The new CLIA quality control regulations and blood gas testing

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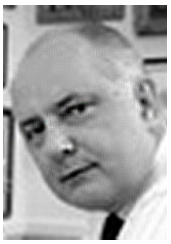
Sharon S. Ehrmeyer Ph.D., Professor
Pathology and Laboratory Medicine
Director, Medical Technology Program
Department of Pathology and
Laboratory Medicine
University of Wisconsin
1300 University Avenue, Room 6175
Madison, WI 53706
USA



R. H. Laessig
Population Health
Pathology and Laboratory Medicine
University of Wisconsin Medical School
Madison, WI 53706
USA

In the U.S. all clinical laboratory determinations, including blood gas testing performed at point of care (POC) or in the central laboratory, is regulated by the Clinical Laboratory Improvement Amendments of 1988 (CLIA).

Congress passed CLIA to ensure accurate, reliable, and timely test results regardless of testing location. The initial quality control (QC) requirements that all test sites must follow are found in the February 28, 1992 Federal Register.

These requirements were updated by the "Final Rule" published in the January 24, 2003 Federal Register. On January 12, 2004, the Centers for Medicare and Medicaid Services (CMS) published Appendix C of the State Operations Manual, a companion document to the Final Rule, which describes three "equivalent quality control" (EQC) options for laboratories to follow in lieu of adhering to the basic QC requirements described in the Final Rule.

Introduction

The QC and calibration requirements of CLIA have been in effect for over 10 years [1, 2]. All are based on test method complexity or difficulty to perform the testing. Currently, blood gas instrumentation used for POCT as well as that used in the central laboratory is classified as moderately complex.

The initial minimum QC standards for blood gas testing, described in the February 28, 1992 Federal Register, included: following manufacturers' directions; having a procedure manual that specifies how to perform tests and report results; performing and documenting calibration procedures (or verifying calibration) at least once every six months; assaying at least one QC sample every eight hours of testing and including a calibrator or control in each run unless the instrument is calibrated or

self-calibrates at least every 30 minutes; performing and documenting remedial actions; and maintaining records of all quality control activities for two years.

When CLIA's requirements were first promulgated, electronic quality control was unknown.

Eventually CLIA allowed electronic controls to fulfill the daily QC requirement provided the manufacturer specified their use. These as well as other mandated quality practices were discussed previously [3].

The basic QC requirements changed on January 24, 2003 with the publication of the CLIA "Final Rule" [4]. In this rule, the former quality practices described in Subparts K (Quality Control), J (Patient Test Management), and P (Quality Assurance) for tests of moderate and high complexity were updated and combined into a new Subpart K (Quality Systems for Nonwaived Testing).

To ensure that test sites focus their quality efforts on all phases of the testing process, this new subpart adopts a quality systems approach and is organized to reflect the flow of a patient specimen through the laboratory.

Most of Subpart K centers on the analytical phase of testing and introduces a new term, "nonwaived testing." Nonwaived replaces the former and differing QC requirements for the moderate- and high-complexity test categories with a single set of QC requirements for both.

Changes in QC blood gas requirements under the Final CLIA Rule

Method validation

Test sites must verify or establish the performance of all methods or test systems introduced after April 24, 2003 (§493.1253), the effective date for the Final Rule. If a test site has been using a method or instrument prior to the effective date, it does not have to revalidate the method.

For unmodified FDA-cleared or approved nonwaived blood gas systems, this includes evaluating: accuracy, precision, reportable range, and reference intervals (normal values).

Practically, this requirement is met when the laboratory evaluates the method or test system's performance characteristics prior to placing the method into routine use, determines that the performance is adequate to meet the needs of the test site's clientele, retains documentation, and follows the manufacturer's instructions for operation, including calibration and QC.

If the system has been modified or is non-FDA-cleared, additional characteristics must be evaluated and documented.

Quality control procedures

Section §493.1256 describes the new requirements for the routine QC procedures. This section is quite different from the minimum requirements published in the February 28, 1992 Federal Register. Specifically, the general QC requirements that are relevant to blood gas testing are (emphasis added):

(a) For each test system, the laboratory is responsible for having control procedures that monitor the accuracy and precision of the complete analytical process.

(b) The laboratory must establish the number, type, and frequency of testing control materials using, if applicable, the performance specifications verified or established by the laboratory as specified in §493.1253(b)(3).

(c) The control procedures must--

1. Detect immediate errors that occur due to test system failure, adverse environmental conditions, and operator performance.
2. Monitor over time the accuracy and precision of test performance that may be influenced by changes in test system performance and environmental conditions, and variance in operator performance.

(d) Unless CMS approves a procedure, specified in Appendix C of the State Operations Manual (CMS Pub. 7), that provides equivalent quality testing, the laboratory must—

1. Perform control procedures as defined in this section unless otherwise specified in the additional specialty and subspecialty requirements at §493.1267.

