

# Considerations for Maintaining Laboratory Quality During the COVID-19 Pandemic

Version 1 • June 28, 2021



Ensuring quality laboratory testing is at the core of public health laboratories' mission. The COVID-19 pandemic has disrupted almost all aspects of laboratory operations diverting significant resources, requiring hiring and/or training of large numbers of new staff and implementing or modifying many tests. These factors along with frequent changes to Centers for Medicare and Medicaid Services (CMS) requirements make it challenging to maintain documentation and procedures necessary to adhere to regulatory requirements. Supply shortages have further exacerbated the issue as laboratories determine how to make efficient use of limited resources while maintaining the highest standard of quality and regulatory compliance.

This document outlines some of the common issues public health laboratories have faced and provides best practices and considerations for maintaining quality laboratory practices and adhering to regulatory requirements under the challenging circumstances presented by the COVID-19 pandemic within quality control, verification and validation, proficiency testing, personnel competency assessment and equipment.

## Quality Control

Quality control (QC) measures help ensure a standard level of testing quality, detect immediate errors and monitor the accuracy and precision of the complete analytic process over time. Controls should be able to detect problems with test system failure, adverse environmental conditions and operator performance. CLIA regulations specify the minimum frequency of general QC requirements as each day of use, unless specified separately for individual subspecialties.

### Individualized QC Plans

#### *Challenge*

QC expends laboratory reagents and test kits. When faced with critical reagent shortages, laboratories must identify efficiencies while meeting regulatory requirements and ensuring test result accuracy.

#### *Considerations*

When the general guidelines for daily default QC are not optimal or compatible with the test system being controlled, an individualized QC plan (IQCP) can allow laboratories to develop their own QC plan based on risk management with evidence to support where QC is not necessary. IQCP is **not** an option to establish QC procedures that are less stringent than those specified by the manufacturer of the test system or reagent, but are an option if deemed safe (according to a risk assessment) in place of default daily QC. If using IQCP, a laboratory should establish a plan to monitor the effectiveness of the QC plan.

Although IQCP has not historically been applicable to tests with Emergency Use Authorization (EUA), CMS updated this in 2020 for the COVID-19 public health emergency. IQCP can be performed on SARS-CoV-2 assays with EUA to assist laboratories in preserving reagents while maintaining quality testing only during the COVID-19 public health emergency (see [CMS FAQ #15 \[12-17-2020\]](#)).

When considering IQCP, laboratories must ensure they adequately consider and document the risks for the entire testing process: pre-analytic, analytic and post-analytic. The IQCP must address all potential hazards that may result due to incorrect test results and rate and mitigate the risks in the QC plan. The following five areas must be addressed in each IQCP risk assessment:

1. Sample/Specimen
2. Testing Personnel
3. Reagents
4. Laboratory Environment
5. Test System

While developing an IQCP can be daunting at first, there are some helpful resources and templates:

- American Society for Microbiology (ASM)'s [materials for implementation of IQCP](#) and [updated IQCP resources](#)
- CDC and CMS's [Developing an IQCP: A Step-by-Step Guide](#)

- The College of American Pathologists (CAP) [website](#) has a variety of information available through e-LAB Solutions Suite under Checklist Resources, IQCP Toolbox (log in required)

## QC Failure

### Challenge

Under CLIA regulations, a laboratory cannot report results when QC is out of compliance. When external or internal QC failures occur, a laboratory may observe potentially actionable positive results for individual patient specimens but cannot report them.

### Considerations

Control material results must meet acceptability criteria before patient results can be reported. To address this challenge:

- Have a written laboratory policy that includes actions to be taken when QC fails.
- Ensure laboratory procedures clearly detail what to do when external and internal QC is out of compliance. For example, for a molecular nucleic acid amplification test, written procedures should include when to repeat amplification and extraction, and when and how to report results.

## Using Expired Reagents

### Challenge

Throughout the COVID-19 response, laboratories have faced limited reagent, kit and material inventories, with some reagents approaching or passing expiration dates. Critical supply shortages may necessitate the use of expired reagents to maintain testing.

