CLIA and Equivalent Quality Control: Options For The Future

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The QC for the Future Workshop was convened by Clinical and Laboratory Standards Institute (CLSI) to provide an objective forum for discussing Equivalent Quality Control (EQC) theory and practice, respond to EQC questions, and provide interested members of the laboratory community, accrediting organizations, industry, and government agencies an opportunity to provide input.

When the final CLIA rule was published in the Federal Register in January 2003, the laboratory community took an immediate interest in the regulation that allowed CMS to consider alternative approaches to QC practices for laboratory testing. Laboratory professionals awaited the publication of the CLIA Surveyor Guidelines, which would contain detailed information about these acceptable alternative approaches (EQC). The guidelines containing EQC options were published in January 2004, and from the day they were published, they have been controversial. Just about everyone with an interest in laboratory testing—from laboratory directors to professional organizations to test system manufacturers—weighed in with an opinion. Some thought the requirements were too stringent; others thought they were too lenient. Many stated that the EQC options provided in the Guidelines are not flexible enough to accommodate the wide variety of sophisticated testing devices available in today’s marketplace. What almost everyone agrees on, however, is that alternative approaches to QC are very much needed, even if the approaches approved so far by CMS are not exactly what they had in mind. Many individuals and organizations felt that CMS needed broader input from the affected parties in crafting alternative options for QC. CMS heard these concerns.

Background and History

On February 28, 1992, the final Clinical Laboratory Improvement Amendments of 1988 (CLIA) rule with comment period was published in the Federal Register.¹ This rule established requirements for laboratories that are subject to CLIA, such as uniform requirements based on the complexity of testing performed by laboratories, regardless of the laboratory’s location, size, or type. It was recognized that it would take time and resources for laboratories to understand and implement new requirements contained in the February 28, 1992 final rule. Therefore, a phase-in of certain requirements was allowed. The phased-in provisions included several basic QC requirements applicable to moderate complexity tests. They also included the date by which doctoral degree holders are required to possess board certification to qualify as high complexity laboratory directors.

The final CLIA rule, Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications, was published in the Federal Register on January 24, 2003.² In this final rule, the phase-in period for QC requirements applicable to moderate complexity testing was ended. Effective April 24, 2003, all laboratories are required to meet and follow these final QC requirements. In addition, qualification requirements for an individual with a doctoral degree serving as a director of a laboratory performing high complexity testing were set forth.

To supplement the CLIA regulations, CMS published a set of updated Surveyor Guidelines³ in January 2004 that contains interpretations and detailed explanations of the regulations. Not only are these Guidelines used by surveyors to assess compliance, they are also used by laboratories as aids to achieving compliance with CLIA. Surveyor Guidelines can be modified by CMS as new information is learned from experience or provided by supporting data.

Major Changes in the Final CLIA Regulations

With the goal of making the revised regulation easy to read and understand and more flexible, the CLIA rule was reorganized and some of the language was revised. The requirements in the final regulation were ordered to reflect the flow of a patient specimen through the laboratory; that is, from receipt of the specimen with the test request through test performance and test result reporting. Many of the former regulatory requirements were not changed but similar requirements were renamed, reorganized, and consolidated into 1 section, duplicate requirements were deleted, and others were reworded to clarify their original intent.

A single set of quality control requirements was developed for moderate and high complexity testing (collectively known as non-waived testing), thus creating a set of simplified and standardized requirements. As a result, many specialty QC requirements were actually decreased. For example, certain reagents used for bacteriology testing were formerly required to be checked daily using a positive and a negative control material. The final rule requires 1 check to be performed on each new batch, lot, and shipment. For many laboratories that receive new shipments

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These QC changes reflect the evolution of CLIA regulations from their previous form as a set of discreet requirements to their current form, which promotes the concept of Quality Systems and reflects data from laboratory surveys since CLIA’s inception. In keeping with this Quality Systems concept, the requirements for quality assessment (QA) are now integrated into the 3 phases of the testing process, pre-analytic, analytic, and post-analytic, to highlight the vital and important role QA plays in ensuring quality services are provided by the laboratory throughout the entire testing process, and to facilitate the incorporation of QA into the laboratory’s routine operations.

Finally, the phase-in for non-board certified PhD directors of laboratories that perform high complexity testing was discontinued. As of the effective date of the final regulation, all new PhD directors of these laboratories must be certified by a CMS-approved board. Directors previously grandfathered before the effective date will continue to be exempt from the requirement.

