COLA'S 3rd Quarter 2022

inSIGHTS

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LETTER FROM THE CHAIR

3rd QUARTER 2022

The 2022 Laboratory Enrichment Forum offered the opportunity for continuing education, professional networking, and productive discussions about the future of the clinical laboratory. Throughout the Forum we solicited attendee feedback to better understand the educational topics that are of the most value to our audience of laboratory professionals. COLA takes customer feedback seriously and we thank our attendees for sharing their valuable insights. We found several common themes in the responses and have focused this edition of inSights on the main topic areas identified by our Forum attendees: molecular diagnostics, proficiency testing and regulatory compliance.

Staying informed about regulatory changes is imperative to maintain regulatory compliance. Adapting quality assessment activities to address change is necessary to assure the laboratory's overall operational quality. In this edition, we review some upcoming changes to the CLIA regulations affecting proficiency testing and reporting. We also provide guidance on how to develop a meaningful and personalized QA Plan that will allow you to learn more about how your laboratory is performing.

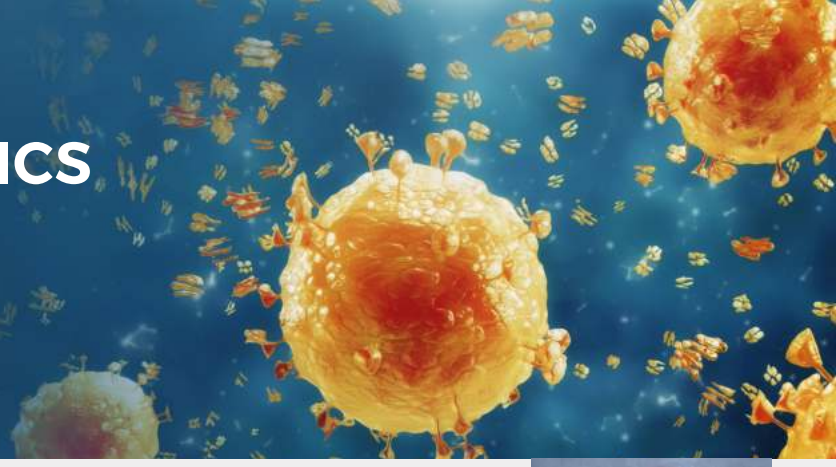
In the article, Molecular Diagnostics – A Brief Overview and Regulatory Requirements we review the regulatory requirements surrounding initiating molecular testing. Molecular testing is no longer only the domain of specialized reference laboratories and is now performed in many physician offices laboratories nationwide. Understanding the regulatory framework around these tests is important if you are considering offering them to your patients.

COLA is currently developing additional educational sessions that will address these and other trending topics in further depth during the 2023 Laboratory Enrichment Forum in Ft. Worth, TX. We hope to see you there.

William E. Kobler, MD
Chair, COLA Board of Directors

MOLECULAR DIAGNOSTICS

A Brief Overview and Regulatory Requirements



By: Kobina Shaffa

Kobina has extensive experience in clinical laboratories, including in molecular, immunology and the core lab. He has BS in Medical Laboratory Science and a Masters in Immunology and Molecular Diagnostics. Kobina joined COLA as a Surveyor in 2021.

A very important component of healthcare is accurate and timely diagnosis. According to the CDC[1], about 70% of all medical decisions depend on diagnostic test results. The clinical laboratory is vital to clinical care, from prenatal genetic tests to hematological and microbiological testing. New tests and methodologies are constantly evolving, and the recent widespread adoption of molecular diagnostic techniques in the clinical laboratory has greatly revolutionized diagnostic testing.

In the early 2000s, the human genome project was launched and has since been completed.[2]

The sequencing of thousands of human genes by research teams worldwide has resulted in vital genetic information stored in gene databases for international clinical reference. In addition, the genomes of thousands of microorganisms, including genes of many bacteria, fungi and parasites are now well-characterized.

Molecular diagnostics techniques can be used to accurately identify very specific genetic sequences.

