

COVID-19 Vaccines Under Development: Where are we?

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***No Relevant Financial Relationship
with Piedmont Healthcare or Companies
Discussed in the Presentation***





Agenda

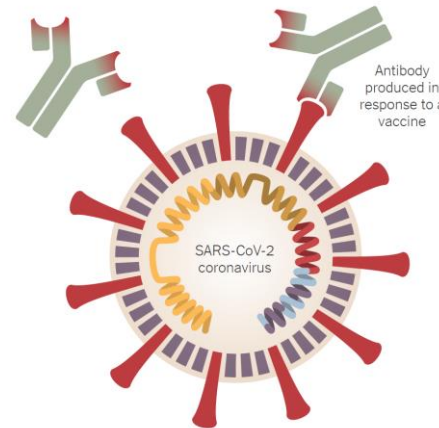
- Definitions
- Emergency Use Authorizations
- Vaccine Development & Clinical Trials
- COVID 19 Vaccine Development
 - Genetic Vaccines
 - Moderna Vaccine
 - Pfizer/BioNTech Vaccine
 - Viral Vector Vaccines
 - Protein Vaccines
 - Inactivated or Attenuated Vaccines



Definitions

What is a Vaccine?

- A **vaccine** stimulates the immune system to produce antibodies, exactly like it would if you were exposed to the disease. [CDC]
- A **vaccine** is a substance that helps in protecting against certain diseases. **Vaccines** contain a dead or weakened version of a microbe. It helps your immune system recognize and destroy the living microbe during a future infection. [Web MD]



<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>



Definitions

What is COVID-19?

- It is a coronavirus disease identified in 2019. Symptoms usually appear from 2-14 days after exposure to the virus.
- People with the following symptoms may have COVID-19
 - Fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea

What is an Emergency Use Authorization (EUA)?

- It is a legal mechanism in the US that allows FDA during a public health emergency to facilitate the availability of medical products.
 - Use of an unapproved medical product (e.g., drug, vaccine, or diagnostic device) or
 - Unapproved use of an approved medical product during an emergency to diagnose, treat, or prevent serious or life-threatening disease or condition
 - Emergency is caused by a chemical, biological, radiological, nuclear (CBRN) agents

Note: For current FDA information on COVID-19 go to <https://www.fda.gov/emergency-preparedness-and-response/counterterrorism-and-emerging-threats/coronavirus-disease-2019-covid-19>



Emergency Use Authorizations (EUA) Related to COVID 19

- **314 Diagnostics Authorized for Testing**
- **25 Personal Protective Equipment and Related Devices**
- **27 Ventilators and Other Medical Devices**
- **Drugs/Biologics**
 - Moderna COVID vaccine
 - Pfizer/BioNTech vaccine
 - Convalescent Plasma
 - Remdesivir (Veklury)
 - Casirivimab and Imdevimab combination
 - Baricitinib (Olmiant) in Combination with remdesivir (Veklury)
 - Bamlanivimab
 - REGIOCIT replacement solution that contains citrate for regional citrate anticoagulation (RCA) of the extracorporeal circuit
 - Fresenius Propoven 2% Emulsion (Fresenius Kabi) to maintain sedation for patients who require mechanical ventilation.
 - Fresenius Medical, multiFiltrate PRO System and multiBic/multiPlus Solutions

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



Vaccine Development

First-in-Human Trials

- As per FDA's COVID guidance toxicity studies from previously approved platforms for delivery of the vaccines if scientifically justified can be used as a surrogate to start clinical trials.
- FDA is willing to use draft toxicology reports to start clinical trials provided the reports are available within 120 days of the start of trials
- Identify a safe dose and dosage regimen in humans
 - No adverse effect level (NOAL) and safety factor
- Phase I – Healthy and diverse population considered to be low risk for severe COVID 19, people older than 55 are acceptable to be enrolled provided they do not have any other medical comorbidity
- Phase 2 or 3 trials – Placebo-controlled randomized trials in diverse population with one to two year follow-up.
- COVID-19 vaccine is effective, the **primary efficacy endpoint** for a placebo-controlled efficacy trial should be **at least 50%**, and the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate is >30%.
- **Data and Safety Monitoring Board** is monitoring the data coming out of the trials.

