Overview from FDA

2021 Preparedness Summit
Tri-Agency Task Force for Emergency Diagnostics Session
April 2021

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Office of the Chief Scientist
Office of the Commissioner/ FDA
Outline

• Why are emergency use authorities needed?
• What is an Emergency Use Authorization (EUA)?
• EUA Interactive Review
• EUA vs. IVD Premarket Review
• Post EUA
• Declarations and IVD EUAs
• FDA Engagement in TTFED
Why are legal/regulatory mechanisms for emergency use of medical products needed?

Without these mechanisms, certain preparedness and response activities could otherwise violate provisions of the Federal Food, Drug, and Cosmetic (FD&C) Act:

- Some products needed for a response might not be approved, licensed, or cleared by FDA
- Some products needed for a response might be approved by FDA, but not for the emergency use (e.g., for a new indication)
- Also, to ensure any available HHS Public Readiness and Emergency Preparedness (PREP) Act liability protections apply
- Import or Export
What is an EUA?

• FDA may issue an EUA to allow use of an unapproved medical product, or an unapproved use of an approved medical product, if certain criteria are met (section 564 FD&C Act)

• Before FDA can issue an EUA, HHS Secretary must make an EUA Declaration based on 1 of 4 Determinations described in statute

• Statutory criteria must be met:
  – agent referred to in a declaration is one that can cause a serious or life-threatening disease or condition
  – Based on totality of scientific evidence, reasonable belief:
    • product may be effective (in preventing, diagnosing, or treating)
    • Known/potential benefits outweigh known/potential risks
  – No adequate, approved, available alternative to the product
What is an EUA? (continued)

- Conditions of authorization = safeguards, such as:
  - Information on emergency use, including “not FDA-approved”
    - fact sheets for recipients and health care providers
  - Record keeping and monitoring of adverse events
  - Collection of information
  - Conditions of authorization also clarify roles (e.g., CDC, laboratories)

- Publicly available EUA packages:
  - Consist of:
    - Letter of Authorization
    - Accompanying materials (e.g., fact sheets for health care professionals and patient/recipients, instructions for use, labels)
  - FDA must publish in the Federal Register a notice of each authorization, termination, and revocation
  - FDA posts all of this information near real-time on FDA’s website
Summary of Process for EUA Issuance

In the case of a DOD determination, the HHS Secretary shall determine within 45 days whether to issue an EUA declaration.

- **DOD SECRETARY**
  Determination of Military Emergency or Significant Potential for Military Emergency

- **DHS SECRETARY**
  Determination of Domestic Emergency or Significant Potential for Domestic Emergency

- **HHS SECRETARY**
  Determination of Public Health Emergency or Significant Potential for Public Health Emergency

- **DHS SECRETARY**
  Identification of Material Threat

**HHS SECRETARY**
Declaration that Circumstances Exist Justifying the EUA

**FDA COMMISSIONER**
Issuance of EUA (if criteria for issuance met)

**Termination of Declaration & EUA**

Consultation with ASPR, CDC, NIH
COVID-19 Determination and Declarations Supporting EUAs

• On February 4\textsuperscript{th}, 2020, the Secretary of Health and Human Services (HHS) announced the determination and declaration
  – COVID-19 presents a public health emergency that has a significant potential to affect national security or the health and security of US citizens living abroad
  – Circumstances exist justifying the authorization of emergency use of \textit{in vitro diagnostics} for detection and/or diagnosis of the virus that causes COVID-19

• On March 24, 2020, the Secretary of HHS declared circumstances exist justifying the authorization of emergency use of \textit{medical devices} during the COVID-19 outbreak.

• Additional declarations for other products
Draft IVD EUA Review Templates

• Draft **EUA Review Templates** developed to streamline data submission as well as data review and review documentation

• **Outlines** FDA’s current **recommendations** for the **analytical and clinical validation studies** needed in support of an EUA submission for various IVDs.

• **Dynamic Template**: Draft document, adapted depending on specific circumstances of the outbreak, Analyte & Technology (e.g., molecular, serology), starting point

• **Assist EUA Submitter and FDA Reviewers**:  
  – Submitter fills out the template  
  – Template serves as basis for interactive review  
  – Template will later serve as sponsor’s EUA Submission AND  
  – Review memorandum
EUA Interactive Review

Firm and FDA Interact

Draft EUA Review Template

Pre-EUA Submission

EUA Submission

Emergency Use Authorization

Firm and FDA Interact

Draft EUA Review Template

Pre-EUA Submission

Firm and FDA Interact

Slide credit: K.Sapsford
# EUA Vs. Premarket: In Vitro Diagnostics

<table>
<thead>
<tr>
<th>Requirements</th>
<th>Emergency Use Authorization (EUA)</th>
<th>Premarket Notification or Application</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Special Circumstances</strong></td>
<td>Requires declaration by the HHS Secretary that circumstances exist justifying the EUA There is no adequate, approved, and available alternative to the product</td>
<td>No</td>
</tr>
<tr>
<td><strong>Analytical Evaluation</strong></td>
<td>Limited</td>
<td>Extensive</td>
</tr>
<tr>
<td><strong>Clinical Evaluation</strong></td>
<td>Limited</td>
<td>Extensive</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Temporary - remains in effect for the duration of the declaration unless revoked sooner</td>
<td>Not Limited</td>
</tr>
<tr>
<td><strong>CGMP</strong></td>
<td>Expected but limits or waivers may be granted in an EUA on a case-by-case basis</td>
<td>Required</td>
</tr>
</tbody>
</table>

