CLIA Waiver from an Industry Perspective

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Disclaimer

The information in this presentation are my views regarding the CLIA waiver requirements taking in both IVD industry and laboratory perspective.

IVD Experience

Began my IVD journey as a recent grad in immunology and medical microbiology from the UW - Madison.

Spent those first few years in an immunology lab performing assays and teaching medical technologists and medical students the finer points of testing specimens and what those patient values meant.

Next phase followed, the R&D tech within the IVD industry years

In the beginning within the PHS Act is found the Clinical Laboratories Improvement Act (CLIA) of 1967

” Was to extend and expand...to broaden and improve the authorization for research and...delivery of health services, to improve the performance of clinical labs...and to authorize activities between the PHS hospitals and community facilities.”

- Creation is a reaction to pathology testing errors
- Scant amount of details were available at that point in December of 1967 from a mere ten page law.

(81 Stat. 536, Public Law 90-174, Sec.5)

Clinical Lab Improvement Amendments (CLIA) of 1988

At this point, definitions, certificate requirements, approval of accreditation bodies, proficiency testing programs, training, testing results, standards, inspections, compliance with requirements standards and much more are necessary to comply with CLIA.

Hospitals and independent labs were now included in the regulations

- Widened coverage for all labs that tested human samples that reported patient results
- Not only are the labs regulated, but so too are the education and training requirements of all lab personnel

Note – if you are not reporting testing results back to a patient, CLIA rules do not apply

(102 Stat. 2903, Public Law 100-578)

Medical Technology (MT) Schools accelerate Closing

- Low pay, attrition, retirement and staff shortages made it difficult for staffing labs
- Pay had not kept up with the demands of the job
- Therefore, the simple automated tests or foolproof manual assays are necessary to fill the void with the lack of employees
- Industry was hiring the MTs

Waived assays are therefore all the more important to conduct patient specimen testing with the limited, skilled personnel

My Perspective was that CLIA…

Is very much about personnel requirements, and if lab personnel are leaving the profession, industry is filling the void by;

- Creating simple tests that require minimal steps
- Developing automated tests that require little manipulation
- The result is that waived tests are the lowest denominator
  - Placed the responsibility to develop waived tests on industry when possible
  - Since not all tests are waived, more is still expected of the testing site staff education and the lab director credentials

Result of MT schools closing…

Placed the responsibility on the IVD industry to make up the loss of lab personnel.

CLIA Waivers were to fill the MT personnel void.

What is a CLIA Waiver?

The FDA categorizes IVDs for CLIA purposes basically by degrees of complexity for site user(s) and low risk to the patients. Some assays are already waived by regulation.

- 42 CFR 493.15(c), cleared or approved for home use **are waived**.
- Therefore the assay complexity is determined by the FDA based on review of the package insert (PI) instructions. The assay will be either moderate or high complexity.
- As a previous regulatory approver of 510(k)s or PMAs, the companies would provide a CLIA Categorization within the FDA submission based on the Scorecard.

CLIA Categorization Criteria

1. Knowledge
2. Training and Experience
3. Reagents and Materials Preparation
4. Characteristics of Operational Steps
5. Calibrations, QC, and Proficiency Testing Materials
6. Test System Troubleshooting and Equipment Maintenance
7. Interpretation and Judgement

Scoring Assays

A score of 1 is at the lowest level and a score of 3 is the highest level per each of the seven criteria. A score of 2 falls at a halfway point.

- Total Scores above 12 are considered “high complexity”
- Total Scores 12 or less are considered as “moderate complexity”

1. Knowledge

- Score 1. Very little scientific and technical knowledge necessary to operate the test. This knowledge could be obtained with on-the-job instruction(s)
- Score 3. Specialized scientific & technical skills is essential to perform and analyze testing

Remember – the more simple the test, the lower the score. Design for simplicity.

2. Training & Experience

- Score 1. Minimal training required for pre-analytic, analytic, and post-analytic phases of the testing process
- Score 3. Specialized training is essential to perform all three steps of the process or substantial experience may be necessary.

NOTE – Did I mention SIMPLE?

3. Reagents and Materials Preparation

- Score 1. The reagents and materials are generally stable and reliable. And reagents/materials are prepackaged and/or premeasured, or require no special handling for precautions or storage.
- Score 3. Reagents & Materials may require special handling for reliability or their preparation may include gravimetric/volumetric measurements.

NOTE – Stress prepackaged, premeasured and stable

4. Characteristics of Operational Steps

- Score 1. The steps (pipetting, timing,..) are either automatically performed or easily controlled
- Score 3. The steps require close monitoring or control, and may require special specimen prep, precise temperatures, or timing, accurate pipetting, or extensive calculations.

NOTE – Fewer, automated steps with the analyzer performing the calculations.

5. Calibration, QC, & Proficiency Testing Materials

- Score 1. Stable calibration materials are readily available. QC & proficiency materials are stable and readily available.
- Score 3. Calibration & QC materials may be labile or not available. Or External proficiency testing materials if available, may be labile. (Basically unstable).