<https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders>



Phases in Clinical Trials

	Phase I	Phase II	Phase III	Phase IV
Primary Goal	<ul style="list-style-type: none"> Establish the overall safety 	<ul style="list-style-type: none"> Establish the activity of a drug for a specific group of patients with a specific disease 	<ul style="list-style-type: none"> Confirm the safety and effectiveness of a drug for a specific group of patients with a specific disease 	<ul style="list-style-type: none"> Monitor ongoing safety in large populations and uncontrolled use of drug
Secondary Goals	<ul style="list-style-type: none"> Establish the maximum tolerated dose Determine serious side-effects Determine the metabolism and pharmacologic actions of drugs 	<ul style="list-style-type: none"> Determine the common short-term side effects and risks. 	<ul style="list-style-type: none"> Evaluate the overall risk-benefit ratio 	<ul style="list-style-type: none"> Identify additional, unusual side-effects Identify additional potential uses of the drug

Ref: https://cisncancer.org/research/how_cancer_is_studied/clinical/ct_cytotoxic_therapies_02.html



US: ClinicalTrials.gov

Total of 4110 clinical studies on COVID-19

- Phase 1 – 378
- Phase 2 – 911
- Phase 3 – 552
- Phase 4 – 112

World Health Organization Database

- 3,369 studies on COVID-19

Ref: WHO Trial Registry Network:

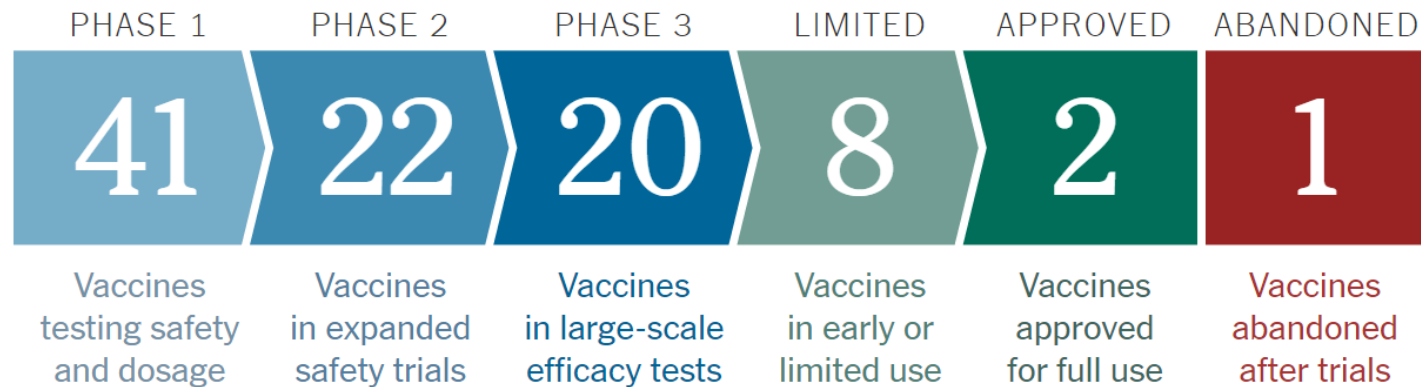
[COVID-19 studies from the ICTRP database](#)



COVID 19 Vaccines Development

Coronavirus Vaccine Tracker







By Carl Zimmer, Jonathan Corum and Sui-Lee Wee Updated Jan. 14, 2021



<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>



Leading Vaccines from Around the World

Developer	How It Works	Phase	Status
 Pfizer-BioNTech	mRNA	2 3	Approved in Saudi Arabia and other countries. Emergency use in U.S., E.U., other countries.
 Moderna	mRNA	3	Emergency use in U.S., E.U., other countries.
 Gamaleya	Ad26, Ad5	3	Early use in Russia. Emergency use in Belarus, other countries.
 Oxford-AstraZeneca	ChAdOx1	2 3	Emergency use in Britain, India, other countries.
 CanSino	Ad5	3	Limited use in China.
 Johnson & Johnson	Ad26	3	
 Vector Institute	Protein	3	Early use in Russia.
 Novavax	Protein	3	
 Sinopharm	Inactivated	3	Approved in China, U.A.E., Bahrain. Emergency use in Egypt.
 Sinovac	Inactivated	3	Limited use in China.
 Sinopharm-Wuhan	Inactivated	3	Limited use in China, U.A.E.
 Bharat Biotech	Inactivated	3	Emergency use in India.