Slide credit: K.Sapsford
Post EUA

FDA’s role once an EUA is issued:

• Review, Revision, and Revocation
  – Review the circumstances and appropriateness of each authorization
  – FDA may revise or revoke if:
    • The emergency circumstances no longer exist
    • The criteria for the issuance of the EUA are no longer met, or
    • Other circumstances make revision or revocation appropriate to protect public health and safety
EUA is not a substitute or shortcut for approval or clearance

FDA issued a De Novo classification order for the BioFire Respiratory Panel 2.1 (RP2.1) as a Class II (Special Controls) device under the generic name “Device to detect and identify nucleic acid targets in respiratory specimens from microbial agents that cause the SARS-CoV-2 respiratory infection and other microbial agents when in a multi-target test.” (to be codified in 21 CFR 866.3981) on March 17, 2021.
## HHS Secretary Declaration of Emergency or Threat

<table>
<thead>
<tr>
<th>Virus/Pathogen</th>
<th>Date of Declaration</th>
<th>In Vitro Diagnostic Tests for Detection and/or Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV-2</td>
<td>February 4, 2020</td>
<td>Emergency Use of In Vitro Diagnostic Tests for Detection and/or Diagnosis of the Virus that Causes COVID-19</td>
</tr>
<tr>
<td>Zika Virus</td>
<td>February 26, 2016</td>
<td>Emergency Use of In Vitro Diagnostic Tests for Detection of Zika Virus Infection</td>
</tr>
<tr>
<td>Enterovirus D68</td>
<td>February 6, 2015</td>
<td>Emergency Use of New In Vitro Diagnostics for Detection of Enterovirus D68</td>
</tr>
<tr>
<td>Ebola</td>
<td>August 4, 2014</td>
<td>Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus</td>
</tr>
<tr>
<td>MERS-CoV</td>
<td>May 29, 2013</td>
<td>Emergency Use of In Vitro Diagnostics for Detection of Middle East Respiratory Syndrome Coronavirus</td>
</tr>
<tr>
<td>Influenza H7N9</td>
<td>April 19, 2013</td>
<td>Emergency Use of In Vitro Diagnostics for Detection of the Avian Influenza A (H7N9) Virus</td>
</tr>
</tbody>
</table>

## IVD EUA Summary

<table>
<thead>
<tr>
<th>EUA Declaration</th>
<th>H1N1</th>
<th>H7N9</th>
<th>MERS-CoV</th>
<th>Ebola</th>
<th>Enterovirus D68</th>
<th>Zika</th>
<th>SARS-CoV-2</th>
</tr>
</thead>
</table>

### EUA Diagnostics:

<table>
<thead>
<tr>
<th>Test Type</th>
<th>H1N1</th>
<th>H7N9</th>
<th>MERS-CoV</th>
<th>Ebola</th>
<th>Enterovirus D68</th>
<th>Zika</th>
<th>SARS-CoV-2</th>
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<tbody>
<tr>
<td>Molecular</td>
<td>17</td>
<td>2</td>
<td>2</td>
<td>9</td>
<td>1</td>
<td>13**</td>
<td>258</td>
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<tr>
<td>Molecular with Self/Home-collection</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>42</td>
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<tr>
<td>Antigen</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>3*</td>
<td>0</td>
<td>0</td>
<td>16</td>
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<td>Immune Response</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
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<td>IL-6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

*Includes one product that was authorized for two different intended uses

**Includes one product that was authorized but later withdrawn by the company

Table data as of March 26, 2021; slide credit: K.Sapford
FDA Engagement with TTFED

- Recommendation to include conditions of authorization for laboratories from EUA letter in the manufacturer’s instructions
- Recommendation to require external control materials
- Agency FAQs
- Fact-sheets for patients, HCPs
- Challenge: communicating early and often while moving quickly to address an evolving public health emergency
Resources

• FDA FAQs on Testing for SARS-CoV-2

• COVID-19 IVD Templates for EUA Submission

• Guidance: Emergency Use Authorization of Medical Products and Related Authorities
  https://www.fda.gov/media/97321/download

• List of all EUAs
Questions?

• Contact the Division of Microbiology devices: CDRH-EUA-Templates@fda.hhs.gov. Stakeholders interested in pursuing an EUA may submit a pre-EUA to begin discussions with the FDA or may submit an EUA request to this mailbox.

• Virtual Town Hall Series - Coronavirus (COVID-19) Test Development and Validation