

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

CLIAC Meeting, Atlanta, September 2, 2009

**Sally Hojvat, M.Sc,Ph.D
OIVD/CDRH/FDA**

sally.hojvat@fda.hhs.gov

Topic

- 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

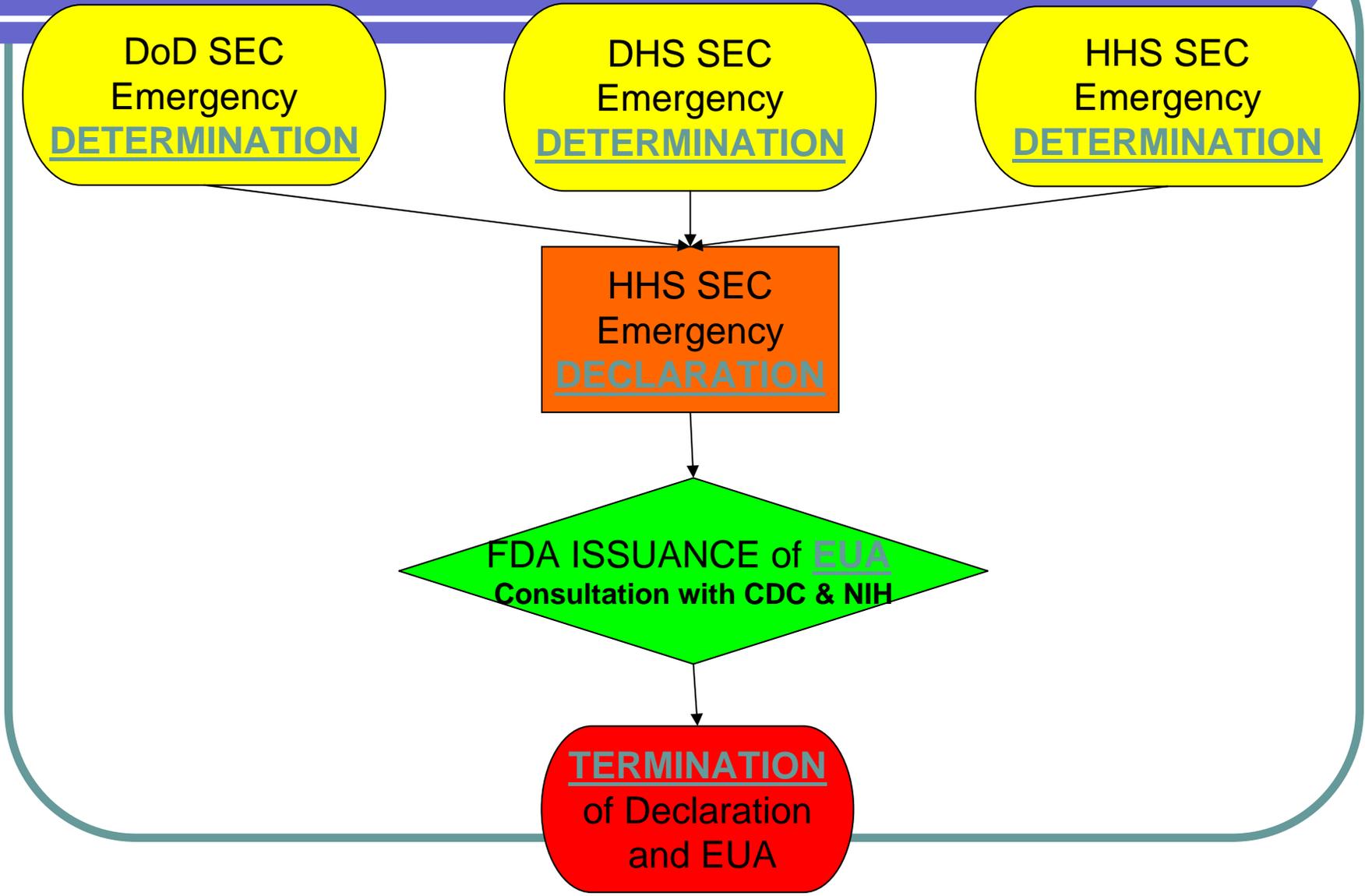
DHS SEC
Emergency
DETERMINATION

HHS SEC
Emergency
DETERMINATION

HHS SEC
Emergency
DECLARATION

FDA ISSUANCE of EUA
Consultation with CDC & NIH

TERMINATION
of Declaration
and EUA



Statutory Criteria (§ 564(c))

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
3. 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



**Ensure that
devices/systems
on the market are
safe and effective**

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

Safety and Effectiveness

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
- CDC Human Influenza RT-PCR Panel- FDA/ABI Fast 7500.Cleared 2008, added specimen types/alternate extraction rgt. - **First step assay** FluA, Flu B, H1,H3 H5 subtyping
Issued May 2nd

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