Warming Up to Frozen Distribution

The race is on to provide temperature-controlled packaging systems that can safely ship and store different COVID-19 vaccines

Clive Bryant at Softbox

Since the turn of the century, the eyes of the world have spent much time focusing on the fervent work of research scientists in pharmaceutical laboratories across the globe. SARS, Swine Flu, Ebola, and Zika Virus have each had their unwanted moments in the spotlight. However, with the global death toll now surpassing the million mark, no one needs reminding of the threat that COVID-19 carries. The impact has been so devastating that we wait with bated breath for news of a vaccine.

At some point in the near future the vaccine race will be won. However, it has only given rise to another issue of equal importance, which may not be at the forefront of everybody's minds. Vaccine product development is invariably followed by the need for distribution, and it is in the supply chain where questions are now being asked. One critical question is: once a vaccine has been found, how will it be safely shipped and stored prior to its final administration? The solution to this part of the COVID-19 conundrum is loaded with potential pitfalls, as well as possibilities.

One Size Doesn't Fit All

The pressure on the vaccine distribution industry is ramping up. Currently, there are around 150 vaccine initiatives in development worldwide, including more than 20 that have begun human trials (1). The US, China, Germany, and the UK all have vaccines in phase III trials; this final stage involves testing thousands of people to determine rare side effects that only show up in groups (2). Russian authorities have already approved their vaccine, so as the finishing line beckons, there will be several diverse therapies primed for circulation in all likelihood.

Potential vaccines are being developed on multiple platforms, with each platform generating the immune response through a different mechanism. For example, four out of the six vaccine frontrunners are based on relatively new or even experimental platforms, while two are based on traditional platforms. Different platforms will likely come with different temperature requirements for transportation and storage (3). It is already evident that some will pose more complex logistical challenges than others. Temperatures, timescales, volumes, safety, and security will all be considerations. However, the ability to provide more temperature controlled packaging (TCP) solutions to match demand, including new, ultra-low temperature systems as part of a global pandemic immunisation programme, is one of the most pressing dilemmas facing the industry. With stringent temperature requirements likely to be imposed (out of caution, producers of certain vaccines and their logistics providers can choose to adhere to extreme temperature requirements [as low as -80°C] to ensure that the efficacy of the vaccines is maintained during storage and transport), the cold chain will need to adapt as it comes under new time and temperature pressures (3). Given the scale of the problem and the speed with which solutions must be found, the pharma sector is approaching the TCP supply chain with some apprehension; it is a space, however, that is synonymous with innovation.

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If it's Commercial, it's Covered

The nature of the vaccines themselves (be they virus vaccines, viral vectors, nucleic acid-based, such as DNA or messenger RNA [mRNA], or protein-based) will typically determine the environmental conditions under which distribution and storage at site must operate. COVID-19 product stability testing is being accelerated, and fast-tracked drug approvals are being sought. Ultimately, the safety and efficacy of some COVID-19 vaccines may be upheld by existing TCP systems, while a host of others are going to require innovative new packaging solutions to meet emerging transport and storage requirements.

As it stands, TCP companies have a variety of systems that fulfil typical shipping requirements. Where COVID-19 is concerned, affordable, widely-available, low-dose steroid treatments, such as dexamethasone (which is already being used to reduce the risk of death in seriously ill patients) can be transported and stored in qualified, recyclable pallet shippers that maintain ambient temperatures of +15 to +30°C. No issues there. Similarly, high-performance, re-usable parcel shippers can be sourced, which operate at chilled (+2 to +8°C) or frozen (-20°C) levels typically found in both scientific and domestic refrigerators and freezers. To cope with acute global climatic temperature variations, advanced packaging materials, such as vacuum insulation panels and phase-change materials that freeze and thaw within specific temperature ranges for different products, can be combined to great effect. This guarantees the integrity of next-generation, temperature-sensitive biopharmaceutical products derived from live entities, such as cells and tissues, for up to 120 hours.

The main crux of the transportation and storage debate for existing vaccines centres around the levels to which products have been commercialised. This is driving the work currently being done at the research facilities at the University of Cambridge, UK. Scientists there are currently in the process of developing a standard, freeze-dried vaccine that can be shipped and stored at +2 to +8°C. While this affords the use of more conventional TCP solutions (sparing many countries and dosing facilities far-reaching complications), it represents only a fraction of the research work currently in development. For some emerging vaccines to remain safe to administer, it is possible that more challenging -80°C temperature requirements will need to be met.