**Description of Surveyor Guidelines**

While the stated audience for the Surveyor Guidelines is the CLIA surveyor, the Guidelines are also widely used by laboratory professionals and others as a guide to achieving CLIA compliance. The Guidelines contain interpretations and explanations of the entire set of CLIA regulations and may describe exceptions where compliance with the technical requirements are not practicable. They also contain questions for surveyors to use when assessing laboratories’ compliance. In addition, the Guidelines provide labels, known as D-tags, which are used to identify survey citations.

Although the Guidelines are cleared by CMS legal counsel, they do not have the regulatory authority of the CLIA rules, and they cannot be more stringent than the regulations. Therefore, in some circumstances, there may be alternative routes to compliance other than those specified in the regulations, which are outlined in the Guidelines. Specifically, the final CLIA regulations were written in a way that would allow CMS to provide new approaches to quality control in the Guidelines. When necessary, the Guidelines may be updated by CMS, a process that is much less onerous and time-consuming than regulation clearance and publication. CMS welcomes input to these Guidelines and will periodically publish updates that will be available on the CMS/CLIA Web site.

**Analytic Systems Requirements: Final Regulation**

Significant changes were made in the QC portion of the CLIA regulation, now entitled “Analytic Systems.” Requirements apply to all non-waived testing. Although the QC requirements are now the same, moderate and high complexity testing continue to have different personnel qualification and responsibility standards.

The changes listed below will most affect laboratories that perform moderate complexity testing. Previously, laboratories performing moderate complexity testing were allowed a phase-in period in which they were not held to the same standards for QC as laboratories performing high complexity testing. The most substantial changes were made in the areas of verification of manufacturers’ performance specifications, calibration and calibration verification, and control procedures.

What follows is an overview of the material contained in the CLIA regulations and the Guidelines. In addition, CMS and CDC have collaborated to produce a series of informational brochures that explain the CLIA regulations in plain English for the above-listed requirements.

**Analytic Systems Requirement: Verification of Performance Specifications**

Manufacturers’ test system package inserts contain specifications for test accuracy, precision, reportable range, and reference ranges. Before placing a test system into use, it is required that these specifications be verified by the laboratory using the test. This verification process helps to assure that the test system is performing as the manufacturer intended and is appropriate for the patient population.

The Guidelines provide helpful suggestions for carrying out this process; for example, it is possible to verify more than 1 specification simultaneously by employing careful sample selection. The number of samples is not prescribed and will vary according to the nature of the test system, as well as the laboratory’s test volume, patient population, and other unique aspects of the laboratory’s operations. Laboratories may obtain assistance from test system manufacturers in the form of materials and procedures for verification; however, the actual process must be performed in the laboratory by that laboratory’s personnel. Each individual test system must be checked, even if multiple devices of the exact same make and model are used. The process of verifying performance specifications may be utilized by the technical supervisor to conduct personnel competency evaluations. The laboratory director can use data obtained during the verification process when determining the laboratory’s QC policies and procedures.

**Analytic Systems Requirement: Calibration and Calibration Verification**

Calibration is the process of testing and adjusting an instrument or test system readout to establish a correlation between the measurement of the substance being tested and the true concentration of the substance. CLIA requires that laboratories calibrate test systems as required by manufacturer’s instructions, and that the calibration be verified by the laboratory at least every 6 months to ensure continued accuracy. Certain tests do not require calibration; for example, manual procedures, microscopic procedures, and procedures involving an instrument where calibration is not practical. Some devices, like unit use, are factory-calibrated, so the laboratory is not required to calibrate them.

CLIA also requires that the calibration be verified by the laboratory at least every 6 months to ensure continued accuracy. Since the purpose of calibration verification is to check whether the test system is providing accurate results throughout the reportable range, 3 levels should be tested—1 at the high end of the reportable range, 1 at the low end or zero, and 1 near the midpoint. An exception for calibration verification is outlined in the Guidelines: calibration verification is met if the manufacturer requires a calibration protocol for and the laboratory tests 3 levels of calibrators, a low, medium, and a high, every 6 months. The Guidelines provide further information on calibration and calibration verification requirements and materials.

**Analytic Systems Requirement: Control Procedures**

Controls are used in laboratories to monitor components of the analytic process that may affect test results. The components monitored consist of the operator, the analysis, and the...
environment. The controls may be either external or internal. External controls, traditionally known as “liquid QC,” monitor all components of the test system. While often commercially obtained, either from the test system manufacturer or from a different manufacturer, or they may also be prepared in-house. Internal controls, on the other hand, are built into the test system. They may be electronic or procedural controls, and they may not monitor all analytic components, specifically, the operator.

