1-56238-963-7 (Print)
ISBN 1-56238-964-5 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2194 (Electronic)

## Contents

## Contents (Continued)

## Foreword

In 1893, Councilman first described preparing transport swabs by wrapping cotton pledgets around the ends of wires, enclosing these wires in test tubes, and sterilizing them in a hot air sterilizer.[1] After sterilization, the test tubes were taken to wards where a wire was removed and used to rub the pharyngeal membranes of patients suspected of being infected with diphtheria. After collection, the test tubes were labeled and sent to a laboratory where specimens were inoculated on a culture medium.

The development of transport devices was a result of public health concerns.[2] Maintaining microorganism viability during transport to the public health laboratory was imperative for the isolation and identification of the agents responsible for relevant infectious diseases. During the 1930s, 1940s, and 1950s, such infections, particularly gonorrhea and bacterial diarrhea, were the driving forces behind the development of transport media and devices.[3] Most studies focused on evaluation of performance rather than establishment of an acceptable standard of expected performance.[4] It is difficult to determine when systematic QC began to be applied to transport systems. However, it was Rubbo, Benjamin, and Stuart[5] who noted that certain batches of cotton wool used on swabs were associated with faster microbial death rates than others and that this phenomenon (toxicity) could be countered by the addition of serum onto the transport swabs.[6] Additionally, the important contributions of Amies, Cary, and Blair for transport medium should be acknowledged.[7,8]

Within the hospital setting, use of transport devices for various "routine cultures" began as investigators determined variability in recovery from specimens plated at the bedside compared to those routed to the laboratory via established mechanisms.[5] Currently, a number of factors contribute to the increasing emphasis on the use of transport devices to maintain specimens for microbiological testing. These factors include an increased use of outpatient treatment that has accompanied shortened hospital stays, and the centralization of laboratory services due to both managed care and a shortage of individuals with expertise in clinical microbiology.

As new technologies provide the opportunity to redefine the method of recovery or detection of microorganisms of interest, standardizing the QC testing and acceptance criteria will become important in order to assure the highest level of care to patients. This document on QC of transport devices will assist in the standardization of the performance of these devices.

Since the publication of the first edition of this document, many studies have followed its recommendations.[9,10-17] In revising M40, the committee updated the document where appropriate, using data generated from studies performed using the protocols that were published in the first edition. Testing protocols were updated to accommodate new types of swab collection devices that have been introduced since the first edition was published, and temperatures under which QC testing and specimen transport are conducted were better defined. Lastly, the committee added to, or expanded sections related to, QC of transport devices used for viruses, urine, and fecal specimens.

In the United States, basic manufacturing requirements for medical devices, including *in vitro* diagnostic devices, were established via the Medical Device Amendments of 1976. This legislation gave the US Food and Drug Administration (FDA) authority to regulate medical devices (premarket notification, [510(k)] and premarket approval), and develop consistent manufacturing requirements (good manufacturing practices [GMP]). GMP include the requirement to perform product QC testing before distribution. Each manufacturer is required to establish the type of testing to be performed, as well as acceptance criteria based on the product and its intended use. Additionally, the European Union has adopted the Medical Devices Directive 93/42/EEC[18] and the *In Vitro* Diagnostic Device Directive 98/79/EC,[19] which have requirements very similar to those in the United States. These directives include provisions to use harmonized standards as a method of demonstrating conformity to the directive requirements. Likewise, the FDA has formalized the use of these types of standards by manufacturers to

demonstrate performance in premarket submissions. Further discussion of regulatory considerations for these markets can be found in Appendix B.

## Key Words

Acceptable performance, acceptance criteria, biological properties, control strains, microbiological, microbiological testing, molecular transport, performance criteria, quality control, regulatory considerations, specimen transport, standards, storage conditions, transport devices, transport medium, transport temperature, viral transport

# Quality Control of Microbiological Transport Systems; Approved Standard—Second Edition

## 1 Scope

The transport of clinical specimens is a critical component for accurate diagnosis. Preservation of inherent, interpretive attributes of microorganisms and/or nucleic acids can be quickly compromised when the transport conditions or transport devices are suboptimal. The advent of antigen detection methods, methods for amplification and detection of genetic elements, and the requirement for local or distant transport of these specimens to a testing facility has imposed further considerations on manufacturers to provide products that will not compromise reporting of clinically relevant laboratory data to physicians. Clinicians should be able to collect and submit specimens to the laboratory and laboratorians should be able to retrieve specimens from containers, devices, and transport media with a reasonable assurance that the viability of microorganisms and/or preservation of nucleic acids present in the specimen will be maintained.

