

WHY THIS MATTERS

SARS-CoV-2 causes COVID-19, and developing a vaccine could save lives and speed economic recovery. The United States is funding multiple efforts to develop vaccines. Developing a vaccine is a complicated process that is costly, typically requires 10 years or more, and has a low success rate, although efforts are underway to accelerate the process.

SCIENCE & TECH SPOTLIGHT:

COVID-19 VACCINE DEVELOPMENT

THE TECHNOLOGY

What is it? Vaccines protect people from disease by triggering the immune system to produce antibodies that will fight the pathogen attacking the body. In the case of COVID-19, the pathogen is the virus SARS-CoV-2. Developing a vaccine is an expensive, lengthy process that involves a rigorous series of steps to first identify a potential vaccine “candidate” and then assess it for safety and effectiveness.

How does it work? A vaccine can use a virus that has been modified to be safe or a molecule that resembles a part of the virus. Once antibodies are produced, if the vaccinated person is exposed later to the virus, their body will produce those antibodies again, increasing their chances of fighting off infection.

Development starts with identifying a “target,” such as a protein, that can induce an immune reaction. Researchers create a vaccine candidate similar to that target that will induce production of antibodies effective against the virus. The vaccine candidate is then moved through phases of development, assessment, and approvals (fig. 1).

Under normal circumstances, the entire process typically takes 10 to 15 years, with more than 65 percent of candidates failing, according to an MIT study. There is an effort to expedite this process for SARS-CoV-2. As of May 15, 2020, there are more than 110 COVID-19 vaccines in development globally; of those, at least three are being developed in the United States with federal funding. These three use different mechanisms to prompt the body to produce antibodies (fig. 2).

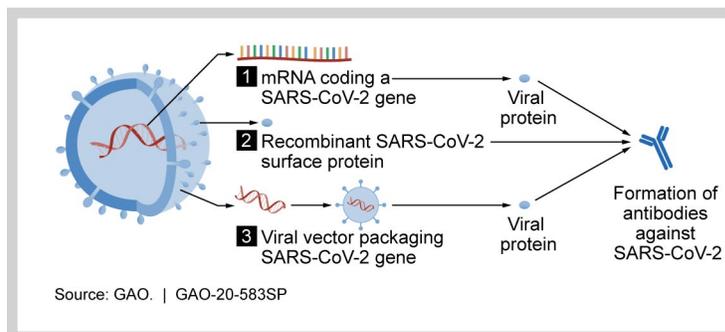


Figure 2. Vaccine candidates use different mechanisms, such as those shown above, to prompt the body to produce antibodies against SARS-CoV-2.

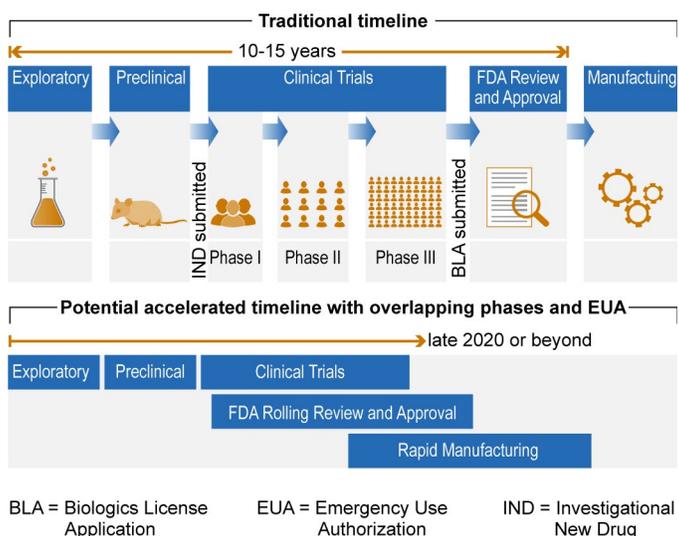


Figure 1. The vaccine development process typically takes 10 to 15 years under a traditional timeline. Multiple regulatory pathways, such as Emergency Use Authorization, can be used to facilitate bringing a vaccine for COVID-19 to market sooner.

The first candidate, developed by National Institute of Allergy and Infectious Diseases scientists and their collaborators, uses a molecule called mRNA specifically coded to generate proteins that will induce an immune response. This is a newer method of vaccine development that has shown promise in animals during the preclinical phase.

The second candidate uses a recombinant protein, which is produced by genetically engineering bacteria or other cells to produce a protein that mimics part of the spike protein found on the surface of the SARS-CoV-2 virus. The spike protein alone does not cause an infection but may be sufficient to produce an immune response. Recombinant protein vaccines are already being used successfully against other viruses, such as the human papillomavirus (HPV), which can cause cervical cancer.