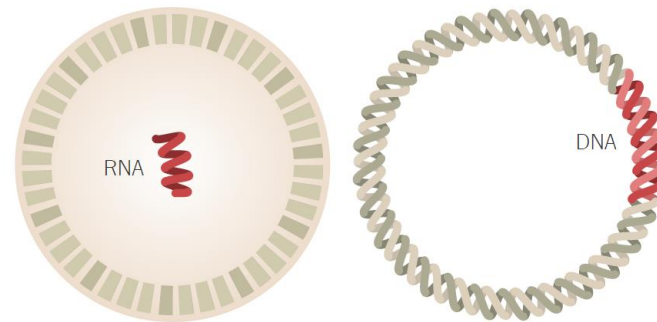
<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>



Genetic Vaccines

Vaccines that deliver one or more of the coronavirus's own genes into cells to provoke an immune response.

- DNA Vaccines – mRNA – protein (antigen) – antibodies and cell-mediated immunity
- RNA Vaccines (mRNA) - protein (antigen) – antibodies and cell-mediated immunity
- **COVID-19: Moderna and Pfizer/BioNTech Vaccine are mRNA vaccines that have the Emergency Use Authorization**



<https://www.fda.gov/vaccines-blood-biologics/consumers-biologics/vaccines-children-guide-parents-and-caregivers#types>
<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>



Moderna Vaccine

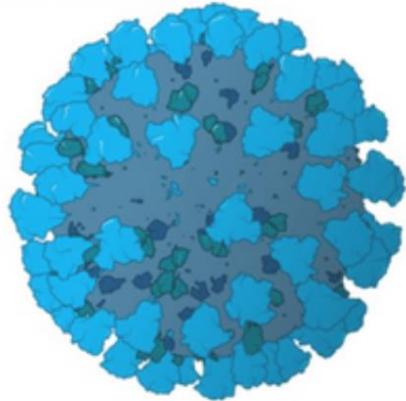
- The vaccine contains strands of mRNA for the spike protein that facilitates the entry of the virus into the cell.
- It is authorized for use for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in **individuals 18 years of age and older**.
- The Moderna COVID-19 Vaccine is a suspension for intramuscular injection administered as a series of two doses (0.5 mL each) **1 month apart**.
- A vaccination card is provided to the recipient or their caregiver with the date when the recipient needs to return for the second dose of the Moderna COVID-19 Vaccine.