### Considerations

During the COVID-19 public health emergency, CMS will allow laboratories to use expired COVID-19 test kits, reagents and swabs, as long as the appropriate testing and documentation is maintained and unless the manufacturer instructions prohibit use of the expired material (see [CMS FAQ #27 \[12-17-2020\]](#)) (CMS, 2020).

To address this situation, establish written policies and procedures regarding use of expired reagents. When possible, request that the manufacturer provide a letter of expiry extension for the reagent or test kit (e.g., as occurred with [BinaxNOW test kits](#)), or document in writing that the manufacturer would vouch for the accuracy and reliability of the reagents while in use past the expiration date. Place these letters in the laboratory's reagent QC binders.

It is important to note that regardless of CMS enforcement discretion, laboratories remain responsible for ensuring the accuracy of their test results. Setting expiration dates is historically the manufacturer's responsibility. Expiration date establishment requires considerable effort, particularly for a testing laboratory during a pandemic. Expiration date practices are outlined in: *CLSI EP25-A Evaluation of Stability of in vitro Diagnostic Reagents and Approved Guideline* and *ISO EN 13640, Stability Testing of in vitro Diagnostic Reagents*, and involve stability studies, sampling plans, transport and storage simulation for worst-case conditions. If using expired reagents in a laboratory, QC must be closely monitored and consider doing additional QC.

## Verification and Validation

### Challenges

**Specimen/Panel Availability:** Early in the COVID-19 response, laboratories had difficulty obtaining sufficient specimens or commercially available panels to perform verification or validation of performance characteristics for molecular and serologic SARS-CoV-2 testing. Emerging SARS-CoV-2 variants are creating similar issues for variant detection assays that laboratories want to bring under CLIA.

**Staff Time:** During an emergency response, laboratories may have less time to focus on developing and performing an extensive verification plan on top of the many steps required to implement a new test, including a [biosafety risk assessment](#), personnel training/competency and qualification of multiple instruments. Shortages of supplies and reagents may necessitate additional verifications or validations to add new specimen types, media types or other testing components.

## Considerations

Before sufficient specimens are available, spiking *in vitro*-translated viral mRNA into various specimen types may be the only way to obtain positive specimens. As additional positive specimens become available, partnering with other public health and clinical laboratories to share known-positive and -negative specimens can help bolster the original validation with true clinical specimens.

Validation and verification approaches for a novel pathogen must be both sufficient and efficient to ensure the test performs well while also rapidly implementing testing. For tests with FDA EUA, only test verification is required, which is shorter and less involved than validation of a laboratory-developed test. ASM has published resources for the verification of molecular and serologic tests:

- Molecular Test Verification: [Understanding, Verifying and Implementing Emergency Use Authorization Molecular 2 Diagnostics for the Detection of SARS-CoV-2 RNA](#)
- Serologic Test Verification: [Verification Procedure for Commercial Serologic Tests with Emergency Use Authorization for Detection of Antibodies to SARS-CoV-2](#)

For efficient implementation of a new test, laboratories can use some aspects of verification testing for other purposes. For instance, reproducibility or precision testing of a small panel of samples (e.g., three positive and three negative samples) for a verification can simultaneously be used as a training/competency panel for personnel and to qualify multiple extraction and real-time instruments for the test.

For additional verifications due to shortages of supplies and reagents, the exact type of verification may differ based on the shortage. For example, verification of a new nucleic acid extraction platform may necessitate a more extensive evaluation than verification of a new type of pipette tip on an automated instrument; for the latter, a “mini-verification” may suffice. The concept of a “mini-verification” panel is described in [Mitchell, 2020](#).

## Proficiency Testing

[According to CMS](#), even during the COVID-19 public health emergency, “if the laboratory is performing testing and providing patient results, [proficiency testing (PT)] is still required and must be performed, as required by the CLIA regulations. (CMS)” If a laboratory adds a new test regulated for a regulated analyte, they must enroll in PT as soon as possible and complete PT for this test/analyte for the rest of the year. If the laboratory adds a test for a non-regulated analyte, external quality assurance must be performed twice a year, and CMS-approved PT may be used for this purpose (and is a requirement of CAP) (CMS, 2017).

## PT Availability during an Emergency

### Challenge

During a public health emergency, PTs may not be available immediately. With SARS-CoV-2 testing, PTs were not initially available, but within a few months, several PT providers were offering programs for nucleic acid amplification tests and PT for antigen and serology testing followed shortly after.