The third candidate uses a virus—adenovirus 26, or Ad26—but researchers have removed its infectious aspects, making it safe as a “vector” to deliver a piece of SARS-CoV-2 to trigger a protective immune response. This method is also in clinical trials against HIV and Ebola.

How mature is it? The process for developing a new vaccine as outlined by the Food and Drug Administration (FDA) is well established. In the exploratory phase, the target and candidate vaccine are identified. In the preclinical phase, researchers use cells and animals to assess safety and produce evidence of clinical promise, evaluated by the candidate’s ability to elicit a protective immune response.

During clinical trials, more human subjects are added at each successive phase. Safety, efficacy, proposed doses, schedule of immunizations, and method of delivery are evaluated.

The next phase is FDA approval and licensure, which includes oversight of manufacturing and postmarket surveillance, and may include Phase IV trials to monitor safety and efficacy, potency, purity, and other potential uses.

At any phase, the process can be terminated for various reasons including detection of adverse events, such as serious side effects.

FDA has four programs to facilitate and expedite the review and approval of new therapies for the treatment and prevention of serious or life-threatening conditions, such as COVID-19. Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review allow for expedited processes, such as overlapping vaccine development phases, to bring vaccines to market more quickly. Vaccine developers could potentially use any or all of these programs for vaccine candidates in the United States.

FDA can also issue Emergency Use Authorizations (EUA) for review of vaccine candidates that have not completed all phases of development if there is sufficient scientific evidence on the product's safety, effectiveness, risks, and benefits.

/// OPPORTUNITIES

Several technologies and initiatives offer opportunities to accelerate vaccine development. For example:

- **Genomic tools.** Tools that provide information about a pathogen's genetic makeup can reduce the length of time for target selection.
- **Collaboration and partnerships.** The National Institutes of Health's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) effort is a public-private partnership intended to provide a collaborative framework for vaccine development.
- **Multiple vaccine mechanisms.** Simultaneous testing of multiple vaccine mechanisms can improve the chances of developing a successful vaccine faster.

/// CHALLENGES

- **Virus mutations.** RNA viruses, such as SARS-CoV-2, can mutate and potentially reduce or eliminate a vaccine's effectiveness, potentially creating a need for new vaccines.

- **Risk from accelerated process.** According to FDA, accelerating vaccine development could increase risk of adverse effects, since less time would be allocated to proving safety and effectiveness.
- **Manufacturing and supply issues.** Some production process and materials needs vary by vaccine type, complicating early expansion of manufacturing. Increasing export restrictions, dependence on imported supplies, and competition for materials may constrain access to supplies.

/// POLICY CONTEXT AND QUESTIONS

- What mechanisms could be used for quickly scaling up vaccine manufacturing, production, and distribution?
- If a vaccine becomes available, who will have priority to be vaccinated? How will the vaccine be purchased and distributed, particularly if distribution requires special handling (e.g., maintaining a specific temperature)?
- How could vaccines developed or manufactured internationally be made more accessible for use within the United States?
- If a vaccine is not developed and widely available soon, what preparations are needed for a possible second wave of the COVID-19 outbreak this fall and winter?

/// SELECTED GAO WORK

In addition to ongoing work that will provide additional details on this topic, GAO has previously issued the following products related to vaccines and FDA's expedited processes:

- Drug Safety: FDA Expedites Many Applications, But Data for Postapproval Oversight Need Improvement, [GAO-16-192](#).
- Influenza Vaccine: Federal Investments in Alternative Technologies and Challenges to Development and Licensure, [GAO-11-435](#).

/// SELECTED REFERENCES

Department of Health and Human Services. Food and Drug Administration. *Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics*. Silver Spring, MD: 2014.

Le, Tung T., Zacharias Andreadakis, Arun Kumar, Raúl G. Román, Stig Tollefsen, Melanie Saville, and Stephen Mayhew. "The COVID-19 vaccine development landscape." *Nature Reviews Drug Discovery*, vol. 19 (2020): pp. 305-306.

GAO SUPPORT:

GAO meets congressional information needs in several ways, including by providing oversight, insight, and foresight on science and technology issues. GAO staff are available to brief on completed bodies of work or specific reports and answer follow-up questions. GAO also provides targeted assistance on specific science and technology topics to support congressional oversight activities and provide advice on legislative proposals.

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Staff Acknowledgments: Karen Howard, PhD (Director); Sushil Sharma, PhD, DrPH (Assistant Director); Laura Holliday (Assistant Director); Chi Mai, PhD (Analyst-in-Charge); Louise Fickel; Eliot Fletcher, PhD; Anika McMillon; and Cindy Korir-Morrison, PhD.

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