2. -
3. -
4. -
5. -
6. Perform control material testing as specified in this paragraph before resuming patient testing when a complete change of reagents is introduced; major preventive maintenance is performed; or any critical part that may influence test performance is replaced.
7. Over time, rotate control material testing among all operators who perform the test.(8) Test control materials in the same manner as patient specimens.
8. -
9. When using calibration material as a control material, use calibration material from a different lot number than that used to establish a cut-off value or to calibrate the test system.
10. Establish or verify the criteria for acceptability of all control materials.
    (i) When control materials providing quantitative results are used, statistical parameters (for example, mean and standard deviation) for each batch and lot number of control materials must be defined and available.
    (ii) The laboratory may use the stated value of a commercially assayed control material provided the stated value is for the methodology and instrumentation employed by the laboratory and is verified by the laboratory.

The specialty requirements for blood gases in §493.1267 are identical to those published in the February 28, 1992 Federal Register under section §493.1245.

(a) Calibrate or verify calibration according to the manufacturer's specifications and with at least the frequency recommended by the manufacturer.

(b) Test one sample of control material each 8 hours of testing using a combination of control materials that include both low and high values on each day of testing.

(c) Test one sample of control material each time specimens are tested unless automated instrumentation internally verifies calibration at least every 30 minutes.

(d) Document all control procedures performed, as specified in this section.

We have underlined three of the above requirements that in our view are noteworthy – "having control procedures that monitor … the complete analytical process," "detect immediate errors" and " equivalent quality testing."

Complete analytical process

The complete analytical process typically means from sample aspiration through measurement to generation of the test result.

In reading the new QC requirements, one is led to believe that electronic controls that monitor only the instrument's readout and/or electronics and do not evaluate the complete analytical process would need to be used as described under "equivalent quality testing" (see below).

Detect immediate errors

By just meeting the minimum CLIA requirement for blood gases, one control every eight hours, it would be impossible for sites to immediately detect errors without some additional quality assurance activities such as frequent calibration. Certainly in deciding how much QC is necessary, the test site must strictly adhere to the manufacturer's minimum operating requirements, consider the instrument's performance specifications (long-term precision and accuracy), personnel's competence, etc.

Equivalent quality testing

Subpart K launches another new QC concept – equivalent quality testing or control – and states that Appendix C, Regulations and Interpretive Guidelines for Laboratories and Laboratory Services, of the State Operations Manual (SOM) will provide more information [5].

In the past, CMS surveyors primarily used these Interpretive Guidelines during the inspection process to determine a laboratory's compliance with a CLIA standard. The 500+ pages of Guidelines now are designed to be a companion to the Final CLIA Rule

to help laboratories better understand and meet the CLIA requirements and to provide additional regulatory information not included in the Final Rule.

Test sites using methods employing procedural controls can choose to meet the general QC requirements (above) or to qualify the use of procedural controls as "equivalent quality control" by following either of the EQC options (below).

The specific option selected depends on the characteristics of the blood gas instrument being used. Notice that in the context of the SOM, "EQC" stands for equivalent quality control, not electronic quality control. Both of the options allow the daily, routine, use of non-traditional control procedures once the test system has been proved to be sufficiently stable over time. This stability must be demonstrated and documented. The two applicable options for blood gas systems are as follows:

EQC Option 1. Test Systems with internal/procedural control(s) that monitor the entire analytic process

If a test system uses one or more **internal/procedural** control(s) to monitor all of its analytic components and the laboratory using the test system successfully completes the evaluation process described below to demonstrate test system stability over time, the laboratory may use the equivalent quality control procedures described below in lieu of performing the applicable procedures specified in the regulations at §493.1256(d)(3)(i-ii for blood gases) and the applicable specialty requirements listed for routine chemistry §493.1267.

Evaluation process: The laboratory must perform the test system's internal control procedure(s) in accordance with the manufacturer's instructions (but not less frequently than once each day of testing) and test two levels of external control material daily for 10 consecutive days of testing.

If the internal and external control results are acceptable throughout the evaluation process, the laboratory may reduce the frequency of testing two levels of external control material from daily [or for blood gases, once per 8 hours of testing] to **once per calendar month** unless the manufacturer requires more frequent and/or additional external control testing.

The laboratory must continue to perform and monitor the internal control(s) in accordance with the manufacturer's instructions, but not less frequently than once each day of testing.

EQC Option 2: Test Systems with internal/procedural control(s) that monitor a portion of the analytic process

Some internal/procedural controls monitor only certain components of the test system. Although the test system's manufacturer may suggest other mechanisms to monitor the component(s) not checked by the internal/procedural controls, the laboratory is ultimately responsible for ensuring that all components of the analytic process are monitored.

The laboratory may use the equivalent quality control procedures listed below in lieu of performing the applicable procedures specified in the regulations at §493.1256(d)(3)(i-ii for blood gases) and the applicable specialty requirements listed for routine chemistry §493.1267, when it can demonstrate the test system's stability over time.

Evaluation process: The laboratory must perform the test system's internal control procedure(s) in accordance with the manufacturer's instructions (but not less frequently than once each day of testing) and test two levels of external control material daily for 30 consecutive days of testing.

