FDA Emergency Use Authorizations

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This practice note provides guidance on Food and Drug Administration (FDA) Emergency Use Authorizations (EUAs).This practice note offers an overview of the legal and regulatory framework for EUAs, provides practical tips for obtaining an EUA, introduces considerations for importing and exporting under an EUA, and highlights certain recent EUAs, including some relating to coronavirus disease 2019 (COVID-19).

This practice note covers the following topics:

For information about FDA approval of drugs and medical devices generally, see FDA Regulation of Pharmaceuticals and FDA Regulation of Medical Devices.

EUA Framework

In an emergency, and when there are no adequate, approved, and available alternatives, Section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act),21 U.S.C. § 301 et seq., authorizes the FDA Commissioner to allow unapproved medical products or unapproved uses of approved medical products to diagnose, treat, or prevent serious or life-threatening diseases or conditions. These medical products, also known as “medical countermeasures” (MCMs) include drugs, biologics, and devices (including *in vitro* diagnostics and personal protective equipment).

The FDA’s authority to allow EUAs was created through multiple amendments to the FD&C Act, including the Project Bioshield Act of 2004, 108 P.L. 276, the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA), the 21st Century Cures Act of 2016, 114 P.L. 255, and Public Law 115-92 of 2017.

In 2017, the FDA finalized its guidance Emergency Use Authorization of Medical Products and Related Authorities (2017 Guidance). The 2017 Guidance replaces two prior guidance texts: Emergency Use Authorization of Medical Products (July 2007) and Emergency Use Authorization Questions and Answers (April 2009).

In February 2020, the FDA issued its guidance Policy for Diagnostics Testing in Laboratories Certified to Perform High Complexity Testing under CLIA Prior to Emergency Use Authorization for Coronavirus Disease-2019 During the Public Health Emergency (COVID-19 Guidance).

How to Obtain an EUA

As explained in the 2017 Guidance, obtaining an EUA involves:

- A determination of the justifications for an emergency use
- Meeting criteria for issuance
- Participating in pre-EUA activities and submissions
- Formally requesting an EUA
- The FDA's processing, approval, and issuance of an EUA letter
- Meeting conditions of authorization

Justification

Before an EUA can issue, pursuant to FD&C Act § 564(b)(1), 21 U.S.C. § 360 bbb-3(b)(1), the Secretary of the U.S. Department of Health and Human Services (HHS) must declare that at least one of four circumstances exist. The four circumstances are:

- A domestic emergency or a significant potential for a domestic emergency involving a heightened risk of attack with a chemical, biological, radiological, or nuclear (CBRN) agent, as determined by the Secretary of Homeland Security (FD&C Act § 564(b)(1)(A), 21 U.S.C. § 360bbb-3(b)(1)(A))
- A military emergency, or significant potential for a military emergency, with a heightened risk of an attack with a CBRN agent on U.S. military forces, as determined by the Secretary of Defense (FD&C Act § 564(b)(1)(B), 21 U.S.C. § 360bbb-3(b)(1)(B))
- A public health emergency, or a significant potential for a public health emergency, affecting or with the significant potential to affect national security or the health and security of U.S. citizens living abroad, that involves a CBRN agent or related disease or condition, as determined by the Secretary of HHS (FD&C Act § 564(b)(1)(C), as amended by the PAHPRA, 21 U.S.C. § 360bbb-3(b)(1)(C))
- A material threat sufficient to affect national security or the health and security of U.S. citizens living abroad, identified by the Secretary of Homeland Security (FD&C Act § 564(b)(1)(D), 21 U.S.C. § 360bbb-3(b)(1)(D))

Criteria for Issuance

After the HHS Secretary makes an EUA declaration, the FDA can authorize unapproved products or unapproved uses of approved products, subject to the criteria discussed below. Even if there has been an EUA declaration, for an EUA to issue, four criteria must be met:

- **Serious condition.** The CBRN agent(s) must be capable of causing a serious or life-threatening disease or condition. 2017 Guidance § III.B.1.a.
- **"May be effective."** There must be a showing that the unapproved product or unapproved use may be effective in treating the disease or condition. This is lower than the effectiveness standard used for other product approvals. 2017 Guidance § III.B.1.b.
- **Risk benefit analysis.** The FDA must determine that the known and potential benefits of the product outweigh the known and potential risks of the product. 2017 Guidance § III.B.1.c.
- **No alternatives.** There must be no adequate, approved, and available alternative. 2017 Guidance § III.B.1.d.
    - An alternative may be "inadequate" if, for example, there are contraindications for a population, the dosage form is inappropriate, or the CBRN agent is resistant to approved and available products.
    - An alternative may be "unavailable" if, for example, there are insufficient supplies to meet the emergency need.

