U.S. FOOD & DRUG ADMINISTRATION

Transitioning Diagnostics from Emergency Use Authorization (EUA) to Marketing Applications

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Overview

- Emergency Use Authorization (EUA) authority
- EUA vs. Premarket Study Requirements
- RWE/RWD Guidance

Emergency Use Authorization (EUA) Authority

EUA Authority

- Section 564 of the Federal Food, Drug and Cosmetic Act (FD&C Act)
  - Amended by the Project Bioshield Act of 2004
  - Amended by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA)
  - The 21st Century Cures Act of 2016
  - Public Law 115-92 of 2017

EUA Authority

FDA can authorize:

- Use of unapproved MCMs (despite lacking the amount of data that would be necessary for approval)
- Unapproved use of approved MCMs (e.g., for a new indication)

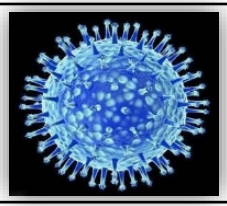
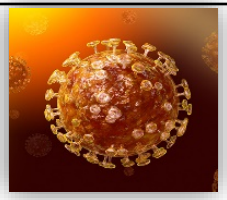
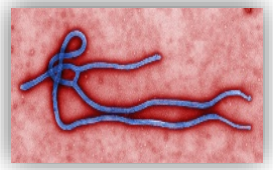
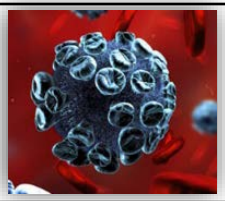
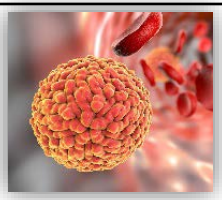
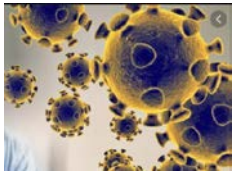
to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents when certain criteria are met.

EUA and IVD

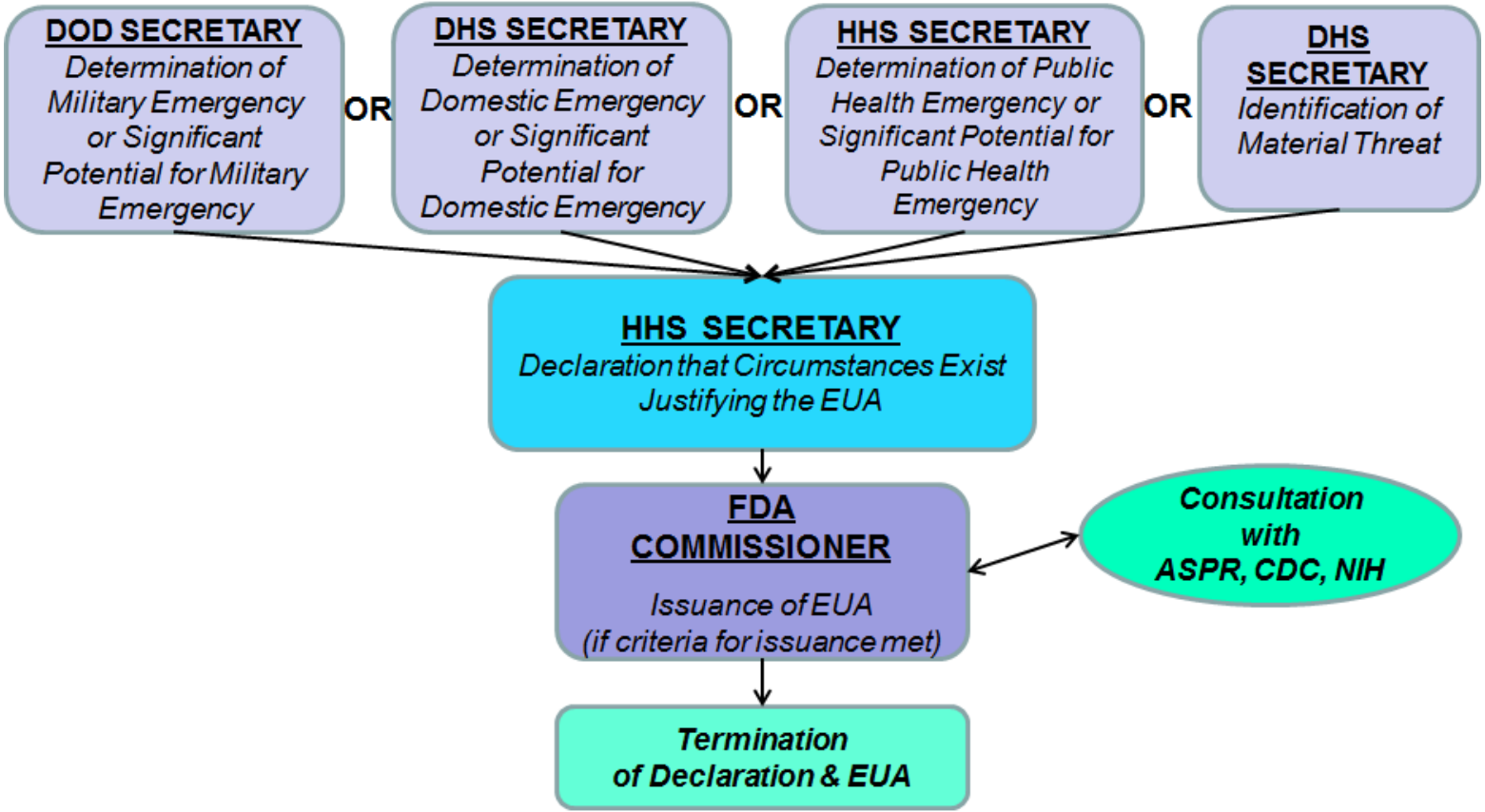
- In vitro diagnostics play a very important role in any emergency response involving an emerging infectious disease - from initial outbreak detection, diagnosis, patient management and infection control.

