THE *NEW* POOR LAB'S GUIDE TO THE REGULATIONS (CLIA, The Joint Commission, CAP & COLA)

2021

Successful Strategies & Specific Applications of the Regulations

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Library of Congress Control Number: 2021935711

ISBN 1-886958-35-1
ISBN-13 978-1-886958-35-7
Published by Westgard QC, Inc.
7614 Gray Fox Trail
Madison, WI 53717

Phone 608-833-4718

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- updates on new developments in compliance and regulations
- additional articles, lessons, and advice on compliance, quality, and regulatory topics

Foreword

The circumstances now afflicting humanity cast a bright focus on this new edition of the Poor Lab's Guide to the Regulations. Not just because every human activity is being impacted by the tragic pandemic of the third decade, but because its topic sharply explains one of the two redeeming lights of the COVID-19 calamity: testing and vaccines. The latter have been in development for decades, as manufacturers took heed from the predictions repeatedly announced by research and public health professionals since the SARS and MERS epidemics of the 1990's and have been perfecting their techniques since. But clinical laboratories were caught by surprise just like everybody else. Yet, with speeds that can only be described as miraculous, laboratory equipment manufacturers and diagnostic laboratories rose to the occasion and, in a blink, were able to start diagnosing infections at public health scale. Literally within days of the awkwardly delayed public realization of the large pandemic spread in our area, clinical laboratories were able to deploy fast and accurate molecular testing[i], a feat the prescient fictional movie "Contagion" could only have imagined a decade before. But we were able to do it without any ad hoc preparation. All we needed was to struggle with supply shortages while following the ingrained clinical laboratory quality practices this small tome masterly addresses.

A colleague recommended[ii] that we should always carry our bag of tricks and have it ready to open at a moment's notice. And what a toolset clinical laboratory professional instantly drew to confront the raging pandemic! As we are the members of the healthcare team that count, we were ready to deal in more ways than one with the large and rapidly increasing numbers associated with COVID-19 without any ad-hoc preparation. In fact, our field had been preparing for more than 70 years. We have not only been measuring the content of patient samples but also the exactitude of our measurements and the efficiency and robustness of our processes with as much care. And since once you can measure, you can improve, we have become the leading practitioners of quality management among those who take care of patients.

Retrospectively, it makes sense that the near-patient activity that arguably most resembles industrial production and specializes in measuring, eagerly took to the mid-century revolution in industrial statistical quality led by Shewhart, Juran, Deming and others[iii] soon after these techniques demonstrated their value in the Japanese industrial revolution, even before U.S. industry fully warmed to it. We can milestone the beginnings of this journey with the adaptation of Shewhart's quality control chart to the clinical laboratory by Levey and Jennings in 1950 [iv] and track its explosive growth since the 1970s thanks in good part to Jim Westgard's persistent efforts.[v,vi]

Since you can only improve what you can measure and you can only correctly measure what you know, the virtuous cycle of mutually reinforcing statistical literacy and quality improvement has brought the clinical laboratory and their industry suppliers to the vanguard of quality practices among healthcare specialties. This practice also compels the laboratorian to intimately understand every moving part of the operation in order to measure it. It follows that they can quickly and effectively pivot the laboratory operation to adapt to new technology – or to a new virus – without severe disruption it and without ending up with too many missing parts.

That is how, one week after the first patient had been diagnosed in the New York Metropolitan area, on March 8th with help from New York State Department of Health, our laboratory brought up SARS-CoV-2 RNA testing using a manual polymerase chain reaction (PCR) method to generate a couple of hundred results per day, scaled up to cartridge-based PCR the following week and to automated amplified RNA testing only 8 days later on March 16th, expanding to provide close to 3,000 tests per day[i]. All of this testing was also validated and carried out under rigorous quality control! It was not easy, requiring heroic staff efforts, massive redeployment of resources and shrewd management of supply chains. But it followed the

familiar script inculcated by our culture of quality and carried out countless times in the past. Peer laboratories throughout the world tell similar success stories of effort and cunning bred out of this shared culture.

Nevertheless, I would venture to say that every clinical lab is poor in several regards. Poor in appreciation: a neurosurgeon who separates conjoined twins can justly be recognized as fit to become the country's president, but the clinical laboratories that provide the main defense against the pandemic in near-miraculous ways are often only recognized by the testing they are *unable* to do or by the delays they cannot avoid. We have made clinical laboratories so accurate and efficient, that they only appear in the public conscience when they err or fail to meet demand.

We are also poor in financial resources: while providing the information for more than two-thirds of all medical decisions, our share of the U.S. healthcare budget is so tiny to almost fall within its margin of error. Even though we are the healthcare experts in counting, we are usually not appreciated by the accountants who allocate institutional moneys: precisely because we can accurately count every test we report, we attract budget-cutting zealots like flies to honey. But many ignore the value each individual test delivers to patients, providers and the community and the intense expert work behind their accuracy.

We are also poor in human resources, at least in the U.S., as medical technologists, full-time clinical pathologists and other professionals are becoming acutely scarce. Even within wealthy commercial institutions devoted to clinical laboratory testing, the laboratory does not always win the competition for resources. In fact, I have never been to a clinical laboratory on a day or evening when they were not "short-staffed."

But in many countries, including the U.S., and especially in New York State, clinical laboratories are rich in regulatory oversight. As annoying as they sometimes seem, regulations and voluntary accreditations codify and standardize the minimal tenants of clinical laboratory quality. They provide cookbooks of instructions based on the long tradition described above so that laboratorians do not have to start from scratch. Laboratory professionals who take regulatory and accreditation compliance as opportunities are at a great advantage over those who consider them a tiresome burden. We simply need to smartly apply the letter and intent of the requirements to ensure minimal satisfactory operational and test result quality.