Pre-EUA Activities and Submissions

Before applying for an EUA designation, a product sponsor should contact the FDA. This will allow the sponsor to coordinate with the FDA on appropriate clinical trials and the proper form for supplying data prior to a formal submission.

Submission of an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) is not required for potential EUA products. Sponsors submitting data, however, as part of pre-EUA activities should follow FDA recommendations for submitting pre-IND, IND, and device pre-submissions, as well as the recommendations in the 2017 Guidance at § III.C.

Early discussions with the FDA allow sponsors to address the factors that the FDA considers in prioritizing EUA requests. 2017 Guidance at sections III.C and III.D.4.a. These factors include:

- Seriousness and incidence of the disease
- Public health need for the product
- Urgency for the treatment need
- Availability and adequacy of information on safety and efficacy
- The potential role of the product in ensuring national security
- Whether the product is included in government stockpiles
- The extent of meeting a significant unmet medical need in particular subpopulations or stages of emergency response
- Whether the request is from or supported by a government stakeholder
- The availability of the product
- Whether other mechanisms, such as an IND or IDE, would be more appropriate(e.g., where there is little or no safety or efficacy data available)

Requests for an EUA

Many formal requests are made by a government sponsor (e.g., an executive branch agency), although industry sponsors are free to make formal requests. Obtaining a government sponsor or supporter can be a key component in the attention given by the FDA to a request. The actual authorization is a letter to the sponsor that includes a description of the product, its uses, contraindication, criteria for issuance, the scope of authorization, waiver of any requirements, and any conditions. The letter will also be issued with certain materials, for example, instructions for use and fact sheets.

Section III.D.2.a of the 2017 Guidance recommends that the following information be included in any request for an EUA:

- Description of the product and its intended use
- Description of the product's FDA approval status
- The need for the product, including whether there are adequate, approved, and available alternatives
- Safety and efficacy information:
    - Required safety information will vary by product and emergency. It can include, for example, controlled clinical trials, bench testing, and/or clinical experience if the circumstances warrant. 2017 Guidance § III.D.2.b.
    - Early discussions with the FDA about the required safety and efficacy information are critical.
- A discussion of risks and benefits:

- A discussion of risks and benefits should include (1) measures taken to mitigate risk or optimize benefit; (2) limitations, uncertainty, and data gaps; (3) contraindications; and (4) actual and potential threats posed by CBRN agents that may be relevant.

- Information on chemistry, manufacturing and controls, and the sites of manufacture, including the current good manufacturing practices (CGMP) status of those sites
- Information on the quantity of product on-hand and surge manufacturing capabilities
- Information comparable to an FDA-approved package insert or instructions for use, drafts of fact sheets for healthcare professionals and recipients of the product, and a discussion of the feasibility of providing this information in an emergency (a sample of instructions used for an EUA diagnostic panel for the novel coronavirus is available on the FDA's website)
- Information to support an extension of a label's expiration date, if sought –and–
- Any right of reference (a right of reference means "the authority to rely upon, and otherwise use, data submitted from reports of an investigation or data previously submitted to FDA in support of an application, including the ability to make available the underlying raw data for FDA audit.")

A formal request to issue an EUA should generally not be submitted until there has been an EUA declaration. If required and if the FDA has adequate information, the FDA can issue an EUA within hours or days of a request. To facilitate a fast approval, sponsors should provide as much information to the FDA as possible as part of its Pre-EUA Activities and Submissions.

Waivers and Conditions of Authorization

The FDA may waive certain requirements or impose conditions for an unapproved product or unapproved use.

The FDA will waive requirements on a case by case basis. See FD&C Act § 564(e)(3), 21 U.S.C. § 360bbb-3(e)(3). These waivers can include:

- **CGMPs.** The FDA will consider alternatives to ordinarily required compliance with CGMPs.
- **Prescription requirements.** The FDA will allow waivers to prescription requirements where, for example, the emergency requires large-scale administration outside of traditional healthcare settings, called "points of dispensing" (PODs). Note that emergency mass dispensing of FDA-approved products is allowed under certain conditions set forth in section IV.D. of the 2017 Guidance.
- **Risk Evaluation and Mitigation Strategy (REMS).** REMS is a drug safety program for certain medications with serious safety concerns. If needed, the FDA will waive REMS requirements.

The FDA will impose conditions similar to conditions for approved products and uses. The following is a non-exhaustive list:

- **Notice to healthcare professionals.** The FDA requires adequate notice to healthcare professionals and authorized dispensers that the FDA has authorized the emergency use, the benefits and risks, and available alternatives.

  - In practice, this is accomplished by including a factsheet for healthcare professionals or authorized dispensers with the request for an EUA.

  - The fact sheet should target the healthcare professional with the lowest level of training, generally be very brief, and contain no more than a few pages. If necessary, this information can be given through mass media, videos, or direct communication. For an example of a healthcare provider fact sheet for the novel coronavirus, see this document.

