CLIA CORNER

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Quality Control (QC) Requirements for Non-waived Test Systems

For each non-waived test system, the laboratory is responsible for monitoring the accuracy and precision of each phase of the analytic testing process by using control procedures. In this issue of the CLIA Corner, we will discuss Quality Control (QC): what is it, when to perform it, how to assess acceptability for it, and what to do when it fails.
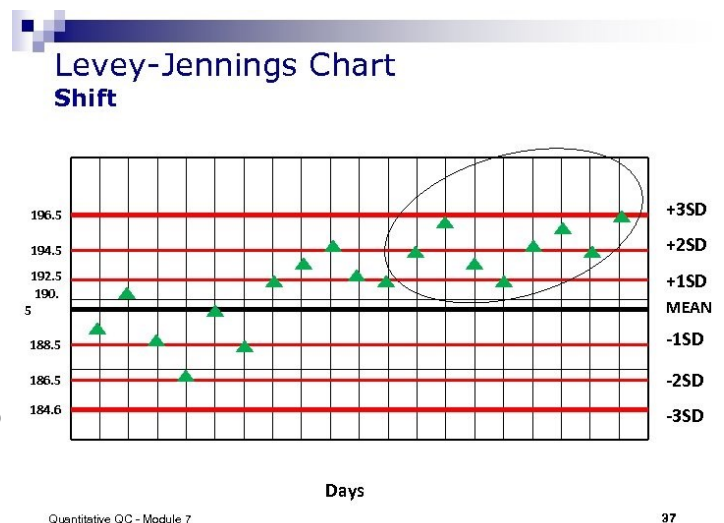
What is Quality Control?

CLIA requires each laboratory to have QC procedures that monitor the accuracy and precision of the complete testing process, which includes the test system, environment, and operator.

- **Test system** failures may result from reagent contamination or deterioration, reagent lot variances, reaction temperature fluctuations, inadequate sampling, improper or loss of calibration, electronic or mechanical failure, etc.

- **Environmental** conditions that may affect test system performance include temperature, airflow, light intensity, humidity, vibrations near an instrument, altitude, etc.

- **Operator** performance can also affect test system performance and may include improper specimen preparation and handling, incorrect test result interpretation, failure to follow the manufacturer's test system instructions, etc.

The laboratory's control procedures must:

- Detect immediate errors that occur due to test system failure, adverse environmental conditions, and operator performance.

  o The laboratory must review the QC on every run prior to reporting patient results. This review must happen in real time as opposed to a retrospective study.

- Over time, monitor accuracy and precision of test performance that may be influenced by changes in test system performance, environmental conditions, and variance in operator performance.

  o A retrospective review of QC results may help to identify shifts and trends and may include the use of Levey Jennings graphs and/or external peer group QC statistics and data.

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Written QC procedures may be incorporated into each test procedure or in an overall laboratory QC procedure. They must include the number, type, and frequency for testing QC materials.

When is Quality Control performed and what are the requirements?

At a minimum, two levels of external QC materials must be run each day patient specimens are assayed or examined. There may be additional or different requirements for special procedures such as molecular amplification, test systems with extraction phases, electrophoretic procedures, thin layer chromatography procedures, and some specialty/sub-specialty procedures (i.e., bacteriology, cytology, histopathology, etc.). Refer to the CLIA Regulations and Interpretive Guidelines for specifics.

- If the test system manufacturer or the state in which the laboratory operates has more stringent QC requirements than CLIA, then the laboratory must follow the more stringent requirements.

- If the test system manufacturer has less stringent QC requirements than CLIA and the laboratory would like to follow the manufacturer's requirements, the laboratory must develop an Individualized Quality Control Plan (IQCP) for the test system.

The laboratory must also perform QC before resuming patient testing when a complete change of reagents is introduced, major preventative maintenance is performed, or when any critical part that may influence test performance is replaced. The QC results must meet the laboratory's acceptability criteria before patient testing may resume.

Additional requirements that must be met include:

- Over time, QC testing must be rotated through all testing personnel who perform the test.

- QC must be tested in the same manner as patient specimens.

- The laboratory must follow the manufacturer's requirements for using reagents, media, and supplies to the extent that they do not conflict with any regulatory requirements.

- QC results must meet the laboratory's and, as applicable, the manufacturer's test system criteria for acceptability before reporting patient test results and all control procedures performed must be documented by the laboratory.

