



Keeping Vaccines Safe: Cold Chain Monitoring During COVID-19 and Beyond

Cold storage has long been a fixture in food distribution. By 1900, compression refrigeration replaced ice harvesting in most applications. In the 1930s, mechanically refrigerated trucks debuted, and cold chain distribution launched at scale. Fleets of trucks kept perishables, such as food and medicine, cold as they moved anywhere. Soon, the need for cold chain monitoring at all points and with more items like pharmaceuticals became evident.

Cold chain monitoring has two objectives. First is monitoring storage conditions to maximize quality and shelf life. Second is identifying if a temperature excursion occurs, and ideally when and where, to contain and correct problems and ensure consumer safety. Four cold storage points are common: “banana” (13°C), chill (2°C), frozen (-18°C), and deep frozen (-29°C)¹.

Today, cold chain complexity is increasing. Pharma items like COVID-19 vaccines carry tiered storage requirements. Vaccines must stay at precise temperatures from manufacturing to point of use (POU). Effective cold chain monitoring

implies technology and process work together. Failures at any point in a vaccine cold chain can be costly and hazardous. Here, we’ll look at the brief history of cold chain in pharma and the key requirements for COVID-19 vaccines. Then, we’ll see how IoT technology enables configurable, scalable, real-time cold chain monitoring.

Stakes rising for pharma cold chain monitoring

Before the onset of World War II, cold chain operations were in-house. Each local food distributor oversaw handling of perishables in their network. Fighting a global conflict and rebuilding afterwards called for moving food and medical supplies across continents quickly. Third-party logistics companies appeared in the 1950s with growing opportunities in regional and national networks. More hands and longer distances meant distributors began losing sole control of their cold chain².

Pharmaceuticals also entered a growth phase during the 1950s. Initial large-scale global



Image courtesy Pfizer

vaccination efforts scored successes against diseases like smallpox and polio. Those wins stimulated demand and investments. Longer distances, more transport modes, and higher volumes became routine for lower risk cold chains. But high-value goods like biologics and vaccines stressed pharma cold chain technology.

Growth in pharma cold chains has increased the stakes. In 2020, \$341B of pharma products flowed through cold chains, with estimates showing a 48% CAGR. A 2019 study by IQVIA shows direct pharma product losses of \$15B during temperature excursions. Add in replacement products and root cause analysis of failures, and the amount rises to \$35B. ^{3, 4}

Those figures alone justify improved pharma cold chain monitoring. Yet, COVID-19 has renewed attention on the concept. Many new vaccines are entering markets, some with messenger RNA (mRNA) needing ultra-cold storage at -70°C. mRNA instructs human cells to produce pieces of spike protein found on the surface of some viruses like ones causing COVID-19. It is extremely

fragile and breaks down quickly with improper handling, losing its potency. ^{5, 6}

Billions of mRNA-based vaccine doses in production highlight the need for better solutions in cold chains. Process alone cannot manage growing transit and storage risks. Organizations are now searching for enhanced, automated pharma cold chain monitoring technology.

mRNA-based vaccine cold chain requirements

Common vaccines, such as for the flu, need only basic refrigeration. mRNA-based vaccines introduce tiered storage requirements, with temperature and time of the essence. Sheer distances and volumes of doses in transit from manufacturing sites to POUs across the globe are also challenges. One lean manufacturing expert identified what may be the biggest challenge for COVID-19 vaccination efforts. ⁷

"... no single organization has responsibility for the entire [vaccine journey]."

