What Passive Packaging Options Are Available when Shipping Clinical Trials at Frozen Temperatures?

Within the clinical trials sector there is an increasing demand for high performing thermal packaging to meet the rising requirements of protecting pharma payloads, needing be shipped at extreme lower temperatures.

Consequently, thermal packaging vendors are responding to the growing trend to transport clinical trial materials at significantly lower temperatures including frozen, deep frozen and ultra-deep frozen.

The main driver for this rising demand in such specialist shippers is due to the rapidly rising rate of clinical trials being conducted. After the initial impact of the pandemic, the industry is now seeing multiple trials initiating from their first phase and successfully moving through all four phases.

A clinical trial starts initially with an experimental treatment on a small group of often healthy people to judge a developed drug's safety, side effects and establish the correct drug dosage required.

Through the second and third phases the quantity of participants is increased alongside the emphasis on effectiveness. The fourth phase of a trial for drugs or devices takes place after the FDA agrees the trial results are positive and approves their use.

As a device or drug's effectiveness and safety are monitored in large, diverse populations this can present temperature challenges for pharma payloads being deployed. Throughout all the phases of a clinical trial, the temperature requirement can change across, cryogenic frozen (-180°C), deep frozen (-80°C), frozen (-20°C), 2–8°C and even 15–25°C.

As a trial moves through its phases, the quantity of participants increases as does the spread of countries these participants are located in. This presents considerable challenges from a logistics standpoint to ensure the drug remains at the right temperature.

Clinical research organisations (CROs) need to ensure they can meet some if not all of these temperature requirements if they are to be chosen to manage the clinical trial. To do this they will need to assess the packaging options they have, and which packaging is the most appropriate to utilise to protect the valuable medical materials being shipped.

Temperature Requirements

More recently there has been an increase in trials materials needing to be kept at a frozen temperature and this can create additional complications. There are considerations to take into account including what packaging is available within the industry, how does this packaging work and crucially, how long will it maintain the set temperature for?

The passive packaging options available are uncontrolled ambient, controlled ambient, refrigerated, frozen and deep frozen. Deciding what packaging to use will be based on the drug's temperature stability, the temperature band the drug can be exposed to without impacting on its performance and effectiveness when administered.

The majority of packaging being utilised for clinical trials will use foam and/or vacuum insulation panels (VIP) for insulation and a phase change material (PCM) for the engine and power of the packaging to maintain temperature. The different materials used will affect the thermal performance the systems can achieve with the following systems being used during clinical trial phases:

- Uncontrolled ambient: A simple expanded polystyrene (EPS) box with the no specific temperature control and a large tolerance of drug stability.

- Controlled ambient (referred to as "controlled room temperature" or "CRT"): This would require EPS boxes with a PCM for a specific temperature requirement of +15°C to +25°C. (freeze point of phase material 20°C)

- Refrigerated: (freeze point of PCM 4°C) This would require EPS boxes with a PCM for specific temperature requirement of +2°C to +8°C. To maintain this demanding temperature a VIP would be used as the insulation.
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- Frozen: (freeze point of phase material -20°C) This would require EPS boxes with a PCM for specific temperature requirement of below -15°C. To maintain this challenging temperature a VIP would be used as the insulation.

- Deep frozen: Traditionally deployed would be EPS boxes with use of dry ice for a deep frozen requirement of -80°C. Or for -50°C temperature requirements a PCM with an enforced VIP would be used as the insulation.

With all these various options available with variable performance and price points, it can be a challenge to decide what packaging to use. Many of these passive packaging solutions currently being deployed within the marketplace have extensive qualification to demonstrate their cold chain capabilities.

Clinical Trial Trends

Companies operating in the clinical trials space want to have a bandwidth to maximise their options and will start as many clinical trials as they can that have as much chance of being successful as possible.

Therefore, they are now starting clinical trials with much less tolerable stability data. Because there is less stability data available, trials are often started at frozen temperatures, utilising frozen performance packaging to ensure the efficacy of that drug or pharma product is met.

Later in the clinical trial, when the stability data is available, there might be a move to packaging which is able to maintain a temperature of 2°C–8°C.

Another key driver for the rising requirement for frozen packaging systems has been due to increasingly stringent Good Distribution Guidelines (GDP) that organisations need to comply with when storing, transporting and handling medical materials within the supply chain.

Updated GDP regulations resulted in the introduction of CRT, a newer temperature level implemented within the clinical trial space with mandatory requirements to demonstrate temperature control is in place.

With the advent of more stringent guidelines, pharma products must be kept frozen by using specialised temperature-controlled packaging (TCP) engineered and designed for this purpose. The subsequent rise in requests for TCP for frozen shipments is in response to ensure adherence to these increased regulatory requirements. There has also been a rise in requests for ambient controlled shippers.

