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