However, even though regulatory and accrediting guides contain similar requirements, they do vary in detail and process so that selection and compliance requires the comparison of multiple documents and sources. Dr. Ehrmeyer's modestly-titled book significantly eases the task by placing descriptions of the major regulatory and accreditation norms in one place alongside knowledgeable explanations and sources. It constitutes essential help for laboratories that cannot afford dedicated compliance and quality departments.

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Preface

In the early 1990's, Dr. Ron Laessig and I often found ourselves teaching courses or giving lectures on the newly emerging federal regulations. They were based on the 1988 federal law, the "Clinical Laboratory Improvement Amendments of 1988" (CLIA'88 or CLIA) for short.

In 2003 CLIA was revised and in 2004, CMS published Appendix C of the State Operations Manual, *Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services*, which "interprets" the CLIA'03 regulations for both inspectors and laboratories. And, the CMS-deemed accreditation agencies continually "tweaked" their requirements along the way. This *Poor Man's Guide* is up to date with CLIA regulations along with the latest requirements for CAP, The Joint Commission and COLA.

Various organizations asked us to repeat the presentations because of the significant implications for laboratories and the complexity of the regulations. We initially arranged our lecture notes in a series of booklets that were later pulled together into a single volume for our AACC, ASCP, etc., workshops. Now the information is continually updated.

One objective in compiling these materials was to give the reader an easy to understand, practical means of addressing the complexities of the CLIA regulations as well as the testing requirements from the CMS-deemed accreditation agencies. In the process, the Guide tries to provide practical solutions to the problems facing laboratories such as:

- How to extend reportable range beyond the highest calibrator the "Poor Lab's Way"?
- How "good" is "good enough" – QC tolerances, QC rules and empowerment?
- What's going on with POCT – is everyone getting into the act?
- What about electronic and process controls and the "equivalent" QC options?
- What is Risk Analysis and how will it eventually replace "equivalent" QC?
- Where does QC and quality assurance fit into the new term – Quality Assessment?
- How should the mandated proficiency testing requirements and on-going accuracy assessments be met?

For the record, Dr. Ronald Laessig conceived of the idea for what is now "THE NEW POOR LAB'S GUIDE TO THE REGULATIONS: CLIA, The Joint Commission, CAP & COLA." The name came out of the concept of extending the calibration beyond the highest calibrator using a patient specimen with an appropriately elevated result. Since the technique did not cost much (it's actually free), this approach led to the working title of "Poor Man's Guide." I insisted on making the document politically correct and added "Person's" to the title. For the sake of simplicity, we changed from the NEW POOR MAN'S (PERSON'S) GUIDE to the more concise (and neutral) POOR LAB'S GUIDE.

The earlier editions included the disclaimer that no federal, state or professional inspector, company or professional organization necessarily agreed with what we said or endorsed our approach. It still holds! However, it should be noted that on more than one occasion inspectors have suggested, during the inspections, this Guide as a practical way to understanding the myriad of complexities associated with implementing the regulations.

Finally, special thanks go to a friend, mentor and colleague, Dr. Laessig who died unexpectedly, but peacefully, in his sleep on March 29, 2009. Ron enriched my life immensely and, like me, those he touched miss him tremendously.

Sharon Ehrmeyer, PhD

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What's new in the 2021 Edition

Obviously, the global pandemic has changed virtually everything. However, the regulations are resistant. Instead, we are temporarily in an "Emergency Use Authorization" period, where there are rules about when to suspend the normal rules. Even when the emergency ends (soon, we hope) and normal regulations resume, some significant changes will endure. In particular, the regulations around Laboratory-Developed Tests (LDTs) may be permanently altered by the experience of the pandemic. These are just a few of the significant changes that today's laboratories must confront. Of course, the accreditation organizations, The Joint Commission (TJC), the College of American Pathologists (CAP), and COLA have issued updated requirements. All this and more is covered in the 2021 edition of the *Poor Lab's Guide*.

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Tribute to Ron Laessig

Ron Laessig was Emeritus Director of the Wisconsin State Laboratory of Hygiene and Emeritus Professor of Population Health Sciences (and he liked to say "sometimes clinical chemist") at the University of Wisconsin Medical School. He retired after over 40 years of service to the University and the State of Wisconsin.

The best description of Ron is a "quality builder." And there were many dimensions to his building, from furniture to his home, from clinical chemist to Director of a large testing service, from proficiency testing to total quality management, from in-service training to statewide training seminars, from classroom instruction to national workshops, from committee member to President of NCCLS (now CLSI), from staff building to a new laboratory building that represents the state-of-the-art in environmental and toxicology testing in the US today.

I met Ron in graduate school where we shared a research laboratory. Two memories stand out – coffee that would make your hair stand on end and a work schedule that began at 6:00 am and went until at least 12 midnight, 6 days a week. Having come from ND and grown up working on a farm, I always believed that I had a strong work ethic and could outwork almost everyone. But not Ron! I don't think anyone had the dedication and commitment that he showed as a graduate student and throughout his career. And his accomplishments reflect that willingness to work hard at everything he did!

