COVID-19 Vaccine Development and Approval

The vaccine approval process is an extensive, phased process that, under normal circumstances, takes years to complete. As millions of lives are being lost around the world due to COVID-19, the global vaccine development effort has moved full speed ahead, leaving many to wonder if safety has been compromised as a result. This resource explains the COVID-19 vaccine development process and how these vaccines have been developed at unprecedented speeds, without compromising safety.

Steps in the COVID-19 vaccine development and approval process

Scientists Develop Vaccine Candidates: Vaccine platform selected (e.g., subunit vaccine, viral vector, mRNA) and designed to induce an immune response against SARS-CoV-2 virus

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Preclinical Trials: Investigations in animals, leading up to viral-challenge studies in nonhuman primates

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Clinical Trials: Under investigation in human volunteers for safety and efficacy in three phases; compared against a control group

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Review by FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC): A committee of independent health experts who review the scientific evidence and evaluate safety, efficacy, manufacturing quality, and conditions for use

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FDA Emergency Use Authorization (EUA): A temporary access mechanism used during public health emergencies

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CDC Advisory Committee on Immunization Practices (ACIP) Recommendation: A committee of independent health experts who review available data to make recommendations about vaccine use and prioritization

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Allocation and Distribution: The vaccines become available to the public. When supplies permit, pharmacists order and administer the vaccine to priority patients based on CDC ACIP and state allocation and recommendation plans.

Ongoing Safety Monitoring: Multifaceted programs provide ongoing monitoring and reporting (e.g., VAERS, Vaccine Safety Datalink, V-SAFE, and other systems).

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Biologics License Application: Vaccines that receive an EUA still need to undergo full review in the same way as all vaccines licensed by FDA's Center for Biologics Evaluation and Research (CBER).

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Quick Links

- APhA: COVID-19 Vaccines in Development Webinar
- APhA: COVID-19 Vaccine Clinical Trial Process Webinar
- FDA: Vaccines in Development 101
- FDA: The Path for a COVID-19 Vaccine from Research to Emergency Use Authorization
- CDC: COVID-19 Vaccination
- HHS: Fact Sheet: Explaining Operation Warp Speed
- NEJM: Developing COVID-19 Vaccines at Pandemic Speed
- *New York Times:* Coronavirus Vaccine Tracker

Vaccine Development

How is it possible that vaccine candidates were developed so quickly?

1. **SARS-CoV-2, the virus that causes COVID-19 disease, may be new. But coronaviruses are not.** COVID-19 is very similar to the coronaviruses responsible for Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), so scientists were able to leverage previous research on coronaviruses, other viruses, and various vaccine technologies to identify dozens of vaccine candidates quickly.
2. **Unprecedented financial support from governments around the world** empowered scientists to tap into innovative vaccine technologies and removed the financial risk normally involved in vaccine development.
3. **The sheer number of vaccine candidates is one of the reasons we expect to have an approved COVID-19 vaccine available to the public in record time.** More than 50 vaccines are in clinical trials on humans around the world, and almost two times as many are in preclinical trials, where vaccine candidates are under investigation in animals.

What are the different types of SARS-CoV-2 vaccines, and why are they different?

Several different vaccine types are being evaluated as COVID-19 vaccines. How vaccines stimulate an immune response can vary depending on the type of vaccine it is.

- **mRNA Vaccines** deliver a short segment of RNA that acts as a kind of blueprint, so that the body will make a protein that is part of the virus.
- **Protein-based Vaccines** use a part of the virus, such as a protein from the virus's surface, to evoke an immune response.

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- **Inactivated Vaccines** are made using chemicals to kill the virus, which prevents the virus from multiplying when injected to stimulate an immune response.
- **Viral Vector Vaccines** take a part of the coronavirus and insert it into another harmless virus to deliver the blueprint for a protein that the body makes itself.

The mRNA platform is new. How can we know that the Pfizer/BioNTech and Moderna vaccines are safe?