This technology can be used to detect pathogens with high specificity to determine the causative agent of infection, and detect targeted human DNA or RNA sequences for cancer risk screening, tumor profiling and pharmacogenomics testing. Clinicians rely on laboratory test results for diagnosis and treatment decisions. Some molecular assays are qualitative, designed to determine whether or not a target is present. Others may be quantitative or semi-quantitative, to assess how much of the target is present. Many types of molecular techniques are currently used in specialized clinical testing, including micro-arrays, next-generation sequencing, plasmid profiling and methods for identifying restriction fragment length polymorphisms (RFLPs). To date, the robust polymerase chain reaction (PCR) technique or one of its many modified approaches is still the most commonly used molecular technique in the clinical laboratory.

As the SARS-CoV-2 virus spreads globally, new variants continue to emerge, and molecular diagnostic tools with very high sensitivity and specificity were needed to advance our understanding of SARS-CoV-2 composition and the mutations that lead to new variants. The COVID-19 pandemic accelerated the adoption of PCR-based molecular techniques in clinical laboratories, physician offices and other settings as a means to increase public access to testing.

These tests help to direct mitigation approaches used globally to respond to the pandemic.

Many of these tests are laboratory-developed or are operating under an Emergency Use Authorization from the FDA. Thus, there is a need for adequate regulations and oversight of these tests to ensure patient safety.

Test Validation/ Verification Requirement

All laboratories performing FDA-approved, non-waived testing must complete the verification of the manufacturer's test performance specifications before the test is used in the clinical laboratory[5]. COLA accreditation criteria require that all laboratories that perform moderate or high complexity testing meet CLIA's specific validation or verification requirements for all non-waived tests performed; in addition, some COLA-specific requirements regarding test validation must be met to be compliant with accreditation[3].

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The Verification Of Performance Specifications

Laboratories are required to verify the performance of all non-waived tests prior to clinical use; for FDA-approved tests, this means that they must verify that they can achieve the performance specifications established by the manufacturer. Laboratories are required to ensure that all test methods, including molecular test methods, are verified for accuracy, precision, reportable range, and reference range, when applicable[3,5]. Many laboratories go further under good laboratory practice to confirm the limit of detection (LOD) of the test and to perform carryover studies, when these are applicable to the test system.

COLA requires that all verification studies be reviewed and approved by the Laboratory Director or a qualified designee prior to the start of patient testing.

The Establishment of Performance Specifications

For all molecular tests that are not FDA-approved, including laboratory-developed tests, and those that are FDA-approved but modified by the laboratory, a more extensive validation study is required prior to patient testing. To be compliant with regulatory requirements, the laboratory must establish parameters for the tests, including accuracy, precision, analytical sensitivity, analytical specificity, reportable range, reference range, and specimen stability[3,4,5]. They are also required to complete a cross-contamination study if the test method involves an automated extraction step. The laboratory must evaluate the test for the impact of potentially interfering substances, perform a limit of detection study, and assess the matrix effect of transport media, if applicable. These performance parameters must be established for every specimen type and/or specimen source. For example, if a laboratory is testing both nasal swabs and throat swabs for the presence of a virus, then two separate validation studies are required.

An accurate and effective diagnosis directs treatment, which is paramount to patient safety; therefore, as new technology enters the clinical laboratory, COLA will continue to revise criteria and develop new criteria which align with our mission to promote health and patient safety through accreditation and education.

References:

1. CDC, Strengthening Clinical Laboratories, https://www.cdc.gov/csels/dls/strengthening-clinical-labs.html. Accessed 8/16/2022

2. Nurk S, et al. The complete sequence of a human genome. Science. 2022 Apr;376(6588):44-53. doi: 10.1126/science.abj6987. Epub 2022 Mar 31. PMID: 35357919; PMCID: PMC9186530.

