Regulation of POCT and LDTs, an FDA’s perspective

SoGAT- Clinical Diagnostics III
London, January 13, 2011

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Highlights

• Point of Care Testing (POCT)
  – Innovative Methodology - Public Health Impact
  – Clear Current Regulatory Pathway
  – Future Challenges

• Laboratory Developed Tests (LDTs)
  – Innovative Methodology - Public Health Impact
  – Clear Current Challenges
  – Future Regulatory Pathway
Point of Care Testing

- POCT is commonly defined as clinical laboratory testing performed at or near the site where clinical care is delivered, typically by patients or personnel whose primary training is not in the clinical laboratory sciences.

- POTC may also be referred to as decentralized testing, ancillary testing and bedside testing. Based on CLIA criteria, point-of-care testing is generally divided into two categories of complexity (waived and non-waived testing).
POCT Provides Value

• POCT can provide benefits:
  – Rapid TAT
  – Smaller specimen
  – Rapid delivery of results
  – Early diagnosis. Rapid response
    *Improve quality of care while reducing costs*

• Also challenges:
  – Less controlled environment
  – Pre-, post-, and analytic phase errors
  – Limited training (procedures/limitations)
  – Failures in instruments, reagents, software
    *Increased access to test results vs. potential degradation of quality of results*
FDA can Add Value

• Risk-based oversight
  – Basic controls, independent premarket review, postmarket monitoring

• Reasonable assurances:
  – Predictable performance
  – Uniform and appropriately controlled manufacturing
  – Detection/correction of malfunction, failure
Regulatory Pathway for a POC

• POC-OTC:
  – First 510(k), then OTC, review and clearance (all OTC are home use and qualify for waiver)

• POC-Lay user (POL, ED, nursing facilities, clinic):
  – Waived test: First 510(k) review, then CLIA waiver application (e.g., respiratory virus: FluA/B)

• POC-Centralized clinical lab:
  – Non-waived test; 510(k)/PMA review
CLIA Waiver

CLIA Waiver application

Negligible likelihood of erroneous results,
No risk of harm if performed incorrectly

FDA guidance: “Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices”
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm079632.htm
Meeting CLIA Waiver Criteria

• Is the test system simple?

• Does the test system have an insignificant risk of producing an erroneous result?
  – Failure alerts and fail-safe mechanisms
  – “Accuracy” (Traceable Method)

• Adequate labeling
Laboratory Developed Tests

Tests developed by a single lab for use only in that lab

• Originally:
  – Local, non commercial; small volumes
  – Well established test methods
  – Strong clinician/pathologist/patient relationships
  – Used mostly for diagnosis or monitoring
  – Unmet need, rare diseases
  – Specialists with advanced training/expert interpretation

FDA’s enforcement discretion
Newer LDTs

• More LDT tests using unregulated devices
• Some promoted directly to the consumer (DTC)
• Explosion of “LDTs” with:
  – Increasing complexity
  – Dependence on instrumentation function
  – Prefabricated reagents/kits
  – Use on patients while still investigating clinical utility (no informed consent)
  – No established clinical validation
  – No pre- or postmarket control
Result

- Enforcement discretion becomes a loophole
  - Potential risk of newer LDT
  - Business models leverage enforcement discretion for rapid market access, avoid FDA oversight
  - Parallel industry with traditional IVD mfrs
  - Industries that engage the FDA regulated pathway are at a commercial disadvantage
FDA Approach*

• Long-running discussion on need for oversight of LDTs
• Framework to implement oversight of LDTs
  – Public meeting to initiate stakeholder input (July 2010)
  – Meetings with industry groups
  – Appropriate risk stratification
  – Phase-in timelines; review; QS
  – No intention to disrupt testing
• Framework document TBD

* CAUTION-Everything I say here is provisional!The statements made in this presentation do not represent a final decision by FDA. Statements are intended to provide insight, but not guidance
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Possible Elements of Framework

- Risk-based oversight
  - FDA has always regulated on risk
  - Risk stratification
  - Phase-in. Address highest risk first

- Some type of registration and listing
  - Look at ALL LDTs
  - How many, what is tested, what is risk?

- Classification panels
  - Classify tests with no predicates or existing regs
  - Avoid numerous *de novo* actions
Possible LDT Exceptions

• Rare disease LDTs
  – Current HUD, for <4,000 patients tested

• “Traditional” LDTs

• No alternative available
  – Continued enforcement discretion?
  – Minimal phased-in requirements?
Operational Plan

• Develop oversight plan
• Publish guidance
  – General requirements
  – Information on complying
• Continue stakeholder interaction
www.fda.gov/cdrh/oivd

- Guidance
  - Documents/Recommendations
- Regulation
  - Device Requirements
- Databases
  - OTC/510(k)/PMA/CLIA

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Supplementary Information
Clinical Laboratory Improvement Amendments of 1988 (CLIA)

Implemented increased oversight of laboratory testing:

- Certification process
- Accreditation requirements
- Periodic inspections
- Education and training requirements
- Proficiency testing

Focus is on the quality of the lab performing the tests, not on the tests themselves

CLIA regulation of labs and FDA regulation of tests are complementary for diagnostic testing
CLIA

- **Total Number of Laboratories** 241,875
  - *Compliance* (surveyed by CMS) 19,178
  - *Accredited* (by Accred. Orgs) 16,095
  - *Waived* 134,778
  - *Provider Performed Microscopy* 38,509
  - *Exempt* 6,315
    - NY (partial) 3,103
    - WA 3,212

CMS database 10/2009
CLIA Categorization Criteria

• 7 criteria per CMS 42 CFR 493.17
  – Knowledge
  – Training and experience
  – Reagents and materials preparation
  – Characteristics of operational steps
  – Calibration, QC, PT materials
  – Troubleshooting and maintenance
  – Interpretation and judgment

• 7 criteria scored as 1, 2, or 3
  – 1 = minimum
  – 3 = specialized
  – Total scores of 12 or <= moderate complexity
  – 13 or >= high complexity
# Clinical Laboratory Improvement Amendments of 1988 (CLIA)

<table>
<thead>
<tr>
<th></th>
<th>CLIA/CMS</th>
<th>FDA</th>
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<tbody>
<tr>
<td>Registration/Listing</td>
<td>Registration and Certification of Lab</td>
<td>Registration of establishment</td>
</tr>
<tr>
<td></td>
<td>List of tests maintained by CMS</td>
<td>Public list of marketed tests</td>
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<tr>
<td>Analytical validation</td>
<td>Post hoc sampling</td>
<td>Premarket review</td>
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<tr>
<td>Clinical validation</td>
<td>No</td>
<td>Pre/postmarket review</td>
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<tr>
<td>Research Phase</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Quality System</td>
<td>Laboratory Quality System</td>
<td>cGMPs, QS Regulations</td>
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<tr>
<td></td>
<td>Assessed by inspection</td>
<td>Assessed by inspection</td>
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<tr>
<td>Design Controls</td>
<td>Not required. Software not addressed by CLIA</td>
<td>Required for Class II and III tests</td>
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<tr>
<td></td>
<td></td>
<td>and all other devices with software</td>
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<tr>
<td>Report Adverse Events</td>
<td>No requirement; no system</td>
<td>Yes</td>
</tr>
<tr>
<td>Postmarket surveillance</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Recalls</td>
<td>No</td>
<td>Yes</td>
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