CLIA Categorization Processes

Perspectives on In Vitro Diagnostic Devices Regulated by the Office of Blood Research and Review/CBER; Public Workshop

July 15th, 2019

Peter Tobin, Ph.D.

Division of Program Operations and Management

OHT7: Office of In Vitro Diagnostics and Radiological Health (OIR)

Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

The Clinical Laboratory Improvement Amendments of 1988 (CLIA)

- Established quality standards for laboratory testing
  - Tests are categorized into three complexity levels:
    - **Waived**
    - **Moderate**
    - **High**
  - The more complex the testing, the more stringent the requirements for the laboratory

CMS, FDA, and CDC work together to administer CLIA and support laboratory quality

CMS

- Issues laboratory certificates
- Collects user fees
- Conducts inspections and enforces regulatory compliance
- Approves accreditation organizations, approves state exemptions, oversees survey & cert. by state agencies
- Monitors Proficiency Testing (PT) and approves PT programs
- Publishes CLIA rules and regulations

FDA

- Categorizes tests based on complexity
- Reviews requests for Waiver by Application
- Develops rules/guidance for CLIA complexity categorization

CDC

- Develops technical standards and laboratory practice guidelines
- Conducts laboratory quality improvement studies
- Develops and distributes educational resources
- Manages the Clinical Laboratory Improvement Advisory Committee (CLIAC)

If you are new to CLIA Categorizations, start with these final guidances:

- CLIA Categorizations
  - Administrative Procedures for CLIA Categorization
- CLIA Waivers
  - Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices

When are In Vitro Diagnostic (IVD) test systems categorized by FDA?

- Following a cleared/approved/licenced premarket submission:
  - IVDs reviewed by CDRH/OIR
  - IVDs reviewed by CBER
- Or, upon request:
  (optional, but needed for use in non-high complexity labs)
  - IVDs with name and/or distributor changes
  - New test systems (instrument & assay combinations) covered by the Replacement Reagent and Instrument Family Policy
  - IVDs exempt from premarket review
  - IVDs that are legally marketed and for which the sponsor is seeking a waiver categorization

FDA CLIA categorizes IVDs that are CLIA test systems

- *"Test system means the instructions and all of the instrumentation, equipment, reagents, and supplies needed to perform an assay or examination and generate test results."*

