FDA Regulation of Testing

Direct-to-Consumer Genetic Testing
A Cross-Academies Workshop
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FDA Regulation

Center for Food Safety and Applied Nutrition

Office of Regulatory Affairs

Center for Devices and Radiological Health

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Center for Biologic Evaluation and Research

Center for Drug Evaluation and Research

Center for Veterinary Medicine

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FDA Regulation

- Federal Food, Drug, and Cosmetic Act of 1938 (The Act)
- Medical Device Amendments of May 28, 1976 – classified all existing IVDs
  - Good manufacturing practices
  - Reporting of adverse events
  - Risk based regulation by intended use

In Vitro Diagnostic Devices

"Reagents instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae in man. … for use in the collection, preparation, and examination of specimens from the human body." [21 CFR 809.3]

- "Diagnosis" = diagnosis, screening, prevention, risk assessment, etc…
- Used in clinical laboratories
- Other settings (e.g., Point-of-Care/Over-the-Counter)

Diagnostic Testing

FDA is concerned that molecular diagnostic tests be reliable and that patients and health care professionals understand both the

Value and the Limitations

of such testing

FDA Premarket Review

All IVDs must establish adequate:

Analytical performance

- How accurately does the test measure the analyte?
- How reliably?

Clinical performance

- How reliably does the test measure the clinical condition?

Labeling (21 CFR 809.10)

- Adequate instructions for use
- Intended use, directions for use, warnings, limitations, interpretation of results, performance summary

Clinical Performance

- Test developers must establish the clinical validity of their tests

- Challenges:
  - Biomarker associations should be discovered and validated in separate, independent data sets

    (i.e., GWAS is a great **exploratory** method, findings should be validated)
  - Validation testing should be done in the intended use population
  - The right study can be challenging

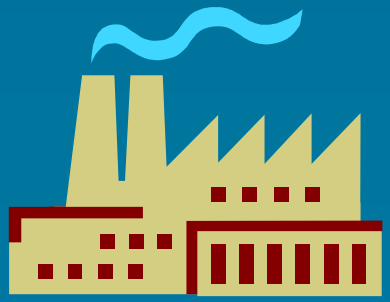
FDA Premarket Review

IVDs for consumer use (OTC) have additional requirements:

- Data submitted to demonstrate that the tests are accurate in the hands of lay users (including sample collection)
- Studies are performed to evaluate how well lay users can understand the instructions without prompting, perform a self-test (or collect a sample), and obtain an accurate result
- **Lay users' ability to understand the results of the test are also evaluated**
- Human factors are also considered in the review, where applicable

IVDs – Unequal Regulation

CLIA

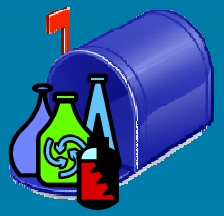


"test kit" manufacturer

Longstanding FDA policy results in a non-level playing field for IVD manufacturers.

Distributed "Test kits" must undergo FDA review prior to marketing while lab developed tests enter the market without review

lab



FDA

FDA "enforcement discretion"

Laboratory Developed Tests

Lab Developed Tests:

Tests *developed* (i.e., designed, manufactured, assembled, and validated) by a single lab for use only in that lab

- Different regulatory threshold than FDA reviewed tests – non-parity
  - No premarket review
  - Used on patients while still investigating clinical utility (no informed consent)
  - No requirement for clinical validity
- Varying quality in test development and validation
- No post-market reporting/recall requirements
- Industries that engage the FDA regulated pathway are at a commercial disadvantage
- Lack of regulatory clarity adds business risk/uncertainty

Laboratory Developed Tests

- FDA has authority over medical devices
- An LDT is a medical device
- If a laboratory makes an LDT, then they are a medical device manufacturer
- FDA has applied enforcement discretion over most LDTs
- Just because you have a CLIA certificate, doesn’t mean that you are not a medical device manufacturer and everything you do is under FDA enforcement discretion

Laboratory Developed Tests

- This policy has not changed, but it could.
- In the meantime, FDA will take actions if patients are being put at risk
- Significant public health and policy decisions need to be made, but
  - Should be done in an open transparent manner with stakeholder input
  - Should not be a surprise

Laboratory Developed Tests

- LDTs do not include:
  - Distribution of tests between sites within an organization

    (e.g., within a corporate entity or coalition of labs)
  - Contract manufactured tests
  - Custom manufactured devices
  - Tests obtained through agreements, purchase, from others
  - Non-laboratory services (software analysis, web tools, etc.)

Laboratory Developed Tests

Many groups publicly discussing the regulation of LDTs:

- Kennedy bill (2007)
- Genentech Petition
- Hopkins Genetics and Public Policy Center proposal
- HHS SACGHS Report on Oversight of Genetic Testing
- AdvaMed "Risk-based Regulation" proposal
- American Clinical Laboratory Association (ACLA)
- Coalition for 21st Century Medicine
- etc…

Should tests be regulated by risk rather than by business model?

Challenges

- What is the proper level of federal oversight for LDTs?
- What level of clinical evidence for new tests would assure FDA approval, adoption by clinicians, and **payor reimbursement**?
- We are able to test, but should we test?
- How to balance innovation and patient protection?

Summary: Bad News

- Biological and clinical nuances
- Financial uncertainties
- Regulatory uncertainties

Summary: Good News

- Broad menu of regulatory tools
  - Pre-IDE
  - Expedited reviews
  - De novo classification
- Mandate to be least burdensome
- New resources – MDUFA

- **New Personalized Medicine Staff**
  - Director = Dr. Elizabeth Mansfield
  - 20 new staff for IVD group in 2009

Thank you!

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