- **Information for recipients**. The FDA does not require informed consent for administering or use of an EUA product. See 21 C.F.R. part 50; 2017 Guidance § III.E.1.b. But to meet FDA disclosure requirements, sponsors should include an additional fact sheet for patients.

- To the extent applicable, the fact sheet should specify that the FDA has authorized the emergency use, benefits and risks, the patient's option to accept or refuse the product, consequences of refusing administration, and available alternatives.
- The fact sheet should also include the product name and an explanation of its intended use, a description of the disease or condition, a description of items to discuss with the patient's healthcare provider, adverse event information, and dosing information and instructions.
- Like the healthcare provider factsheet, the information should be easily understood, and may be communicated through mass media, videos, or direct communication. Translations into multiple languages may be needed. For an example of a patient fact sheet for the novel coronavirus, see this document.

• **Monitoring and reporting of adverse events.** Sponsors should provide proposals for data collection and follow-up for adverse events to the FDA during pre-EUA interactions.

Duration and Revision of an EUA

An EUA generally remains in effect for the duration of the related EUA declaration. The effective date will be specified in the EUA. The FDA will periodically review EUAs and may revoke an EUA for a number of reasons, including the following:

• Justification for its issuance no longer exists

• Criteria for issuance are no longer met–or–

• Revocation is needed to protect public health or safety(e.g., adverse manufacturing inspections, reports of adverse events, product failure, product ineffectiveness)

Practice Tips on Submissions

Keep the following in mind for EUA submissions:

• References to previously submitted data (e.g., in an Investigational Device Exemption (IDE) or Drug MasterFile (DMF)) should identify prior submissions by submission date, name, reference number, volume, and page number.

• Submissions with a cover letter may be provided in electronic format. If submitted by paper, sponsors should provide at least three hard copies.

• Because of the emergency nature of EUAs, product sponsors should contact the FDA before submitting any materials for directions on format by emailing the appropriate center.

• In addition to other submission requirements outlined in the 2017 Guidance, a message highlighting the urgency and including the cover letter and submission should be sent to EUA.OCET@fda.hhs.gov, as well as to the appropriate center and any other contacts familiar with the submission.

• Given the fact that the FDA's resources will likely be relatively taxed during the health emergency, contacting the agency both early and often is recommended throughout the process.

• Contact information for each center can be found in the 2017 Guidance.

Import and Export Considerations

A medical product authorized for emergency use under an EUA may be legally imported and exported under Section 801 of the FD&C Act, 21 U.S.C. § 381. According to Section VIII of the 2017 Guidance, the EUA letter of

authorization is the appropriate documentation or certification to show that the product may be imported or exported.

Snapshot of Select EUAs

COVID-19

The HHS Secretary determined on February 4, 2020, that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad, and that involves the virus, SARS-CoV-2, that causes the disease COVID-19. On March 4, 2020, the HHS Secretary also declared that there was justification to authorize emergency use of personal respiratory protective devices during the COVID-19 outbreak.

In the early stages of the coronavirus outbreak, the FDA issued letters of EUA on February 4, February 29, and March 4, 2020, to allow for emergency uses of diagnostic panels and protective devices. The FDA has issued specific guidance for diagnostic tests that have not received EUA. The policy sets recommended limits of detection, standards for clinical evaluation in the absence of known positive samples, and reporting suggestions, among other things.

The FDA has also provided a template for a COVID-19 EUA request. The template, which practitioners should consult before preparing a request, is available on the FDA's website.

Keep in mind that the FDA's website contains historical letters of authorization, fact sheets, and instructions for use.

Practitioners should consult the FDA's website for the latest developments.

Entorovirus D68 (EV-D68)

In contrast to the response for COVID-19, the HHS Secretary issued a determination on Enterovirus D68 on February 6, 2015, but it was not until May 12, 2015, that FDA issued a letter of EUA. The slower time to issuance can be explained by the significantly lower scale of the Enterovirus D68 outbreak compared to SARS-CoV-2.

Zika

The FDA issued its EUA determination on tests for detection of Zika Virus and/or Diagnosis of Zika infections on February 26, 2016, the same day that it issued an EUA letter for the CDC's Zika immunoglobulin M Antibody Capture Enzyme-Linked Immunosorbent Assay. Additional EUA letters issued in March, April, May, June, July, September, November, and December 2016, as well as August and September 2017.

As is frequently the case for emergency conditions lasting several years, the authorizations were amended multiple times. Practitioners can review the FDA's template for Zika-related EUA submissions by contacting the FDA at CDRH-ZIKA-Templates@fda.hhs.gov.

Examples of healthcare provider and patient fact sheets, as well instructions of use are available on the FDA's website.

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