COVID-19 Vaccine Storage and Stability

Article Published: May 25, 2021 | Jennifer Welsh

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COVID-19 vaccines are here, they are headed out globally and the world is faced with a giant logistical task: keeping these vaccines in their desired storage conditions to ensure stability and efficacy of every dose that goes into an arm. This is an even more complex problem because some of these vaccines have requirements to be kept frozen or refrigerated for optimal safety and efficacy.

While many places in the US have had good success in administering vaccines at local drugstores, community centers or clinics, there are many places within the US and outside of it in which these cold-storage chains are not adequate.

Many middle- and low-income countries do not have adequate storage facilities. In warmer areas of the world, including South America, Asia and Africa, the challenge of keeping things cold is even greater, especially in remote villages or areas off the grid.[1] This means that their options for COVID-19 vaccines are limited.

COVID-19 vaccine storage and stability

There are several different types of COVID-19 vaccines that have been – or are in the process of – receiving Emergency Use Authorization (EUA) (Table 1). Each vaccine has unique storage requirements, and as companies conduct more testing, we are seeing these requirements be updated continually.

Two different types of vaccines are being distributed across the US. This includes two mRNA vaccines created by Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273). These vaccines deliver a dose of viral mRNA, which our cells turn into viral proteins. The immune system reacts to these proteins, mounting a defense that lets us fight off the infection the next time we come into contact with it. The issue with these vaccines is that the mRNA molecules are fragile. In the vaccine they are encased in a lipid-based bubble to keep them safe, but this fragility means they must be kept cold to retain their efficacy.

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The second major type of vaccine we are seeing used against COVID-19 is the adenovirus vector-based vaccines, like Johnson & Johnson's Janssen one-shot COVID-19 vaccine (Ad26.COV2-S [recombinant]) and Oxford/AstraZeneca's Vaxzevria.[2,3] These use a non-dangerous virus that has been genetically engineered to not cause symptoms. The virus presents SARS-CoV-2 genes to the body's cells. The genes are transcribed into proteins and presented to the immune system, which mounts a defensive response against SARS-CoV-2. Because the genetic sequence is contained within a virus, it is potentially more stable than a naked piece of mRNA and can be stored at fridge temperatures.

A third type of vaccine on the horizon is the protein subunit vaccine by NovaVax. The vaccine is not yet approved by the Food and Drug Administration (FDA) or other regulatory authorities, however it is expected to be approved in the third quarter of 2021. Subunit vaccines only include SARS-CoV-2 proteins, not any of the genetic material of SARS-CoV-2 or any other virus, so they are stable at refrigerated temperatures, according to NovaVax. However, because the vaccine is not yet approved for emergency use, we do not have specifics on its storage and stability requirements.

Table 1. A summary of some of the different types of approved COVID-19 vaccines and their storage requirements.[4,5,6,7,8]

ⓘ Please use the scroll bar at the bottom of the table to view more.

Type	Vaccine	Shipping	Storage	Stability

mRNA	Moderna	Shipped and delivered at a temperature of -20 °C.	Can be stored for up to three3 months in the refrigerator at 2-8 °C. Can be stored in the freezer (-50 °C to -15 °C) for 7 months.	Stable for up to 24 hours at room temperature.
	Pfizer/BioNTech	Shipper containers can be stored for up to 10 days at 15-25 °C without opening.	Vials can be stored in the refrigerator at 2 °C to 8 °C for up to 1 month. Previously, thawed, undiluted vaccine vials could be stored in the refrigerator for up to 5 days.	After diluting, the vaccine is stable for up to 6 hours at 2-8 °C or room temperature.
Adenovirus	J&J	Shipped at 20 ° C.	Can be stored at -20 °C for 2 years. Can be stored for up to 3 months in the refrigerator at 2-8 °C.	After being punctured, the vial can be stored in the refrigerator for up to 6 h.
	AstraZeneca/Oxford		It can be stored in the refrigerator 2-8 °C for up to 6 months.	

“Each COVID vaccine requires different storage conditions, whether it's in the same category or not,” Michelle Holm, PharmD, MPH a pharmaceutical contract portfolio manager in supply chain management at Mayo Clinic, said. “Some vaccines have to be refrigerated, some vaccines come frozen and all vaccines can be stored at room temperature, for specific amounts of time based on each vaccine’s EUA criteria.”

The companies that create these vaccines determine their required storage and stability conditions based on the clinical trial data. During development, they test the vaccine after storage in different conditions to determine if there are any changes in efficacy, loss of active pharmaceutical ingredients and whether the solution has grown any microbes.

“These storage conditions are based on how the drug manufacturer conducted the clinical trials. Pfizer tested and verified ultra-cold storage as the best mechanism to assure its safety and efficacy while ensuring no bacteria would be present in the vials,” Holm said. “And it worked, Pfizer was the first to receive EUA approval.”

After approval, the companies can continue testing to see if the storage and stability conditions can be updated. They then send updated details to the FDA, which reviews the data and determines if these new storage requirements are approved.

