TITAN CONTAINERS

# Tackling the $35 Billion Problem

## Cold Storage Challenges in Pharma

Why Cold Storage in the Pharmaceutical Sector
Has Never Been More Important

White paper 2024

# Executive Summary

**$35 BILLION**

**In annual losses due to inefficiencies in temperature-controlled logistics in the pharma industry**

Our starting point for this white paper was a single statistic that has been widely reported on a number of pharmaceutical websites.[1] For a sector generating over a trillion dollars annually[2], this might seem like a drop in the ocean.

However, with annual projected ROI in research and development for global pharmaceutical companies falling to 1.2% in 2022[3] – according to Deloitte – there is little room for complacency. While many drugs within the pharmaceuticals sector need no cold storage whatsoever, the need for refrigeration is growing – driven by new vaccines and biologics.

Increasing life expectancy, emerging Cell & Gene Therapies (CGT), mRNA Vaccine technology, Therapeutic mAbs and other factors are all fuelling growth in demand for pharma cold storage. According to the American Society of Health-System Pharmacists,

**43% of the 292 new drugs approved from January 2018 to March 2023 needed to be stored in a temperature-controlled environment.[4]**

In fact, the needs for robust cold storage within the supply chain are poised to accelerate exponentially. One study – by French financial newspaper Les Echos – predicted a 70% growth in temperaturesensitive products by 2025.[5]

For an industry that is clearly so reliant on cold storage supply chains, the need for effective solutions has never been more pressing. he complexities of providing reliable cold storage, however, are hard to overstate.

While CGTs present a beacon of optimism, their end-to-end operation is riddled with multifaceted challenges impacting supply chain, manufacturing and quality.[6]

- PwC

But effective cold chain processes do exist. Finding them in the face of increasing demand has become a modern business imperative. Established in 1987, TITAN Containers is the world's largest family-owned shipping container company, and since expanding into the cold storage market 16 years ago, has amassed considerable experience in a very specific niche: cold storage for the pharmaceutical sector.

With the global pharmaceutical logistics market growing at a rate of 8.8% per year[7], according to market research and consulting organisation Precedence Research, we believe we have a role to play in helping the industry understand the challenges inherent in cold storage.

**In this white paper, we also strive to illustrate what best practices within the pharma cold chain look like and offer some key insights into the effective procurement of reliable cold storage solutions.**

# Cold Storage in the Pharmaceutical Sector

# A $35bn Problem

At the heart of the industry's cold chain conundrum are biologicals – also known as biologics and biopharmaceuticals – which includes vaccines, allergenics, antitoxins, stem and gene therapies, tissues, blood and blood products such as platelets, somatic cells, and more.

Demand for these is growing, as biologics offer hope when it comes to treatment for everything from osteoporosis and rheumatoid arthritis to Crohn's disease and certain types of leukaemia and cancer. The drawback, according to the FDA, is that: Biological products tend to be heat sensitive and susceptible to microbial contamination.[8]



# Ever-moving goalposts

To complicate matters further, many biologics can be stored safely at different temperatures. The Pfizer-BioNTech COVID-19 vaccine, for example, can be stored in a refrigerator for up to a month and, longer term, at -60°C until it reaches its expiration date.[9] Thus, a delicate balancing act must be managed by biologics manufacturers as they plot out their products' most likely life cycles and try to predict their future storage needs.

The prize for getting this right, however, is beyond the scope of any meaningful metric. The FDA notes that biological products often represent the cutting edge of biomedical research and may, in time, "offer the most effective means to treat a variety of illnesses and conditions that presently have no other treatments available."[10]

To say biologics have a critical role to play in the story of modern medicine would be an understatement.

To provide them to an eager public, however, manufacturers have their work cut out. As well as being reliant on flawless temperature control and the ability to categorically prove that product has been maintained at the correct temperature throughout its life cycle (as part of the whole traceability process), pharmaceutical companies engaged in the biologics space also need supply chain oversight that takes into account:

- **Safety and security** of the product (to avoid fraud, contamination and theft) and other GDP (Good Distribution Practice) requirements.

- **International transportation** – often to isolated, poor populations – plus 'last mile' packaging and the challenges of maintaining safe temperatures for products being delivered. The sheer volume of biological products out for shipment can sometimesseem overwhelming – between 3.5 and 5.5 billion vaccine doses alone are manufactured each year.[11]

- **Their overall sustainability endeavours and future decarbonisation plans** (the pharma sector generates 52 megatons of CO2 annually).[12] The incalculable costs of defective products entering the marketplace – including the damaging effects on users' health, stakeholder confidence, the company's reputation and other factors.