Fact sheet: <https://www.fda.gov/media/144637/download>

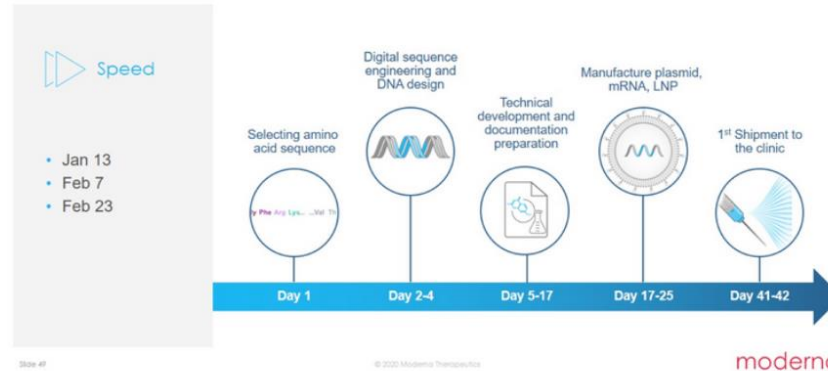


Schematic Diagram for Manufacturing the Moderna Vaccine

SARS-CoV-2 Antigen

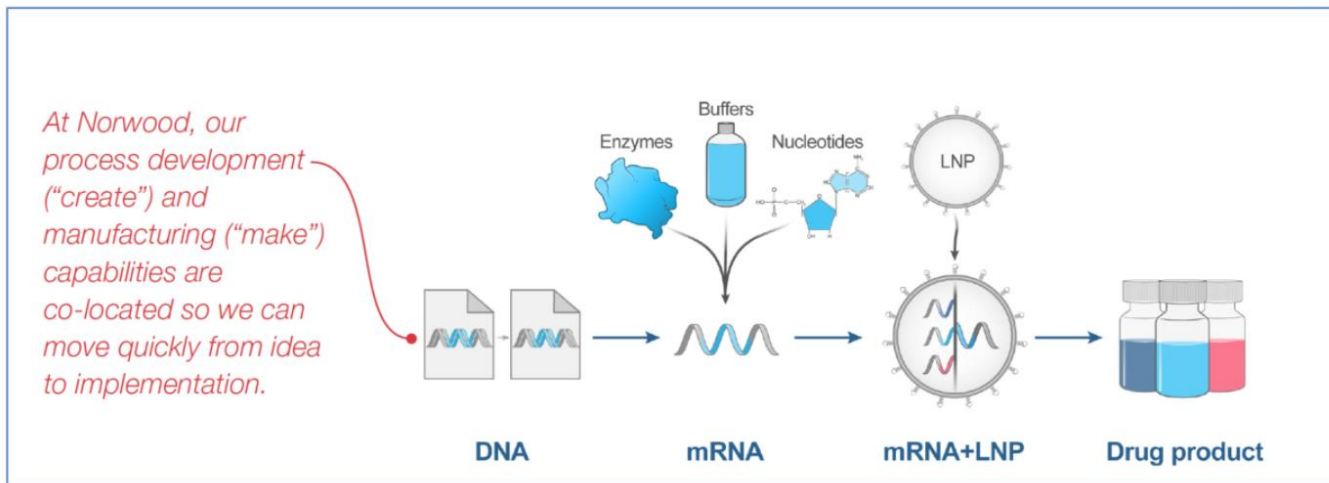


SARS-CoV-2



Each 0.5 mL dose of Moderna COVID-19 Vaccine contains 100 mcg of nucleoside modified messenger RNA (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2 virus.

Each dose of the Moderna COVID-19 Vaccine contains the following ingredients: a total lipid content of 1.93 mg (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine [DSPC]), 0.31 mg tromethamine, 1.18 mg tromethamine hydrochloride, 0.043 mg acetic acid, 0.12 mg sodium acetate, and 43.5 mg sucrose.



<https://ericbender.co/2020/03/12/modernas-vaccine-dream-machine/>



Moderna Vaccine

- The vaccine is supplied in multiple-dose vials and stored frozen between -25° to -15°C (-13° to 5°F). Store in the original carton to protect from light.
- Adverse reactions reported in a clinical trial following administration of the Moderna COVID-19 Vaccine includes pain at the injection site, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, axillary swelling/tenderness, fever, swelling at the injection site, and erythema at the injection site
- All providers of the vaccine have to commit to certain requirements such as reporting of adverse events to FDA, entering information into the state/local jurisdiction's Immunization Information system.

Fact sheet: <https://www.fda.gov/media/144637/download>



Pfizer/BioNTech Vaccine

- The vaccine contains strands of mRNA for the spike protein that facilitates the entry of the virus into the cell.
- The vaccine is authorized for use (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in **individuals 16 years of age and older**.
- The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a series of two doses (0.3 mL each) **3 weeks apart**.
- A vaccination card is provided to the recipient or their caregiver with the date when the recipient needs to return for the second dose of the Pfizer-BioNTech vaccine.

Fact Sheet: <https://www.fda.gov/media/144637/download>



Pfizer/BioNTech Vaccine

- The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen suspension in multiple dose vials; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine.
- Each dose of the Pfizer-BioNTech COVID-19 Vaccine contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2.
- Each dose of the Pfizer-BioNTech COVID-19 Vaccine also includes the following ingredients: lipids (0.43 mg (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.



Pfizer/BioNTech Vaccine

- The Multiple Dose Vials will arrive in thermal containers with dry ice. Once received, store in an ultra-low temperature freezer between -80°C to -60°C (-112°F to -76°F). Vials must be kept frozen between -80°C to -60°C (-112°F to -76°F) and protected from light until ready to use. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Do not refreeze thawed vials.
- Adverse reactions following the Pfizer-BioNTech COVID-19 Vaccine that have been reported in clinical trials include injection site pain, fatigue, headache, muscle pain, chills, joint pain, fever, injection site swelling, injection site redness, nausea, malaise, and lymphadenopathy. **Severe allergic reactions have been reported following the Pfizer-BioNTech COVID-19 Vaccine during mass vaccination outside of clinical trials.**
- All providers of the vaccine have to commit to certain requirements such as reporting of adverse events to FDA, entering information into the state/local jurisdiction's Immunization Information system.

