Facilitating Development and Utilization of Genome-Based Diagnostic Technologies: A Workshop

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Agenda

- Barriers to successful test development
- Potential Solutions
- Obstacles
- Overcoming Obstacles

1976 – Medical Device Amendments

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

Standard

Safety

- There is reasonable assurance … that the probable benefits … outweigh any probable risks. [21CFR860.7(d)(1)]

Effectiveness

- There is reasonable assurance that … the use of the device … will provide clinically significant results. [21CFR860.7(e)(1)]

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*

Program Implementation

- Premarket: Industry provides the evidence, FDA reviews and clears or approves
- Postmarket: Industry's responsibility, FDA monitors and provides guidance
- Compliance: FDA monitors companies to make sure they comply with the law and and regulations

FDA Review

- Technology a factor but not determinative
- Intended use and indications for use
- Different administrative packages
- Same core – science

Elements of Review

- Analytical validity
  - Correctly detects analyte
- Clinical validity
  - Correctly identifies disease/condition
- Labeling

Laboratory Developed Tests 1976

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

LDT Then (continue)

- Tests usually for diagnosis or monitoring
- Often for rare diseases, unmet needs
- Performed by specialists with advanced training and require expert interpretation (karyotype, IHC)
- Small test volumes

LDTs Now

- Many are the same
- Still often for unmet needs, rare diseases
- Still need for expert interpretation (IHC, cytogenetics, culture, etc.)

But Also Much More

- Volume and types of LDTs has grown significantly
- Often a mechanism for market entry of novel tests
- Higher proportion in commercial labs and biotechnology companies
- Often no clinician/pathologist/patient relationship
- Tests developed for broad, commercial use

And …

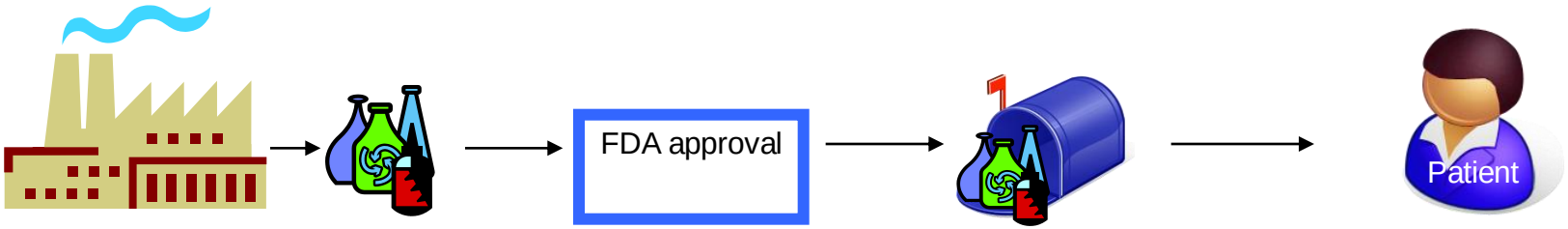
- Often require complex software
- Many incorporate automated interpretation
- Tests increasingly empirical, non-transparent
- Rely on complex statistical methods
- Clinical validity not well understood
- More tests for predicting drug response, risk of disease
- Novel tests often developed by companies and “licensed” to a lab

And More

- Tests broadly advertised
- Aggressively marketed to clinicians
- DTC advertising
- Internet sales, overnight shipping
- Nationwide, international reach

Current Regulatory Reality

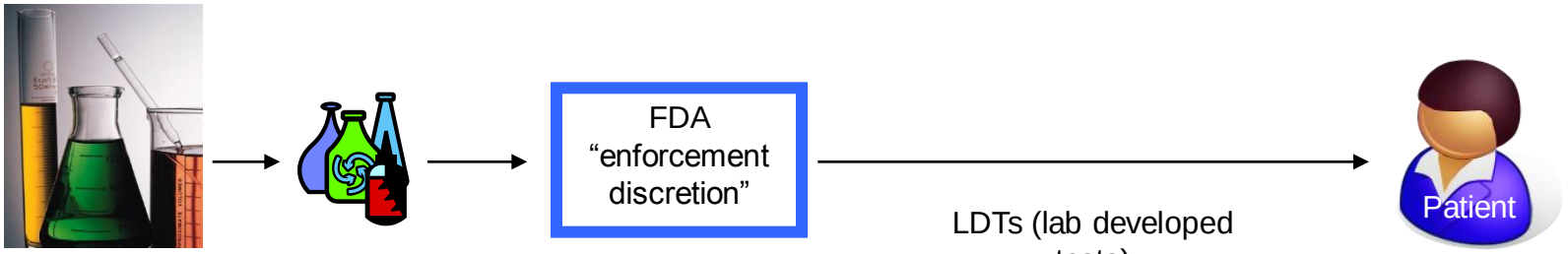
1) Commercially Distributed Test Pathway:



"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

IVDs – 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

Barriers to Successful Test Development

- Return on investment
- Regulatory Clarity
- Evidence based Medicine
- Standards
- Integration of knowledge in to Medical Practice

Potential Solutions

- No easy answers
- Collaboration between CMS and FDA?
- Collaboration with FDA?
- Collaboration with standards developing bodies?
- Piece meal approaches?

Obstacles

- Chaotic health care system
- Financial interests in status-quo
- Political interests
- Financial constraints

Overcoming Obstacles

- It is about Patients!
- All sectors need to work together to pose solutions
- Working in the political arena is bound to be contra productive