### Considerations

Now that they are available, PT should be performed for SARS-CoV-2 molecular, antigen and serology testing. These are all available from multiple CMS-approved PT providers:

- [American Association of Bioanalysts](#)
- [American Proficiency Institute](#)
- [College of American Pathologists](#)
- [WSLH Proficiency Testing](#)

## PT for Multiple Platforms or Instruments

### Challenge

PT can be challenging when there are multiple testing platforms all testing for the same analyte (i.e., SARS-CoV-2 RNA) or if multiple instruments are running the same test.

### Considerations

If a laboratory tests for the same analyte using more than one system or platforms, PT should be performed on the designated “primary method” for patient testing during the PT event (CMS, 2017). Comparability testing is required for

any other instrument/method performing patient testing. To comply with CLIA regulations, PT is prohibited on multiple platforms/instruments, as this would not be treating the PT sample the same way a patient sample is treated.

Laboratories must monitor the performance of a test across multiple instruments and systems/platforms and may opt to do any of the following to ensure reliable results for all test methods:

- Perform a self-assessment
- Participate in an inter-laboratory comparison
- Participate in a commercially available program (e.g., [CAP Quality Cross Check](#))

## Maintaining Compliance during Testing Suspension

### Challenges

During an emergency response, laboratories may have to temporarily suspend other, lower priority testing at times, and PT may be postponed, suspended or canceled by the PT provider. Despite suspensions of testing or PT, these laboratories are required to remain in compliance.

### Considerations

If a test is temporarily suspended, and therefore a laboratory does not perform scheduled PT, it must be documented in the laboratory's PT response that testing is not currently being performed for that test and cite the reason why (e.g., supply or reagent shortage, staff shortage, etc.). The inspecting agency and PT program in which the laboratory is enrolled must be notified within the timeframe of the expected PT results for that event. Do not let the event run past due without proper communication; this may result in a PT failure.

If a PT provider postpones, suspends or cancels a PT event, they must notify CMS (and obtain CMS approval) and all affected laboratories. The laboratory will not be penalized in this situation but should still consider some form of performance monitoring, such as self-assessment.

## Personnel Competency Assessments

### Accommodating a Large Influx of New Staff

#### Challenges

Many laboratories have added new staff or have had to cross-train staff from other sections during the COVID-19 response. Providing and documenting training and competencies for the influx of staff can be challenging, and providing personnel competency assessments can put additional strain on limited reagents and consumables.

Doing competency assessment with diverse roles, limited sample availability and different organizational structures across laboratories. Additionally, the COVID-19 response has necessitated new skill sets, such as bioinformatics, and there are not necessarily supervisors with proper knowledge to perform competency assessments.

#### Considerations

According to CLIA regulations, competency assessments must be performed twice during the first year an individual performs testing and annually thereafter.

Competency assessment requires six main components:

1. Direct observation of testing
2. Monitoring of recording/reporting or results
3. Reviewing tests results, worksheet, QC, PT and preventive maintenance
4. Direct observation of instrument maintenance and operations
5. Assessment of test performance (e.g., testing previously analyzed specimens, PT, etc.)
6. Assessment of problem-solving skills

According to CMS, all six procedures must be addressed for personnel performing testing for all tests performed; however, the competency assessment can be done throughout the entire year as long as all six procedures are addressed (CMS, 2012). Coordinating competency assessment with routine practices and procedures such as PT can help make efficient use of staff time and supplies. Other suggestions include enrolling in a commercially available competency assessment program (e.g., CAP). Utilization of document control programs (e.g., MediaLab) that have modules or workflows that allow for electronic tracking and monitoring of staff competency as well as workflows that

help streamline electronic completion of specific elements of competency can aid in the management and tracking of staff competencies and related documentation.

## Equipment

### Moving Instruments or Equipment

#### **Challenge**

In order to effectively respond to the COVID-19 pandemic, many laboratories have had to relocate existing equipment, expand testing capacity by purchasing multiples of the same equipment or diversifying the types of equipment capable of testing for the same analyte.

