



FDA Considerations

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Why are we here?

- New era of molecular diagnostics and personalized medicine
- Broad agreement that diagnostics are the linchpin of personalized care
- Public needs assurances that diagnostics are sound and reliable

FDA Mission

Benefits

Getting safe and effective devices to market as quickly as possible. . .



Risks

While ensuring that current devices on the market remain safe and effective. .

LDTs provide value

- Motivated to create new tests for unmet needs
 - Smaller volume tests
 - Geographic proximity/rapid TAT
 - Specialty tests requiring specific technical expertise/training
 - Rapid response to critical need



FDA adds value

- Risk-based oversight
 - Basic controls, independent premarket review, postmarket monitoring
- Reasonable assurances:
 - Predictable performance
 - Uniform and appropriately controlled manufacture
 - Detection/correction of malfunction, failure

What's happening now

- Re-assessment of bifurcated regulatory strategy
 - LDTs and traditional commercially distributed IVDs
 - Today, logical basis of bifurcation has faded
 - LDTs have evolved to be more like commercial IVDs
 - Unlevel playing field
 - Stifle high-quality innovation?
 - Introduce unreasonable risk?
 - Uncontrolled design/manufacture
 - Unsupported claims
 - Unreported malfunctions, failures

Current issues

- “LDT” status is self-applied
 - No formal regulatory definition of “LDT”
 - Many labs offer tests created by others as LDTs
 - LDT = loophole, in some cases
- Preliminary information often packaged as medically actionable
- Formalized control of design is lacking
 - Direct guide to what and how to validate
- Software is often uncontrolled
 - Software design and validation principles are critical

Considerations

- Assuring that LDTs are safe and effective...
- ...while facilitating innovation
- Avoiding duplication with CLIA
- Utilizing CLIA or deemed inspectors
- Avoiding disruption of testing

Risk-based Classification

- How would an undetected false result affect a patient?
 - Serious injury or death, difficult to detect false result, high public health risk
 - Incorrect and harmful clinical management, invasive procedure, failure to follow up
 - Companion diagnostics, cancer diagnosis, tests that direct or very strongly influence patient management of serious disease, tests for serious/fatal communicable diseases
 - Non-serious injury, relatively easy to detect false result, adjunctive test
 - Delayed test results, uncertain clinical management, continued testing, psychosocial issues
 - Tests where phenotype is already known, tests where multiple findings used to direct clinical management, tests to monitor already-detected disease
 - Little potential for injury, easy to detect false result, highly adjunctive test
 - Unlikely to directly affect clinical management, knowledge only without change in management, evaluation without directed management
 - Tests that identify one among many defining characteristics of a tissue or cell, tests that have little clinical impact, certain instruments and equipment

Our approach

- FDA regulates tests, not labs
- FDA authority can address oversight, to the benefit of labs and consumers
- LDT problems not applicable across the board, but FDA oversight brings value as a uniform system
- Risk-based framework appropriate for all manufacturers adds value

Elements that may be helpful

- Resource management: revisit of currently regulated tests to assess potential for downclassification
- Risk-based phase in over time to allow for predictability, planning
- List of who offers what
 - Coordinate with NIH's Genetic Test Registry?
 - Expanded registration and listing?
- Implement modifications to current oversight structure where appropriate

How will FDA manage this?

- Plan for some re-assessment across the board
 - Goal to focus on risk, will adjust oversight if needed
- We will use and build our resources according to need
 - Phase-in?
 - Downclassification?
 - Pilots for 3rd party accreditation?
 - Review
 - Inspection

How will stakeholders get information?

- Understood that lots of outreach and education may be needed
 - Guidance
 - IVD Forum
 - PreIDE program
 - Informational meetings
 - Advisory panels
 - Direct questions to FDA staff

Framework

- To be determined—questions to be addressed
 - Who is offering what
 - Appropriate risk stratification
 - Advisory panels?
 - Which tests/labs (if any) can remain under enforcement discretion
 - Phase-in timelines: review, QS
 - Costs to labs
 - Inspection needs
 - No intention to disrupt testing