
A CLIA Carol – FDA Perspectives

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CLIA Past

- FDA regulatory after thought
 - Good thought grounded in FDA mandate of premarket review of lab tests (IVDs)
 - Role for quality control recommendations
 - Role for complexity determinations
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Quality Control

- Internal FDA committee – a look at conventional recommendations (technology driven)
 - More uncertainty about how to handle unconventional claims – the trade-off between improvements in internal control and use of surrogate (external QC)
 - Suspect – CMS options 1-3
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Complexity Determinations

- Notion that following premarket review, FDA staff would have insight into nuances of test design, performance and labeling
 - Lead to logical complexity decisions
 - FDA with direction from CDC did perform complexity determinations for a brief time
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Budgetary Shortfall

- Categorization assigned to CDC (smooth transition)
 - Quality control deferred
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Complexity Determinations at CDC

- Integrated internal system for high and moderate complexity – work of art by Dr. Collins and Rosemary Bakes-Martin
 - Waiver – not entirely original but in part derived from FDA home use model
 - Codified in Proposed Rule 1995
 - Never finalized but used as operational template for decisions for some ten years
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Pax Romana: FDA Not Active Partner

- Connections established
 - Very good for FDA
 - CMS – eyes and ears to real world
 - CDC – insights into standards, educational programming, global outreach
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CLIA Present

- FDA back on first base
 - Complexity transfer late 1999, early 2000
 - Revitalized interest in QC reviews in 2004
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CLIA Complexity

- Re-visit of the idea of one stop shopping for premarket reviews and classifications
 - HHS decision
 - Complexity decisions assigned to FDA (smooth transition)
 - High/moderate program unchanged
 - Originally continued use of CDC model for waivers (most decisions have until recently been based on that model)
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CLIA Waiver Determinations

- Revisit of waiver criteria (based on input from AdvaMed, vetting through CLIAC)
 - Supplementing accuracy with traceability
 - Broadening methods for establishing accuracy
 - More naturalistic users
 - Stronger hazard analysis
 - Draft Guidance – 2005
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CLIA Waiver Determinations

- New principles included
 - introduction of traceability requirements,
 - stronger hazard analysis (what CDC called stress testing),
 - more contingent clinically based performance standards,
 - use of real world operators (non-lab medical workers rather than lay users) under stress of multi-tasking
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CLIA Waiver Determinations

- Comments received, some rather late in cycle
 - Comments quite helpful
 - Changes made in design and statistical recommendations were simplified
 - Balance between real and artificial samples
 - Controlled challenges of cut-off points
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Controlled Cut-off

- Guidance not binding
 - Encourage protocol reviews through pre-ide
 - Scientific issues addressed through controlled cut-off studies are a critical issue to be addressed
 - Sponsor must understand and control assay at critical cut points
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Document Finalized

<http://www.fda.gov/cdrh/oivd/guidance/1171.pdf>

Alternative QC

- CMS set base lines
 - CMS provided options in surveys manuals based on running external QC over varying periods of time
 - Desire for more flexibility and stronger science
 - FDA approached; CLSI workshop and project initiated (2004)
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Alternative QC

- FDA overestimated regulatory authority
 - FDA underestimated complexity of using risk based analysis to provide lab specific or minimum/maximum surrogate (external) QC recommendations
 - Everyone underestimated the weakness of the science to pedigree alternative QC
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CLSI Projects

- Two aligned projects addressing issue
 - EP 22 directed toward information to be provided by manufacturers to FDA or labs
 - EP 23 directed towards labs or CMS at how to translate risk analysis and design control info into authentic and reasonable frequency recommendations for surrogate (external) QC
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Detailed and Intricate Documents Drafted

- In fact several versions
 - Some with statistical base – derived from non-lab industry uses
 - No supporting scientific models, evidence, literature, or experience *
 - FDA signaled that these documents might be helpful to labs, probably not an activity FDA could undertake
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FDA Believes Use of these Documents May Be Problematic

- FDA believes documents are replete with excellent information
 - Uncertain if practical or useful for decision making by labs, FDA, or CMS
 - Risk of harm if used as marketing tool instead of a tool to identify residual risks
 - Needs simplification
 - Needs vetting
 - Needs piloting
 - Uncertain of future course of action
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CLIA Future

- Powerful collaborative framework to build on between FDA, CMS, and CDC
 - Weekly, sometimes daily consults
 - Improved understanding programs
 - Information and expertise sharing
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Real Need for Integrative Thinking

- Technology is amazing (Field of Dreams)
 - Change in menu of waiver tests
 - Change in quality of all tests
 - Change in need for QC
 - All three agencies juggling to keep up
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Challenge to Labs

- Maintain broad focus on big picture
 - Lab Errors
 - Pre analytical – 41 to 68%
 - Analytical – 4 to 13%
 - Post analytical – 18 to 55%
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Institute of Medicine

- To Err is Human - 1999
 - Lab results impact patient safety (false negative and false positive results)
 - Lab results impact quality of care (correct use of results)
 - Ordering right tests at right time
 - Interpreting results properly
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Pathology 2008

- Pre analytical performance being extended to test selection
 - Post analytical performance being extended to test interpretation
 - Track record for old tests not good
 - One can only imagine how health care providers will deal with new tests
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Rand Report (2004)

- Established measures
 - Established quality criteria
 - Established review mechanisms
 - Concluded quality care was hit or miss – 50% chance
 - Lab use no exception – 30 to 80% chance lab tests will be ordered correctly
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Challenge to Lab Professionals

- Follow CLIA
 - Build on CLIA principles and processes
 - Exploit knowledge of tests into strategies for test use
 - Be more proactive, visible, and involved
 - Chip away at the artificial distance between patient bedside and laboratory
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CLIA Future – transcend regulations

■ Exigency

- ❑ Health care spending now 15% on a trajectory toward 25% *
 - ❑ Principles of evidence based medicine are now well established and moving into the world of laboratory medicine
 - ❑ Need for leadership that builds on CLIA quality as a starting point but does not stop there
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Common Theme – Good Science

- Challenges are great
 - Work will be tough
 - Stakes are high
 - Our specialty depends on the outcome
 - we can become marginalized with lab work a commodity or
 - galvanized with lab work a value added service
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Little Gidding -- Eliot

We shall not cease from exploration
And the end of all our exploring
Will be to arrive where we started
And know the place for the first time.
Through the unknown, unremembered gate
When the last of earth left to discover
Is that which was the beginning.