> "Manufacturers have their work cut out. As well as being reliant on flawless temperature control and the ability to categorically prove that product has been maintained at the correct temperature throughout its life cycle"

# Calculating the pharma sector's cold storage needs

According to business consulting firm Grand View Research, the global cold storage market is currently estimated at around $138bn[13], approximately one-seventh of which (circa $20bn) is spent by pharmaceutical companies. The same organisation also estimates the global pharma logistics market at $92bn[14]. Extrapolating from this, just under a quarter of all pharmaceutical sector spending on logistics goes on cold storage.

This is an astronomical amount to spend on keeping products cool. However, as was widely reported at the time, the COVID pandemic highlighted critical weaknesses in pharma cold chains and brought home the need for improved resilience. Evidently, the $20bn that is being spent on cold storage in the pharmaceutical sector is either not enough or, as our opening statistic suggests, propping up a system that is not as efficient as it could be.

Whichever is true, there is a compelling need for pharmaceutical companies to find innovative and reliable cold supply chain partners who can help improve current processes and prevent future losses.

# The Challenges of Meeting the Sector's Demands

No sector has more onerous cold storage compliance requirements than biopharmaceuticals. These stringent demands – which are in place to avoid potentially catastrophic consequences in the event they are not followed – weigh heavily on the shoulders of companies in the biologics sector.

The need for faultless cold chains is far greater than most people could imagine: the World Health Organisation estimates that up to 50% of all vaccines are wasted globally every year, a large part of the issue being a lack of temperature control and cold chain failures.[15]

Industry website Pharmaceutical Commerce recently reported on a study by the University of St. Gallen in Switzerland – an authority on supply chains – who found that the transport of temperaturesensitive products within the pharma sector often failed to meet quality requirements. In around one-third of instances when this happened, the net result was the complete loss of goods.[16]

In many ways, businesses in the biopharma space could scarcely have picked a more capricious field in which to work. As California-based life sciences company Beckman Coulter Diagnostics notes:

Biologics are subject to more inherent variability (in form, function, and efficacy) than totally synthesised pharmaceuticals. They are also more susceptible to small changes in environmental conditions, whether during production, storage or use.[17]



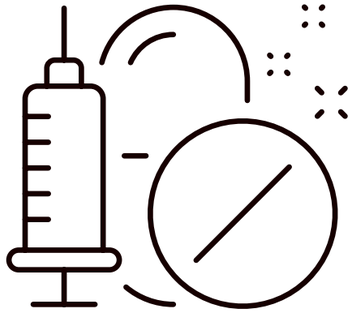
**The journey from laboratory to end user The ability to reliably trace the voyage of biological products is a non-negotiable within the industry. That doesn't, however, make it any the less challenging. With long journeys involving numerous moving parts come multiple risks. These include:**

- Temperature excursions during storage caused by everything from inaccurate measuring systems to mechanical breakdowns.
- Cross contamination.
- Lack of necessary training and bad handling practices.
- Unexpected events such as extreme weather or vehicle failure.
- Ineffective packaging and other supplier issues.
- Theft.
- Variations in local infrastructure.
- Sudden drops in demand and the resulting need for chilled 'holding' areas.

The safe storage of products in temperature-controlled environments plays a significant role in the biologics supply chain. Most commonly, cold storage planning is focused on the period during which products are stored after manufacture but before distribution.

However, requirements are rarely black and white. For example, manufacturers are not always able to ascertain in advance the precise temperature range they will need – as is the case when conducting stability trials or when products need to be stored for longer periods than initially anticipated.

Furthermore, overproduction and underproduction are not uncommon when producing biologics. In the initial phases of development especially, yields may be an unknown quantity. Similarly, spikes in demand can be difficult to predict.



A third complication when trying to manage the safe cold storage of biologicals is time. FDA approval can take several years – making it challenging for manufacturers of biological products to accurately predict their cold storage needs. One answer to this issue may be temporary cold storage solutions that can be rapidly deployed on demand.

Mahesh Veerina, President and CEO of supply chain specialists ParkourSC, summed up the issue of pharma cold chains rather succinctly in a recent article on the Pharmaceutical Commerce website: "In an ideal world, the pharmaceutical supply chain is consistent and problem-free," he said.

**"Demand doesn't change, there are no disruptions, weather and traffic are perfect, and there are ample logistic resources to meet the needs of all pharma manufacturers."[18]**

This fantasy world, of course, does not exist. A quest for quality
While quality control is integral to the biologics supply chain, it doesn't necessarily follow that this mentality is 'baked in' to all of the sector's service providers – just as it isn't across the industrial landscape. The research firm Boston Consulting Group found that across all sectors, only 6% of executives and quality managers strongly believe their whole company contributed to meeting quality standards.[19]

Pharmaceutical companies have the edge over other sectors somewhat, thanks to the regulations that are in place to ensure proper storage and handling. As global transport and logistics firm Geodis notes, the pharmaceutical industry must comply with good manufacturing practices and good distribution practices to ensure product integrity.[20]



Some countries, they point out, have tightened their application of GDPs even further – Germany and Austria among them.