Our careers started out in a parallel fashion, beginning as clinical chemists in different labs of the University of Wisconsin, but we diverged as Ron acquired more and more management and leadership responsibilities at the State Lab and nationally, while I became more specialized in Quality Control. Yet things also converged at certain periods in time, such as when Ron mentored Sharon Ehrmeyer in her graduate program on External Quality Control, or Proficiency Testing, which paralleled some of my own studies in Internal Quality Control. Ron and Sharon maintained an ongoing collaboration and were spurred on by the laboratory regulatory environment. They co-authored this "Poor Man's Guide" which explained the regulations in a down-to-earth manner to help laboratories adapt to the "CLIA rules." With the advent of the Final CLIA rule in 2003, our interests again converged in opposition to CMS's proposed "equivalent QC" guidelines. And Ron enjoyed it when CMS admitted they "blew it," as Ron and Sharon discussed in an editorial in *Lab Medicine* in October 2005.

Ron always had fun in whatever he was doing! That was part of his formula for life. He liked to tell stories and I can testify that he was very good at it, since I was sometimes on the receiving end of those stories. My worst fear was to have him precede me on a program and have to adjust my presentation on the fly to respond to his statements, such as "…enjoy this because Jim is going to be as dry as cornflakes without milk" or "…Jim will tell you more about that" (and usually mentioned a topic I knew nothing about).

It is a distinct privilege to be able to continue Ron's work in the form of this Poor Lab's Guide. While we have now published five editions since his passing, Ron's spirit still guides this manual. And while I might not agree with everything he and Sharon recommend, I do not dispute the usefulness of having this easy-to-read guide to the labyrinth of regulations, standards, accreditation guidelines that face laboratories in the US.

James O. Westgard, PhD

THE NEW POOR LAB GUIDE TO THE REGULATIONS (CLIA, The Joint Commission, CAP & COLA)

Successful Strategies & Specific Applications of the Regulations

Chapter 1: Regulations – An Overview

REGULATIONS – AN OVERVIEW

Historical View of Laboratory Regulations

The first national requirements regulating laboratories were issued as the Clinical Laboratory Improvement Act of 1967. These were followed closely by the Medicare regulations. The individual states and the College of American Pathologists (CAP) provided the major inspection programs.

Beginning with Dr. Sunderman and his pathology colleagues in 1945, and thanks to the CAP's efforts soon thereafter, proficiency testing (PT) programs by states and professional organizations provided a means of documenting the quality of laboratory performance. The state and federal programs monitoring laboratories incorporated PT into the regulatory process. Today, PT is a cornerstone of CLIA – successful participation is a primary indicator of quality in laboratories performing moderate and highly complex tests. These two complexity levels are now combined in the **nonwaived** category.

The CLIA'67 and Medicare regulations covered only a small percentage of U.S. laboratories (basically large hospitals and reference laboratories). The Clinical Laboratory Improvement Amendments (CLIA), replaced these regulations. On February 28, 1992, the Health Care Financing Administration (HCFA) [now renamed the Centers for Medicare and Medicaid Services (CMS)], working with the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA), published the requirements covering all test sites needing to meet CLIA regulations. Since February 28, 1992, the government has made changes to the regulations published in a series of Federal Registers. The most up to date electronic edition of CLIA can be found at:

https://www.ecfr.gov/cgi-bin/text-idx?SID=1248e3189da5e5f936e55315402bc38b&node=pt42.5.493&rgn=div5

[An index for the updated CLIA waived regulations is shown in Section 1.1.]

CLIA is unique in that it requires *every* testing site examining *"materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease..."* to be regulated. In short, *all* clinical laboratories (testing sites) are subject to the CLIA regulations and testing must be conducted under the appropriate CLIA certificate.

As of March 2021, approximately 267,000 laboratories were registered under CLIA (this includes laboratories in exempt states). CLIA requires all laboratories to have a certificate that identifies the complexity of testing performed. (http//www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/statupda.pdf)

	# of Labs	# of POLs
Total labs registered	266,516	121,125
Total labs registered in non-exempt states	256,747	118,715
Moderate & high complexity (CMS inspected labs)	17,432 (7%)	10,785 (9%)
Accredited Labs (CAP, TJC, COLA, etc.)	15,721 (6%)	4,971 (4%)
Provider-Performed Microscopy (PPM)	30,120 (11%)	23,273(19%)
Waived testing only	193,474 (73%)	78,686(66%)

Section 2.2: The Poor Lab's View of PT

(A Quick Summary of PT Issues)

How it works

Whether you call it Proficiency testing (PT), external quality assurance (EQA) or inter-laboratory comparison, the idea of PT is to evaluate a laboratory's ability to produce the *right* answer. The concept is simple. The PT provider sends several samples from common pools. Each laboratory analyzes these samples just as they would patients and reports its results to the provider. The PT provider evaluates the results according to the specified criteria and then notifies each laboratory as to the quality or correctness of the results. Obviously, right answers indicate good performance. Wrong answers imply poor performance. A preponderance of wrong answers suggests a need for corrective action.

The role of PT

The primary benefit of PT is to provide laboratories with *independent and external* evaluations of their testing capability. The strength of PT lies in the ability to observe simultaneously data from many laboratories. For example, if 30 laboratories analyze the same PT sample and each achieves nearly the same result for a particular analyte, each laboratory would assume that its instrument was measuring the analyte correctly. On the other hand, if 29 of the 30 laboratories fall within the specified PT acceptable range and one laboratory reported a value significantly outside the range, that individual laboratory probably has a problem, analytical or otherwise.

Accuracy and PT

PT, both voluntary and regulatory, is a means for laboratories to establish a method's accuracy. (If an analyte is measured in the laboratory but not included in the CLIA list of regulated analytes, PT still plays a valuable role. In terms of CLIA, this falls under "voluntary" PT and is primarily a QA or Quality Assurance or assessment activity.) A laboratory's method that passes PT is assumed to be accurate. A method that consistently fails PT is questionable. CLIA (CMS) includes, and accrediting organizations incorporate, the concept of PT participation as one means for **accuracy verification** in their QA requirements.