If the internal and external control results are acceptable throughout the evaluation process, the laboratory may reduce the frequency of testing two levels of external control material from daily [or for blood gases, once per 8 hours of testing] to once per calendar week unless the manufacturer requires more frequent and/or additional external control testing. The laboratory must continue to perform and monitor the internal control(s) in accordance with the manufacturer's instructions, but not less frequently than once each day of testing.

Both Options have the same requirements when a control (internal and/or external) result is unacceptable:

If any internal or external control result is unacceptable during the evaluation process or after the laboratory has reduced the frequency for testing external control materials, the laboratory must repeat the unacceptable internal and/or external control.

In effect, EQC Options 1 and 2 have the potential to allow a test site to continue to use internal/procedural controls on a daily basis and to analyze external QC only once per calendar month or once per calendar week instead of once every eight hours as specified for blood gas testing. In deciding whether to pursue EQC Options 1 or 2, the test site must balance the cost and convenience of enacting the 10- or 30-day evaluation against the benefits of doing external QC only on a monthly or weekly basis. In addition, and more importantly, CMS in Appendix C clearly reminds laboratory directors that the quality of test results delivered to patients and legal responsibility need to be considered:

Since the purpose of control testing is to detect immediate errors and monitor performance over time, increasing the interval between control testing (i.e., weekly, or monthly) will require a more extensive evaluation of patient test results when a control failure occurs (see §493.1282). The director must consider the laboratory's clinical and legal responsibility for providing accurate and reliable patient test results versus the cost implications of reducing the quality control testing frequency.

CAP and JCAHO requirements

While all testing sites performing blood gases must meet the minimum CLIA requirements, not all sites follow the specific regulations cited. Instead, test sites voluntarily choosing to adhere to the requirements of professional accrediting organizations such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) or the Laboratory Accreditation Program of the College of American Pathologists (LAP-CAP) [6,7].

Each of these organizations has test performance standards that meet or exceed those of CLIA and each has been "deemed" or approved by CMS. At this time, it is not known whether JCAHO and/or CAP will adopt the concept of EQC. Until this is known, test sites being inspected by either of these organizations must follow the existing requirements of their accrediting organization.

Summary

Test sites performing blood gases and inspected by CMS for CLIA compliance must comply with the Final CLIA Rule published on January 24, 2003. The major changes in the Final Rule focus on quality practices identified in Subpart K. These include requirements for preanalytical, analytical and postanalytical phases of testing. While the pre- and postanalytical quality assurance requirements have been rearranged and renamed "quality assessment" requirements, they remain essentially the same as those published in the February 28, 1992 Federal Register. CMS now has established one set of QC requirements for both moderate- and high-complexity testing and terms this combined category "nonwaived testing". For any test method introduced after April 24, 2003, the effective date for the Final Rule, test sites must verify and document the performance characteristics. The new requirements for QC procedures include monitoring the accuracy and precision of the complete analytical testing process and immediately detecting errors. In addition, test sites can choose to qualify internal/procedural controls as EQC. The two EQC options open to blood gas testing are discussed in the SOM. Test sites being inspected by JCAHO or CAP do not have to be concerned with these options at this time, since it is unknown whether either accrediting organization will adopt the CLIA EQC concept.

References

- If the repeat control result(s) are within range, no further corrective action is necessary and the laboratory may, as applicable, resume the evaluation process or continue the reduced frequency of external control testing.

- If the repeat control result(s) are not acceptable, the laboratory must identify the problem, take appropriate corrective action and follow the requirements at §493.1282(b)(2) before reporting patient test results. The laboratory must restart and successfully complete the evaluation process before reducing the frequency of testing external control materials.

  Specifically §493.1282(b)(2) for corrective actions state: Results of control or calibration materials, or both, 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 test results have been adversely affected. The laboratory must take the corrective action necessary to ensure the reporting of accurate and reliable patient test results.

- All evaluation process and corrective action activities must be documented.

- Public Law 100-578, Section 353 Public Health Service Act (42 U.S.C. 263a) October 31, 1988.

- U.S. Department of Health and Human Services. Medicare, Medicaid and CLIA programs: Regulations implementing the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Final rule. Fed Regist 1992; 57: 7002-186.

- Ehrmeyer SS. U.S. quality assurance regulations for decentralized testing. Available at: http://www.bloodgas.org

- US Centers for Medicare & Medicaid Services (CMS). Medicare, Medicaid, and CLIA Programs: Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications. Final Rule. Fed Regist Jan 24 2003; 16: 3640-3714. Current CLIA Regulations (including all changes through 01/24/2003) available at:http://www.phppo.cdc.gov/clia/regs/toc.aspx.

- CMS State Operations Manual Appendix C, Regulations and Interpretive Guidelines for Laboratories and Laboratory Services. Available at: http://www.cms.gov/clia/appendc.asp.

- Joint Commission on Accreditation of Healthcare Organizations. Comprehensive accreditation manual for pathology and clinical laboratory services. Oakbrook Terrace, IL: JCAHO, 2004. Available at: http://www.jcaho.org.

- College of American Pathologists. Laboratory Accreditation Program's Checklists. Northfield, IL. 2003. Available at: http://www.cap.org.