3. COLA Accreditation Manual 2022

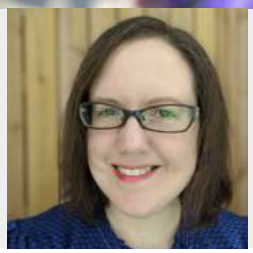
4. LDT and CLIA FAQ, https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/LDT-and-CLIA_FAQs.pdf. Access 8/16/2022

5. CLIA Interpretive Guideline for Laboratories, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/som107ap_c_lab.pdf. Accessed 8/16/2022

LOOK OUT: CHANGES IN PROFICIENCY TESTING

By: Jennifer MacCormack, MLS (ASCP) CM

Jennifer is an experienced science and medical writer with a background in clinical laboratory testing, medical & health science, and regulatory oversight. She received her Bachelor of Science in Physiology from McGill University.



The CLIA regulations were developed decades ago, and while clinical laboratory testing has changed significantly since the 1990s, regulatory changes have not entirely kept up with advancements in the science and practice of laboratory medicine. In July of 2022, CMS published a Final Rule (CMS-3355-F) in the Federal Register to implement revisions to the proficiency testing (PT) sections of the CLIA regulations. The final rule incorporates input from a PT workgroup within the Clinical Laboratory Improvement Advisory Committee (CLIAC), which included key industry stakeholders such as PT program officials, laboratory professionals and representatives from accreditation organizations and state CLIA programs.

The Final Rule includes changes to the required content of PT modules and changes in the acceptable ranges used for scoring PT results.

The list of regulated analytes will be updated, with some deletions and many additions. For more details, a summary of the changes and the rationale behind them can be found in memorandum QSO-22-21-CLIA, published by the CMS Center for Clinical Standards and Quality/Quality, Safety & Oversight Group.

Changes to PT Referral and Sanctions

CMS sanctions relating to proficiency testing (PT) sharing or improper PT referral will now also apply to proficiency testing performed on waived tests. The effective date of this change was August 10, 2022. Enrollment in PT modules for waived testing is still optional and not a CLIA requirement; however, it is recommended as good laboratory practice. Note that PT on some waived analytes may be required under certain state regulations or required by accreditation organizations.

Immunohematology Changes

Under the specialty of immunohematology, the acceptable score for unexpected antibody detection (antibody screen) will be 100%, where it was previously 80%. This brings it into alignment with ABO/Rh testing and compatibility testing, which also require 100% scores to be considered acceptable.

Hematology Changes

With the implementation of the new PT rules, laboratories performing both automated differentials and manual differentials will be required to enroll in PT for both the automated and manual methods. Currently, a laboratory is only required to enroll in a PT module for their primary method of performing WBC differentials, whether this is automated or manual.

Chemistry, Toxicology, Endocrinology and Immunology Changes

CMS has approved several additions to the list of regulated analytes for which a laboratory is required to enroll in PT. See Table 1 below for the newly regulated analytes. Several analytes have also been removed from the list, as they are rarely used in current clinical testing: LDH isoenzymes, ethosuximide, quinidine, primidone, procainamide and its metabolite N-acetyl procainamide.

