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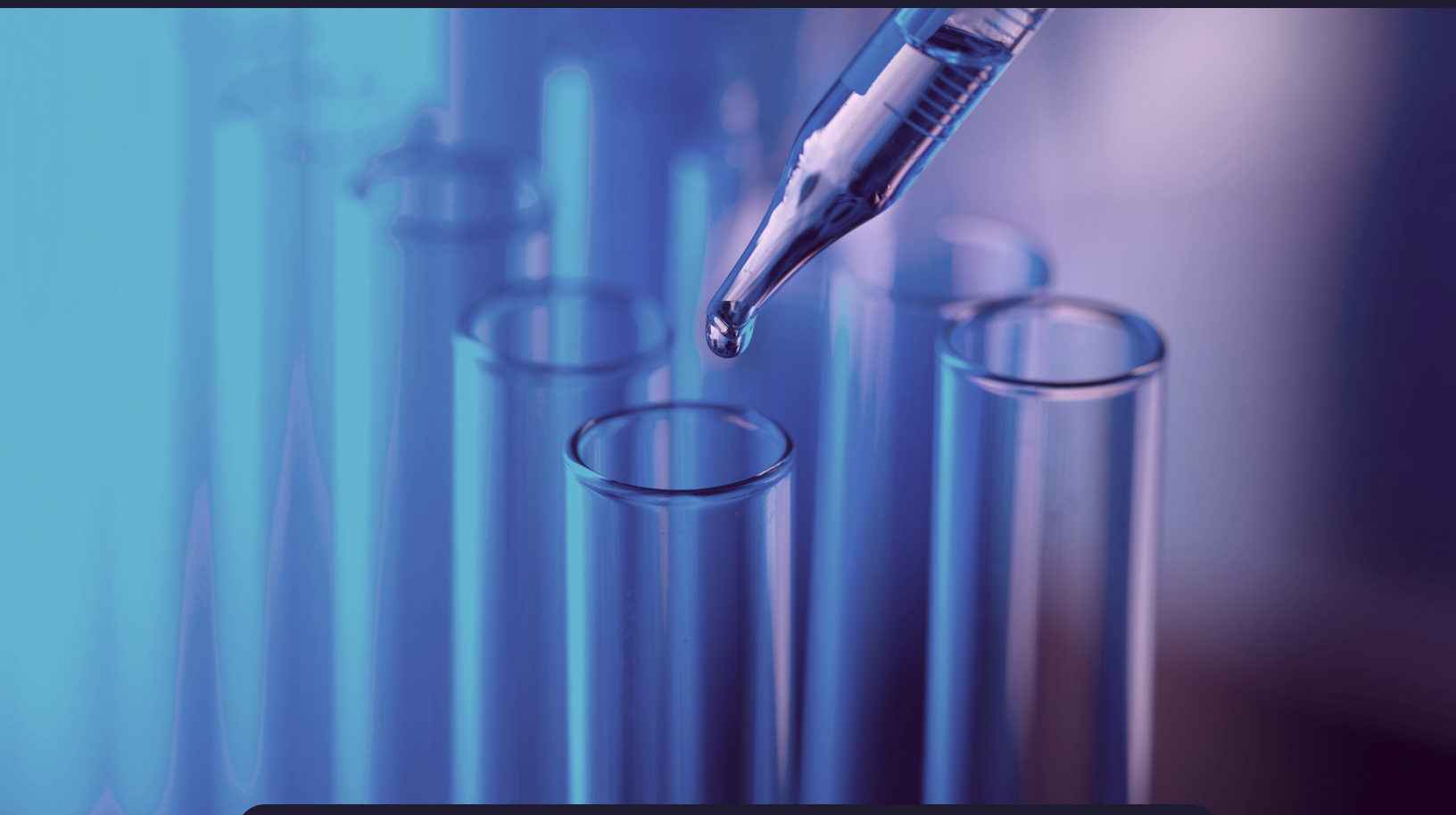
Standard Operating Procedures for CLIA Compliance

The Most Important SOPs and Instructions for Laboratory Staff



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Standard Operating Procedures for CLIA Compliance: The Most Important SOPs and Instructions for Laboratory Staff

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Part 1: What should a molecular diagnostics laboratory SOP include to be CLIA- compliant?

