CryoPod™ Carrier: Standardized Cryogenic Temperature Handling of Cellular Therapies

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Abstract

Temperature control during sourcing, manufacturing, and delivery of cell therapies is crucial, as fluctuations can affect viability and function of the cells, and potentially, the overall efficacy and safety of the therapeutic product. In many cell therapy workflows, source cells arrive cryopreserved at LN2 temperatures (-150 to -196°C), and post-manufacturing, cells are again cryopreserved and stored in vapor- or liquid-phase LN2 prior to their use in the clinic. In either case, containers filled with dry ice (-50° to -75°C) or liquid-phase LN2 are frequently used to transport cryopreserved cells around the manufacturing or clinical setting. However, these approaches introduce temperature cycling (LN2 to dry ice temperatures), can be unsafe for users, and are an unstandardized means of internal transport. Furthermore, multiple studies have shown that transient warming events affect cell viability and function and that tracking the temperature of the cells during any transit period is essential.

To improve standardization in how cell-based therapies are transported, BioCision and Brooks Life Science Systems have jointly developed the CryoPod™ Carrier, a safe, portable solution that, once charged with LN2, maintains a stable < -150°C environment for over 4 hours. LN2 is contained in the CryoPod Carrier in a manner that prevents sloshing or spilling, and there is no direct contact between the contents and the LN2. Additionally, the on-board electronics display and log temperature and time to provide assurance that the contents have not been subjected to temperature variation, and it accommodates one standard freezbox or multiple small bag cassettes.

The CryoPod Carrier standardizes internal cryogenic transport and provides researchers, manufacturers, and clinicians a solution for safeguarding the cryogenic cold chain for valuable cell therapy products and those handling them.

Introduction

There are hundreds of cellular therapy products currently under clinical development, from islet cells, to immune cells, to stem cells.[1] The global cell therapy market is projected to grow to over $3 billion by 2020. Maintaining cold chain integrity from point of manufacture all the way to patient administration at the clinic means that temperature should be tracked and monitored at all times, including during short term handling and transport that may include sample transfer within a facility, across campus, or across town. The CryoPod™ Carrier is the result of a year-long joint development project and is specifically aimed at addressing a critical gap in the cold chain by minimizing temperature fluctuations during short term transport. The carrier protects cryogenically frozen biospecimens by holding a stable temperature of less than -150°C, below the glass transition temperatures of water, where biological activity is believed to cease. The carrier incorporates a special material that holds and minimizes LN2 movement and prevents LN2 from coming in contact with either the samples or the handle. It also features a LN2 autofill option, ensuring hands-free replenishing of the LN2 charge in less than 15 minutes.

The CryoPod™ Carrier is a novel year-long joint development project and is specifically aimed at addressing a critical gap in the cold chain by minimizing temperature fluctuations during short term transport. The CryoPod Carrier delivers integrated temperature tracking and logging, providing assurance of patient safety in terms of product quality and efficacy upon arrival at the delivery site.

• Up to 4 hour hold time at < -150°C with lid on
• Minimizes or eliminates LN2 contact
• +3 L liquid nitrogen (LN2) charge
• Temperature monitoring, logging, and alarms
• Portable and easy to handle
• Fits one 2” high cryobox or 2-3 small cassettes
• Magnetized lid helps protect samples

Methods

To obtain temperature hold time data, a prototype CryoPod™ Carrier was loaded with ~2.8 L of LN2 and the interior basket air temperature was monitored by thermocouples at different heights above the bottom of the basket.

To measure temperature profiles during toting, a fully charged prototype CryoPod Carrier at steady state temperature was loaded with a partially filled cryobox equilibrated to LN2 vapor phase temperatures. The lid was closed and the unit was carried around the local vicinity for 1.5 hours. The temperature in 4 sentinel vials was measured the entire time by thermocouples. At the end of the toting, the cryobox was removed from the carrier and returned to LN2 vapor phase.

To test cherry-picking, a charged prototype CryoPod Carrier at equilibrium was loaded with a cryobox that had been equilibrated to vapor phase LN2 temperatures. The temperatures of 4 sentinel vials were monitored by thermocouples as well as the temperature of the air directly above the open cryobox. 30 vials were cherry-picked from the cryobox using gloved hands and the fluctuations (if any) in the sentinel vials were recorded.

Results

Stable Environment for Cherry-Picking Samples: The CryoPod™ Carrier maintains samples below -150°C - even with the lid open - allowing cherry-picking of samples without exposing "innocent vials" to unwanted temperature fluctuations.

Stable, Reliable Toting Solution: Unlike homemade dry ice carriers or carriers containing free LN2, the CryoPod™ Carrier can be used to transport samples without damaging temperature fluctuations. Temperature was stable and remained below -170°C for each cryovial throughout transport with little variation between vial positions.

Conclusions

In conclusion, the CryoPod™ Carrier is a hand-portable liquid nitrogen-based system for handling and transporting frozen biological samples or cell therapy products over short distances. Its ability to maintain, track and log temperature, as well as its unique safety features give the CryoPod Carrier a clear advantage over other common cryogenic shipping methods.

CryoPod Carrier Use Scenarios

• Transporting vials or cassettes within GMP laboratory or manufacturing area
• Cherry-picking samples
• Transporting samples within hospital or pharmacy setting

References and Acknowledgements