

CLIA Corner

The University of Iowa Hygienic Laboratory

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Requirements to perform streamlined quality control for microbial identification systems

QUALITY CONTROL FOR COMMERCIALY AVAILABLE MICROBIAL IDENTIFICATION SYSTEMS

Background

Commercially available microbial identification systems (MISs) are test systems that utilize multiple substrates and/or reagents to **identify** aerobic or anaerobic bacteria, yeast, molds, or yeast-like algae grown from culture. The CLIA quality control regulation for MISs is found at 42 CFR section 493.1256(c)(1), which states, *a laboratory must check each batch (prepared in-house), lot number (commercially prepared), and shipment of identification systems (systems using two or more substrates, or two or more reagents, or a combination) when prepared or opened for positive and negative reactivity, as well as graded reactivity, if applicable.*

For microbial identification systems (MISs), this means the laboratory must use a varying number of control organisms to verify the positive and negative reactivity. Laboratories and manufacturers expressed concerns to the Clinical Laboratory Improvement Activities Committee (CLIAC) in late 2004 suggesting the CLIA quality control (QC) requirements for commercial MISs were excessive. The American Society of Microbiology (ASM) surveyed microbiology laboratories to determine QC failure rates of commercial MISs and reported these results in 2006. The data showed a failure rate of less than 0.1% for all commercial MISs surveyed. Based on the survey information, ASM recommended that the Clinical Laboratory Standards Institute (CLSI) develop guidelines for more appropriate MIS QC. On August 29, 2008, CLSI released document M50-A, "Quality Control for Commercial Microbial Identification Systems, Approved Guideline."

CMS Revises Policy for Commercial MISs QC

The Centers for Medicare and Medicaid Services (CMS) issued a memorandum on October 17, 2008, which revised the CLIA policy on quality control for commercially available microbial identification systems. The policy revised the CLIA *Interpretative Guidelines for Laboratories and Laboratory Surveyors* by incorporating the information on streamlined QC of commercial MISs provided in the CLSI document M50-A. CMS approved the procedure detailed in the CLSI document, M50-A, as equivalent to the requirements at 42 CFR 493.1256(c)(1) under certain conditions. The CLSI document defines criteria whereby users of commercial MISs may qualify to perform streamlined QC (i.e. reduce the number of organisms necessary to ensure quality of the test systems). The criteria apply to all non-modified commercial MISs (e.g. manual, semi-automated or automated systems.)

Process for Streamlined QC of Commercial MISs

In order for a laboratory to reduce the number of organisms used to QC its commercial MIS, the laboratory must follow a four-step process that includes:

1. A quality assessment program;
2. General requirements and responsibilities (more details to follow);
3. Specific requirements to initiate the performance of streamlined QC; and
4. Requirements to continue to qualify for streamlined QC.

Step 1 – Quality Assessment Program

The laboratory must have a quality assessment (QA) program in place to ensure accurate and reliable MIS testing. The QA program needs to encompass the four quality systems:

- 1) General: patient confidentiality, specimen identification and integrity, compliant investigation, personnel competency, proficiency testing performance, and record retention.
- 2) Pre-analytic: test request and specimen collection, submission, handling and referral.
- 3) Analytic: test procedures; accurate and reliable test systems, equipment, instruments, reagents and supplies; specimen and reagent storage conditions; equipment and test system maintenance and function checks; verification of method performance specifications; calibration and calibration verification; control procedures; corrective actions and test records.
- 4) Postanalytic: test reports, notification of test results and test reporting systems.

Step 2 – General Responsibilities

As described in CLSI, M50-A, Section 5.3, the laboratory must perform or meet the following:

- Develop procedures and comply with manufacturer recommendations for MIS storage and handling from the time of delivery through the time of testing.
- Ensure that personnel are qualified and trained, and are shown to be competent to perform MIS testing.
- Retain and follow the manufacturer's current technical information and/or product insert containing instructions for testing, including, but not limited to:
 - accurate inoculum preparation;
 - proper incubation conditions; and
 - correct interpretation of end points and results.
- Adhere to processes and procedures for initial and continued qualification.
- Document all MIS QC activities and any corrective action taken and report any QC failures to the manufacturer and/or distributor, as applicable.
- Comply with all applicable regulations for testing and retaining documents, including any state or local requirements that are different and/or more stringent than federal requirements.

Step 3 – Initial Qualification

To initiate performance of streamlined QC, the laboratory must maintain documentation of the manufacturer's compliance with ISO 13485 and FDA quality system requirements (QSR). Certification of the manufacturer conformance can be in the form of a Certificate of Analysis, Certificate of Compliance or a certification statement in the manufacturer's instructions for use.

The laboratory must meet **one** of the following options:

- A. Perform and document MIS verification study as required in 42 CFR 493.1253(B)(1). If the user has performed a verification study for the MIS to demonstrate it can obtain performance specification comparable to the manufacturer, streamlined QC may be implemented immediately. The documentation of the verification study must be available.
- B. If a verification study has not been performed, or documentation is not available, but the laboratory has been performing comprehensive MIS QC, it may conduct and document a historical review of QC performance with that MIS as follows:
 - Review QC performance for at least three consecutive lot numbers of MIS from three different shipments that span at least three consecutive seasons to assess seasonal variation of shipping conditions.
 - QC testing must have been performed using positive and negative controls and/or organisms producing positive and negative reactions for reagent and/or substrate according to the manufacturer's instructions.
 - Performance is considered satisfactory if at least 95% of the reagent/substrate results are within the results specified by the manufacturer.
 - If data is not available to conduct a historical review of QC performance or data does not meet the 95% threshold for expected results even after corrective action, the user may prospectively assess QC performance or perform verification study.
- C. If the laboratory has not performed a verification study and has not been performing comprehensive MIS QC, or does not have documentation of one of these options, it must perform comprehensive QC and may not initiate streamlined QC until it has documentation that it has met either option A or B described above.

Step 4 – Continued Qualification

Once a laboratory has implemented streamlined QC for its MIS, in order to continue performing streamlined QC, it must perform the following on an ongoing basis:

- Maintain current documentation of manufacturer conformance to QSR requirements.
- Maintain documentation of results of verification study or historical QC review.
- Test all key indicator strains specified in the manufacturer's instructions for streamlined QC with each batch, lot number and shipment of MIS.
- Perform testing according to the manufacturer's instructions and use only the manufacturer's recommended reagents for testing.
- Monitor and document streamlined QC performance.
- Investigate and resolve any QC failures, including any reagents and/or substrates that repeatedly do not perform as expected, and verify that the key indicator strains detect any product failures that occur.

- Report QC failures to the manufacturer and distributor.
- Have effective QA mechanisms in place to identify the cause of failures, and to resolve and prevent future QC failures whenever possible.

Important – The process for streamlined QC **only** applies to microbial **identification** systems and does **NOT** apply to antimicrobial susceptibility tests.

More Information

To obtain more information and the specific documents mentioned please access the following websites:

<http://www.clsi.org> – M50-A, Quality Control for Commercial Microbial Identification Systems; Approved Guideline

<http://www.cms.hhs.gov/clia> – Interpretative Guidelines for Laboratories and Laboratory Surveyors

<http://www.cms.hhs.gov/SurveyCertificationGenInfo/downloads/SCLetter09-06.pdf> – Memorandum-Revised CLIA Policy on Quality Control for Commercially Available Microbial Identification Systems (MISs)

NEW EMAIL ADDRESS

***Just a reminder that our email addresses have changed:
nancy-grove@uiowa.edu and kristine-rotzoll@uiowa.edu***

