Oversight of Laboratory Developed Tests

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Overview

- **Background**
  - IVD regulation
  - Need for greater oversight of LDTs
- **Initial public feedback in 2010**
  - Oversight framework suggestions
- **FDA's current proposal**
  - Continued enforcement discretion in some areas
  - Timeframe for enforcement in other areas
- **Next Steps**
  - Discussion of FDA's current proposal

1976 – Medical Device Amendments

- Provided definition of ‘medical device’
- Defined the standard to be used
- Provided Regulatory Paradigm
- Risk-Based regulation of medical devices

Risk-Based Classification

- **Class I: common, low risk devices**
  - Most exempt from premarket submission
  - General controls
- **Class II: more complex, higher risk**
  - Premarket Notification [510(k)]
  - Substantial equivalence, special controls
- **Class III: most complex, highest risk**
  - Premarket Application [PMA]
  - Safety, effectiveness

Laboratory Developed Tests Circa 1976

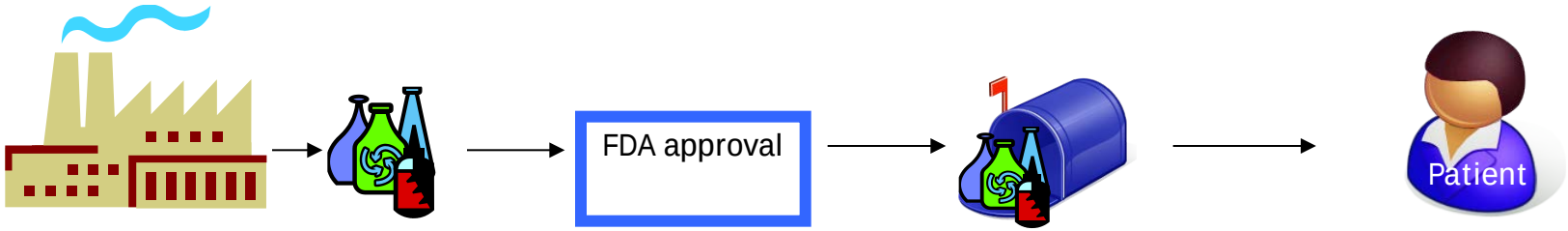
- Local
- Mostly non-commercial
- Test methods generally well established, accessible
- Clinician/Pathologist/Patient relationships
- Simple software – calculations

Enforcement Discretion

- Not unique to LDTs
- Does not change the fact that the law applies
- Many different reasons for this practice (risk, history, timing, resources, etc.)
- Practices like this do occur, but may change (often because of changes in risk profile of the products)
- Policy often not written or well defined

Current Regulatory Reality

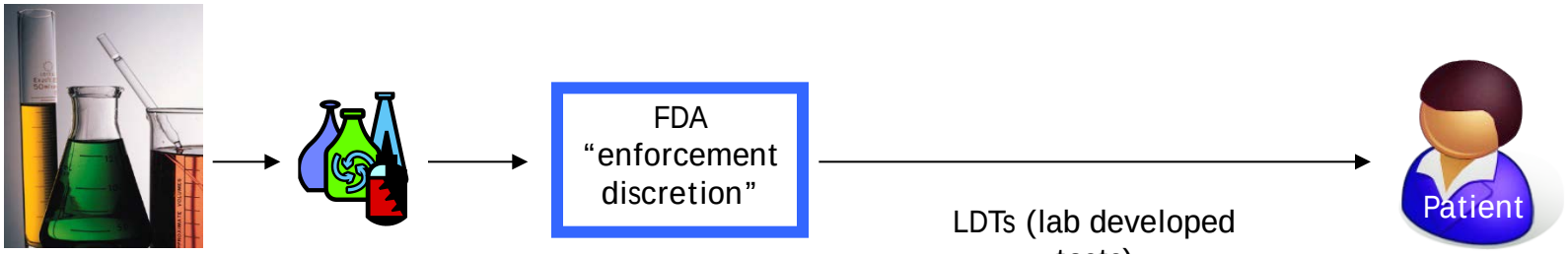
1) Commercially Distributed Test Pathway:



"test kit" manufactured for distribution to multiple labs

"Test kits" distributed to patients, hospital, or clinical lab

2) Lab Developed Test (LDT) Pathway:



Test designed, manufactured, and used in a single lab

LDTs (lab developed tests) enter the market without review

Need for Oversight

- LDTs, while offering innovations, have proliferated, essentially unregulated as devices, to a point where serious public health issues could easily arise
- CLIA "not enough" for manufacturers of LDTs
- No record of which labs offer which LDTs
- No way to distinguish a "good" lab from a "bad" one

Common Regulatory Themes

- National Human Genome Research Institute (Department of Energy & National Institutes of Health;1997)
- Secretary's Advisory Committee on Genetic Testing (2000)
- Secretary's Advisory Committee on Genetics, Health, and Society (2008)
- Institute of Medicine (2012)

Two Regulatory Paths

	CLIA	FDA
Research Phase	No	Yes
Analytical validation	Post hoc sampling	Yes
Clinical validation	No	Yes
Report Adverse Events	No requirement; no system	Yes
Transparent Results	No public information	Published review summary

Quality Systems

- **CLIA not sufficient**
  - CAP
  - NYSDH
  - AABB
  - ISO15189
  - etc…

Initial Public Feedback (2010)

FDA held a public meeting *PRIOR* to developing the proposed regulatory oversight framework

Initial Public Feedback (2010)

- **Oversight Framework Suggestions**
  - Process should allow for stakeholder input and leverage external experts
  - Should use risk-based, phased-in strategy
  - Should provide reasonable transition period
  - Should provide clear definition of LDTs
  - Registry of all tests
    - Partnerships with other agencies
  - Process to address emerging diseases/emergency situations

Initial Public Feedback (2010)

- **Oversight Framework Suggestions (continued)**
  - Less oversight for certain categories of tests
    - Rare Diseases
    - No FDA approved/cleared alternative
    - Hospital based tests
    - Tests with extensive peer review
    - Tests performed in accredited lab or already approved by NY state
  - Post-Market Surveillance needed to protect public health
  - Significant Education/Outreach needed

Draft Framework

- **Risk-based (highest to lowest)**
- **Phased-in (9 years)**
- **Carve outs:**
  - Rare Dx, unmet needs, traditional LDTs, etc
- **Notification and MDR reporting**
- **Classification panels for new intended uses**

What is Next

- **Had a Public Meeting**
- **Received more that 300 comments**
  - We plan to address all comments
- **Have invited all accreditors and CMS to meet**
- **Working on next steps**

FDA vs CLIA

- **FDA regulates articles, i.e., test systems, reagents, instruments, software, etc.**
- **CLIA regulates laboratory operations**
- **Non-conflicting regulations because they are for different purposes**
  - Some similarities that can be leveraged

FDA/CMS Task Force

- Senior leadership and SMEs from both Agencies
- Effort to identify similarities in regulations
- Streamline requirements for labs regulated by both CMS and FDA
- Public outreach

DTWG (Hall) Proposal

- Recognizes that laboratory developed tests can be regulated similarly to distributed tests
- Recognizes that laboratories perform some functions that distributed manufacturers do not
- Recognizes the need for all test to be clinically valid
- Recognizes that regulation can be risk-based

Goal: Optimal Public Health

- **Additional oversight:**
  - Improve patient healthcare
  - Improve public health
  - Allow for timely, good innovation

Questions?

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