This standard provides criteria to the manufacturers and end users of transport devices to assist in providing and choosing dependable products for the transport of microbiological clinical specimens. Manufacturers will be able to state whether or not the performance characteristics for specific groups of microorganisms and transport devices of a particular product satisfy the performance standards as specified in this document. Furthermore, manufacturers shall state whether or not any additional testing is required before the use of a particular product.

Secondary distributors and end users must assume the responsibility for storage and transport conditions of specimen collection devices before and after use, by adhering to the conditions specified by the manufacturer or those deemed optimum by the laboratory in order to ensure microorganism viability/stability.

In this document, except as specifically noted, QC consists of an assessment of the performance characteristics of a complete device, and not the individual components. There are multiple variables involved in the manufacture of a transport device, including, but not limited to, the container, transport medium, collection device, packaging, and environment. It is fundamental that the assessment of the device be based on measurable performance characteristics for the particular device.

This document is not intended to provide proprietary information on product development, but rather to provide assurance to the device's user that manufacturer claims are met following standardized testing and acceptance criteria. It provides guidance to the manufacturer in addressing critical issues related to specimen integrity specific to the type of testing to be performed, eg, bacterial and viral culture, or nucleic acid detection. This document does not address the technique of transport device manufacturing, but focuses on the methods for QC testing and acceptance criteria in order to provide a product suitable for the analysis of clinical specimens for agents of disease.

Transport devices are essential components of the preexamination process of microbiology laboratory testing. It is recognized that these early steps in the total testing process are critical to the production of clinically relevant information. Patients, physicians, health care providers, and laboratorians expect products that meet the highest standards of laboratory practice. This document will facilitate this goal.[a] And while it is beyond the scope of this document to address the design of devices, it is imperative that

[a] In the United States, the Clinical Laboratory Improvement Amendments guidelines place the responsibility for acceptance of quality specimens on the laboratorian.



device design promotes correct use, and that laboratorians select devices that best serve the needs of the physician and the patient.

Although a discussion of specimen transport conditions is beyond the scope of this document, it is recognized that temperature has a significant effect on the preservation of microorganisms in various transport devices. A number of recent studies[12,20] have compared performance of transport devices inoculated with various organisms at controlled room temperature (20 to 25°C) and cold temperature (2 to 8°C). These studies have established that simulated transport performance at cold temperature yields superior results compared to transport at room temperature. These data support the suggestion that the current recommendations of room temperature transport do not represent the optimal holding temperature for maximum preservation of microbiological samples.[9-11,21-27] If transport conditions of the end user differ from those validated by the manufacturer, actual transport conditions should be tested in order to determine viability and overgrowth of microorganisms (eg, in insulated coolers with cold packs).

Manufacturers are encouraged to perform QC of microbial transport devices at both controlled room temperature and cold temperature as defined in Section 4.2 and, furthermore, to specify this practice in their package inserts and regulatory submissions. Inclusion of this information will permit users who wish to transport specimens for testing by their laboratories at cold temperature reasonable assurance that manufacturers performed testing at the temperature used by their laboratories. If further investigations lead to changes in the current recommendations for controlled room temperature specimen transport, manufacturers performing QC at both temperatures would not have to make any subsequent changes in their QC procedures or package inserts. Finally, to emphasize that few standards for QC have been suggested for many microbiology transport devices, some of the protocols provided are general outlines designed, in part, to promote discussion among the manufacturers, laboratories, and users regarding what would constitute an appropriate standard, as well as promote research and publication that may serve as the foundation of new standards as activity in this area moves forward.

## 2 Introduction

Before publication of the first edition of this document, there was no recognized standard procedure for determining the effectiveness of microbiological transport devices. As a result, manufacturers did not have the benefit of external guidelines and standards to measure the performance characteristics of their products, and relied on internally developed protocols for testing product performance. For this reason, it was difficult to independently validate manufacturers' performance claims.