NOTE- Never under estimate the value of providing **stable** reagents.

6. Test System Troubleshooting and Equipment Maintenance

- Score 1. Test system troubleshooting is automatic, or self-correcting, or clearly described or requires minimal judgement, and Equipment maintenance is provided by the manufacturer, is seldom needed, or can be easily performed.
- Score 3. Troubleshooting is not automatic and requires decision making and direct intervention to resolve problems, or Maintenance requires special knowledge, skills and abilities.

NOTE – Ensure as a manufacturer to automate if all possible

7. Interpretation and Judgement

- Score 1. Minimal interpretation & judgement required to perform pre-analytic, analytic, and post-analytic processes, and Resolution of problems requires limited independent interpretation and judgement.
- Score 3. Extensive independent interpretation & judgement are required to perform pre-analytic, analytic, and post-analytic processes, and resolution of problems requires extensive interpretation and judgement

NOTE – Labs with minimal training and skills would have difficulties

IF Your assessment is not Black and White… Default to a Score of 2

A Final **score of 2** will be assigned to a criteria heading when the characteristics for a test are intermediate between the listed descriptions of scores 1 and 2

Allows some “wiggle room” for interpretation of the categories when necessary.

COVID- 19 and Point-of-Care (POC) and Home Self Testing Devices

1. POCT - Provides rapid results at the bedside, doctor's office etc., with no sample transport issues to delay a diagnosis

    CMS allowed a lab/testing site to use its current Certificate of Waiver for COVID-19

2. Home self testing for SARS-CoV-2 were allowed on the market under an Emergency Use Authorization (EUA)

A Decision for Laboratories

CLIA Application for Certification – OMB # 0938-0581 Highlights

- “Lab directors performing non-waived tests must meet specific education, training and experience under subpart M of the CLIA regulations.”
  - Certificate for Provider Microscopy Procedures (PPM)
  - Certificate of Compliance
  - Certificate of Accreditation
- Proof of qualifications must be submitted
- Decide upfront on the the type of lab tests to be performed

[Form CMC-116 (12/21)]

CLIA Personnel Qualifications

1. **Waived**: No Standards

2. **Moderate Complexity** Testing: Minimum requirement is a high school diploma or equivalent and documented training for the testing performed

3. **High Complexity** Testing: Minimum of an Associate degree, including 24 semester hours in science and completion of either:

- An accredited or approved clinical lab training program, or three months lab training in the specialty(ies) in which the individual performs high complexity testing

Labs Using Waived Tests – 493.15

The lab may qualify for a **certificate of waiver under 353 of the PHS Act** if it restricts the tests it performs to one or more of a small set of these nine tests currently

- For example some non-automated tests such as ESR, hemoglobin, fecal occult blood, urinalysis
- Visual urine pregnancy tests
- Blood glucose monitoring tests cleared by the FDA
- Spun microhematocrit

FDA Submissions that are Currently Waived Analytes

The design and development of your assay should contain requirements to arrive at a CLIA Waiver Determination

- Over **140 analytes** as of September 30, 2023 **listed on the FDA website with data supporting a CLIA waiver approval**
- All appear to be included in the FDA submissions as either 510(k)s or PMAs with the CLIA Waiver
- Excellent site to routinely check for additional tests and keep track of the competition

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm

Some Highlights of the CLIA Waiver Determination Decision Summary

FDA review includes the (CW number) along with the biologics or CDRH 510(k)s and/or PMA

- Simple - Minimal operator steps and maintenance, test is automated and requires little or no service
- Insert is written for a grade school level of comprehension
- Risk analysis according to ISO 14971
- Built controls
- Human factors
- Demonstrating Accuracy
- Specimen integrity and assay stability and more

Design Goals should reflect ease of use and intended user(s) performing some of the testing

If your goal is to market a waived test:

- Human factor testing critical,
- Your in-house technicians should reflect the same training as the proposed intended users in performing the in-house testing for the CLIA Waiver, also
- “Clinical testing” of your modified, investigationsal proposed package insert (PI)
  - Create a Likert scale questionnaire and have the internal “waived” staff provide the answers to an assay they have not worked on during development
  - Next, send out the “clinical” version of the PI to 10-20 labs with the Likert procedural questions and review for test comprehension. Determine next steps if changes are made.

Clinical Testing of Package Insert

Once the PI has been sent to sites, tabulate and determine if those results impact the clinical protocols and the whether the labs in the next phase of development.

If the comprehension results are sufficient, clinical trials may commence.

Words of Advice

Again, Design your IVD to fall into the "Waived" Analytes criteria

1. PHS Act 493.15 list of current tests or FDA submissions on the website
2. Include the CLIA Categorizations in your FDA submissions
3. Many examples are out there, therefore review comparable tests found on the FDA submissions site
4. Include CLIA expectations in your product design
5. If not, determine if a modification might be in your best interest

Thank You