EUA - Emergency Use Authorization

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization

About Emergency Use Authorizations (EUAs)
The Emergency Use Authorization (EUA) authority allows FDA to help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats including infectious diseases, by facilitating the availability and use of medical countermeasures (MCMs) needed during public health emergencies.

Under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), when the Secretary of HHS declares that an emergency use authorization is appropriate, FDA may authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents when certain criteria are met, ***including there are no adequate, approved, and available alternatives*** (emphasis added). The HHS declaration to support such use must be based on one of four types of determinations of threats or potential threats by the Secretary of HHS, Homeland Security, or Defense.

https://www.yalemedicine.org/news/what-does-eua-mean

Emergency Use Authorization Vs. Full FDA Approval: What's the Difference?
By Carrie Macmillan March 7, 2022

A primer on the two and why it matters, especially when it comes to COVID-19 vaccines.

Before COVID-19, most of us probably weren't familiar with the term "emergency use authorization." And two years into the pandemic, the meaning of this regulatory step is still a little foggy—even though it's constantly mentioned in news reports about COVID-19 vaccines, tests, and treatments.

Put simply, an emergency use authorization (EUA) is a tool the Food and Drug Administration (FDA) can use to expedite the availability of medical products, including drugs and vaccines, during a public health emergency. An EUA can only be granted when no adequate, approved, available alternatives exist, and when the known and potential benefits outweigh the potential risks. An EUA also only lasts as long as the public health emergency for which it was declared.

It is the job of the FDA to ensure medical products meet rigorous safety and efficacy standards, a process that can take years for what's called "full approval." Though that timeline is condensed when an EUA is granted, the FDA still upholds its strict standards.

Since the start of the pandemic, the FDA has granted numerous EUAs related to COVID-19. So far, two vaccines (Pfizer-BioNTech, for ages 16 and up, and Moderna, for 18 and up) and one treatment (Gilead Science's remdesivir) have gone on to receive full FDA approval.

So, does getting a vaccine or taking a drug that is under emergency use authorization mean it's any less safe than one that has full FDA approval? And how does the process work? Below, we take a closer look at the details.

How long have EUAs been around?

The FDA established its EUA program in 2004 in response to threats of bioterrorist attacks, including anthrax. Later, it was used for H1N1 (swine flu), Ebola, avian flu, Middle Eastern Respiratory Syndrome

(MERS), and other major public health threats. EUAs in these instances included tests, an anthrax vaccine, antiviral treatments, and personal protective equipment.

An EUA can be revised or revoked by the FDA at any point as the agency evaluates the most current needs and available data. For example, the FDA issued an EUA for hydroxychloroquine during the first phase of the COVID-19 pandemic. Later, when it became clear that the treatment posed a risk but did not offer significant benefit, the FDA retracted the EUA.

How does the EUA process differ from the full FDA approval process?

Amid the myriad paperwork/administrative differences between the two options (more detail below), there are two standout differences—and they have nothing to do with the scientific rigor of the trials.

For an EUA for a COVID-19 vaccine, for example, the FDA requires that at least half of the clinical trial participants be followed for at least two months after vaccination. For full FDA approval of a COVID-19 vaccine, participants are followed for at least six months.

The full approval requires more data about the vaccine-maker's processes and facilities, including inspections of manufacturing plants.

What does the normal full FDA approval process entail?

The FDA's full approval process varies depending on the product. For vaccines and therapeutics (a treatment, therapy, or drug), companies file what is called a "biologics license application"—or a BLA.

But before filing an application for a vaccine BLA, development and testing must follow a standard set of steps. Here is the typical process:

Research and discovery stage: Scientists conduct laboratory research—often in animals—to test their vaccine candidate.

Pre-clinical stage: Researchers perform additional lab testing in animals to gather information on how the vaccine works and whether it's likely to be safe and perform well in humans.

Clinical development stage: When studies are ready to begin in humans, the company compiles results of their pre-clinical testing and information about the manufacturing technology, and submits them to the FDA for assessment. If all looks good, the FDA green-lights clinical trials, which include four phases:

Phase I: Small groups of volunteers receive the trial vaccine to gather safety data. Generally, this involves about 20 to 100 volunteers.

Phase II: If there are no safety concerns from Phase I, more people (in the hundreds), with varying health statuses and from different demographic groups, are given various dosages.

Phase III: The vaccine is given to thousands of people and tested for efficacy (the percentage reduction of disease in people who received the trial vaccine versus those who received a placebo), safety, and immune response.

Phase IV: Monitoring trials (more below)

Assessment of manufacturing stage: While clinical trials are being conducted, FDA investigators review the manufacturing processes. This step includes visits to the facility to ensure it operates in compliance with FDA regulations.