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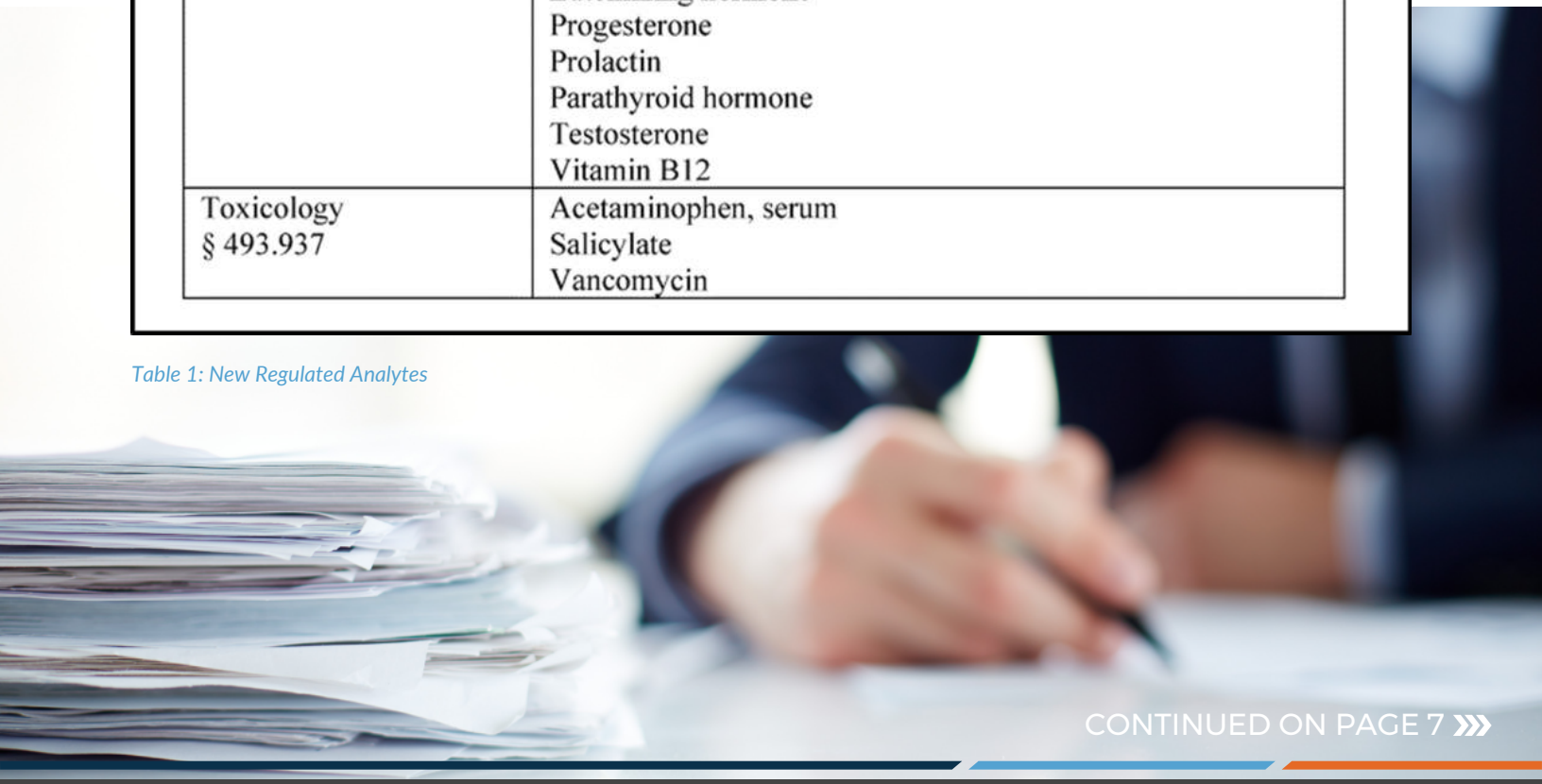
TABLE 1: Analytes Proposed for Addition to Subpart I

CLIA Regulation	Analytes
General Immunology § 493.927	Anti-HBs Anti-HCV C-reactive protein (high sensitivity)
Routine Chemistry § 493.931	B-natriuretic peptide (BNP) ProBNP Cancer antigen (CA) 125 Carbon dioxide Carcinoembryonic antigen Cholesterol, low density lipoprotein, direct measurement Ferritin Gamma glutamyl transferase Hemoglobin A1c Phosphorus Prostate specific antigen, total Total iron binding capacity (TIBC), direct measurement Troponin I Troponin T
Endocrinology § 493.933	Estradiol Folate, serum Follicle stimulating hormone Luteinizing hormone Progesterone Prolactin Parathyroid hormone Testosterone Vitamin B12
Toxicology § 493.937	Acetaminophen, serum Salicylate Vancomycin

Table 1: New Regulated Analytes



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Microbiology Changes

CMS will require PT for direct antigen testing in mycology and parasitology; PT is already required for direct antigen testing in both bacteriology and virology. Bacterial toxin detection will now also be part of regular PT challenges for bacteriology. In addition, PT challenges for Gram stains will now require reporting of the bacterial morphology in addition to the Gram reaction.

Any bacteriology PT program is required to include clinically important species of aerobic and anaerobic bacteria appropriate for the sample sources represented. They must include both Gram-negative and Gram-positive bacilli, and Gram-negative and Gram-positive cocci.

