Current Policy Topics in OIVD

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Overview

- 510(k) reviews
- Laboratory developed tests
  - IVDMIA
  - Other
- RUO/IUO labeling
- Personalized Medicine

510(k)

- Opinions from many directions on the adequacy of the 510(k) process for assuring safety and effectiveness
- IOM review, FDA internal review, public workshops held
  - No specific recommendations yet
  - Stay tuned

Laboratory Developed Tests

- Bifurcation in oversight of IVD devices
  - FDA + CLIA
  - CLIA only
- LDTs (CLIA only pathway)
  - No record of who is offering what
  - No premarket review
  - No requirement for clinical validation
  - No postmarket requirements
  - Taking on higher risk, more complex tests

LDTs: the problem

- Can be used as a loophole
  - Bad, unvalidated, or fraudulent tests on market with minimal control
  - High risk tests with unknown performance in use
- Creates an unlevel playing field
  - Traditional Dx manufacturers have higher hurdle than LDT manufacturers

Enforcement Discretion

- LDTs: Currently,
  - Self-defined by labs
  - No way to know what's out there
  - No regulatory definition of LDT
  - More-or-less blanket approach by FDA

Time for Change?
Some questions and possible answers

- Is blanket enforcement discretion appropriate?
  - risk-based approach
- Is self-definition appropriate?
  - define the limits of what is/not an LDT
- Should we know what's being offered?
  - registry of tests
- Is the public health being served?
  - patient and healthcare provider notice of test status

Examples: Benefits/harms

- Possible benefits
  - Tests available for small populations
  - Rapid test development and deployment
  - May save system $$$
- Possible harms
  - Patients, healthcare providers relying on useless tests
  - Labs think they validate better than they really do
  - Puts traditional mfrs with controlled design, product development, manufacture processes at disadvantage = they don't play

Benefits/harms explored

- Emergency use authorization for H1N1 outbreak
  - Devices for diagnosing 2009 H1N1 needed urgently
  - Device regulatory bar lowered
  - EUA not required to offer test
  - Multiple applicants from traditional and LDT manufacturing sectors

2009 H1N1

- FDA makes EUA template available with minimum info/data requirements
  - "fill in the blanks" approach
  - Low data burden
- Result
  - Several devices deemed appropriate
  - Labs—more than one had improperly designed test (already being offered), not enough validation
  - Mfrs—more than one "not ready for prime time"

IVDMIA

- FDA's effort to ensure certain types of difficult-to-validate tests came under regulatory scrutiny
  - Easy to overfit data
  - Easy to introduce bias
  - Easy to choose incorrect validation strategy
  - Easy to get to market if an LDT

Problems We've Seen

- Inappropriate sample size
- Overfit data
- Bias, bias, bias
- Tests not independently validated
- Lack of control mechanisms
  - Reagents
  - Processes
  - Samples

Guidance

- Still on the table
- No prediction for publication date

RUO/IUO Labeling

- Manufacturers inappropriately marketing devices marked:
  - For research use only. Not for use in diagnostic procedures (RUO)
  - For investigational use only. The performance characteristics of this product have not been established (IUO)

Legitimate Uses of RUO/IUO

- RUO
  - Research to determine characteristics of devices to be developed
  - Basic scientific research
- IUO
  - Controlled investigations to gather performance data on products
    - Informed consent, IRB

RUO Inappropriate Marketing

- Labeling
  - Includes intended use
    - See 21 CFR 801.4 on intent
  - Includes clinical information
  - Includes clinical interpretation guidelines
  - References diagnostic use
- Sold for clinical use

IUO Inappropriate Marketing

- Sold for clinical use outside investigation
- “investigation” has no protocol, no ending criteria

Personalized Medicine

- How will OIVD handle novel technologies
- What is different about codevelopment
- What are the regulatory requirements for companion diagnostics
- Other policy areas around emerging diagnostic issues

Novel Technologies

- aCGH
- Whole genome sequencing
- Proteomics
- Highly multiplexed diagnostics

Codevelopment

- What are the issues for diagnostics required for appropriate use of therapies
- How will codevelopment submissions be handled by FDA
- Timing/coordination issues

Companion Diagnostics

- Definition
- Regulatory requirements
- Labeling

Other Issues

- RUO to IVD transition for instrumentation, reagents
- Intercenter coordination for codeveloped products
- Quality systems for laboratories

Thanks!

- Questions?
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