Are you seeking CLIA compliance in your new lab? Tenured former Laboratory Director and Ovation laboratory expert, Pauline Gee, has compiled an extensive outline of exactly what you'll need to get your lab on the road to CLIA certification and laboratory best practices. Not only does achieving CLIA accreditation ensure quality testing standards are achieved, but it also expands the complexity of testing your lab can process. Your commitment to these standards accelerates the creation of new therapies for infectious diseases and rare genetic disorders. Ovation is proud to partner with labs like yours to make more specific, and more accessible treatments for patients in need.

Which labs need CLIA certification?

Before the Clinical Laboratory Improvement Amendments of 1988 or CLIA, testing was limited to independent hospitals and laboratories. Additionally, the complexity of tests and laboratories in which tests were performed was not considered. Now, CLIA has improved the standardization of laboratory testing as well as determining which laboratories have the capacity and ability to process certain test types.

The only laboratories NOT subject to CLIA standards are those that fall under the "waived tests" category. This CLIA-determined category includes simple tests with minimal chance of error or risk. These laboratories are exempt so long as they continue to perform testing in strict compliance with manufacturers' instructions and regulations.

According to CLIA regulations, if your laboratory performs even one applicable test on "materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings", you are subject to CLIA regulation and should aim for accreditation.

How do I create a lab manual or lab standard operating procedure (SOP) to fulfill CLIA compliance?

Before diving into the processes and steps to creating CLIA-compliant lab manuals or SOPs, you need to consider a few things.

- Understand which type of CLIA certification your lab will need
  - Certificate of Waiver: issued to a laboratory to perform only waived tests.
  - Certificate for Provider-Performed Microscopy Procedures (PPMP): issued to a laboratory in which a physician, mid-level practitioner, or dentist performs no tests other than the microscopy procedures. This certificate permits the laboratory to also perform waived tests.
  - Certificate of Registration: issued to a laboratory that enables the entity to conduct moderate or high complexity laboratory testing or both until the entity is determined by a survey to be in compliance with the CLIA regulations.
  - Certificate of Compliance: issued to a laboratory after an inspection that finds the laboratory to be in compliance with all applicable CLIA requirements.
  - Certificate of Accreditation: issued to a laboratory on the basis of the laboratory's accreditation by an accreditation organization approved by CMS.

- Ensure you are up-to-date on local and state regulations as they may include additional steps.
- Ensure that all personnel are qualified by CLIA regulations for the duties they will perform on the outlined SOPs.

Now that you've determined your specific certification type and laboratory staff requirements, you're ready to start building your lab SOPs.

What are the foundational policies and procedures for CLIA compliance?

Begin your SOP documentation by understanding the standards for every person that will interact with a sample. These team members are responsible for upholding CLIA standards, and as such, must have the proper credentials and certifications required to maintain a high level of quality and accuracy in testing.

Compliant with the General Laboratory Systems 42 CFR § 493.1230 and other associated sections.

a. **ERGONOMIC POLICY**: Personnel must have ergonomic work conditions, adjustable height of lab stools, minimization of repetitive motions required, etc.

b. **PERSONNEL DOCUMENTATION**

1. Copies of credentials of testing personnel from Accessioning to QC and release of results to patients include

i. Copy of certifications (Board or otherwise), Degrees, Diplomas, and other professional certifications by ASCP

ii. Copy of transcripts that verify the credentials listed in 1.b.1.i

iii. Awards and other achievements

iv. Job descriptions that succinctly outline authorizations, immediate reporting supervisor and subordinates, and responsibilities

v. Documentation of all Training listed in c below

How do you properly train personnel for CLIA compliance?