For susceptibility testing, CMS will require at least two PT samples per event, including organisms with a predetermined pattern of susceptibility and resistance to common antimicrobial agents. For bacteriology, the PT challenges are required to include one Gram-negative and one Gram-positive organism.

PT modules for other microbiology subspecialties will also be required to include representatives of medically important organisms. Specific organisms may vary from year to year, but requirements are as follows:

- *§ 493.913(a)(3): For mycobacteriology, we are proposing that the annual program content must include Mycobacterium tuberculosis complex and Mycobacterium other than tuberculosis (MOTT), if appropriate for the sample sources.*

- *§ 493.915(a)(3): For mycology, we are proposing that annual program content must include the following major groups of medically important fungi and aerobic actinomycetes if appropriate for the sample sources: Yeast or yeast-like organisms; molds that include dematiaceous fungi, dermatophytes, dimorphic fungi, hyaline hyphomycetes, and mucormycetes; and aerobic actinomycetes.*

- *§ 493.917(a)(3): For parasitology, we are proposing that the annual program content must include intestinal parasites and blood and tissue parasites, if appropriate for the sample sources.*

- *§ 493.919(a)(3): For virology, we are proposing that the annual program content must include respiratory viruses, herpes viruses, enterovirus, and intestinal viruses, if appropriate for the sample sources*[ii].

The changes to the proficiency testing regulations will be effective on July 11, 2024; the delay in implementation will provide proficiency testing providers sufficient time to develop appropriate modules to meet the new requirements.

Laboratories are encouraged to enroll in appropriate proficiency testing prior to the implementation date to ensure they are able to receive appropriate challenges in 2024.

References:

[i] Center for Clinical Standards and Quality/Quality, Safety & Oversight Group. QSO-22-21-CLIA. https://www.cms.gov/files/document/qso-22-21-clia.pdf. Accessed September 27, 2022.

[ii] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments of 1988 (CLIA) proficiency testing regulations related to analytes and acceptable performance. Federal Register. 2022;87:41194-41242. https://www.federalregister.gov/d/2022-14513. Accessed September 27, 2022.

