FDA Updates

Clinical Laboratory Improvement Advisory Committee Meeting
September 20, 2006

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Agenda

- Critical Path Initiatives
- Patient Safety Initiatives
- CLIA Activities Update
- New FDA Guidances
  - →Leftover Samples
  - →Analyte Specific Reagents Q &A
  - →Multivariate Index Assays

Critical Path

- White Paper – 2004
- Infrastructure developed
- Leveraging and academic partners
- Information available at http://www.fda.gov/oc/initiatives/criticalpath/

Critical Path – IVD Highlights

- Juvenile Diabetes Research Foundation (JDRF) - collaborative work on research proposals to answer regulatory and scientific issues
- Plans for a Workshop on Rapid Infectious Disease Diagnostics – November 2006
- Pilot projects being considered on Warfarin
- FDA interested in additional partners/projects
- Special interest in co-development of drugs and diagnostics

Patient Safety Initiatives

Adverse Event Reporting:

- Discussed as important issue at past CLIAC meeting - especially related to monitoring waived test activities
- OIVD trying to clarify user facility requirements
- OIVD learning from MDR data base – passive reporting

Patient Safety Initiatives

LabNet

- Derivative from active surveillance program under MedSun
- Pilot labs selected - Training under way

Goals:

- Provide more active surveillance of IVDs that are on the market than currently available to FDA
- Collaborate on mechanisms needed for monitoring devices used in hospital laboratories

Patient Safety Initiatives

Benefits of LabNet:

- Opportunity to share problems and concerns regarding in-vitro diagnostic devices directly with the FDA and also, in de-identified form, with other sites participating in MedSun
- Help discern if the problems hospital lab staff are experiencing are more widespread
- Provide facility with timely device recall information, safety tips, and articles of interest
- Labs become a significant contributor to the safety of in-vitro diagnostic devices, and thus, improve public health

CLIA Activities Update

- CLIA final guidance is in final form and starting the clearance process
- Technology continues to drive this area
- Most recent example of a notable CLIA waiver - ESA Lead Test - success here a direct result of CDC funding of novel technology

New OIVD Guidance Documents

- Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable

  http://www.fda.gov/cdrh/oivd/guidance/1588.pdf

- Commercially Distributed Analyte Specific Reagents (ASRs): Frequently Asked Questions

  http://www.fda.gov/cdrh/oivd/guidance/1590.pdf

- In Vitro Diagnostic Multivariate Index Assays

  http://www.fda.gov/cdrh/oivd/guidance/1610.pdf

Leftover Specimens

- FDA law and regulations make patient samples subject to human subject protections and requirement for informed consent
- Differs from NIH Common Rule
- Means unidentified left-over discard samples cannot be used for development or research of new tests for FDA submissions

Leftover Specimens

- FDA intends to exercise enforcement discretion, under certain circumstances, with respect to requiring informed consent when human specimens are used in FDA-regulated IVD Device investigations
- Guidance is first step – regulation to follow

Leftover Specimens

Enforcement Discretion when:

- Investigation meets the IDE exemption criteria at 21 CFR 812.2 (c)(3)
- The study uses leftover specimens
- Specimens may be coded but not individually identifiable
- Specimen may be accompanied by clinical information if source not identifiable
- Individuals caring for patients are different from those conducting the study
- Supplier of specimen has established policies and procedures to prevent release of identifiable information
- Study protocol must be reviewed by an IRB

ASR Guidance

- Intended to address confusion in the marketplace and to clarify the regulations regarding commercially distributed ASRs and the role and responsibilities of ASR manufacturers

- Guidance was adapted from a document submitted to FDA by AdvaMed

ASR Guidance

- Intended to clarify the definition of an ASR
- Intended to communicate limitations on marketing of ASRs
- Not intended to eliminate legitimate home brew testing
- 90 day comment period

ASR Guidance

Examples of ASRs:

- a single antibody
  - →e.g., an anti-troponin I antibody
- a single nucleotide primer
  - →e.g., a forward primer for amplification of the ΔF508 locus of the CFTR gene
- a single purified protein or peptide
  - →e.g., purified estrogen receptor protein

ASR Guidance

Examples of entities that are not ASRs:

- Multiplexed reagents
- Test systems
  - → e.g., when it some or all of the products needed to conduct a particular test and/or has instructions for use.
- Control material
- Products that have specific performance claims, or procedural instructions, or interpretations for use.
- Reagents that are extensively processed
  - → e.g., arrayed on beads
- Reagents offered with software for interpretation of results.
- Other products that do not meet the ASR definition
  - → e.g., software for interpretation of assay results, microarrays, etc.

Multivariate Guidance

Identifies a class of laboratory developed devices subject to FDA regulation –

In Vitro Diagnostic Multivariate Index Assays:

IVDMIAs

Multivariate Guidance

IVDMIAs:

- Use clinical data (from one or more IVDs assays and sometimes demographic data) to empirically identify an algorithm
- Employ the algorithm to integrate these different data points in order to calculate a patient-specific result (e.g., a "classification," "score," or "index")
- The result cannot be interpreted by clinicians using prior knowledge of medicine without information from the test developer regarding its clinical performance and effectiveness

Multivariate Guidance

- IVDMIAs are a narrow niche of laboratory developed devices that are not subject to enforcement discretion
- Guidance indicates regulation will be risk-based by intended use (same as all other medical devices)
- 90 day comment period

Summary

- Critical Path Initiatives
- Patient Safety Initiatives
- CLIA Activities Update
- New FDA Guidances
  - →Leftover Samples
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Current Snapshot

- OIVD efforts to improve regulatory programs
- Developing and Evolving regulations
- Focus on good science