How to use PT information

There are two basic uses of PT: (1) Quality assurance/assessment and (2) meeting regulatory requirements. The QA use of PT is illustrated by the simple comparison of results. Technically, this is referred to as **peer group** comparison. In essence, if a laboratory reports the *same* answer as everyone else, it must be right. Conversely, if a laboratory reports different results outside the acceptable limits, something is probably wrong. While PT programs attempt to create more sophisticated interpretations of the data, the central concept of peer-group comparisons remains.

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Chapter 3. Procedure Manual

Procedure Manuals – An Overview

Concept: At least for every nonwaived test procedure performed by the laboratory or at point of care, there must be a written and available set of instructions. (Standard Operating Procedures or SOPs) describing how to perform the test. The regulatory term for these instructions is "Procedure Manual (PM)."

From "A to Z" or "Alpha to Omega" Laboratories need a Procedure Manual (PM) for *all* laboratory operations and *all* testing performed in the laboratory. These can be organized in one or several PMs to best fit the situation. While the testing process begins with ordering the test, the Procedure Manual (PM) begins with patient preparation and sample acquisition, extends to sample processing and analysis, and concludes with reporting results and archiving results and specimen. These stages of testing are referred to as the **pre-analytic**, **analytic** and **post-analytic** processes in the PM.

The basic principles of Procedure Manuals (all you ever wanted to know)

- Prepare one for every test and have it available for the staff. Electronic copies are acceptable.
- Follow the CLIA mandates (Page 54) for preparation.
- Use the 16 suggestions (pages 56 through 58) in the self-assessment checklist.
- Include the manufacturer directions (package inserts) as part of your lab's PM to the extent possible for the analytical phase of testing (about 90% of the PM); add your lab/organization-specific information (10%) and you are done.
- Keep Current:
    - For CLIA, the current director must approve any new PM and any changes made.
    - Laboratories not inspected by CMS for CLIA compliance must adhere to their specific accrediting agency directives and director approval/review signature requirements.
    - Manufacturer product inserts must match the **lot of product** in current use.
    - The PM must be part of the initial orientation to testing and annual competency assessment for personnel.
- Maintain a copy of each procedure with the dates of initial use and discontinuance.
- Keep Master Secure: The content of the master PM must be controlled. Only authorized persons should be allowed to make changes.

Life's most important secret (about PM's): Write and construct the manual to fit *your* laboratory's circumstances. Write for your typical employee, i.e., a clinical laboratory scientist.

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Chapter 4: Method Verification,

Calibration and Calibration Verification

Overview

A quick introduction

Method Verification of performance specifications is a collective term which refers to a series of exercises that the laboratory undertakes to ensure and document that a method is working properly (at minimum, it meets manufacturer claims)" before placing the method into routine use. The process entails performing experiments and collecting data. The information collected from the studies is used in quality planning to ensure quality patient results.

Calibration is "setting the device/system so that it yields correct results." The processes of setting your watch to the correct time (if you remember watches that needed this activity), or initially adjusting the bathroom scale to zero, are calibrations. Calibration implies that changes or adjustments are or can be made, although many devices are "factory" calibrated and cannot be changed by the lab.

Calibration Verification is the process of checking (no changes or adjustments) the "correctness" of the calibration. In the wristwatch analogy, confirming its time against the "correct" time of an atomic clock is equivalent to calibration verification. With CLIA, this process also defines the reportable range of test results or the range of values (low to high) known to be accurate and precise. In previous years, the reportable range was also called the "analytical measurement range (AMR)."

In the clinical laboratory...

Currently CLIA and accrediting agencies' requirements range from quite rigorous protocols to no verification at all. The supposedly simple, waived tests like "dipsticks" used in the physician's office laboratory require *no* method verification. For FDA-approved nonwaived (moderate and high complexity) methods, laboratories must verify the achievement of manufacturer claims. For FDA-approved tests that are modified and Laboratory-Developed Tests (i.e. home-brewed and not FDA-cleared or approved), laboratories at this time *must establish the performance specifications*. This section walks you through the validation and verification process and identifies what needs to be done according to CLIA and the different accrediting agencies.

Waived tests

CMS (for CLIA), COLA, The Joint Commission and CAP have **NO** specific method verification, calibration or calibration verification requirements for waived testing other than to follow, at a minimum, the manufacturer instructions.

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Chapter 5: Quality Control

Overview of Quality Control (QC)

According to the CLIA Requirements

QC and waived test methods. For laboratories inspected for compliance to CLIA, **waived tests are exempt** from specifically mandated QC requirements, although test sites must meet all manufacturer-specified and/or recommended QC requirements. Test sites performing waived methodologies also are expected to follow the manufacturer directions and apply good laboratory practices. CAP, TJC and COLA have specific QC requirements for all test complexities, including those in the CLIA waived classification (see Chapter 10: Point of Care Testing).

> **Note:** Provider-Performed Microscopy, consisting of specified tests performed by physicians, nurse-practitioners, physician assistants, etc., as part of a patient's medical examination, is a subset of moderate complex (nonwaived) testing. QC is required "whenever possible."