The Pfizer/BioNTech and Moderna vaccines are both mRNA vaccines—a novel vaccine type that uses the "blueprint" for SARS-CoV-2 spike protein in the form of mRNA. While no mRNA vaccines have been licensed so far, mRNA vaccines and treatments have been studied for over 15 years.

Vaccine Approval

How is it possible for these vaccines to be approved so quickly?

1. **Governments took the financial risk.** Under normal circumstances, vaccine approval follows a step-by-step process that is designed to balance safety and efficacy with prudent financial investment. One of the major reasons the usual process takes a long time is that the company developing the vaccine must manage the costs involved. Since the global economy hinges on our ability to vaccinate against COVID-19, governments and the private sector took unprecedented financial risks to support promising vaccines, even though they may have to waste effort or discard products if a vaccine is not proven to be safe and effective.
2. **Process improvements.** FDA has allowed for some steps in the vaccine approval process to be conducted simultaneously without additional safety risks.

Were clinical trials conducted differently?

Each vaccine goes through three phases of clinical trials before licensure and approval and safety monitoring continues in a fourth phase of the vaccine life cycle. As described above, these phases typically take a number of years, largely due to cost mitigation. During the pandemic, developers still conducted all three phases of clinical trials and were empowered to conduct these phases simultaneously.

>> **Phase 1:** Emphasis is on assessing safety; includes 20–100 otherwise healthy volunteers who haven't been exposed to the virus.

>> **Phase 2:** In the absence of safety concerns from Phase 1 studies, Phase 2 studies include more people. Various dosages are tested on hundreds of people with varying health statuses and demographic groups. These studies provide additional safety information, as well as preliminary information on effectiveness.

>> **Phase 3:** The vaccine is generally administered to thousands of people, and the study generates critical information on effectiveness and additional important safety data.

>> **Phase 4:** After vaccine release with licensure and approval, monitoring continues after vaccine release. Additional analysis is done regarding coadministration with other vaccines, use in other age groups, etc.

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How is an Emergency Use Authorization different than the normal vaccine licensure process?

Normally, a biologics license application (BLA) is submitted to FDA and reviewed by FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC). During the COVID-19 public health emergency, FDA can issue an emergency use authorization (EUA) to facilitate the availability of various products. FDA has already used EUA authority to give early access to COVID-19 diagnostic tests, convalescent plasma, remdesivir, and monoclonal antibodies. An EUA is a regulatory option for a vaccine once the developer has accumulated enough scientific evidence for efficacy, safety, and product quality. The EUA only lasts during the emergency and is reviewed by the FDA periodically for safety. Later, the developer must seek full approval via BLA as they achieve certain data targets. For more information, see FDA's EUA for Vaccines Explained.

What is the CDC Advisory Committee on Immunization Practices role?

CDC's Advisory Committee on Immunization Practices (ACIP) is a group of independent medical and public health experts who carefully review all available data about the vaccine from clinical trials and other studies to develop recommendations for vaccine use. It advises the CDC Director.

What ongoing safety monitoring is being planned?

CDC is expanding safety surveillance through new systems and additional information sources, as well as by scaling up existing safety monitoring systems. Pharmacists should be aware of these systems and have a role in reporting adverse events. New safety monitoring systems include:

a. **CDC V-SAFE:** A new smartphone-based, after-vaccination data collection system for people who receive COVID-19 vaccines. V-SAFE will use text messaging and web surveys from CDC to check in with vaccine recipients and monitor their health.

b. **CDC National Healthcare Safety Network (NHSN):** An acute care and long-term care facility monitoring system with reporting to the Vaccine Adverse Event Reporting System (VAERS).

c. **CDC and FDA Vaccine Safety Datalink (VSD) and other large insurer/payer databases:** A system of administrative and claims-based data for surveillance and research.

For more information about these new systems as well as existing safety monitoring systems, like the Vaccine Adverse Event Reporting System (VAERS), visit CDC's Ensuring the Safety of COVID-19 Vaccines in the United States.