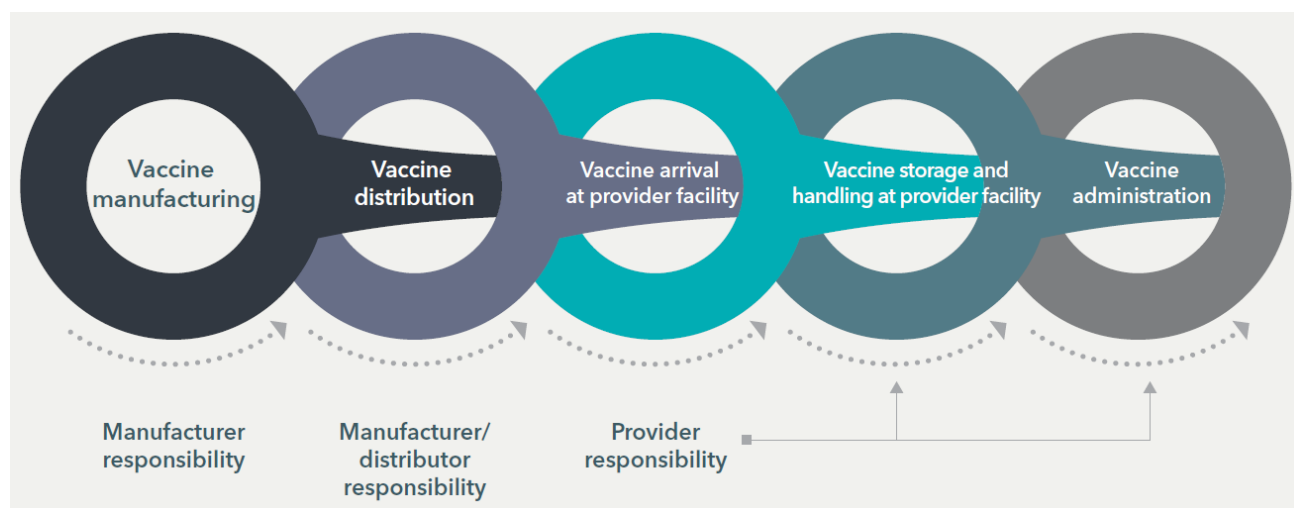


image courtesy US Centers for Disease Control and Prevention

“No single organization has responsibility for the entire vaccine journey.”

Compliance with manufacturer recommendations from shipment until shot administration is critical. Here’s a summary from two leading manufacturers of mRNA-based vaccines for COVID-19 showing what providers are facing.

Pfizer

Teaming with immunotherapy firm BioNTech, Pfizer received the first US Food & Drug Administration (FDA) emergency use authorization (EUA) for a COVID-19 vaccine in December 2020. In the US, Pfizer manufactures vaccines at its Kalamazoo, MI facility and ships directly to providers. They project manufacturing 1.3 billion doses of COVID-19 vaccine in 2021. Two doses of the vaccine 21 days apart provide full effectiveness.⁸

Vaccines ship inside thermal boxes packed with dry ice (about -78°C). Unopened, packed boxes can last 10 days in transit. After opening, vaccines can be stored in the thermal box up to 15 days if the dry ice is refilled every five days. Vaccines can also be placed in an ultra-cold freezer and stored for up to 180 days (six months). New data from the European Medicines Agency (EMA) shows deep-frozen storage between -25 and -15°C provides stability for two weeks as an alternative to ultra-cold storage.⁹

Preparing for administration, vaccines are thawed in chill refrigeration at 2 to 8°C for up to five days. Refreezing is not permitted. Before administration, vaccine vials are brought to room temperature, then diluted within two hours. After the first dose is drawn from a diluted vial, the vial can be stored between 2 and 25°C and must be used or discarded within six hours.

Moderna

The second FDA EUA for a COVID-19 vaccine went to Moderna, also in December 2020. Moderna uses a different model. Their in-house manufacturing for the US is in Norwood, MA. Contract manufacturing of key ingredients is done by Lonza Biologics in Portsmouth, NH. All COVID-19 vaccines manufactured are shipped to distributor McKesson in Irving, TX, then to providers. They project 700 million doses manufactured in 2021. Introducing booster and pediatric-strength doses ups production to as many as 3 billion doses in 2022.