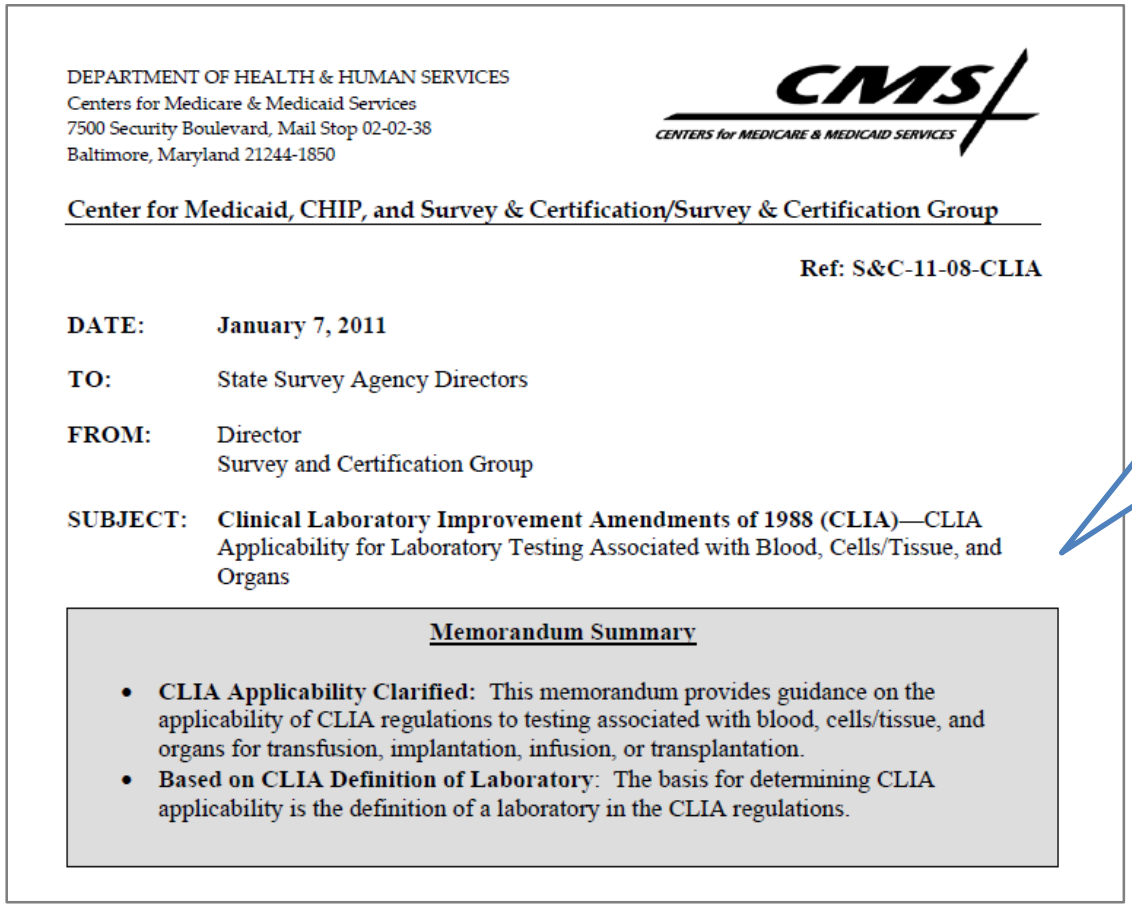
  (42 CFR 493.2)

- Each instrument + assay/analyte combination categorized separately

Uncategorized test systems and test systems used off-label are considered high complexity by default

42 CFR 493.17

CLIA applies to most laboratory testing associated with blood, cells/tissue, and organs



DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard, Mail Stop 02-02-38
Baltimore, Maryland 21244-1850

CMS
CENTERS for MEDICARE & MEDICAID SERVICES

Center for Medicaid, CHIP, and Survey & Certification/Survey & Certification Group

Ref: S&C-11-08-CLIA

DATE: **January 7, 2011**

TO: State Survey Agency Directors

FROM: Director
Survey and Certification Group

SUBJECT: **Clinical Laboratory Improvement Amendments of 1988 (CLIA)**—CLIA Applicability for Laboratory Testing Associated with Blood, Cells/Tissue, and Organs

Memorandum Summary

- **CLIA Applicability Clarified:** This memorandum provides guidance on the applicability of CLIA regulations to testing associated with blood, cells/tissue, and organs for transfusion, implantation, infusion, or transplantation.
- **Based on CLIA Definition of Laboratory**: The basis for determining CLIA applicability is the definition of a laboratory in the CLIA regulations.

See this CMS memo for more information

https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Downloads/SCLetter11_08.pdf

Some IVD devices or components are not categorized

- Samples not taken from the human body (excluded from CLIA)
  - E.g. Breath tests, pulse oximetry, skin reflectance testing
- Separately cleared or approved IVDs that are not complete test systems:
  - Calibration materials & QC materials
  - Sample Collection Kits

CLIA statutory criteria for waiver

CLIA, 42 U.S.C. 263a(d)(3) Examinations and Procedures, as modified by the Food and Drug Administration Modernization Act of 1997 (FDAMA):

"The examinations and procedures [that may be performed by a laboratory with a Certificate of Waiver]… are laboratory examinations and procedures that have been **approved by the Food and Drug Administration for home use** or that, as determined by the Secretary, are simple laboratory examinations and procedures that have an insignificant risk of an erroneous result, including those that −

A) **employ methodologies that are so simple and accurate as to render the likelihood of erroneous results by the user negligible**, or

B) the Secretary has determined pose no unreasonable risk of harm to the patient if performed incorrectly."