Based on the complexity of the testing that your lab intends to perform, your personnel will need specific training, experience, and an understanding of the operational steps involved in processing your specific sample type. To start, your staff should have a lab SOP that meets each of the following standards.

c. **Training of personnel**

1. SOP: Training records for testing protocols
2. SOP: Competency Assessments on the exact protocols used for testing patient specimens
3. SOP: Safety training for handling infectious agents in accordance with CDC protocols
4. SOP: Safety training to meet OSHA requirements including how to handle spills, etc.
5. SOP: Training of HIPAA and IT security

d. SOP: **Biohazardous waste disposal and documentation** thereof, especially pertinent when working with infectious agents

e. SOP: **Environmental monitoring of all temperature and %RH of working spaces and sample storage conditions**

f. SOP: **A single SOP for every instrument used in the laboratory**

g. SOP: **Use of Reagents and the disposal of waste**

How do you ensure the quality and safety standards in your lab meet CLIA standards?

To ensure continued lab sample quality and laboratory efficiency, your team should have the following policies in place.

h. **QUALITY POLICY**: Preventative maintenance and calibration of instrumentation
   1. Installation Quality/Operational Quality
   2. Daily, Weekly, Monthly, Semi-Annually, Annually for each instrument including pipettors
   3. Reconcile with manufacturers' specifications, if operating outside of manufacturer's ranges, validation studies must be performed to extend ranges to show that there is no decrement of performance

i. **QUALITY POLICY**: Instrument calibration of all instruments for equivalency in performance every 6 months with a low, moderate, and high copy number of all channels used for detection

j. **SAFETY POLICY**: Chemical and reagent inventory and chemical hygiene

k. **SAFETY POLICY**:
   1. Weekly safety walkthroughs documented
   2. Emergency drills – evacuation, meeting points, communication policies, etc.
   3. Emergency incidents or any harm to personnel

l**. SECURITY AND ACCESS POLICY: facilities access**
   1. Laboratory facility
   2. Impact by events in the surrounding neighborhood, parking lots, emergency alerts provided by campus and Aurora first responders
   3. Accidents or physical attacks or threats of bodily harm to laboratory personnel
   4. Emergency procedures and documentation easily visible posted
   5. Emergency contact list

PART 2: What does CLIA look for in laboratory validation studies?

According to CLIA guidelines “The Technical Consultant/Technical Supervisor or Laboratory Director are responsible for ensuring the procedure used for verifying the performance specifications is adequate, as well as evaluating the results generated during the verification process.”

It’s vital that your lab compares the performance of the test system in your laboratory with the standards established by CLIA, as well as the manufacturer. This includes the following performance characteristics:

- Accuracy
- Precision
- Reportable range
- Reference intervals/range (normal values) for the laboratory’s patient population

You’ll need to create the following validation studies to prove consistent results and achieve CLIA accreditation. Remember, the more complex your tests are, the more stringent the validation studies required by CLIA become.

2. **VALIDATION STUDIES**:
    a. Optimizing your assay/test
    b. Determining the Limit of Detection (LOD
    c. An appendix that organizes the raw data from all validation studies

As you continue to prepare your laboratory and laboratory staff for meeting CLIA standards and achieving accreditation, you can use the following list to ensure success under the scrutiny of a CDPHE onsite inspection/survey. Please note that this list does not include forms, logs, and work records that result from the execution of these SOPs and Policies but are required. In some cases, no reorganization or revision is needed. The set of SOPs for manufacturing the kit requires little editorial work.

What's the difference between pre-analytic, analytic, and post-analytic phases?

The pre-analytic testing phase occurs first and may include specimen handling issues that occur even before the time the specimen is received by the lab. Because errors with specimen handling and identification can occur in this phase, lab staff must be diligent to avoid allowing errors to funnel into the lab process.

The second phase is the analytic phase. This includes the diagnostic procedures, processes, and products that ultimately provide final results.