Seeking approval stage: Once clinical trials are completed—and if the manufacturing process in place demonstrates that the vaccine can be produced reliably and consistently—the company submits its BLA, containing all the data from steps above, to the FDA.

Full approval granted stage: If the vaccine is approved (or licensed, as it is also known), the company can market it for use in the population for which it was approved.

To decide on approval, FDA scientists evaluate all of the data and information in the BLA. Sometimes, the agency seeks input from its Vaccines and Related Biological Products Advisory Committee (VRBPAC)—a group of outside, independent experts from scientific and public health fields. (The FDA considers input from the committee, but is not bound by its recommendations.

Continued oversight stage: After approving a vaccine, the FDA continues to oversee its production and monitor its safety. This includes periodic facility inspections. There are also Phase IV trials, which are optional, ongoing studies to identify uncommon adverse events and long-term complications, as well as to monitor effectiveness. Vaccines are also monitored by various surveillance systems, including the Vaccine Adverse Event Reporting System (VAERS), which accepts and analyzes reports of possible health problems after vaccination.

What is the process for an EUA?

The EUA process for a vaccine is similar to the BLA, or full approval, process in most ways. A manufacturer must conduct laboratory research, followed by animal testing, and submit an application. Phase I, II, and III clinical trials run as they normally would, as does the FDA assessment of manufacturing practices. But here are some notable steps that have a degree of overlap:

Safety board: An independent data safety monitoring board (DSMB) evaluates data from the Phase III trial and tells the manufacturer whether or not they have met criteria for a clinical endpoint (showing how well a vaccine prevents COVID-19, for example) that had been pre-established by the FDA. Based on the group's findings, the manufacturer decides whether and when to submit an EUA request.

The DSMBs are different than VRBPAC. Safety boards are established by the vaccine manufacturer as part of a trial and have access to unblinded trial data that they review while the trial is ongoing to see if there are any safety or efficacy signals that warrant action being taken before the trial is scheduled to conclude.

DSMBs aren't specific to the EUA or BLA pathways, but for the EUA COVID vaccines, it was their interim assessment that indicated the vaccines were highly effective and prompted submission to the FDA—where VRBPAC then met and reviewed the formal submission.

FDA review: Once an EUA is submitted, scientists and physicians from the FDA's Center for Biologics Evaluation and Research (CBER) evaluate the application. CBER is the FDA office responsible for vaccines, so they directly and formally oversee the vaccine review in both the EUA and BLA pathways.

Public meeting: The FDA convenes a public meeting of its VRBPAC to go over the data from the clinical trials. The VRBPAC is typically consulted for both EUA and BLA submissions. Although the FDA isn't required to consult their advisory committees, they typically do for major decisions, such as authorization of COVID-19 vaccines.

EUA decision: After the advisory committee meeting, CBER's staff will consider the members' input and continue their evaluation. If the FDA determines the criteria for EUA are met, the vaccine will be authorized for emergency use.

Continued monitoring: Manufacturers are expected to have a plan for active follow-up for safety, including deaths, hospitalizations, and other serious adverse events among those who receive the vaccine under an EUA. This includes participation in VAERS. Vaccine-makers are also expected to continue their clinical trials to gain additional information on safety and effectiveness and to pursue full FDA approval of their vaccine.

How long, on average, does full FDA approval take compared with EUA?

According to one study, over the past decade, the FDA approved 21 vaccines, mostly for flu or meningococcus. The median clinical development period (meaning from a Phase I trial to approval) was just over 8 years, including a median FDA review period of about a year.

For comparison, the COVID-19 vaccine from Pfizer-BioNTech, which was the first to receive an EUA, was under clinical development for six months before it submitted its EUA. An EUA was granted in less than a month; full approval was issued eight months later.

If EUA is essentially the same process, only faster, what's the benefit of the full FDA approval process?

It's not really an "apples-to-apples" comparison.

In public health emergencies, the development process may be a little different. The world experienced—and is still experiencing—a global pandemic, which means there was an outpouring of resources and energy on one goal: developing vaccines and treatments against COVID-19.

To that end, early on the FDA provided clear communication to the pharmaceutical industry about the scientific data and information needed to ensure the timely development of vaccines. And among other efforts, the government developed a coordinated strategy involving its own agencies, academia, nonprofit organizations, and pharmaceutical companies to prioritize the development of the most promising vaccines.

That focus—and the resources applied to it—isn't typically available for every vaccine or medical product, especially those that fall outside of a public health emergency.

Also, the processes are not designed to be nimble. They're designed to give people confidence—and peace of mind—that products receiving FDA approval continue to be viewed as the gold standard of scientific rigor.

This article was medically reviewed by Jason L. Schwartz, PhD, an associate professor in the Department of Health Policy and Management at the Yale School of Public Health.