While regulations help keep products safe, following them requires resources, focus and commitment. At the same time, pressure for companies worldwide to reduce their carbon emissions is growing, too. Cold storage has and always will require energy use. Reducing the carbon footprint created by the "energy-intense" cold chain will, says pharma industry tech powerhouse IQVIA, be critical in the pursuit of net zero ambitions.[21]

Failure to provide effective cold storage in the supply chain affects producers of biologics in multiple ways, including loss of revenues, potential lawsuits if temperature control data proves to have been flawed and faulty drugs entered the marketplace, reputational damage and more. When coupled with the challenges of ensuring unimpeachable cold storage in an environmentally-friendly way, it can seem like an uphill battle.

# What Does 'Good' Look Like, and What Does the Market Want Today?

Cold chains across the biopharmaceuticals sector are often complex and fragmented.[22] The more successful ones, however, have found ways to combine reliable partners with good visibility and integration – while maintaining a watchful eye on the wider business landscape and the future possibilities of emerging tech. The following are what we believe to be the top 5 areas for consideration when looking at ways to strengthen your cold chain.

## New Technologies

PwC asserts that "Advanced temperature monitoring technologies, such as IoT-based sensors, are increasingly being em-ployed to ensure the integrity of the cold chain, reducing the risk of costly losses."[23] Additionally, Blockchain has a role to play.

A recent study by researchers in Iran pointed out that: "Blockchain would benefit the pharmaceutical cold chain by bringing data integration, secure transactions, serialisation, and traceability."[24]

A research team from China, meanwhile, recently put forward the notion that deep learning will become increasingly relevant when predicting demand. This would "assist the cold chain inventory management decision-making so as to reduce the warehousing cost of cold chain products."[25]

## Cold Storage

As noted, a key consideration for biologics manufacturers is the need for flexibility in their cold storage capacity. This can help mitigate changing timelines, fluctuating needs, contract uncertainty and risk.

One option that is proving popular is on-demand modular cold storage facilities that are available on rental terms and can be rapidly installed indoors or outdoors as and when needed. Unlike permanent cold storage solutions, they do not normally need planning permission and can also be relocated and reconfigured as required.

Compared with the long list of considerations when installing permanent cold storage – assessment and planning, permitting and licensing, construction work, CAPEX, and more – temporary modular solutions are well suited to the vagaries of changing production yields, market variations and the waiting game synonymous with FDA approval.



## Energy Efficiency

PharmaSource, an online community for pharma and biopharma procurement professionals, noted in a roundup of predictions for 2024 that "Many procurement leaders are working on programmes to engage suppliers with their ESG commitments, recognising that suppliers hold the key to successfully reducing scope three emissions."[26]

Ensuring your partners have an unblemished track record on sustainability and that they are embracing new technologies to minimise energy use during cold storage and transportation is becoming increasingly important.

## Training

In the eyes of automation specialists MasterControl, training in the pharma space is not a onetime event — it is a continuous and dynamic effort. "That not only means that a pharma company's training program itself must be dynamic," they add, "but that the documentation and certification of the individuals being trained must be dynamic as well."[27]

They put forward automated training as a possible solution – which global company training platform Continu says is all about "leveraging digital tools, scheduling regular content updates, and using analytics to adapt and optimise learning paths."[28]

## Delivery Vehicles

Trailers, vans and trucks play a critical role in the biologics cold chain, and as well as having reliable refrigeration technology built-in, the need for unbeatable levels of insulation is paramount. Thermo King, the American refrigeration specialists, say that an important element is the age of the equipment. "For a refrigerated trailer, the average life cycle is seven to 10 years," they note, adding:


For pharmaceutical shippers, the recommended life cycle for temperature control equipment is three to five years, depending on a fleet's equipment capacity and design.[29]

- THERMO KING

# How to Procure the Right Cold Chain System for your Business – 7 Key Questions to Ask

## 1. How do you combat cybersecurity?

In 2020-21, hackers targeted many of the main COVID-19 vaccine developers. IBM's global lead for threat intelligence, Nick Rossmann, told CBS News in 2021 that "Logistics firms are a particularly ripe target. Potentially [hackers] could spoil the vaccine batches that they have in refrigeration units."[30]

Cybersecurity – even today – is sometimes overlooked. According to a report by cybersecurity experts CrowdStrike, only 36% of businesses vetted their new and existing suppliers for security purposes in the previous 12 months.[31]

## 2. What are your quality control procedures?

Zuhal Reed at life sciences insurance specialists Medmarc told the Risk & Insurance website that: Sourcing high-quality biological material like nucleic acid, viral vectors used in gene therapy, cell lines, antibodies and enzymes – and producing them with consistent quality – is difficult.