Two doses are required, 28 days apart.¹⁰

Vaccines are shipped in cartons kept deep frozen at -20°C nominal, never permitted to be below -50°C, so dry ice is not recommended. Preparation for administration starts with thawing in chill refrigeration at 2 to 8°C for up to 30 days, with no refreezing allowed. No dilution is required. Unpunctured vials can be kept between 8 and 25°C for up to 12 hours. After the first dose is drawn, a vial can be stored between at 2 and 25°C and must be used or discarded within six hours.

Limits of infrastructure, process, and older TMDs

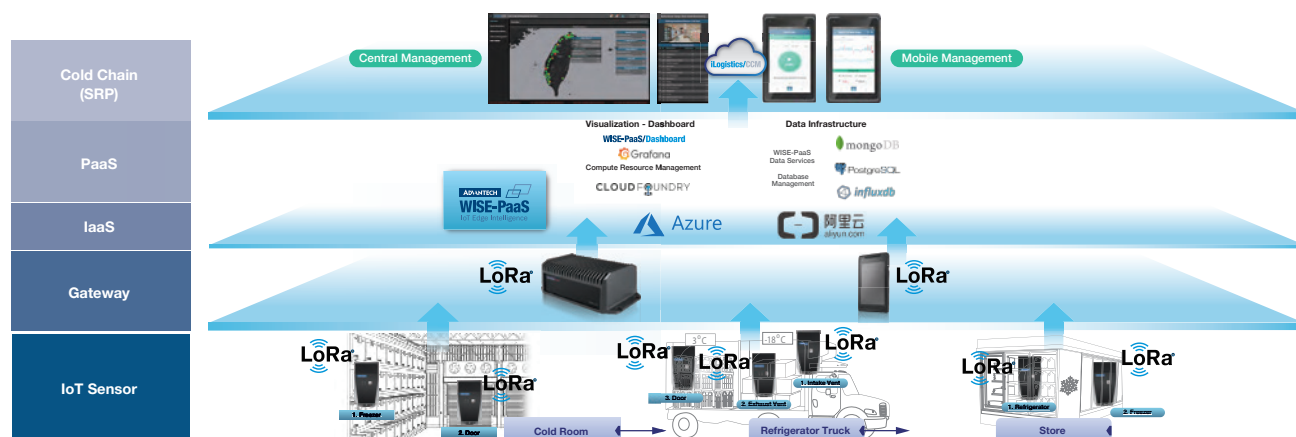
Pfizer ramped up large scale mRNA-based vaccine manufacturing quickly, exposing storage issues. Analysts estimate only 25 to 30 countries have any ultra-cold storage infrastructure. In the US, only research hospitals and large universities typically have ultra-cold storage. New ultra-cold storage units run \$10k to \$20k. This puts many rural healthcare providers at a disadvantage. Also, dry ice availability can make re-icing in the thermal shipping box difficult or costly in many areas.

The latest EMA data on deep-frozen stability may provide some relief.

Moderna avoids ultra-cold storage entirely, using deep-frozen storage many shippers and providers already have. An added distribution step is offset by improved stability while deep frozen. The 30-day at chill gives more time to complete transit to remote locations. Careful monitoring of storage is still required.

These similar, yet different manufacturer requirements add to abundant process risk. On top of them, states and cities have their own plans for distribution and handling. Most providers opt for one vaccine exclusively to simplify their procedures. Still, all it takes is one person anywhere in a cold chain – at a distributor, shippers, or providers – to break effective communication. Failure to share information or log data correctly compromises the cold chain. Cascading failures risk entire shipments, or all vaccines in a storage unit.

To help providers, the US Centers for Disease Control and Prevention (CDC) recently updated



the Vaccine Storage and Handling Toolkit for COVID-19 vaccines. It focuses on reducing process risk and goes a step further. Section 3 addresses storage and monitoring, citing use of a digital data logger (DDL) as a temperature monitoring device (TMD).¹¹

DDLs overcome significant limitations of older TMDs. Basic thermometers need frequent manual observations. Irreversible thermochromic strips show a temperature excursion occurred but give no sign of when. Chart recorders capture history but still need observation. The CDC recommends DDLs with a list of features. These include a detachable buffered temperature probe, an audible alarm, an accuracy of $\pm 0.5^{\circ}\text{C}$, displays showing current, min, and max temperature, and a reading rate of at least every 30 minutes. DDLs provide a way to automate and store readings, and many can also connect to a computer for downloading data.