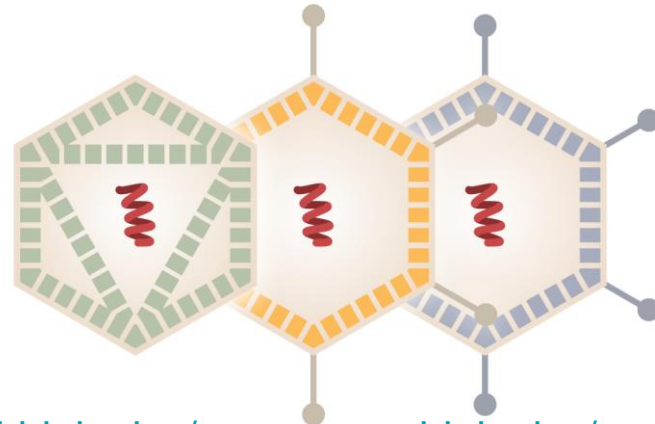
Fact Sheet: <https://www.fda.gov/media/144637/download>



Viral Vector Vaccines

Vaccines that contain viruses engineered to carry coronavirus genes.

- Viral vectors will invade cells and cause the cells to make viral proteins
- The coronavirus proteins go to the surface of the cells causing the immune response.
- **COVID-19: Russian Vaccine (Sputnik) approved for early use and a Chinese vaccine for special use by military; Astrazeneca/Oxford vaccine is approved for emergency use in UK and India. Johnson & Johnson vaccine is still in development**

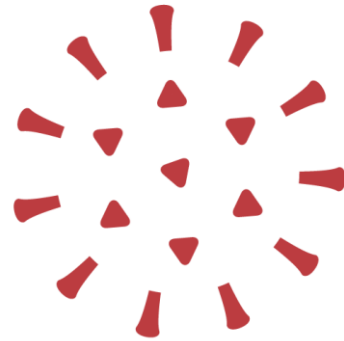


<https://www.fda.gov/vaccines-blood-biologics/consumers-biologics/vaccines-children-guide-parents-and-caregivers#types>
<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>



Protein-Based Vaccines

Vaccines that contain coronavirus proteins but no genetic material. Some vaccines contain whole proteins and some contain fragments of them.



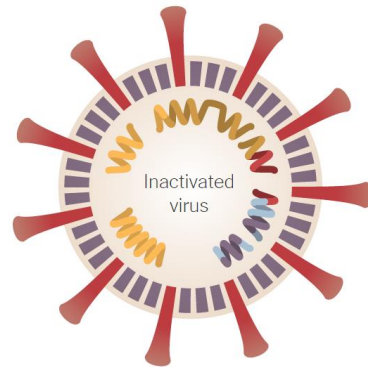
COVID-19: One approved for early use in Russia; Novavax vaccine is under development.

<https://www.fda.gov/vaccines-blood-biologics/consumers-biologics/vaccines-children-guide-parents-and-caregivers#types>
<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>



Inactivated or Attenuated Vaccines

Vaccines created from weakened coronaviruses or coronaviruses that have been killed with chemicals.



COVID-19: Inactivated vaccine approved for limited use in China and emergency use in India.

<https://www.fda.gov/vaccines-blood-biologics/consumers-biologics/vaccines-children-guide-parents-and-caregivers#types>
<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>



Competency Questions

- Quiz #1 – What type of COVID 19 Vaccines are currently authorized for use in the US?
 - a) Protein vaccines
 - b) Viral vector vaccines
 - c) Genetic vaccines
 - d) Inactivated or attenuated vaccines
- Quiz #2 – What are some of the major differences between the authorized vaccines?
 - a) Storage conditions
 - b) Minimum age
 - c) Duration between the two doses
 - d) All of the above



Resources

COVID Cases: <https://www.covid19.uga.edu/tracker.html>

Vaccine Tracker:

- <https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker>
- <https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>

Clinical Trials: <https://clinicaltrials.gov/ct2/results?cond=COVID-19>

WHO Trial Registry Network: <https://www.who.int/ictrp/network/en/>

Vaccines Basics: <https://www.cdc.gov/vaccines/basics/test-approve.html>

NIH: [COVID-19 Treatment Guidelines](#)

UGA College of Pharmacy COVID 19 Resources: <https://rx.uga.edu/about/college-of-pharmacy-coronavirus-covid-19-updates-and-resources/>





Thank You!
Q&A