QC and nonwaived test methods. The original CLIA regulations (1992) broke new ground by mandating **daily** QC for all moderate and high complexity tests. The 2003 CLIA regulations combined these two complexity categories into the **nonwaived** category and both now follow the same CLIA quality control requirements identified in §493.1256. CLIA states that QC must monitor the **complete** analytical process including environmental conditions, the test system and the operator. Section §493.1256 also emphasizes that QC needs to monitor the accuracy and precision for *immediate* error detection *and* facilitate detection of errors *over time*.

> **Note:** While not specifically mentioned, CLIA implied that the QC requirements are met through analysis of **external liquid controls**, the"gold" standard. All other QC approaches (not using external, liquid controls) fall under Section §493.1256(d) Laboratories (particularly POCT) wanting to utilize these other QC approaches to meet daily requirements must develop **Individualized Quality Control Plans (IQCPs).** (See Chapter 6.)
>
> **As of April 2016, the definition of acceptable control material changed.** CMS issued a memo stating that acceptable control materials now include on-board (inside the testing device) ampules/cartridges provided they have matrices similar to patient specimens and follow all elements of the analytic process (https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/Survey-and-Cert-Letter-16-20.pdf). As a result, laboratories may decide after evaluating their testing device(s), that an Individualized Quality Control Plan (IQCP) is not necessary.

Follow manufacturer directions. This is the basic premise of CLIA and all other accrediting agencies. If the manufacturer directions have specific QC requirements, the laboratory must follow these at a minimum. When a test is approved by the FDA, it ensures that the manufacturer QC requirements identified in the product labeling are appropriate.

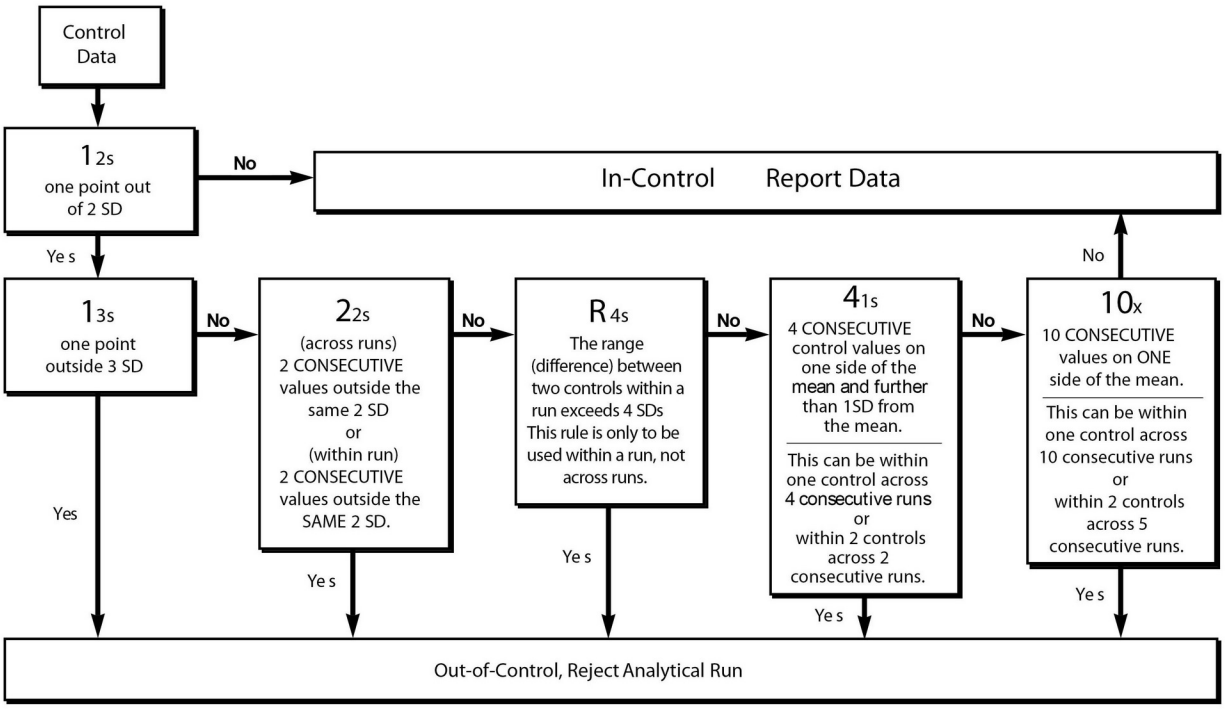

Figure 1: Westgard Multirule Approach, one common combination of rules

"Westgard Rules" – In the 1970s, Dr. James Westgard came up with a unique approach for assessing QC data. This approach is officially known as multirule QC, but more commonly called the "Westgard Rules." Multiple rules are used because different QC rules exhibit different degrees of sensitivity to and specificity for various error situations – bias, drift, imprecision, etc. Together, these rules are more powerful than a single rule. This approach is depicted in Figure 1 and further explained in Figure 2. The classic "Westgard Rules" are evaluated in a two step process – a primary warning or screening rule and a series of secondary rejection rules. Rejection rules are interpreted only after the warning rule is violated. Rejection rules are selected to detect systematic and random errors and a violation of one of these rules assists laboratories in troubleshooting.

In other words, evaluate the QC result with the warning rule and if it is not violated, accept the data and report patient results. If the warning rule is violated, check the rejection rules. If NO rejection rule is violated, the system is "in-control" and patient data can be reported. Violation of any rejection rule is considered an out-of-control situation and requires remedial action. The particular rule violated provides valuable clues to the cause of the out-of-control situation, i.e., imprecision, bias, drift, etc., expediting troubleshooting.