#### **Considerations**

Laboratories should have a written procedure that follows the manufacturer's recommendations and describes the performance verification, function checks and acceptance criteria required when instruments or equipment are moved.

**Prior** to moving the instruments or equipment, communicate with the vendor to determine who can perform a move and the recommended method for re-verifying performance of the instrument (i.e., installation and operational performance (IQ/OQ)).

Laboratories should review appropriate data and documentation to ensure optimal performance and approval before patient testing resumes on the instrument or equipment.

### New Instrument Purchases & Instrument Comparisons

#### **Challenge**

During the COVID-19 pandemic, laboratories have had to scale up the number and diversity of testing platforms to address unprecedented testing demand and reagent availability issues.

#### **Considerations**

Some newly-installed instruments and equipment should have qualifications performed to ensure proper IQ/OQ prior to patient testing; this service may be purchased at the time of instrument procurement.

Maintain written procedure(s) describing the routine operation, emergency shutdown, acceptable function limits, troubleshooting and whom to notify about issues for all new instruments and equipment, and maintain all documents and records relating to the qualification of new instruments and equipment.

Perform instrument comparisons every six months on multiple instruments of the same make and model, as well as between different makes and models used to perform testing on the same analyte. The laboratory's quality assurance manual should describe the procedure for performing instrument comparability, the frequency in which it should be performed, specimen types used, the acceptance criteria for results and corrective actions required when results are not acceptable.

It is recommended that patient samples (single or pooled) be the preferred specimen for instrument correlations to ensure comparisons with the normal matrix in which the analyte is found. However, QC, reference or PT materials can be utilized in circumstances where human specimen integrity may be compromised. Review results generated from the performance of instrument comparisons for acceptance and document approval.

### Equipment Maintenance and Compliance

#### **Challenge**

High demand and other pandemic-related challenges can make it more difficult to access vendors and service technicians may be slower than normal to respond when issues arise.

#### **Considerations**

Normally, all instruments and related equipment should have preventative maintenance and function checks performed as defined by the manufacturer; laboratories should have a procedure that describes the specific maintenance, function checks and cleaning required and the frequency at which they should be performed. Performance verification and function checks need to be performed following any major maintenance or work on instruments or equipment. Laboratories should review all documents and records relating to preventative maintenance,

service or repair and function checks for acceptance and document approval. During times of increased equipment usage and demand, the frequency of preventative maintenance and function checks should be re-evaluated and likely increased.

During the COVID-19 response, a variety of approaches have been used to deal with slow turn-around by vendors:

- Have multiple instruments and/or tests for a single analyte so the laboratory can continue testing if one instrument is out of service.
- Ask the manufacturer what maintenance could be performed by the laboratory without requiring a visit. It may be possible for manufacturers to utilize video conferences for step-through function checks and other maintenance tasks.
- If maintenance is delayed, ask the manufacturer to provide written documentation vouching for the accuracy of the instrument.

## References

- CMS. (2012, November). *What Do I Need to Do to Assess Personnel Competency?* Retrieved from [https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/clia\\_compbrochure\\_508.pdf](https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/clia_compbrochure_508.pdf)
- CMS. (2017, September). *CLIA Proficiency Testing and PT Referral Dos and Don'ts*. Retrieved June 22, 2021, from <https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/CLIAbrochure8.pdf>
- CMS. (2020, December 17). *Frequently Asked Questions (FAQs), CLIA Guidance During the COVID-19 Emergency Updated as of 12/17/2020*. Retrieved from <https://edit.cms.gov/files/document/frequently-asked-questions-faqs-clia-guidance-during-covid-19-emergency-updated-12-17-2020.pdf>
- CMS. (n.d.). *Frequently Asked Questions (FAQs), CLIA Guidance During the COVID-19 Emergency*. Retrieved June 22, 2021, from <https://www.cms.gov/files/document/clia-laboratory-covid-19-emergency-frequently-asked-questions.pdf>
- Mitchell, M, St. George, K, Rhoads, D, Butler-Wu, S, Dharmarha, V, McNult, P, Miller, M. (2020, May 7). Understanding, verifying and implementing Emergency Use Authorization molecular diagnostics for the detection of SARS-CoV-2 RNA. *J. Clin. Microbiol.* doi:10.1128/JCM.00796-20