

Beyond Cold

Vaccines have fundamentally changed with innovative mRNA and viral vector technologies driving their development. These new types of vaccines have unique cold storage requirements, which standard refrigerators and freezers cannot meet. Instead, ultra-low temperature freezers are needed to support vaccine storage

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Without a doubt, 2020 was an unusual year. The SARS-CoV-2 pandemic reshaped how we work, live, learn, and interact at every level. The global response, however, was unprecedented. The imperative to contain the virus pushed the vaccine industry into the public spotlight and the outcome was disruptive: a new generation of vaccines emerged that has redefined immunisation strategies.

A New Era in Vaccine Storage

Vaccines based on novel mRNA and viral vector technologies are in line to bring the world back to normalcy. Developed, tested, and approved in record time, these vaccines have changed how industry produces, manages, and – above all – moves immunisations through the cold chain from manufacturing sites to anxiously waiting end users. Within the span of just 11 months, the transport and storage of vaccines at -70°C became a global priority. Before last year, ultra-low temperature (ULT) had only been used for the highly localised delivery of trial vaccines during Ebola outbreaks.

Until now, most vaccines were commonly stored between 2°C and 8°C worldwide. Consequently, the existing cold chain infrastructure built on standard refrigerators and freezers was insufficient to accommodate these new ULT storage needs. In anticipation and support of these new vaccine modes, and facing the largest immunisation campaign in human history, cold chain infrastructure is expanding to reach far below sub-zero temperatures and adding storage facilities to accommodate massive numbers of doses.

Purpose-Built ULT Freezers Are Made to Meet This Demand

Freezers capable of reaching and holding a temperature between -50°C and -80°C are not new. They have been in use for decades in areas like drug development, cancer

research, and cell therapy. Suppliers have perfected the technology behind these ULT devices, and some have even pioneered advances in design, engineering, and efficiency for over 70 years. What is new today is the global urgency for immunisations and public visibility of vaccine distribution efforts. Therefore, ULT freezers have made a debut in the international dialogue about cold chain management.

At first glance, the concept of ULT freezers seems simple: ultra-cold storage minimises degradation, extending the time over which the functional and structural features of biological materials can be used – be it DNA, proteins, cells, or vaccines. Behind that simplicity, however, is a body of precision engineering that ensures each freezer meets rigorous requirement and qualification needs – repeatedly and sustainably. These devices are designed to operate consistently and reliably, withstanding variation in temperature, handling, users, and environment. They are also designed to facilitate communication with operators and to align with storage recommendations of the US Centers for Disease Control and Prevention, WHO, and numerous other authorities and stakeholders in vaccine programmes around the world. The instruments are available, and agents in the distribution chain are looking to acquire storage capacity not only for this pandemic, but for the reality that these novel vaccines are here to stay.

When Selecting the Right ULT Freezer, Let Doses Guide the Way

Altogether, the market for ULT freezers offers a fleet of purpose-built instruments that cover essentially any storage capacity at just about any temperature point. Freezer size can range from smaller benchtop instruments that hold a few thousand vaccine doses, to large stand-up units that hold several hundred thousand doses.

Purchase	Install	Maintain
Let doses guide the way	Create an installation plan	Observe best practices of refrigeration
Consider dosage configuration and pack-out dimensions	Ensure an independent monitoring system is ready for use	Load freezer to consolidate and facilitate item removal
Confirm electrical requirements	Have appropriate and abundant personal protective equipment on hand	Know what is in the freezer and where
		'Stay in touch' with the ULT freezer
		A little TLC goes a long way

Table 1: Considerations and guidelines to acquiring and managing an ultra-low temperature freezer

Choosing the right ULT freezer for a node in the vaccine cold chain is not as simple as selecting the largest instrument that a budget can buy. The performance of a ULT device is influenced by the volume of material it holds at any given time and traffic it experiences as those materials are removed and replaced. The temperature immediately surrounding a vaccine dose is more stable in a near-full freezer, and lengthy periods in which a freezer stands empty can lead to suboptimal storage conditions. It is, therefore, important to balance storage capacity and content turnover when evaluating freezer options.

Three criteria should guide the selection of a ULT freezer:

- **The maximum number of vaccine doses that must be held:** At any given time, the chosen freezer should accommodate a full inventory.
- **The dosage configuration and pack-out dimension:** How and when a vaccine is dosed as well as the number of people to be vaccinated in a given timeframe determine the frequency and quantity in which vaccines are removed from storage. The chosen freezer needs to have the size and compartmentalisation to minimise how often doors are opened, while ensuring vaccines spend the least time possible outside of cold storage.
- **The electrical requirements:** Of course, electrical outlets and mains voltage differ from country to country. The chosen freezer must match electrical supply and requirements to operate safely and continuously.