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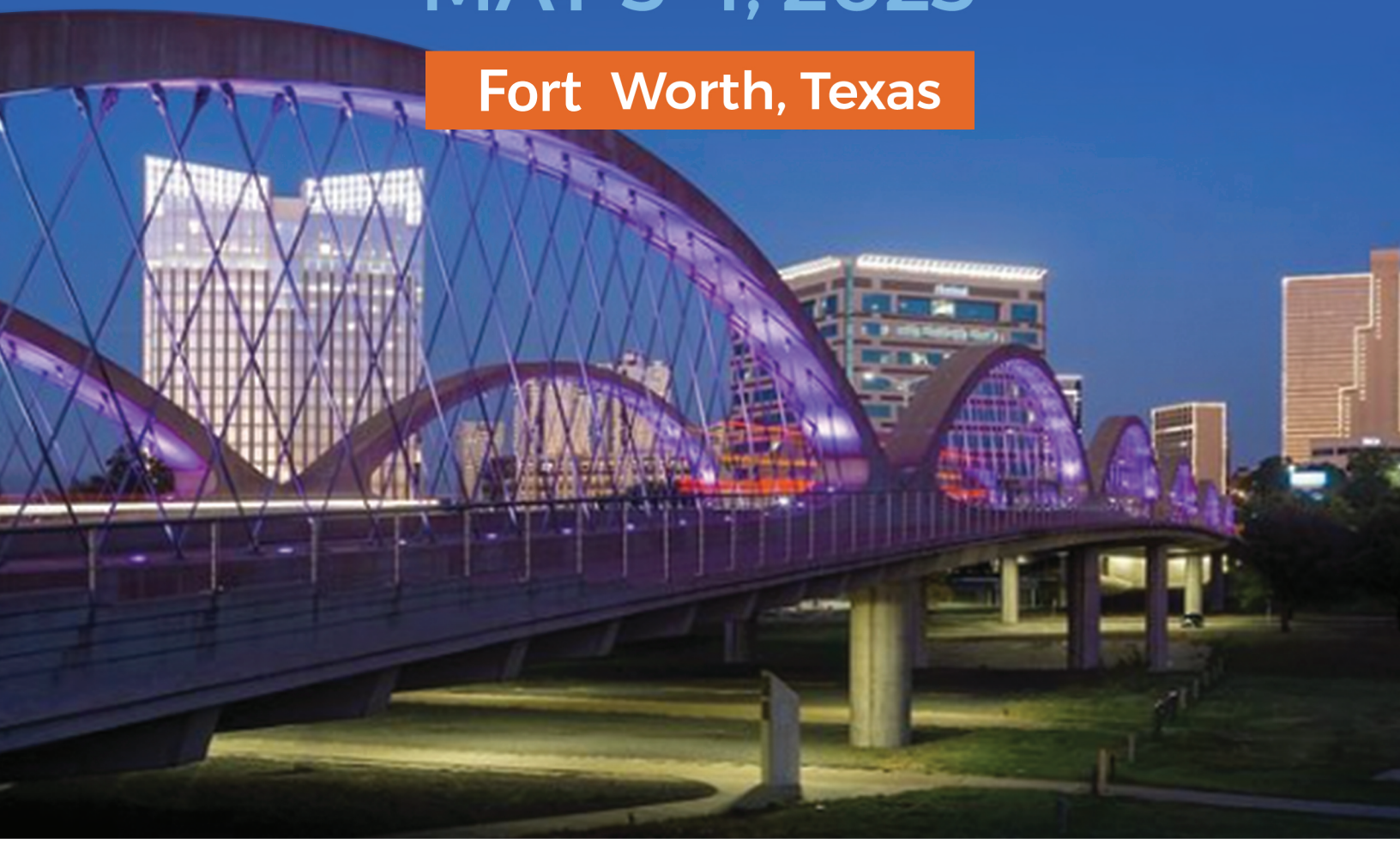

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Editorial:

BEST PRACTICES FOR QUALITY ASSESSMENT AUDITS

By: Jennifer MacCormack, MLS (ASCP) CM

Jennifer is an experienced science and medical writer with a background in clinical laboratory testing, medical & health science, and regulatory oversight. She received her Bachelor of Science in Physiology from McGill University.

Some of the most common questions COLA's technical staff receive from our laboratories relate to the quality assessment (QA) process.
What exactly should be assessed?
How do we measure our performance?
How can we be sure we're performing meaningful quality assessment reviews?

Every laboratory is different, and Quality Assessment Plans will vary considerably depending on the laboratory's size and scope of service. That said, all laboratories must conduct regular reviews of their preanalytic, analytic and postanalytic processes in order to track the laboratory's performance over time and to uncover areas for improvement. The general roadmap for all QA reviews is the same:

1. Select a process to audit
2. Determine the target quality metric
3. Collect and review data
4. Perform a root cause analysis when targets are not met
5. Implement corrective actions
6. Re-audit the process to determine effectiveness of corrective actions

1 Selecting a process to audit

All laboratory processes can be evaluated through quality assessment, but some are better targets for a QA review than others.

Look for areas where there is a high risk of error, or where errors translate to high risk to the patient. For example, specimen labeling and timely reporting of critical values. It's also meaningful to audit areas where there have been recent changes, such as new staff, new instrumentation and IT systems, or changes to procedures. Change creates an environment where errors may increase, and a QA review of new and changed processes a few months after their implementation can provide meaningful data about whether they may need adjustment.

In addition, consider reviewing any areas where problems have recently been noted, either through complaints to the laboratory by patients or providers, or regulatory deficiencies cited during biennial laboratory surveys. Even if corrective actions were implemented to bring processes into compliance or resolve complaints, it is useful to go back months later and reassess whether those corrective actions truly solved any underlying problems.

2 Determining the quality metrics

Target metrics must be set prior to data collection and review. They should be reasonable and meaningful. For example, a target of 100% of laboratory results reported within the established turnaround time may not be realistic depending on the test volume of your laboratory.