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Chapter 6: Individualized Quality Control Plans (IQCPs)

Individual Quality Control Plan (IQCP)

On January 1st, 2016, the **Individual Quality Control Plan (IQCP)**, a new CMS approach to QC, became official. This *voluntary* option replaced Equivalent Quality Control (EQC) procedures. What this means is that test sites, typically point-of-care sites, need to develop and follow their IQCPs to rely on a device's "built-in" quality assessments for daily QC. While CLIA and all accrediting organizations now allow the IQCP option, some specialties and subspecialties are excluded. Test sites need to follow the specifics of their accrediting organizations.

When an IQCP is not developed, performance must be evaluated *daily* with external, liquid QC as described in Chapter 5.

The Backstory of IQCP

When CLIA began in 1992, sites were mandated to evaluate the performance of all testing daily usually using two levels of external, liquid QC materials. In the mid-1990s, point-of-care (near-patient, bedside) testing arrived. Many of these small, self-contained, handheld instruments included manufacturer, *"built-in"* quality assessments – electronic checks, procedural and/or internal controls, and a variety of internal function checks. While CMS did not necessarily agree with these "alternative" assessment approaches at that time, CMS did not require test sites to perform additional daily external QC. However, CMS did state that "future" CLIA revisions would address the issue.

In 2003, CMS added an equivalent quality option (section §493.1256(d). Few laboratories seemed to understand the meaning of "equivalent quality testing" or the "equivalent quality control" (EQC) concept. It took CMS several years to explain the approach and develop studies for labs to qualify manufacturers' alternative quality assessments. This option was only viable from 2003 through 2015. Finally on January 1, 2016, this option was eliminated and IQCP began.

The Birth of IQCP

EQC was controversial from the beginning. Many laboratory professionals thought the equivalency evaluation studies were unscientific and insufficient robust to truly judge the ability of the various manufacturer alternative assessments to detect test device errors. The former director of CLIA at a CLSI/CMS Forum in 2005 even admitted "We blew it." To address the EQC concerns, CMS encouraged CLSI committees develop new guidelines: one for manufacturers to describe the capabilities of their alternative assessment approaches and one for laboratories to facilitate appropriate QC selection. Unfortunately, the CLSI manufacturer guideline was ultimately abandoned. The second guideline, **EP-23: Laboratory Quality Control Based on Risk Management**, was officially released in October 2011. EP-23 describes how laboratories can use risk management concepts to customize their QC activities based on testing technology and potential risks throughout the entire testing process.

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Chapter 7: Quality (Assurance) Assessment

Where QA (Quality Assurance) becomes QA (Quality Assessment)

Introduction

In the 2003 updates to CLIA and the accompanying *Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services* (Appendix C in the SOM), the term "quality assurance" became "quality assessment," with requirements integrated into the entire testing process – pre-analytical, analytical and post-analytical. CMS also suggested that the progression to Quality Assessment is an evolutionary change, which improves and aligns the regulations with current practices in competent laboratories.

Historically, the concept of Quality Assurance is tied closely to the theories of Total Quality Management, Risk Management and Quality Management Systems, which now permeate laboratory activities worldwide. The Joint Commission, CAP, and COLA formally include these concepts in their laboratory inspection process as well.

Quality Assessment

Curiously, while CMS mandates a ***"Quality Management Systems (QMS) Approach"*** for all phases of clinical laboratory operations, QMS is never, in the extensive SOM or the regulations, actually ***defined***. The closest to a definition is in the introduction (§493.1200) where CMS gives three key components (from its viewpoint) of a quality management systems approach:

Subpart K – Quality Systems for Nonwaived Testing

§493.1200 Introduction

(a) Each laboratory that performs nonwaived testing must establish and maintain written policies and procedures that implement and monitor quality systems for all phases of the total testing process (that is, preanalytic, analytic, and postanalytic) as well as general laboratory systems.

(b) Each of the laboratory's quality systems must include an assessment component that ensures continuous improvement of the laboratory's performance and services through ongoing monitoring that identifies, evaluates and resolves problems.

(c) The various components of the laboratory's quality systems are used to meet the requirements in this part and must be appropriate for the specialties and subspecialties of testing the laboratory performs, services it offers, and clients it serves.

Let's extract some of the key ideas:

a) Develop a quality system **appropriate for your particular laboratory** that covers the pre-analytic, post-analytic and analytic components of testing.

b) On an ongoing basis, select Quality Indicators to check on the system to ensure the integrity of the total testing process.

c) Evaluate data collected from Quality Indicators to identify, evaluate and resolve problems.

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Chapter 8. Personnel

Personnel

Requirements under CLIA, COLA, TJC and CAP

Under CLIA, no specific educational requirements apply to personnel performing only waived testing. These tests may be performed by anyone, although the Centers for Medicare and Medicaid Services (CMS) expect personnel to follow the manufacturer's instructions and apply good laboratory practices. CAP, TJC, COLA and other accrediting agencies have training, competency assessment, and other requirements for waived testing. Check your agency.

For the Provider-Performed Microscopy (PPM) category, testing is done by physicians, dentists, and mid-level practitioners – nurse practitioners, nurse midwives, or physician assistants – when the specimen is collected as part of a physical exam. Individuals performing PPM are expected to follow good laboratory practices in terms of training, competency assessment, QC, QA, and comply with all applicable CLIA regulations. CAP's PPM is for physicians or midlevel practitioners credentialed by the institution's medical staff. CAP includes in this category 13 PPM and waived tests. See CAP's POC checklists for details. When others (non-providers) do this testing, the testing is conducted under a certificate of compliance or accreditation and analysts are expected to follow all the requirements identified for the CLIA-specified test complexity.