Finally, the post-analytic phase is last and leads to the production of a final result, value, or in histology, a diagnostic pathology report.

As you create lab training and procedures, be sure to keep each distinct phase in mind. We've separated them to ensure each piece is given the full, individual attention it needs for your lab to achieve CLIA compliance.

1. **Standard Operating Procedures organized according to CLIA requirements;**
    a. **42 CFR § 493.1240 - 1241; 1242** and other associated sections: **Pre-analytic Systems** require the following organization to parallel the specimen journey:
        1. SOP's: Manufacture of specimen kits/tubes for collection
            i. Reagent formulation and Quality Assurance procedures
            ii. Assembly
            iii. Quality criteria for release to use at specimen collection sites with POC professionals who are minimally trained
        2. SOP: Specimen Collection of Saliva TwoStep:
                i. Without electronic records except for tracking documentation on spreadsheets, e.g., Excel
                ii. With the patient portal of your choice
                iii. With API integration of patient portal, Primary to Ovation LIMS
        3. SOP: Instructions and training of personnel at the point of collection
        4. SOP: Accessioning operations to initiate Chain of Custody and procedures for checking specimen integrity, specimen type, and completeness of patient demographics in test requisitions and for communication of specimen rejection to allow for timely recollection
            i. Without electronic records except for tracking documentation on spreadsheets, e.g., Excel
            ii. With the patient portal of your choice
            iii. With API integration of patient portal, Primary to Ovation LIMS

5. QUALITY POLICY: Only specimens that pass Specimen acceptance should go through to the Analytic processing:
    i. Quality metrics for test requisitions/orders
    ii. Specimen integrity criteria for acceptance and rejection
    iii. Journey of requisitions that do not meet quality metrics
    iv. Journey of specimens that do not meet quality metrics
6. SOP: Instructions for use of the Ovation OvDx LIMS for pre-analytic systems and conditions which require manual contingencies.

b. **42 CFR § 493.1289 – 1251; 1283** and other associated sections; **Analytic Systems** to include the following: TEST MENU DEPENDENT

1. SOP: Batch Creation – selection of accepted specimens for processing based on the performance of a set of controls
    i. 46 or 92 specimen batches
    ii. Positive controls
    iii. Negative or NTC controls
2. SOP: RNA Release – (not really extraction since the RNA is not isolated at any point)
    i. Mechanism of action or principle of the method
3. SOP: Plating Configuration – 48 or 96 specimen format
    i. Methods that allow plating of controls in either plate format
    ii. Processing of partial plates and placement of controls
4. SOP: Pre-PCR preparation protocols and plate setup of master mixes of LAMP PCR reagents
    i. Setting up the reagents for a run
    ii. Distribution into plate
    iii. Adding specimen to master mix, etc.,
5. QUALITY POLICY: - maintenance of Chain of Custody throughout Analytic section
    i. Acceptance or rejection criteria for a batch
    ii. Acceptance or rejection criteria for a single specimen in a batch
    iii. Procedures for re-testing and recollection
    iv. Communications to all stakeholders
6. SOP: Instructions for use of the Ovation LIMS in Batch Creation and Plating Configuration if used
7. SOP: Creation and retention of records for every batch which includes lot numbers, expiration dates for all reagents used and instruments used, and calibration due dates

Part 3: How do I create a CLIA-compliant post-analytical validation plan?