CLIA regulations require testing 2 levels of external QC materials each day of testing. New to the final regulation, however, is the flexibility of an option in the Guidelines that allows laboratories to reduce the frequency of external QC testing in certain instances. This option, known as Equivalent QC or EQC, was instituted in recognition of the fact that many of today’s test systems are simple to use, stable, and demonstrate QC failure only infrequently. Manufacturers, large reference laboratories, and hospital laboratories routinely collect QC data that show the stability of test systems. It is not uncommon for certain test systems to rarely, if ever, fail QC, thus leading some to question the necessity of performing external QC each and every day for these test systems. It is important to note, however, that reduced frequency QC testing, or EQC, is optional under CLIA. Laboratories may continue to meet the CLIA requirement for external QC by the traditional means of testing two levels of QC daily.

Only certain test systems are eligible for EQC. The laboratory director determines eligibility using the criteria in the Guidelines. Eligibility is based on the specialty/subspecialty of the test system and the QC frequency instructions in the manufacturer’s package insert, and is subject to certain exclusions based on test method.

Once a test system is determined to be eligible for EQC, the laboratory director must select from among 3 EQC options, based on the extensiveness of internal controls built into the test system. Those systems with internal controls that monitor all analytic components are eligible for EQC option 1, which allows a reduction to monthly testing of external QC material. Eligible test systems with internal controls monitoring some, but not all, components of the analytic system may choose EQC option 2, which allows weekly external QC testing. Finally, those test systems without internal controls are limited to EQC option 3, which also requires weekly testing of external QC material. Written information from the manufacturer, such as package inserts, Web sites or operator manuals, can be consulted to obtain information about internal controls.

Before reducing QC frequency, the prescribed evaluation process found in the Guidelines must be successfully completed. For options 1, 2, and 3, the evaluation process requires the laboratory to obtain acceptable results when testing 2 levels of external controls and internal controls per the manufacturer for 10, 30, or 60 consecutive days of testing, respectively. During the evaluation period, and going forward, all quality systems activities routinely employed for the test system must be monitored as usual, including proficiency testing results, staff competency assessment, analytic systems quality assessment, and calibration verification. Any deviation from expected results in 1 of these areas requires analysis and corrective action, and may result in the need to repeat the evaluation process. If a laboratory’s existing QC data successfully fulfills the requirements of EQC evaluation process, the laboratory may use this data instead.

Finally, 2 key points to remember when implementing EQC: first, the decision on whether or not to implement EQC, and which EQC option to choose, is ultimately the responsibility of the laboratory director. Test manufacturers may provide recommendations and guidance, but the laboratory director is required to consider the recommendation in light of his or her individual laboratory’s unique situation. Points include the frequency and volume of test performance, test system stability, technique-dependence of the test, and type of testing personnel employed in the laboratory.

Second, laboratory professionals should remember that EQC is only 1 part of the comprehensive Quality Systems program needed to fulfill CLIA requirements and to provide good quality testing. Along with EQC, laboratory directors need to consider other required quality assessment activities when monitoring and evaluating the performance of each test system; for example, proficiency testing results and staff competency evaluations. If problems are identified in any of these areas, it may be necessary to revert to daily QC when problems are identified and until they are corrected, and the evaluation process is successfully repeated.

The take home message is that it is more important for the laboratory director to ensure that all of the Quality Systems are working well and producing accurate test results than it is to debate over which or any of the EQC options to select.

Educational Survey Cycle

It was noted previously that many requirements in the final CLIA regulation would be new requirements for laboratories performing moderate complexity testing. In keeping with CMS’ educational approach and its outcome-oriented survey process, these laboratories will receive educational surveys for those requirements that are “new to that laboratory.” Laboratories with problems meeting the new standards will not receive a deficiency, but instead will receive a letter urging them to become familiar with the new requirements so that they are in compliance for the next survey. Of course, any non-compliance with existing regulations will continue to be cited on a deficiency statement. CMS will continue the educational survey cycle until the quality control issues in the CLIA final regulation are resolved. Laboratories that are not surveyed by CMS, but receive CLIA certification by virtue of accreditation, must continue to meet the requirements of their accreditation organization. CMS is actively working with its approved accreditation organizations to standardize inconsistent policies in order to reduce confusion in the laboratory community.

Conclusion

The CLIA final regulations elevated quality requirements for laboratories to the systems level and provided a platform for the development of innovative quality control standards that reflect new technologies. CMS is committed to working with its partners in industry and the laboratory community to even further enhance quality patient testing through novel approaches to quality based on future scientific data and best practices.