FDA’s Role in Ensuring Laboratory Testing Quality During Public Health Emergencies

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Case Study: EUA for 2009 H1N1 Influenza Devices
Influenza Testing Status: April 24th

- FDA cleared: Influenza A/B rapid /DFA antigen tests; nucleic acid based flu A/B and flu A/B, subtype H1, H3, H5 devices

- No cleared test available to definitively detect/differentiate influenza A subtype 2009 H1N1 from seasonal influenza A

- CDC request review and authorization of new device to detect novel H1N1 virus under EUA
Emergency Use Authorization (EUA)

- Emergency declared April 26th
  Section 564 of the Federal Food Drug and Cosmetic Act, as amended by the Project BioShield Act of 2004

- EUA allows lawful interstate shipment, use of unapproved medical products or unapproved uses of approved medical products, during a declared emergency
EUA PROCESS

DoD SEC Emergency DETERMINATION

DHS SEC Emergency DETERMINATION

HHS SEC Emergency DETERMINATION

HHS SEC Emergency DECLARATION

FDA ISSUANCE of EUA Consultation with CDC & NIH

TERMINATION of Declaration and EUA
Device must meet four statutory criteria for EUA:

1. Serious or life-threatening illness or condition caused by a specified agent
2. Reasonable to believe that product may be effective in diagnosing, illness/condition
3. Known & potential benefits outweigh known & potential risks of the product
4. No adequate, approved, available alternative to the product
EUA : Review of Data

- EUA is based on “totality of scientific evidence available to Secretary… including data from adequate and well-controlled clinical trials, if available…” (§ 564(c)(2))
FDA’s Mission

- Get safe and effective devices/systems to market as quickly as possible
- Ensure that devices/systems on the market are safe and effective

Benefits

Risks

Get safe and effective devices/systems to market as quickly as possible
Safety

- Are there reasonable assurances, based on valid scientific evidence that probable benefits to health from use of the device outweigh any probable risks? [860.7(d)(1)]

Effectiveness

- Is there reasonable assurance based on valid scientific evidence that the use of the device in the target population will provide clinically significant results? [860.7(e)(1)]
Information Requested for 2009 H1N1 Influenza EUA Devices

- Detailed description of test system. Discussion of risks/benefits of product
- Availability of instruments, manufacturing capacity, testing throughput
- Intended use, specimen types claimed
- Specimen collection, handling, storage, processing
- Instrument/software validation
- Analytical performance: LoD, analytical reactivity, crossreactivity, precision
- Clinical performance: minimum of 10-20 specimens positive by comparator authorized H1N1 EUA (or alternate algorithm) & 50-100 negatives by acceptable H1N1 comparator method
- Proposed labeling, information for health care provider and recipient, “fact sheets”
H1N1 EUAs Issued to Date : CDC

- CDC Swine Flu rRT-PCR Panel / ABI 7500 - not previously FDA cleared - **Second step assay** for testing Flu A positive/unsubtypable specimens. Detects 2009 H1N1 virus. Issued April 27th.

Commercial/DoD EUAs

- Focus Diagnostics (Quest) Influenza A H1N1 (2009) Real Time RT-PCR/ ABI 7500. **First step assay** detects Flu A 2009 H1N1, multiple respiratory specimen types
  Issued July 23rd

- rRT-PCR Swine Flu Panel on JBAIDS. Manufactured by CDC for Department of Defense (DoD)/Joint Biological Agent Identification and Diagnostic System. **First step assay** detects Flu A 2009 H1N1, nasopharyngeal swabs.
  Issued August 24th
Current Status of EUA Requests

- Many “official” requests and “unofficial” inquiries
- Sources = commercial companies/reference laboratories/academia etc.
- Most nucleic acid-based tests. Complex multiplex to RT PCR systems. Time to results range from :40 min/ 4 hours/4 days.
- Interactive reviews. Turn around time for EUA authorization, several days to 4 weeks
Prioritized Review Process Based on Public Health “Unmet Need”

EAU requests prioritized on basis of “Unmet Need”

- **Support for Public Health Surveillance**
  Request of another gov. agency: CDC

- **Support for Diagnostic Testing**
  Surge manufacturing capacity *
  Availability of instruments in US laboratories *
  Complexity*. Doctors’ office vs CLIA high complexity
H1N1 Influenza IVDs: FDA Short /Long Term Strategy

- Track potential shortages of influenza diagnostic devices
- Track and act on false claims for diagnosis of 2009 H1N1 infection
- Make widely available information required for EUA authorization and establish a standard template for validation of all H1N1 diagnostics
- Continue to balance “need” vs “safety and effectiveness” of 2009 H1N1 influenza diagnostic devices
H1N1 Influenza IVDs: FDA Short /Long Term Strategy

- Prioritize EUA review of existing/new diagnostic devices if virus reassortment occurs
- Prioritize devices capable of detecting resistant strains
- Encourage submission of 510(k)s for H1N1 detect/differentiation
- Continue to work closely with CDC /NIH/HHS on preparation/testing needs strategy for upcoming influenza season