Safeguard Contents: The Principle Behind Preparing for and Maintaining a ULT Freezer

Informed by decades of experience and feedback from users, as well as an understanding of evolving cold storage needs, manufacturers of purpose-built ULT freezers have designed units for longevity, notwithstanding standard day-to-day traffic. With advances in computer technology and connectivity, devices are now also equipped to provide status updates, schedule maintenance, track usage, and warn about any issues affecting performance.

Today's purpose-built ULT freezers offer a seamless and informed user experience with the priority of safeguarding what's inside. Accordingly, safeguarding the contents inside a ULT freezer should be the guiding principle in how any user interacts with the unit, from preparing for its arrival and installation to using it throughout its lifecycle. Three elements are important in a usage plan to maximise the benefits of a ULT freezer: preparation, best practices, and communication.

Anticipate and Prepare

Working with a ULT freezer begins before the device arrives. Depending on the instrument size and where it will be located, installing a ULT freezer can be a complex operation. Preparing for the day it arrives means ensuring all installation steps can be carried out without delay.

To begin, delivery should be scheduled within a time window that ensures support by facilities management. The timeline should include a buffer for any troubleshooting, and allow the newly installed freezer to reach the targeted temperature before loading contents – usually between 12 and 24 hours. Additionally, an installation plan can ensure a smooth procedure. The plan should include measures to create a clear path and provide adequate tools for unloading the unit from its transport and accessing the room where it will be installed. At times, overcoming hurdles like staircases and narrow



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hallways or door thresholds may require creative workarounds. What's more, actions and controls are needed to align with institutional quality management system requirements for the safe installation of new equipment.

The final location of the ULT freezer must also meet specific requirements to ensure optimal operation. The chosen room must have good ventilation yet maintain a relatively stable ambient temperature. Also, the ULT freezer must be connected to a dedicated and appropriate electrical outlet. Finally, an independent digital data logger must be purchased to serve as a separate monitoring system. All these requirements should be cleared before the instrument arrives.

Keep Cold In

Just like with a standard freezer, observing best practices to minimise temperature fluctuations within a ULT device should be the focus of access behaviour – how the contents are configured inside a ULT freezer is important. When loading a newly installed device, always load from the top down. Subsequently, the cargo in the freezer should remain consolidated to assist in keeping the temperature around individual items as constant as possible. Therefore, it is good practice to plan how contents are added and removed from the freezer to firstly avoid cargo fragmentation and secondly, minimise how frequently external and internal doors are opened.

In fact, frequent door openings are the most common mishandling of cold storage. Implementing an inventory management system grants all users transparency about the used onboard capacity and location of specific cargo in the ULT freezer so content access is fast and efficient.

Pay Attention to 'Freezer Talk'

In general, maintaining visibility of a ULT freezer's status and operation is a cornerstone of its long-term care and management. Luckily, today's devices communicate with users to make that information readily available. With onboard connectivity and

integrated displays with operation dashboards, a modern ULT freezer provides continuous feedback about its performance. This information is meant to guide decisions about instrument management, so users should be familiar with steps to take in response to common messages and alerts.

Given the reality of modern work environments, and especially the circumstances of this global pandemic, most ULT freezers also connect to mobile devices and cloud-based systems to allow remote monitoring. Some manufacturers can also integrate that connectivity with support and maintenance plans that, for example, allow support teams to diagnose issues remotely, notify response teams in the rare case of malfunction, or help keep a regular maintenance schedule. These systems enable reliable and uncomplicated everyday use of a ULT freezer, while maximising its lifecycle.

Putting in Place the Pieces of a New Ultra-Cold Chain

The arrival of novel vaccine forms requiring ultra-low temperature storage has drawn attention to the need for a reliable ultra-cold chain from manufacturer to distribution sites. Existing purpose-built ULT freezers meet the demand for this pandemic, and any other situation that calls for reliable and secure storage options.

Looking into the future, however, the relevance of these ULT systems goes far beyond vaccines. Already today, the long-term storage of biological materials plays an essential role in the biopharmaceutical industry, from biobanking specimens for research, development and validation of novel drugs, to using biomolecules, cells and tissues as therapeutic agents themselves. The specific requirements of each use case are met by these purpose-built ULT freezers. Firstly, they are robust instruments engineered to perform within narrow tolerances of deviation. Secondly, and perhaps more importantly, manufacturers have constructed an ecosystem of support to ensure every ULT freezer meets user expectations of simple, reliable, and long-term protection of the contents that really matter.



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