Pathways to waived complexity

CLIA Waiver by Regulation

Clearance/Approval of test type listed in 42 CFR 493.15, or

Clearance/Approval for home use (by prescription or Over-the-Counter (OTC))

→ **CLIA Record (CR): Waived**

Stepwise CLIA Waiver by Application

Marketing Submission (PMA, 510(k), De Novo) → **CR: Moderate** → **CLIA Waiver by Application (CW)**

Dual 510(k) and CLIA Waiver by Application (For CDRH 510(k)s)

Pre-Submission → **Combined 510(k) and CW**

CLIA Waiver by Application

Summary of the CLIA Waiver Guidance* Recommendations:

- **Is the test system simple?**
  - Simple test characteristics
  - Quick Reference Guide at 7th grade level
- **Does the test system have an insignificant risk of erroneous result?**
  - Risk Analysis
  - Flex Studies
  - Accuracy Studies

* Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices

Moderate vs. High complexity is determined using the seven categorization criteria:

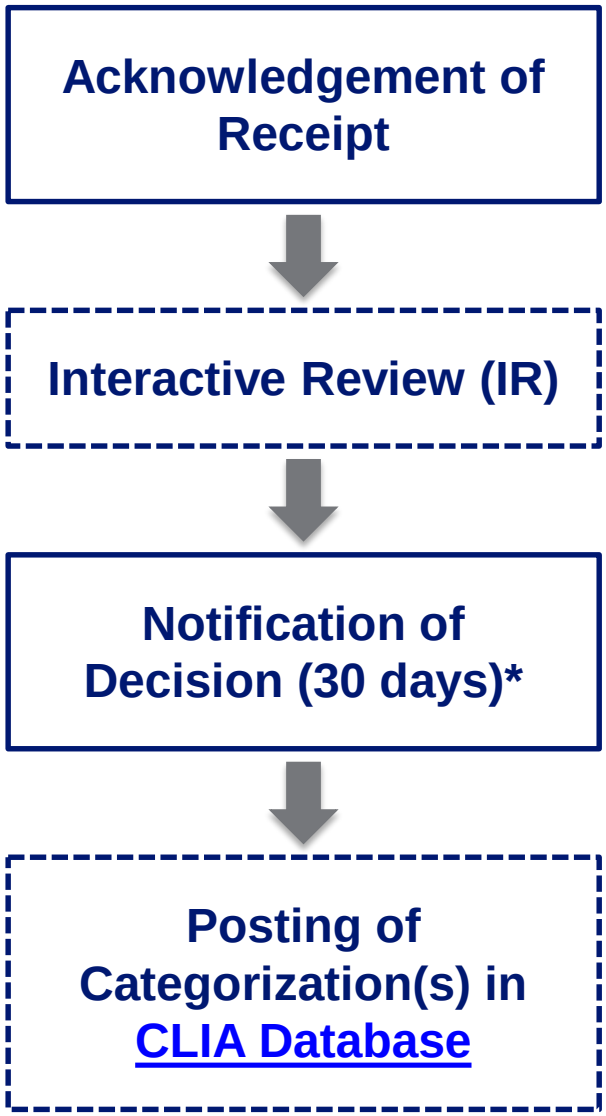
1. Knowledge
2. Training and experience
3. Reagents and materials preparation
4. Characteristics of operational steps
5. Calibration, QC, PT materials
6. Troubleshooting and maintenance
7. Interpretation and judgment

3-point scoring system for each criteria

Total score ≤ 12: moderate complexity

(42 CFR 493.17)

The CLIA Record (CR) process



No User Fee, eCopy recommended but not required

Questions about a CR?

CLIA@fda.hhs.gov

*10 Days for Cleared/Approved CDRH Premarket Submission

CR “Document” Number and marketing application “Parent” Number

Questions?

CLIA@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION