DEPARTMENT OF HEALTH & HUMAN SERVICES
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CENTERS for MEDICARE & MEDICAID SERVICES

Center for Medicaid and State Operations / Survey and Certification Group

Ref: S&C-09-06

DATE: **October 17, 2008**

TO: State Survey Agency Directors

FROM: Director
Survey and Certification Group

SUBJECT: Revised Clinical Laboratory Improvement Amendments of 1988 (CLIA) Policy on Quality Control for Commercially Available Microbial Identification Systems (MIS)

Memorandum Summary

- This memorandum revises the analytic system information for microbial information systems found in the Centers for Medicare & Medicaid Services' Interpretative Guidelines (IG) for Laboratories and Laboratory Surveyors.
- It incorporates the information on streamlined quality control (QC) of commercial microbial identification systems (MIS) provided in the Clinical and Laboratory Standards Institute (CLSI) document, "Quality Control for Commercial Microbial Identification Systems, Approved Guideline," M50-A, into the IG for Laboratories and Laboratory Surveyors.
- The process for streamlined QC of commercial MIS is a 4 step process that includes quality assessment program requirements, general requirements, specific requirements to initiate the performance of streamlined QC, and requirements to continue to qualify for streamlined QC.

Currently, the CLIA regulations at 42 CFR section 493.1256(e)(1) require a laboratory to 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.

In addition, the IG for Laboratories and Laboratory Surveyors at 42 CFR 493.1261(a) state:

> "For microbial identification systems (MIS) utilizing two or more substrates, the laboratory must check each media using control organisms to verify positive and negative reactivity of each substrate."

At 42 CFR 493.1250, CMS may approve an alternate procedure if we find that such procedure provides equivalent quality testing. We are therefore approving the procedures detailed by CLSI in the document "Quality Control for Commercial Microbial Identification Systems, Approved Guideline," M50-A (issued by CLSI on August 29, 2008) as equivalent to the requirements at 42 CFR 493.1256(e)(1) under certain conditions. This CLSI document defines criteria whereby users of commercial MIS may qualify to perform streamlined QC as recommended by the manufacturer in lieu of meeting the control requirements specified at 42 CFR 493.1256(e)(1).

These criteria apply to all commercial MIS (e.g., manual, semi-automated, or automated systems). However, a commercial MIS that is modified by the laboratory does not qualify for streamlined QC.

The process for streamlined QC of a commercial MIS is the following;

A. The laboratory must first have a quality assessment (QA) program in place to ensure accurate and reliable testing.

B. The laboratory must meet the general responsibilities for testing as described in Section 5.3 of CLSI M50-A (listed in attachment).

C. Using CLSI M50-A to initiate performance of streamlined QC, the laboratory must meet the following specific requirements:

    1. Maintain current documentation of the manufacturer's conformance with ISO 13485 and Food and Drug Administration quality system requirements (QSR). Certification of 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.

    2. Meet one of the following:

        a. If the laboratory has performed a verification study for the MIS as described at 42 CFR 493.1253(b)(1), streamlined QC may be implemented immediately. Documentation of the verification study must be available.

        b. If the laboratory has not performed a verification study as described at 42 CFR 493.1253(b)(1) above or does not have the required documentation, but has been performing comprehensive MIS QC as required at 42 CFR 493.1256(e)(1), it may conduct and document a historical review of QC performance with that MIS as follows:

            i. Review QC performance for at least three consecutive lot numbers of the MIS, from three different shipments that span at least three consecutive seasons to assess seasonal variation of shipping conditions.

            ii. QC testing must have been performed using positive and negative controls for each reagent and/or substrate according to the manufacturer's instructions.

iii. Performance shall be considered satisfactory and the user may initiate streamlined QC if at least 95% of the reagent/substrate results are within the results specified by the manufacturer.

iv. If sufficient data are not available to conduct the historical review of QC performance, or the data do not provide expected QC results, after corrective action (as applicable), the laboratory may choose to assess QC performance prospectively as described above, or may verify and document the performance specifications for the MIS as described at 42 CFR 493.1253(b)(1).

3. If the laboratory has not performed a verification study and has not been performing comprehensive MIS QC as described in the CLIA regulations, or does not have documentation of one of these options, they must perform comprehensive CLIA QC and may not initiate streamlined QC until they have documentation that they have met either option a or b described above.

D. As mentioned in CLSI M50-A, the laboratory must perform the following to continue to qualify for streamlined QC:

1. Maintain current documentation of the manufacturer's conformance to QSR requirements.

2. Maintain documentation of the results of the verification study or historical QC review.

3. Test all key indicator strains specified in the manufacturer's instructions for streamlined QC with each batch, lot number, and shipment of MIS.

4. Perform testing according to the manufacturer's instructions and use only manufacturer-recommended reagents for testing.

5. Monitor and document streamlined QC performance.

6. 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.

7. Report QC failures to the manufacturer and distributor.

8. Have effective QA mechanisms in place to identify cause, resolve and prevent future QC failures whenever possible.

We agree with the CLSI guidelines for initiating streamlined QC for MIS and for continuing to qualify for streamlined QC of commercial MIS. This information will be included in the next revision of the IG for Laboratories and Laboratory Surveyors.

Effective Date: Immediately. Please ensure that all CLIA staff are fully apprised of this information within 30 days.

Training: The information contained in this announcement should be shared with all survey and certification staff including managers and surveyors and their manager. The policies and procedures will be formalized in the appropriate sections of the IG.

For questions concerning this memorandum, please contact Judy Yost at 410-786-3407 or via email at Judith.Yost@cms.hhs.gov.

/s/
Thomas E. Hamilton

Attachment

cc: Survey and Certification Regional Office Management

Attachment

General Responsibilities Described in Section 5.3 of CLSI M50-A

The laboratory must meet the following:

- Develop procedures to ensure adherence within the laboratory's institution to the manufacturer's recommendations for MIS storage and handling from the time the MIS is received by the institution's central receiving area (loading dock) until delivery to the laboratory.

- Comply with the manufacturer's recommendations for MIS storage and handling from the time the MIS is delivered to the laboratory storage area until it is used for routine *in vitro* testing.

- Assure that all individuals who perform testing with the MIS are qualified and trained to conduct testing, and have been shown to be competent in use of that MIS.

- Retain and follow the current technical information and/or product insert containing instructions for use provided by the manufacturer. The testing information should include instructions for:
  - accurate inoculum preparation;
  - proper incubation conditions; and
  - correct interpretation of end points and results.

- Document all MIS QC activities and corrective action.

- 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.

In addition, the laboratory should integrate the manufacturer's risk mitigation information with the unique characteristics of their environment to develop effective QC protocols for *in vitro* diagnostic devices. Environmental characteristics can include unique factors (e.g., personnel competency, testing location, test volume, temperature) that may impact test results.