CLIA Categorization Processes

Perspectives on In Vitro Diagnostic Devices Regulated by the Office of Blood Research and Review/CBER; Public Workshop
July 15th, 2019

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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

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<thead>
<tr>
<th>CMS</th>
<th>FDA</th>
<th>CDC</th>
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<tbody>
<tr>
<td>Issues laboratory certificates</td>
<td>Categorizes tests based on complexity</td>
<td>Develops technical standards and laboratory practice guidelines</td>
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<td>Collects user fees</td>
<td>Reviews requests for Waiver by Application</td>
<td>Conducts laboratory quality improvement studies</td>
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<td>Conducts inspections and enforces regulatory compliance</td>
<td>Develops rules/guidance for CLIA complexity categorization</td>
<td>Develops and distributes educational resources</td>
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<td>Approves accreditation organizations, approves state exemptions, oversees survey &amp; cert. by state agencies</td>
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<td>Manages the Clinical Laboratory Improvement Advisory Committee (CLIAC)</td>
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<td>Monitors Proficiency Testing (PT) and approves PT programs</td>
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<td>Publishes CLIA rules and regulations</td>
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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.

See this CMS memo for more information.

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 7\textsuperscript{th} 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

- **Acknowledgement of Receipt**
  - No User Fee, eCopy recommended but not required

- **Interactive Review (IR)**
  - Questions about a CR?
    - CLIA@fda.hhs.gov

- **Notification of Decision (30 days)**
  - *10 Days for Cleared/Approved CDRH Premarket Submission

- **Posting of Categorization(s) in CLIA Database**
  - CR “Document” Number and marketing application “Parent” Number
Questions?

CLIA@fda.hhs.gov