Once you've created procedures for pre-analytical and analytical validation, it's time to conclude your lab SOPs with post-analytical validation. In this final phase of the testing process, your focus should be on assessments and validation.

a. **42 CFR § 493.1299 – 1291** and other associated sections; - **Post-analytic Systems Quality Assessments**

1. SOP: Evaluating the run when completed for quality checks of the run including:
    i. Scoring of controls (manual entry into LIMS?)
    ii. Batch pass/fail – instructions as a consequence of each
    iii. Individual Specimen pass/fail – instructions as a consequence of each
2. SOP: Entering results
    i. Manual into electronic spreadsheets
    ii. Manual upload to the patient portal of your choice
    iii. Manual entry into LIMS or batch upload spreadsheet file of results
3. Verify and sign out results for Lab Director approval
    i. Manual workflow for quality checks and release
    ii. LIMS quality release
4. SOP: CDPHE reporting of SARS-Cov2 results
5. QUALITY POLICY –
    i. Criteria for pass/fail for a batch
    ii. Criteria for pass/fail of a single specimen in a batch
    iii. How to evaluate tests results in accordance with the metric of 'Expected Test Results' for the population that is being tested – addressing changes in patient populations over time
    iv. Communications policies for instances and to whom when warranted

1.**VALIDATION STUDIES**: of Saliva TwoStep

a. Rearrange so that it is consistent with an LDT validation study instead of the FDA EUA
b. The first page should have just a table that summarizes the Sensitivity, Specificity, and LOD for Saliva TwoStep (see the table at the beginning of this document)
c. Should start with Validation Plan, then Validation Design, Protocols used for the Validation, Validation Results, Conclusion with analytic performance characteristics
d. Clinical Evaluation to provide clinical sensitivity and specificity
e. An appendix that organizes the raw data

2. **VALIDATION STUDIES**: **Computer Systems Validation**
    a. Performance of the patient portal and/or Ovation LIMS in your lab's production environment testing the system with edge cases
    b. Disaster recovery and business continuance plan if there is a loss of internet access
    c. Cybersecurity and Privacy policy

3. **QUALITY MANAGEMENT SYSTEMS MANUAL**
    a. Manual that provides policies to address CLSI's 12 quality essentials
    b. Plan for continual improvement
    c. Proficiency or accuracy verification plan
    d. Competency assessment of personnel plan
    e. Business continuance plan for physical disasters

4. **An organizational chart** that delineates responsibilities and authorities
    a. Specify positions with clearly delineated responsibilities and authorities
        1. **Key and mandatory positions to fill the requirements of CLIA personnel**
            i. Laboratory Director
            ii. Technical and General Supervisors
            iii. Safety Officer
            iv. Privacy Officer
            v. Cybersecurity or Information Security Officer
    b. **Policies that hold those responsible accountable**
        1. Policies to identify deficiencies in personnel performance
        2. Policies to retrain personnel, invoke performance improvement plans for testing and quality personnel
        3. Policies to remove incompetent personnel that might impact the quality of patient test results and patient care
        4. Risk matrix of Segregation of Duties to identify and resolve conflict

Once you've completed all of these pieces, you can begin the application for your CLIA certificate.

How do I apply for a CLIA certificate?

The CMS CLIA website or your local State Agency can provide the application (Form CMS-116) that you must complete. Send your completed application to the address of the local State Agency for the State in which your laboratory is located.

Note: If your laboratory is outside of the United States, or is not one of the territories of the United States and seeking CLIA certification, before completing a CMS-116, contact CLIA-IOIntake@cms.hhs.gov

You've reached the end of the necessary lab policies and procedures needed to prepare for CLIA accreditation. After you've implemented the lab procedures and best practices outlined in this eBook, you're ready to move on to determining which tools and platforms will help your lab scale. For the next steps in your lab's growth journey, the Ovation team can help. We provide LIMS and sample data assistance to labs at any stage of growth and we pride ourselves on the security and compliance baked into our LIMS and ORN (Ovation Research Network)

Contact us today at sales@ovation.io.

Where can I find additional information and resources?

CDC: https://www.cdc.gov/CLIA
CMS: https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index
FDA: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCLIA%20/search.cfm

https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/types_of_clia_certificates.pdf

https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/060630BackgrounderrlEG.pdf

https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/howobtaincliacertificate.pdf

https://www.cdc.gov/clia/clia-documents.html

https://www.aafp.org/family-physician/practice-and-career/managing-your-practice/clia/quality-assurance.html