Network-wide cold chain monitoring with IoT technology

Connectivity holds the key for many providers in improving vaccine cold chain integrity. One DDL

coupled directly with a single storage unit is an improvement. Yet, a provider facility likely has several storage units for different temperatures – one for ultra-cold, one for deep frozen, and one for chill. Bigger facilities may have many different storage units. Larger providers may have a network of facilities with hundreds of storage units to monitor.

What if DDLs could integrate with a provider IT network using wireless networking technology? Adding IoT technology to facilities automates measurements and speeds up communication. One dashboard can oversee all storage units anywhere in the provider network. Provider teams could check on storage units using mobile devices without walking to each unit. Vehicles with in-transit monitoring carrying vaccines between provider facilities could also be checked easily. A provider's entire vaccine cold chain status could be in a single, always available view.

Advantech has developed a complete Solution-Ready Package (SRP) for cold chain monitoring applications. These SRP components are proven reliable in food and pharma deployments. Flexible configuration allows teams to deploy monitoring

Deep-freeze sensing: Advantech TREK-120

An example of an advanced LoRa-based sensor ready for use in deep-freeze vaccine cold chain monitoring is the Advantech TREK-120. This small, durable battery-operated device is installed inside a storage unit near vaccines being monitored, measuring temperatures from -30°C to $+70^{\circ}\text{C}$. It has an IP65 rating, with its electronics sealed from water and contaminants. Its battery lasts up to 3 years in typical conditions. Readings can be logged, transmitted in real-time on a LoRa network, or captured via NFC in a smartphone or tablet. Programmable network alerts along with an LED indicator on the panel give notification of any temperature excursion.



fast and adapt as needs change. This IoT-enabled cold chain monitoring system has several pieces:

- **Sensors** - Highly accurate battery-operated sensors can be set up and connected on a network like LoRa without any wiring. Sensors deliver readings automatically in real-time and need little maintenance.
- **Gateways** - LoRa has several hundred meters of range through common construction materials. Sensors can spread across campuses or, with mobile LoRa gateways, vehicles. Gateways combine a network of sensors into groups, transmitting sensor readings into a facility network or the cloud.
- **Network infrastructure** - Rather than relying on a commercial network provider, creating a private, scalable LoRa network is easy. An IaaS (infrastructure as a service) such as Microsoft Azure configures and connects sensors and gateways.
- **Application platform** - Scalability from a few sensors to hundreds of connected sensors across many facilities is important. A PaaS (platform as a service) combines data infrastructure, processing, and visualization applications. Open interfaces enable real-time sharing of data between providers, manufacturers, distributors, and shippers.

IoT-enabled cold chain monitoring frees people from the tedious task of recording readings. Programmable alerts trigger when a temperature excursion happens. Rapid response to any problem contains losses, reduces costs, and

ensures safety. Effective monitoring lets providers focus on giving shots with confidence vaccines have been stored properly.

Investing in the future for public health

The potential for mRNA technology is massive. Rapid vaccine creation and ramp-up for billions of doses is critical in fighting any out-of-control pandemic. An important mRNA feature is the ability to modify a vaccine quickly as virus variants emerge. mRNA can also be used in developing therapeutics. All these point to the need for more effective cold chain management.

Public health officials are certain that COVID-19 will not be the last global pandemic. Cold chain monitoring capability is a good investment for providers now, and well into the future. Evolving IoT technology is making cold chain monitoring easier to implement and use.

Advantech continuously innovates solutions with customers and partners. Marketing and application engineering teams are ready to work with providers looking for expert help with cold chain monitoring. For more information, visit:

<https://www.advantech.com/srp/cold-chain-management-solutions>

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