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Freezing Up Distribution

Labs and research centres are no strangers to developing and storing biopharmaceuticals at ultra-low temperatures. For tissue and cell preservation, cryogenic (liquid nitrogen) storage will typically be used. However, when it comes to transportation, dry ice-based shippers are widely sought after and readily available (long-term product stability is better maintained when bulk drug substances are transported in a frozen rather than a liquid state) (4). Operating at below -80°C, dry ice has triple the refrigeration power of water ice. However, with little in the way of product stability data where the latest COVID-19 vaccines are concerned, new shipping and local storage challenges may need to be overcome.

Furthermore, medical staff at the point of dispensation may not have complete familiarity with the processes involved in receiving, handling, and storing vaccines packed and shipped in this deep-frozen state. It's a problem that will doubtlessly be exacerbated in emerging or underdeveloped countries. The issue of commercialising the supply of products that require ultra-low temperature storage is a matter of some urgency. SVB Leerink analysts have noted that two frontrunner mRNA-based COVID-19 vaccines, Moderna and Pfizer, could run into logistical supply issues over the ultra-cold storage needs for both shots. Experts expressed concern that the temperatures required to store mRNA vaccines were 'severely limiting' to distributors' ability to ship the shots, and to clinics' ability to administer them to a large number of patients (5). Analysts argue that the correct conditions could only be met at tertiary hospitals and labs. This could be accommodated in intensive one-day vaccination events at such sites, but would still only cover a fraction of the healthy population (6). The obvious

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solution is to build out the supply chain to accommodate end-to-end storage and dispensation, but that is far easier said than done.

Supply Chain Roadblocks

Fast-tracking new COVID-19 vaccines poses a massive challenge for both the pharma and distribution industries that reaches beyond temperature stability and packaging. Current logistical setbacks have clearly constrained the supply chain; land, sea, and air transportation have been hit by shrinking capacity, rising costs, delays, or a lack of workers due to the coronavirus. It's a torrid scenario. The infrastructure powering the global economy is scaling down for a protracted downturn just as pharma companies need to scale up for the biggest and most consequential product launch in modern history (7). Nevertheless, there seems to be a consensus among leading global logistics companies that, while the cold supply chain isn't currently ready, with a coordinated global strategy, much can be overcome.

It is likely we will witness an unprecedented number of TCP systems moving through cold chain (providing, of course, that the appropriate packaging systems are available and in sufficient quantities). Consequently, vast amounts of dry ice may be required to pack new, low-temperature products. Consignors will need to apply very specific IATA-based dangerous goods labelling and handling instructions on their shipments, while logistics providers will be mindful of the legal limitations in aircraft cargo holds that could hamper the uplift and subsequent delivery of deep-frozen shipments.

The fact that vaccines, which will be box-transited from point of manufacture to an immunisation or dosing centre, could well be in storage for up to a week only adds to the scale of the logistical task. Place this whole scenario in large parts of Africa, South America, or Asia where logistics systems can be less sophisticated, and it begs the question: just how realistic is it to expect industries to come together to move frozen vaccines around the globe in new, totally safe, durable, cost-effective, ultra-low temperature transport and storage devices, in what seems like the blink of an eye?

A Cause for Optimism

With a combination of therapies and treatments that require different storage and distribution methods likely to emerge in the not-too-distant future, it is perhaps understandable that the market is currently questioning the ability of the pharma cold chain and the TCP companies to deliver. It certainly looks like there's a new cold chain logistics mountain to be climbed.

While the likes of non-mRNA vaccines that utilise a protein sub-unit approach may facilitate the use of more readily-available storage conditions, in the absence of their proliferation an innovative TCP system that possibly leverages common methods, such as dry ice or phase-change materials needs to materialise. The question, of course, is how?

History is often a reliable indicator. In the face of challenges arising from the progressive nature of pharma development, global distribution companies have usually managed to respond conclusively; necessity has often been a springboard for innovation and may prove to be so again. What we know for sure is TCP production will need to be dramatically scaled up while vaccines are in production. The industry trailblazers will be pushing ideas around right now, almost certainly looking at existing practices and seeing how creative combinations and modifications can be made to form new, qualified, fit-for-purpose, elite systems that will pass regulatory scrutiny. Given what's gone before, dare we bet against them?

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