Note: PPM testing can be excluded from the laboratory's and/or POCT CAP inspection when a separate CLIA number is obtained for testing.

CMS in the January 24, 2003 CLIA update combined moderate and high complexity testing into the **nonwaived** testing category. However, for the purposes of personnel, the two categories **remain separate**. For a laboratory performing FDA-approved moderate complexity testing, individual(s) need to be identified for 4 positions: (Subpart M, §§493.1403 – .1425)

- Director
- Technical Consultant
- Clinical Consultant
- Testing Personnel

For high complexity testing, 5 positions are needed: (Subpart M, §§493.1441 - .1495)

- Director
- Technical Supervisor
- Clinical Consultant
- General Supervisor
- Testing Personnel

Note: It is important to consider the CLIA implications before modifying any FDA-approved tests (even waived tests). Modified tests become Laboratory-Developed Tests (LDTs), which are high complexity, requiring appropriate personnel and additional validation studies.

Note: Specific qualifications for each position vary according to test complexity. The position titles identified above by CMS do not have to correspond to working titles.

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Chapter 9: Preparing for Inspection

Keep your laboratory inspection ready!

The Clinical Laboratory Improvement Amendments (CLIA) mandate in Subpart Q that all test sites performing nonwaived testing undergo an inspection every two years. CMS or state agencies inspect laboratories for CLIA compliance. Professional accrediting organizations have their own inspectors/surveyors or use practicing laboratory professionals to assess compliance. All inspections are unannounced (but normally conducted within a known timeframe). All have a similar focus. And all inspections need to take place while the test site's CLIA certificate is valid.

Certainly being "inspection ready" makes good sense for many reasons. While readiness can't guarantee a stress-free inspection, it should make the process less of a hassle and, hopefully, the preparation will impress the inspector. First impressions count! Make sure that all of the inspecting agency's requirements are met and the proof (documentation) to show compliance is understandable and readily available for the inspector's review. In preparing, take full advantage of your agency's "get inspection ready/self-assessment" tools so that problems are found and corrected *before* the actual inspection. CMS and all the accrediting organizations want test sites to be ready and to successfully pass inspections.

Laboratories being inspected for CLIA compliance need to make sure to review the testing mandates (the regulations) in the Federal Register and the *Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Service,* which serve as a companion to CLIA. For every CLIA requirement, the *Guidelines* clarify and emphasize what is expected of laboratories. They provide probes for inspectors to use in determining compliance. All CLIA requirements are associated with a "D" or deficiency tag. When a laboratory is found to be noncompliant with a particular requirement, the inspector cites the "D tag" rather than repeating the specific requirement.

Hints: Be Inspection-Ready; Be Ready to Successfully Pass Inspection

- Regulatory compliance is a MUST! Know and comply with your inspecting agency's requirements.
- Be aware of your agency's top deficiencies. Don't get caught in the same traps.
- Be prepared – leadership saves the day. Find problems before inspectors do. Be proactive and look carefully at all the laboratory's practices and procedures; don't assume all is fine. Self-inspection is important, so "do" what surveyors "do" during the inspection process.
- Make sure activities are consistently monitored; have a QA plan and a continuous quality improvement philosophy.
- Look good! Keep food/drink out of lab, have "no food"/"no flammables" signs on refrigerator doors, understand hazardous chemical labels, unclutter and clean workspace, practice safety first.

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Chapter 10. Point of Care Testing

All POCT is Regulated by CLIA

All testing, regardless of where performed, is regulated by CLIA. CLIA regulates *every* testing site examining "materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease..." In short, *all* testing sites are subject, at a minimum, to CLIA's testing regulations.

CLIA Certificates

All POCT must be done under an appropriate CLIA certificate. Information on applying for a CLIA certificate is discussed in Chapter 1 and available on the CLIA website. POCT conducted in most organizations fits into one of two broad scenarios: 1) the central laboratory holds a single CLIA certificate that covers all testing, including POCT, or 2) one or more POCT sites within the institution have separate CLIA certificates. There is no one right way; the choice is organizational and most often depends on who wants to be in charge, cost and administrative concerns.

Each certificate has a fee schedule, which is dependent upon test volume, number of specialties, and test complexity. CLIA regulations divide test methods into three categories: waived, moderate and high complexity. CLIA'03 combined moderate and high complexity into a single, **nonwaived** category with essentially the same testing requirements. Typically, POCT sites perform only *waived and nonwaived* (moderately complex) testing. Under CLIA and the other accrediting agencies, the *waived and nonwaived* categories have DIFFERENT regulatory requirements in terms of personnel, QC, performance verification, proficiency testing, etc. These will be discussed in detail.

Note: While most POCT uses waived methods, if a site develops its own test procedure or chooses to ***modify*** an existing FDA-approved procedure, the test automatically becomes **high complexity**. Modifications include not following the manufacturer's directions and/or performing the test on a sample or patient, e.g., pleural fluid, serum, etc., not specified in the manufacturer's labeling. As a result, the modified method now is subject to *all* of CLIA's more stringent nonwaived (high complexity) personnel and performance specification requirements mandated for modified, FDA-approved tests and/or Laboratory-Developed Tests.

Note: In 2014 the FDA published draft guidelines for glucose meters used to test "critically ill" patients. Most currently-used POCT meters are **not** FDA-approved for this patient population. Consequently, testing "critically ill" patients with these glucose meters is considered a modification ("off-label") use and automatically makes the device *highly complex*, and subject to the high complexity performance and personnel qualifications. Test sites can continue to use these meters, but must develop and follow a policy that defines "critically ill" and how to test these patients with an "approved" method (typically by sending the specimen to the central laboratory), perform validation studies for modified FDA-approved tests, or implement a FDA-approved (for "critically ill" testing) glucose meter. As of 2021, very few methods were officially cleared by the FDA for use with "critically ill" patients.