However, perhaps that 100% target is appropriate when applied more narrowly to cardiac panels coming from the emergency room. Remember, too, that targets can change over time. If the laboratory sets a target of 80% for annual competency evaluations performed on time, and consistently meets that target, they may consider pushing the target up to 90%. The goal of quality assessment is to improve quality over time.

3 Collect and review data

Depending on the target, the personnel conducting the audit should collect and review relevant documentation and records and make notes on their findings. In smaller laboratories, it may be possible to review all relevant documents from a set timeframe.

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In most cases, though, it is more realistic to review a random selection of records that are representative of the whole. Take care to ensure selection is indeed random. Include records from different days, different shifts, different personnel and so on, to reduce the possibility of bias.

Use of standardized forms for data collection can ensure that all personnel who perform a QA review will collect data in the same manner. The laboratory's QA Plan should describe the data collection process, including how to select items to review and how to assess those items for acceptability. COLA-accredited laboratories have access to sample QA review forms in the Solutions Library on COLAcentral.

4 Perform a root cause analysis

After collecting and evaluating the data, determine whether or not the target metric has been met. If not, the next step is to investigate why the laboratory did not meet the goal. It is very important to dig deeper and find the true root of the problem. Remember that QA is not about blaming individuals for not following policies or not completing paperwork; it is a chance to uncover whether there is a systemic problem behind the unacceptable audit results. Perhaps new employee training is inadequate, work instructions are unclear, or forms are missing areas to record important information. The goal is to correct and adapt policies and procedures in response to QA findings and make it harder for the same errors to reoccur by putting safeguards in place.

Even if the metric is met, there may be room for improvement.

It is good laboratory practice to investigate any non-perfect scores on QA reviews, in case there are steps that the laboratory can take to bring those scores up higher. Just as a score less than 100% on a proficiency testing event should be investigated, extra effort in exploring QA review results can lead to improvement in the laboratory's overall quality.

5 Implement corrective actions

Once the likely root cause is determined, consider what corrective actions are required.

If the QA review uncovered any errors or risks of harm to patients or to staff, it is important to act immediately to address the root cause or eliminate the danger. For example, if errors are discovered in results that were manually transferred from a worksheet into the laboratory information system, those patients' healthcare providers must be notified immediately and the results corrected in the system. After completing any required immediate corrective actions, step back and look at the details to determine what actions can be put into place to avoid it happening again.

When possible, include the entire laboratory team when considering solutions. Each team member brings different experience to the conversation, and may have ideas that laboratory management has not considered. In addition, including all staff in quality assessment discussions serves as excellent training. They can use the information learned through QA reviews when they encounter unusual or difficult situations themselves; a deeper understanding of laboratory QA can improve critical thinking and troubleshooting skills.

5 Re-audit the process to determine effectiveness of corrective actions

Not all corrective actions will be effective. Sometimes the investigation lands on the wrong root cause, or the corrective action is not adequately implemented. This is why it is good practice to re-audit the same area after some time has passed, to determine whether or not the actions taken achieved the goal and corrected the underlying problems.

Establish a calendar for reviews

To ensure that all areas of the laboratory are adequately assessed over the course of the year, it is recommended to plan out specific areas of review using a calendar. Select one or two specific audit targets per month, depending on the needs of your laboratory. This gives ample time for audit preparation and planning, and spreads out the workload so that staff are not overwhelmed performing several audits in a short timeframe to meet regulatory requirements.

OUR COMMITMENT TO YOU

We are a physician-directed organization whose purpose is to promote health and safety through accreditation and educational programs.

ABOUT COLA:

For more than 30 years, COLA's accreditation program has provided an extra pair of eyes for laboratories striving to produce quality test results. COLA's laboratory accreditation program consists of quality-engineered processes that are certified to ISO 9001. This means our customers benefit from unique services that are standardized and represent a commitment to customer satisfaction. Just as importantly, COLA provides materials to guide successful completion of inspections and adherence to regulations; and has a dedicated staff of subject matter experts steered by a coaching approach.