

COVID-19 Vaccine Approval Process Overview

November 2020

The purpose of this document is to provide state and territorial health officials with snapshot information about the COVID-19 vaccine approval process, vaccine candidates, and other information. Recently, FDA indicated it will likely approve a COVID-19 vaccine through an **Emergency Use Authorization** or a **Biologic License Application**.

Definitions

A [Biologic License Application \(BLA\)](#) is approved only if FDA determines there is substantial evidence of safety and effectiveness from adequate, controlled trials.

An [Emergency Use Authorization \(EUA\)](#) is used during an emergency to facilitate the availability of unapproved products that diagnose, treat, or prevent serious or life-threatening diseases. Standard for an EUA is the product “might be effective.” EUAs have historically been used to allow deployment of a medical countermeasure when known potential benefits outweigh known potential risks. The risk and benefit analysis can vary across populations.

FDA recently signaled that a COVID-19 vaccine may be approved through an EUA that utilizes standards much closer to that of a BLA. [FDA guidance released on Oct. 6, 2020](#), requires two months of follow-up after patients’ second vaccination prior to EUA approval.

An approximate timeline of the benchmarks for approval of a COVID-19 vaccine are as follows:

Phase 1 Trial	Involves 20 to 100 healthy volunteers. Assesses the safety, side effects, and immune response to the vaccine. The study also determines the most effective safe dose.
Phase 2 Trial	Involves several hundred volunteers . Assesses the safety and the ability to stimulate an immune response.
Phase 3 Trial	Involves thousands of volunteers . Assesses safety, efficacy, and common side effects. A control group is used to compare incidence of infection. Testing with a representative population sample is important for determining efficacy and safety.
Manufacture While Awaiting Approval	Large-scale production of COVID-19 vaccine candidates occurs during Phase 2/3 trials to ensure immediate availability of deployment if the candidate is proven safe and effective. If the vaccine does not meet pre-determined safety and efficacy standards, the manufactured doses will be destroyed.
ACIP Work Group	The Advisory Committee on Immunization Practices (ACIP) COVID-19 Work Group meets weekly to review data from Phase 1, 2, and 3 trials. Once Phase 3 data is available, the group will conduct an independent review of safety and efficacy data using the Evidence to Recommendations (EtR) framework and Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method. The

work group will then present policy options to the full ACIP. ASTHO has representatives on both the COVID-19 Work Group and the full committee.

EUA Application and Review

Once Phase 3 data becomes available, the pharmaceutical company will submit an application to FDA for an EUA. FDA will then begin a [review of application](#).

FDA career scientists will review the application. The Vaccines and Related Biological Products Advisory Committee (VRBPAC) will hold a meeting and advise FDA. To come to a determination, VRBPAC will review and evaluate data concerning the safety, effectiveness, and appropriate use of the vaccine candidate.

After determining whether the “vaccine will cause more benefit than harm,” FDA will decide if a EUA shall be granted.

ACIP Review

After an EUA is submitted, ACIP will hold an emergency meeting with a public comment session to review safety and efficacy data using ETR/GRADE. ACIP will vote on recommendations for the vaccine and prioritization of vaccine within populations. ACIP will submit its recommendations to the CDC director.

CDC Review

ACIP recommendations will be submitted to the CDC director for publication in the Morbidity and Mortality Weekly Report (MMWR). The Affordable Care Act requires most health insurance plans to cover ACIP-recommended vaccines without cost sharing. Health plans have one year from MMWR publication to implement recommendations according to CDC immunization schedules. This would not include grandfathered plans or out-of-network providers. Some plans may consider local health departments to be out-of-network providers.

Note: While a vaccine may receive approval through an EUA for use within a specific population, the manufacturer will continue monitoring Phase 3 trials, providing and analyzing data. This expanded data set will be submitted to FDA as a BLA for coverage of broader demographic groups than originally covered in the EUA.

Vaccine Candidates Currently in Phase 3 Trials in the United States

Currently, four vaccines are in Phase 3 clinical trials. Operation Warp Speed has funded two additional vaccine candidates that have not yet entered Phase 3. Below is a snapshot of this information. For additional context please view *The New York Times'* [up-to-date tracker](#), which displays the status of vaccine candidates.

- [Moderna / NIH](#)
 - o mRNA vaccine.
 - o Requires frozen (-20 C^o) temperature storage.
 - o Two injections, 28 days apart.
 - o Phase 1 and 2 trials were underway in January and March 2020.
 - o Phase 3 testing began July 2020 with 30,000 healthy volunteers.
 - o Shared safety protocol information.

- [Pfizer / BioNTech](#)
 - o mRNA vaccine.
 - o Two doses, 21 days apart.
 - o Requires ultra-cold temperature (-70 C^o) storage.
 - o Phase 1 and 2 began in May on two versions of the vaccine.
 - o Phase 2 and 3 trials began July 27 with 30,000 volunteers.
 - o Announced expansion of trial to 43,000 participants on Sept. 12.
 - o Expect to manufacture 1.3 billion doses of the vaccine worldwide by end of 2021.

- [AstraZeneca](#)
 - o Chimpanzee adenovirus, ChAdOx1.
 - o Two doses, 28 days apart.
 - o Phase 1 and 2 trials completed.
 - o Phase 2 and 3 trials are underway.
 - o Global trials were halted on Sept. 6 when a volunteer developed transverse myelitis.
 - o British and Brazilian resumed on Sept. 12.

- [Johnson & Johnson](#)
 - o Adenovirus 26 method.
 - o Two doses.
 - o The first dose [utilizes the same platform](#) that was successful for Johnson and Johnson's Ebola vaccine.
 - o Phase 1 and 2 began in July.
 - o Phase 2 and 3 launched in September with up to 60,000 participants.
 - o Aiming for production of at least a billion doses in 2021.

Important Announcements and Deadlines

Below are links to resources and meeting announcements relevant to the COVID-19 vaccine approval and distribution process:

- CDC released Version 2 of the [COVID-19 Vaccine Program Interim Playbook](#) on Oct. 29.
- On Oct. 2, the National Academies of Medicine released its [Framework for Equitable Allocation of COVID-19 Vaccine](#). This framework was provided to ACIP to help determine which populations should be prioritized to receive the first vaccinations.
- State preliminary distribution plans were submitted to CDC on Oct. 16.
- On Oct. 22, [VRPBAC met](#) to discuss how the EUA process will work for the COVID-19 vaccine.
- HHS released [Answers to National Governor Association Questions on Vaccine Distribution and Planning](#) on Oct. 30.
- FDA released [Emergency Use Authorization for Vaccines to Prevent COVID-19 \(Guidance for Industry\)](#) in October.