- Actual measurements, reactions, and/or observations must be recorded and all records must be retained for a minimum of two years including: QC results; commercially prepared QC package inserts and assay sheets; statistical parameters/ acceptable ranges established for new lot numbers of unassayed QC and the data used to establish them; and documentation of corrective action for QC when it fails to meet the laboratory's acceptability criteria. **NOTE: Exceptions to the two-year retention requirements can be found in the First Quarter 2016 CLIA Corner.**

When is Quality Control acceptable?

The laboratory is responsible for establishing or verifying the criteria for acceptability of all QC materials used. For QC materials used providing quantitative results specifically, statistical parameters (i.e., mean and standard deviation) for each batch and lot number must be defined and available.

- The laboratory may use statistical parameters defined by the manufacturer for commercially *assayed* QC materials as long as the manufacturer's stated values are for the methodology and instrumentation used by the laboratory. The manufacturer's acceptable ranges must be verified by the laboratory prior to use as daily QC.

- Statistical parameters for *unassayed* QC materials must be established over time by the laboratory through simultaneous testing of QC materials with a previously established mean and standard deviation. **NOTE: CLIA does not specify how many times QC material must be tested to establish statistical parameters. In general, a minimum of 20 replicates is recommended.**

The laboratory's written QC policy must define the criteria used to determine control acceptability. For example, does the laboratory require that two levels of QC be run, and both must fall within two standard deviations of the mean? Or, is QC acceptable when one of the two levels falls within two standard deviations of the mean and the other within three? All personnel who perform QC must follow the laboratory's specific policy for determining QC acceptability.

What happens when Quality Control is unacceptable?

When QC results do not meet the laboratory's and, as applicable, the manufacturer's test system criteria for acceptability, the laboratory cannot report patient test results until corrective action has been taken and documented for the unacceptable QC results. The laboratory should have written policies and procedures that define steps to be taken in the corrective action process. Consider the following example:

Amy is responsible for performing QC on the chemistry analyzer. She pulls the QC vials currently in use out of the refrigerator and waits the appropriate amount of time for them to equilibrate to room temperature. She gently inverts each of the vials 10-20 times as directed by the manufacturer's instructions. She aliquots them into the correct sample cups and programs the instrument for the appropriate QC panels, puts them on the instrument, and runs them. Amy correctly followed all instructions for performing QC, but some QC results still have flags. Amy checks the QC samples for bubbles, ensures she has enough sample in the appropriate cups, and reruns the analytes with errors. Some of the flags resolve, but some are still there. What does she do next? Should she rerun the analytes with flags on the same QC samples again or should she pull new QC vials and rerun the out of control analytes? Should she put a different reagent pack on the instrument or calibrate for that analyte? Should she perform maintenance? Should she call service for help?

QC troubleshooting is more than rerunning QC samples; that is why it is important for the laboratory to have written policies and procedures that detail when to perform QC and the corrective action to take when it is out of range. In addition, each step in the troubleshooting process must be documented.

When results of QC materials fail to meet the laboratory's established criteria for acceptability, all patient test results obtained in the unacceptable test run and since the last acceptable test run must be evaluated to determine if patient results have been adversely affected. The laboratory must take the corrective action necessary to ensure reporting of accurate and reliable patient test results.

Analytic Systems Quality Assessment (QA)

The laboratory must establish and follow written policies and procedures for an ongoing mechanism to monitor, assess, and when indicated, correct problems identified in the analytic systems. This means the policies and procedures must:

- Ensure the discovery of errors;

- Detail the actions that must be taken to correct the errors; and

- Include a mechanism to prevent recurrence.

The laboratory must assess each QC run for acceptability prior to reporting patient test results, but what happens if, for whatever reason, an unacceptable QC run is verified and corrective action is not documented? Does the laboratory have checks and balances in place that guarantee the identification of the error in a timely manner? What steps will the laboratory take to immediately correct the error(s), review patient testing performed during the time that QC was unacceptable, and notify providers as necessary? What additional checks and balances will be added to safeguard from recurrence of the error(s)?

QC and QA go hand-in-hand; you cannot have an effective quality control program without an effective quality assessment program and vice versa. When the two programs are designed to work together, your laboratory will produce accurate and reliable test results and optimal patient care.