- In the absence of a cleared/approved FDA assay the EUA authority is a mechanism FDA can use to address a public health emergency.

HHS Secretary Declaration of Emergency or Threat

Influenza H7N9 Orthomyxoviridae	**MERS-CoV** Coronaviridae	**Ebola** Filoviridae	**Enterovirus D68** Picornaviridae	**Zika Virus** Flaviviridae	**2019-nCoV** Coronaviridae
					
April 19, 2013	May 29, 2013	August 4, 2014	February 6, 2015	February 26, 2016	January 31, 2020
Emergency Use of In Vitro Diagnostics for Detection of the Avian Influenza A (H7N9) Virus	Emergency Use of In Vitro Diagnostics for Detection of Middle East Respiratory Syndrome Coronavirus	Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus	Emergency Use of New In Vitro Diagnostics for Detection of Enterovirus D68	Emergency Use of In Vitro Diagnostic Tests for Detection of Zika Virus and/or Diagnosis of Zika Virus Infection	

EUA Determination and Declaration

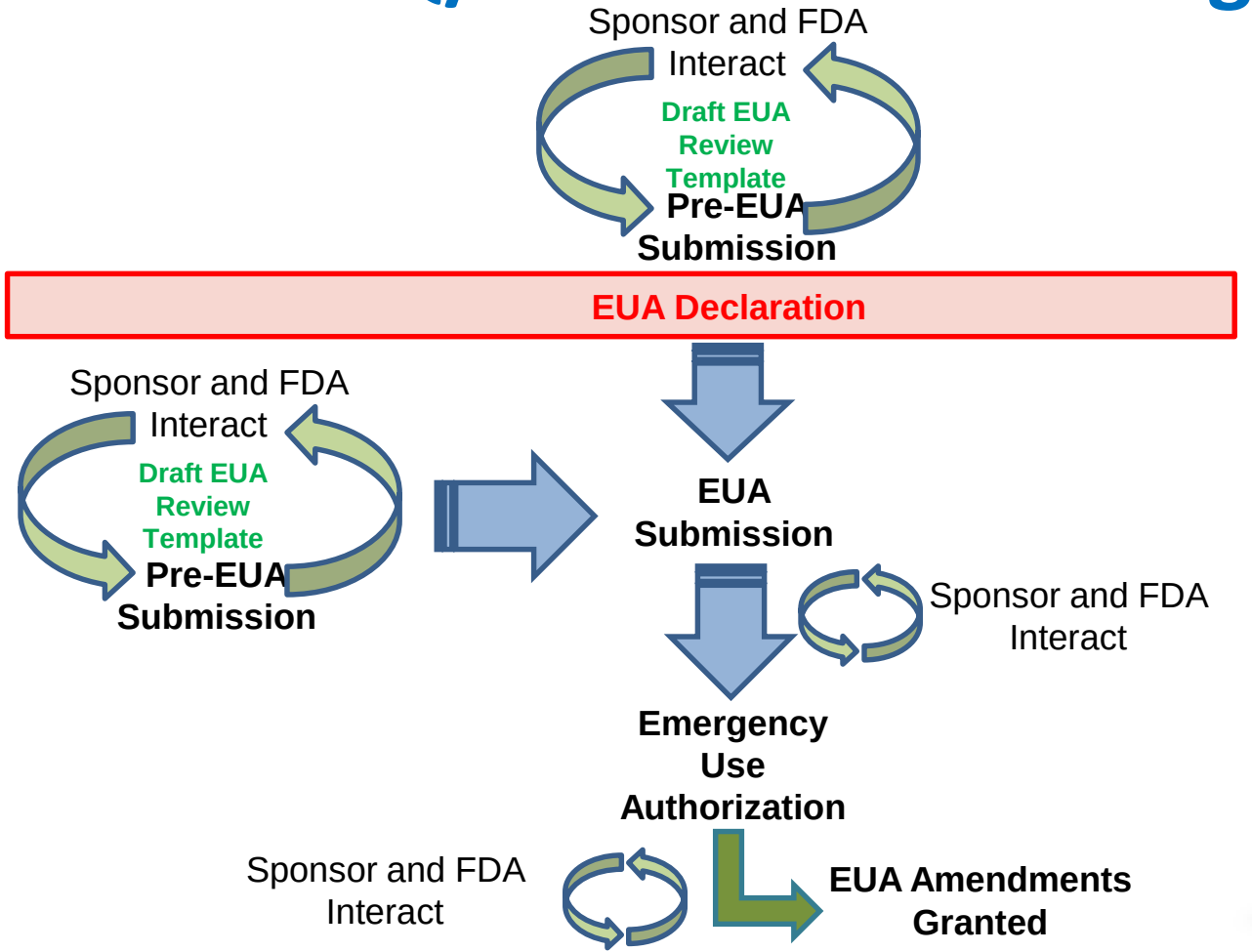


Criteria for EUA

1. The agent causes a serious or life-threatening disease or condition.
2. Based on totality of scientific evidence, reasonable belief:
   - Product may be effective
   - Known/potential benefits outweigh known/ potential risks
3. No adequate, approved, available alternative to the product

EUA program within FDA

OPEQ/OHT7-OIR EUA Program



EUA Documents:

- EUA Review Template

Public Documents:

- Letter of Authorization
- Fact Sheets – Healthcare Providers and Patients
- Manufacturer Package Insert/Instructions for Use

EUA vs. Premarket Study Requirements

EUA vs. Premarket: In Vitro Diagnostics

Requirements	Emergency Use Authorization (EUA)	De Novo/510(k)
Special Circumstances	Requires declaration by the HHS Secretary that circumstances exist justifying the EUA; There is no adequate, approved, and available alternative to the product	No
Duration	Temporary - remains in effect for the duration of the declaration unless revoked sooner	Not Limited
Analytical Evaluation	Limited	Full validation
Clinical Evaluation	Limited	Full validation
cGMP	Expected but limits or waivers may be granted in an EUA on a case-by-case basis	Required

https://www.fda.gov/about-fda/cdrh-transparency/evaluation-automatic-class-iii-designation-de-novo-summaries

Studies EUA vs. De Novo/510(k) - NAAT

NAAT	Emergency Use Authorization (EUA)	De novo/510(k)
Limit of Detection (LoD)	Yes	Yes
Inclusivity	Yes Some *in silico*	Yes Some *in silico*
Exclusivity	Limited Some *in silico*	Full validation Some *in silico*
Interference	Situation specific	Yes
Precision	No	Yes - Multisite
Fresh vs. Frozen	Fresh specimens preferred	Fresh specimens preferred
Clinical Evaluation	Limited – natural clinical specimens	Full validation – natural clinical specimens

EUA IVD to Full Marketing Status

	H7N9	MERS-CoV	Ebola	Enterovirus D68	Zika	
