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 diease, 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