With a global supply chain, it's challenging to regularly audit suppliers. You must ensure thatthe quality is there. The materials must be transported in a way that keeps them safe and viable over a long journey.[32]

Rigorously questioning your cold supply chain partners about their processes will help to reveal any weaknesses.



## 3. How can you help maintain visibility within my partner network?

ParkourSC's Mahesh Veerina sees partner collaborations intensifying to ensure a proactive response to issues across the pharma supply chain. "A modern supply chain should be something other than a game of telephone tag," he notes.[33]

Look for cold chain partners who can seamlessly slot into and enhance your operations and contribute to traceability.

## 4. What is your track record on energy use??

According to the World Economic Forum, around 40% of all emissions in global supply chains could be cut using readily available solutions – efficiencies among them.[34]

Your procurement processes should factor in the projected energy use of thesolutions presented by your prospective cold chain partners.
To assist with your own decarbonisation goals, seek out those whose technologies and innovations provide more energy-efficient solutions than those of other candidates.

## 5. What steps do you take in terms of risk mitigation?

Risk mitigation across the cold supply chain has multiple strands and covers everything from monitoring and backup planning to cybersecurity threat analysis and transportation. Ask how your partners plan for disruptions and unforeseen events.

Inmodular cold storage centres, for example, do they use blast freezers that employ multiple individual cooling units to ensure reliable backup redundancy?

The importance of backup during cold storage is difficult to overemphasise. Last December, research samples that had been collected over decades at a medical university in Stockholm were reportedly destroyed because of a freezer malfunction.[35]

## 6. What is your track record on choosing strategic transport routes?

Your supplier's performance in this area will impact their (and, by default, your own) carbon footprint. Additionally, ineffective route planning may adversely affect the efficacy of temperature-controlled transport systems.

Temperature excursions caused by poor route planning can be disastrous, so drill down into your supplier's methodology and performance record.

## 7. How flexible are your terms?

This is an industry where uncertainties abound, and you need partners who can accommodate this. When it comes to cold storage, for example, renting individual or modular containerised solutions affords the freedom to expand and contract on-demand.

Does your provider offer flexible terms that encourage and facilitate agility, or are they eager to lock you into fixed-term solutions?

# How TITAN addresses these questions

We have provided industry-leading containerised cold storage solutions to pharmaceutical clients such as Novo Nordisk, AstraZeneca, MSD, Sonoco, Pfizer and va-Q-tec for more than 15 years. Among the 100-plus global pharmaceutical clients we help to achieve consistent low temperatures are those who work in biologics and vaccines, MedTech, Therapeutic mAbs, and Animal Sciences.



## Our ArcticStore brand seeks to address many of the industry's key cold chain questions, including:

**Quality control**
Our solutions are offered GDP compliant and provide reliable, safe and secure storage with temperatures ranging from -75°C to +45°C.

**Visibility**
Our collection comes with in-built dataloggers and secure, powerful remote management software.

**Energy use**
All latest-generation ArcticStore models have superior levels of insulation and state-of-theart technology, reducing energy consumption by 20%.

**Risk mitigation**
Multiple separate cooling machines in our ArcticBlast freezers provide reliable backup in the unlikely event of a mechanical failure, ensuring uninterrupted operation.

**Flexibility**
Not only can our cold storage units be rapidly configured into a modular warehouse of any shape or size, but they are available on flexible rental terms to suit changing demands.



ARCTICSTORE BY TITAN CONTAINERS

# Summary

The appetite for new biological products that require temperature-controlled storage is on track for significant growth. Visiongain, a UK market research company, sees the cold chain logistics market that supports the healthcare industry growing at a 9% CAGR rate to 2033.[36]

COVID-19 proved what was possible in terms of the speed with which new vaccines could be created, though this was perhaps just the tip of the iceberg. Many more innovations are coming. The University of Pennsylvania recently wrote that "Vaccines are just the beginning of the potential for messenger RNA."[37] They are well-placed to make such an assertion: their very own sci-entists were behind the technology that helped create the COVID-19 mRNA vaccines.

"Next, come all the rest of the potential new treatments made possible by their discoveries," states the University's website.

**"The technology's potential is virtually unlimited; if researchers know the sequence of a particular protein they want to create or replace, it should be possible to target a specific disease."**

Understandably, there is a ripple of excitement across the pharmaceutical spectrum about the possibilities of what lies ahead.

By identifying, ironing out and then ameliorating legacy cold supply chain is-sues that chip away at the industry's efficiency (and profits), we can all play an important part in making sure that the sector's future is as healthy – in every sense – as it can be.

**If you would like to discuss cold storage solutions or have any questions, please feel free to reach out. We look forward to engaging in further conversation with you.**

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