EUA Declaration	April 19, 2013	May 29, 2013	August 4, 2014	February 6, 2015	February 26, 2016	**Total**
Original EUA Diagnostics:						**39**
Total	**3**	**2**	**13**	**1**	**20**	
EUA Re-authorizations and Amendments:						**18/61**
Total	**1**	**2**	**31**	**0**	**45**	
De Novo or 510(k) Transitions:						**6**
Total	**0**	**2**	**1**	**0**	**3**	

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Guidance for Industry

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

FDA RWE/RWD Guidance

- **RWD** are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.
- **RWE** is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.

Regulatory Context in Which RWE May be Used

- RWD used to generate the RWE are of sufficient quality

- May potentially be used as some or all of the evidence necessary for understanding medical device performance at different points in the Total Product Life Cycle (TPLC)

Characteristics of RWD

RWD must demonstrate:

- **Relevance** – is the RWD data adequate to address the applicable regulatory question or requirement

- **Reliability**
  - Data accrual: how the data were collected
  - Data assurance: data quality and integrity

Example where RWE might be used

- Expanded indications of use
- Postmarket surveillance studies
- Post-approval device surveillance as condition of approval
- Control group
- Supplementary Data
- Objective Performance Criteria and Performance Goals

Questions

- **Can I use the data obtained for EUA authorization?**

  Yes, if no modifications to the device have been made since the EUA authorization. If modifications have been made, a risk assessment of the modifications is required to determine the extend of changes to the device and its influence on performance.

- **Can I use data generated outside the US in an FDA submission?**

  Yes, if the test procedure was performed according to the package insert with no deviations.

Question

- Can RWD be used to help support the advancement of EUA IVD products to full marketing status?

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Additional Resources

- **FDA Medical Countermeasures Initiative (MCMi)**
  - www.fda.gov/medicalcountermeasures
- **FDA EUA Website** (*official updates, current & terminated EUAs, guidance*)
  - www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm
- **FDA Draft Guidance on EUAs and other MCM Emergency Use Authorities**
  - http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm (April 2016)
- **FDA MCM Emergency Use Authorities Website** (*official updates*)
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm411432.htm
- **FDA Zika Response Updates Website**
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm (also available in Spanish and Portuguese)
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