Moderna and Pfizer have already updated their storage requirements, Holm said: “Moderna has doubled the amount of time that their vaccine can be kept outside of the refrigerated space and Pfizer recently announced their undiluted vaccine could be kept in a refrigerated space for up to one month. Pfizer’s previous refrigerated storage requirement was a maximum of five days. Expanded storage requirements are great news for low- and middle-income countries, as well as areas in the United States that don't have access to ultra-cold storage or a plethora of refrigeration options.”

Why vaccine storage matters

The storage and stability features of a vaccine influence how long it can be stored, where it can be stored, who can get a given vaccine and how quickly it needs to move from manufacturing and testing into the patients’ arms.

For mass vaccination, clinics want to work in an assembly-line style to make it quick and easy for patients to get in and get on with their day. To do this, clinics will prefer to draw up an entire vial of vaccine into syringes ready to go for incoming patients. How long the vaccine can sit in those syringes, either in a refrigerator or at room temperature, is the big question. The goal is to have it stable at room temperature for as long as possible.

“The room temperature stability in the syringe is as important as it is in the vial. The extended room temperature stability allows health care professionals the ability to draw up all of the syringes from one vial at one time,” Holm said. "Health care professionals can draw syringes up ahead of time and have them ready to go when the patient arrives. An efficient process is crucial to ensure as many people can be vaccinated in the shortest amount of time therefore the ability to store syringes for longer periods of time at room temperature is vital.”

If the vaccines are not stored correctly, that could impact the vaccine’s efficacy or even lead to contamination. “With the lack of preservatives, the drug companies and the FDA are validating temperature storage frequently to assure increases in room temperature storage continue to provide safe and efficacious vaccine for the public," Holm said. “When you see an article stating, ‘a certain number of doses had to be thrown away because they were removed from the required storage parameters from a greater length of time than allowed’, it is in the public's best interest to discard them so no one receives a vaccine that wouldn't be efficacious and safe.”

The focus on safety starts during vaccine manufacturing and continues through the

clinics and drug stores until the vaccine is administered.

"The FDA monitors the manufacturing plants closely and verified procedures are being followed on a regular basis," Holm said. "If the guidelines and protocols are not followed, the FDA can site the plant and/or shut it down based on the violation. By adhering to the manufacturing guidelines set forth in the EUA, no dose will be administered to a patient that was inappropriately stored or inappropriately manufactured."

When the vaccines are distributed from the manufacturing, testing and quality control plants and enter the distribution chain, they are equipped with specialized temperature monitors to ensure the cold chain is kept intact. The packaging has special QR codes and labels to ensure every dose is stored correctly throughout the journey from plant to needle.

A cold-chain mountain to climb

Updating and improving the stability of these vaccines is essential to overcome the COVID-19 pandemic, Holm said: "To truly get herd immunity, the entire world needs access to the vaccines, not just the US or first-world countries."

Haiti, for example, is the poorest country in the Western Hemisphere, and refrigeration is dependent on the electrical grid. "The grid can go on and off multiple times per day," Holm said. "Globally, we need to continually study how to develop vaccines that can be stored at room temperature for longer periods of time to ensure countries like Haiti have the opportunity and access to them as we have had in the US."

It is not just getting the doses into arms – as of now, the vaccine has to be kept cold through the entire chain of transport. "The process of importing the vaccine into the country, moving it from the airport into the cities and into rural communities, that is the challenge we need to be aware of, understand, and provide support to other countries as we fight this global pandemic," said Holm.

Also, freezers that can store vaccines at -70 °C are very expensive, and there is currently a shortage of them. "Ultra-cold freezers cost around $10,000 each... how many community centers, rural areas and low- and middle-income countries can afford a $10,000 freezer?" Holm said. "There are many places that did not receive the Pfizer vaccine – many nursing homes and long-term care facilities in the US chose to vaccinate with the Moderna vaccine due to the lack of access to an ultra-cold freezer."

Without an ultra-cold freezer, keeping the vaccine cold depends on access to dry ice, frozen carbon dioxide at -78.5 °F. If you add dry ice to Pfizer's shipping containers, they can keep the vaccine stable for up to 35 days, but that requires access to this specialized chemical.[9] "Dry ice is in shortage even in the US," Holm said.

With additional innovation in storage containers, plus additional testing and updates to the requirements for storage and stability of these vaccines, we will hopefully be vaccinating the entire world soon. The wide variety in types of vaccines created against SARS-CoV-2 and new ways of administering them is a hopeful indication that we will quickly have vaccines that will work in every part of the world — not just those areas with ultra-cold storage facilities.

About the author

Jennifer Welsh is a Connecticut-based science writer and editor with several years of bench work in cancer research and anti-viral drug discovery under her belt. She has previously written for Science News, The Scientist, Discover Magazine, LiveScience and Business Insider.

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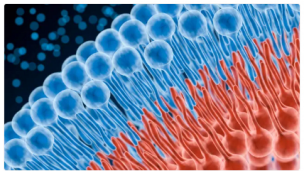

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