A variety of microbiological transport systems, formulations, and devices exist. It is the intent of this document to provide a standard that will enable both manufacturers and end users to systematically evaluate systems for performance effectiveness, ensure standards of performance, and allow for internal validation of product effectiveness.

## 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. The Centers for Disease Control and Prevention address this topic in published guidelines that focus on the daily operations of diagnostic medicine in human and animal medicine while encouraging a culture of safety in the laboratory.[28] 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 disease, refer to CLSI document M29.[29]



# 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 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 as follows:

| | | | |
|---|---|---|---|
| Organization | Personnel | Process Management | Nonconforming Event Management |
| Customer Focus | Purchasing and Inventory | Documents and Records | Assessments |
| Facilities and Safety | Equipment | Information Management | Continual Improvement |

M40-A2 addresses 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 on the following page.

| Organization | Customer Focus | Facilities and Safety | Personnel | Purchasing and Inventory | Equipment | Process Management | Documents and Records | Information Management | Nonconforming Event Management | Assessments | Continual Improvement |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | M29 | | | | X<br>GP16<br>M02<br>M07<br>M22<br>MM13 | M07 | | | | |

## 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 the laboratory's services, namely quality laboratory information.

M40-A2 addresses the clinical laboratory path of workflow step 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 |
| | GP16<br>MM13 | GP16<br>MM13 | X<br>GP16<br>MM13 | GP16<br>M02<br>M07 | GP16<br>M02<br>M07 | M02<br>M07 | M02<br>M07 | MM13 |



## Related CLSI Reference Materials*

**GP16-A3** **Urinalysis; Approved Guideline—Third Edition (2009).** This document addresses procedures for testing urine, including materials and equipment; macroscopic/physical evaluation; chemical analysis; and microscopic analysis.

**M02-A11** **Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard—Eleventh Edition (2012).** This document contains the current Clinical and Laboratory Standards Institute–recommended methods for disk susceptibility testing, criteria for quality control testing, and updated tables for interpretive zone diameters.

**M07-A9** **Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Ninth Edition (2012).** This document addresses reference methods for the determination of minimal inhibitory concentrations of aerobic bacteria by broth macrodilution, broth microdilution, and agar dilution.

**M22-A3** **Quality Control for Commercially Prepared Microbiological Culture Media; Approved Standard—Third Edition (2004).** This document contains quality assurance procedures for manufacturers and users of prepared, ready-to-use microbiological culture media.

**M29-A4** **Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition (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.

**MM13-A** **Collection, Transport, Preparation, and Storage of Specimens for Molecular Methods; Approved Guideline (2005).** This document provides guidance related to proper and safe biological specimen collection and nucleic acid isolation and purification. These topics include methods of collection, recommended storage and transport conditions, and available nucleic acid purification technologies for each specimen/nucleic acid type. A CLSI-IFCC joint project.



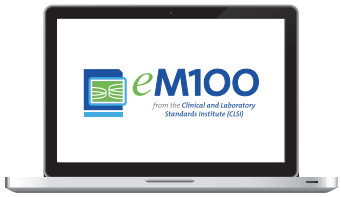
* CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

# Explore the Latest Offerings from CLSI!

As we continue to set the global standard for quality in laboratory testing, we're adding initiatives to bring even more value to our members and customers.




## Shop Our Online Products

Including *e*M100, the interactive searchable database for drug selection, interpretation, and quality control procedures within M100.


## Find Membership Opportunities

See the options that make it even easier for your organization to take full advantage of CLSI benefits and our unique membership value.

CLSI U
Laboratory Standards Education Center

## Visit the CLSI U Education Center

Where we provide the convenient and cost-effective education resources that laboratories need to put CLSI standards into practice, including webinars, workshops, and more.


## Shop Our Online Products

Including eCLIPSE Ultimate Access™, CLSI's cloud-based, online portal that makes it easy to access our standards and guidelines—*anytime, anywhere.*

**For more information, visit www.clsi.org today.**

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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

**P:** 610.688.0100 **Toll Free (US):** 877.447.1888 **F:** 610.688.0700

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

PRINT ISBN 1-56238-963-7

ELECTRONIC ISBN 1-56238-964-5