In other words, ***never*** modify a POCT method unless you are prepared to meet much more demanding regulatory requirements. **Please see the end of this chapter for more advice on how to handle glucose meters with the "critically ill."**

Overview of CLIA Regulations for POCT Testing

When POCT is under the lab's certificate, the lab is responsible for the overall quality of testing and establishing a Total Quality Management (TQM) relationship among all test sites including the central laboratory. While the POCT sites must adhere to the appropriate CLIA regulations, the central laboratory generally is the primary focus of the inspection and is ultimately responsible for POCT oversight.

When the POCT site has its own CLIA certificate, CMS views the site as an independent lab responsible for meeting all regulations. It inspects accordingly.

CLIA and Waived Testing (see Sections 10.1 and 10.2)

In 1992 when the requirements for meeting CLIA were first published in the Federal Register, there were only 8 waived analytes – dipstick/tablet reagent urinalysis (visually read), fecal occult blood, visual urine pregnancy and ovulation tests, non-automated erythrocyte sedimentation rate, blood glucose by monitoring devices cleared by FDA for home use, hemoglobin by copper sulfate (automated), and spun hematocrit. The list keeps expanding and now includes over 100 analytes and 1,000+ methodologies currently tested in more than 180,000 laboratories. This list is updated regularly by the FDA and categories for all test methods are available on the FDA and CMS (CLIA) websites. Section 10.1 has a listing of waived analytes as of January 2021. Reagent/instrument manufacturers also have current information on their products' CLIA classifications.

CLIA has *no* requirements for waived testing and CMS inspectors responsible for determining adherence to CLIA regulations *will not inspect* waived testing unless a specific complaint has been lodged or fraudulent activities are suspected. Section 10.2 compares CLIA's waived testing requirements (none) to those of the CMS-deemed accrediting organizations.

Just because CMS/CLIA has no waived testing requirements does not mean laboratories should assume that waived testing is error free. The 2015 Morbidity and Mortality Weekly Report, "Good Laboratory Practices for Waived Testing Sites" (http://www.cdc.gov/mmwr/pdf/rr/rr5413.pdf), identifies quality and patient safety concerns that can impact patient health, if performed incorrectly. Risks that are still relevant today include:

- Lack of current (and updates) manufacturer instructions
- Failure to follow manufacturer instructions
- Reporting of incorrect results
- Lack of adherence to reagent expiration dates
- Inappropriate reagent storage requirements
- Not performing function or calibration checks
- Lack of documentation – QC, tests performed and results, etc.
- Inadequate training
- Lack of knowledge about good laboratory practices

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Chapter 11. SARS-CoV-2 Testing and Compliance in the Pandemic Era

The COVID-19 Crisis, 2020 and Beyond

It's difficult to remember the world that came before the COVID-19 pandemic. For the US, the 12 months from March 2020 to 2021 were marked by a growing fear that exploded into terror that metastasized into a long, dark despair, and a horrible mourning as the fatalities grew and grew. The SARS-CoV-2 virus presents an almost unending crisis for laboratories, but the challenges inside the lab were often overshadowed by the failures outside the lab.

But even as there appears light at the end of the tunnel, as vaccinations become widespread, this sprint which turned into a marathon which became an ultra-marathon is still deadly strong. It will be years before the globe can be vaccinated. There is an awful chance that variants will continue to emerge, the virus will continue to evolve and inflict more suffering and death, and laboratories everywhere will need to have a robust strategy to deal with supply logistics (shortages), novel methods, and dramatic changes in testing demands (surges, droughts, and everything in between).

Laboratory testing has never been more important to the world and more visible to the global eye. This chapter is meant to help laboratories navigate this new landscape of virus testing.

What we had hoped was going to be a short-term crisis, evolved instead into a long emergency. Temporary regulatory rule-bending will eventually have to be straightened out. Those "Emergency Use Only" (EUA) grants to methods will eventually have to revert back to regular, non-emergency approval and regulation. Learning how to stay compliant, how to assure the quality of these new critical tests, will mark the great challenge of the career of every laboratory professional of this time.

Beyond the regulations, laboratories are grappling with supply shortages (or tests only available on allocation), personnel demands, and financial issues. Most of the early crises (PPE shortages) seem to have been solved in 2021. But reagents, test kits, and even some small things like pipettes or pipette tips for instruments, remain difficult to acquire, and even more difficult to sustain a reliable long-term supply. Many laboratories have resorted to an age-old strategy usually practiced in developing countries – diversification of testing. That is, operating multiple instruments or methods from multiple companies, so that a supply shortage from one company doesn't prevent the laboratory from continuing operation. Of course, this diversification has its own internal cost – more staff required to learn more SOPs, more supplies ordered, more storage needed, more details to manage.

Many laboratories are facing a staffing crisis – on top of the long-building crisis of aging, retiring professionals. While the laboratory has never been more praised by the public, the hours are long, the pressure is high, and the work is unending. Many labs have been working 24-7 in crisis mode for an entire year. This is inevitably causing more retirements, career changes, without any surge in replacements. The public interest in health and medical care has not translated into a boost in medical technologists in training, or in one that will meet the needs of the moment. Laboratories have to be cognizant of the toll of this crisis on their workforce. If only to acknowledge, if not somehow ameliorate this stress.

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