Therefore thermal packaging providers have had to respond to the requirements within the clinical trial industry by adapting product portfolios or engineering and designing new packaging products.

CROs and cold chain organisations will want to partner with TCP vendors who can offer a breadth of products to meet the varying temperature requirements within trial phases to eliminate excursions and ensure the developed drug is effective and safe for patients.

Asia Affect

Another trial trend emerging is that the clinical industry is increasingly enrolling participants for trials from Asia and Asia specific countries. Many more clinical trials are being conducted in Asia because there are numerous different diseases, which are more prevalent in the region than other countries, because these illnesses are being eliminated elsewhere due to vaccine advances.

Asia also appeals due to the low cost of conducting studies and growing patient population, however an Asia-centric approach to clinical trials poses challenges when shipping pharma products, at much lower temperature ranges, to the region.

These logistical challenges, coupled with the rising trend whereby we are seeing a lot of the active pharmaceutical ingredients (APIs) and drugs being manufactured in North America, can present complications when shipping into Asia.

Longer duration capabilities is needed for TCP being deployed to Asia as payloads being transported within the region will have to contend with very different climates. As FDA approval requires proven drug data including its efficacy, ability to work and correct patient dosage, data is needed from all ethnicities of differing age groups, depending on the illness you are trying to prevent or cure.

Therefore it's essential to be able to ship drugs globally and once a clinical trial enters phase three drugs will need to be shipped worldwide to multiple patients employed over a period of time.

Consequently the TCP deployed will need to withstand the various external temperature environments that will be encountered en route.

Clinical trial companies must cover off many elements including managing and manufacturing developed drugs while taking into consideration logistical challenges to ensure they reach participants on a global scale.

These companies will look to TCP vendors who can demonstrate they have a breadth of shipper solutions for all temperature needs and can manage the temperature-control requirement to withstand any external environment temperature challenges. While TCP designed several years ago might be sufficient for shipping within Europe, with the effects of global warming impacting the climates of different countries, it's essential TCP products are fine tuned to provide high-performance and withstand changing climate challenges.

TCP Trends

The industry is seeing a move away from utilising dry ice as companies explore alternatives within the TCP space. A key driver for the shift is because dry ice is a hazardous chemical, a gas, so there are specific safety measures that must be in place when packing a box using it. PPE needs to be worn and packing of the payload must take place in an aerated room so when the dry ice melts, it sublimates, it disperses into the air and is not inhaled.

During shipment clinical trials have a lot of regulation, certification and custom points to navigate, therefore during its journey a box may need to be stalled or held at customs for checks.

If using dry ice, the moment the box is opened or the dry ice escapes, the amount of temperature control you have is limited.

Some of the latest industry developments relate to PCMs, a liquid that will freeze and change phase at a set temperature, negating the need to use dry ice. Newly developed PCMs incorporating different chemical elements will see the liquid freeze at -50°C or -40°C and there's an emerging trend for a -35°C temperature requirement and standard -20°C.

This enables you to freeze panels in advance of shipment without the need to use dry ice or its associated safety measures. The coolants can be packed in a box with standard handling processes and during shipment, should there be a delay, that box can be placed in a freezer and the PCM will stop thawing, won't sublimate so no temperature changes will occur. Once the box continues its journey it will maintain the previous temperature control.

We are seeing PCMs being tailored to specific lower temperature requirements so the performance is available without the potentially hazardous risks related to dry ice, as there is no danger associated with PCM.

As more new PCMs blends become available and packaging advances, we will see dry ice usage reduce further.

Looking ahead we will continue to see the increased incorporation of technology, computers and mobile devices being utilised to make it easier to collect and store live data. This is vital as it allows the CRO to improve the design and conduct of future clinical trials. While the COVID-10 pandemic impacted all aspects of clinical trials, the speed of the trials for developing vaccines proved that processes can be conducted at pace and at a rate not seen before. There are numerous regulatory systems and automated data capturing involved that has been improved as a result of the advancements made during the pandemic, which will improve processes for the future.

A lot of infrastructure has been learned through the pandemic response within the clinical trial world and a key development is the public understanding of clinical trials has increased considerably.

The publics' interest of clinical trials has improved people's awareness overall. This has helped clinical trial companies increase the number of trial participants, which will help improve the success rate of future trials and drug development.

Ross Gregory

Ross Gregory joined Peli BioThermal in 2011 where he works as a Business Development Manager. With over 15 years of experience in commercial sales; customer account management and long-term strategic planning, Ross is a key member of the Peli BioThermal business where he specialises in helping customers facing difficult pharma distribution challenges. Since Ross joined the organisation, Peli BioThermal has experienced significant sales growth throughout its comprehensive single/reusable parcel and bulk shipper products, specially developed for the pharmaceutical and clinical trials market. Before joining Peli BioThermal, Ross spent five years working in retail and the consumables industry as a sales representative and team leader.

Email: ross.gregory@peli.com