Cryogenic Gas Solutions Drive Regenerative Therapies in Life Sciences

By Tamie Joeckel

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Breakthrough innovations in medical research and discovery now dictate the use of cryo preservation, transportation, and storage solutions for therapies that treat chronic and terminal diseases. For years the pharmaceutical industry has been excited about "personalized medicine" to save lives. And recent, innovative medical research is making the dream a reality. Regenerative therapies, immunotherapies, autologous treatments, and allogeneic stem cell discoveries have created treatment protocols that require strict temperature stability.

The manufacturing process for these therapies is complex and usually requires tissue or blood from the patient to make the treatment. Most of the time, there is a single manufacturing facility that serves a global patient population. Traditional shipping solutions such as dry ice not only present hazardous material and handling risks, but the temperature instability can lead to the loss of the cells required to make the treatment.

Cryoport, the leading provider of deep-frozen solutions for shipping and storage for the life sciences industry, understands the importance of temperature stability and patient safety. The Cryoport solutions combine the technology of liquid nitrogen dry vapor shippers with the most advanced logistics management platform in the industry to replace outdated dry ice shipping.

"The cellular therapy, and more broadly, life sciences industry, is investing billions of dollars to advance therapies that are changing the face of modern medicine. It is imperative that companies in this space confer with experts in cold chain logistics as early as possible for feasibility and program execution planning required to help mitigate risk and ensure success in global programs," stated Tamie Joeckel, Senior VP of Consulting for Cryoport. "Whether in Phase I, II, or III in clinical trials or planning for commercial launch of a new therapy, global planning is critical. We recognized this as a great opportunity for Cryoport." The data and experience captured in executing over 30,000 shipments to over 100 countries, affords Cryoport a unique perspective to the challenges of life sciences manufacturers. Cryoport's experts support manufacturers in devising global strategies that help mitigate risk and ensure patient safety.

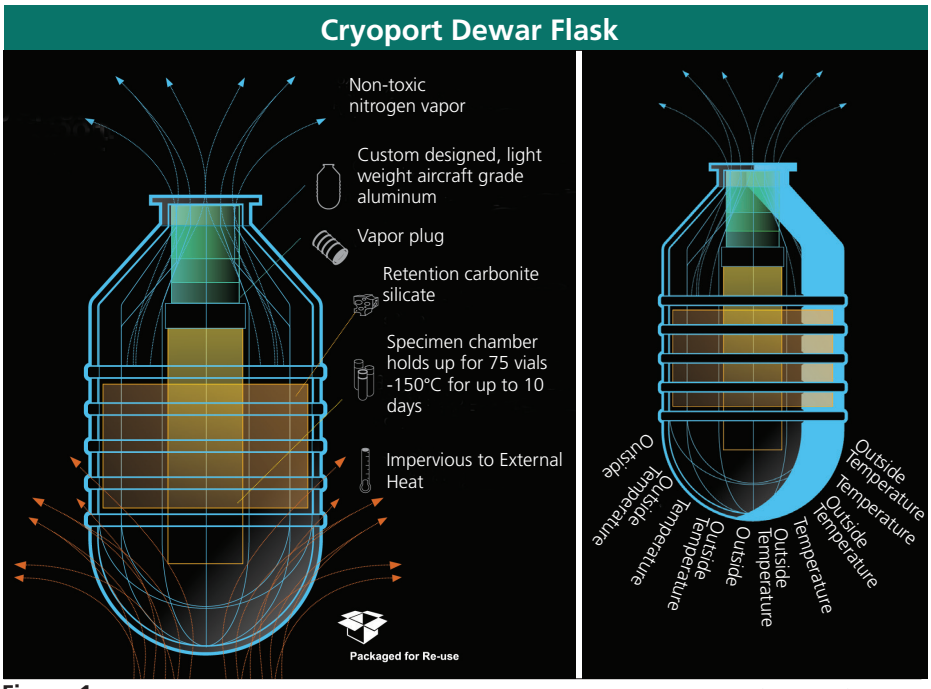

Figure 1

Source: Cryoport

Immunotherapy, also called biologic therapy, is a type of treatment designed to boost the body's natural defenses to fight disease. It uses materials either made by the body or in a laboratory to improve, target, or restore immune system function. One of the most exciting areas of research today is CAR T-Cell therapies to fight cancer. These tumor targeting therapies are generating remarkable results in cancer research. The premise is simple: extract a patient's T-cells from their blood and train them to recognize and kill cancer cells and then re-infuse them back into the patient. The engineered cells recognize and kill cancerous cells, while reactivating other immune players that have been dampened by cancer's inhibitory signals.

While the first CAR T-cells were developed at the Weizmann Institute of Science in Israel in the late 1980s, it has only been in the last few years that the true breakthroughs have occurred. Since 2013, at least half a dozen companies made deals worth hundreds of millions of dollars for research funding. While most of these studies are currently aimed at late-stage disease for which other therapeutic options have failed, researchers in the field anticipate that these immunotherapies could replace standard cancer treatments in the future.

The importance of these therapies has not escaped the notice of regulatory authorities. CAR T-cell treatments are being given priority review for filling unmet medical needs both in the US and globally. Many of these therapies are receiving orphan or breakthrough status from the US Food and Drug

Administration (FDA), bringing expedited regulatory review, which translates into earlier approvals and paths to commercial launch. It's an exciting time that Cryoport has been preparing and waiting for!

The programs that support the production of these therapies are quite complex and require hands-on management of multi-leg components. As an example, some programs require collection of blood or tumor samples from the patients that are then shipped to a manufacturing facility. The treatment for the patient is produced to be shipped back for infusion into the patient. (This is called an "autologous" therapy since the patient's own cells are used to produce their treatment.)

A critical complication in the global transportation strategies for these therapies is the unpredictability of flight schedules and customs brokerage processes. The ability to maintain stable temperatures is critical. Cryoport's patented, custom-built dry vapor shipper (Figure 1) is an aluminum dewar that uses liquid nitrogen (LN_2) and is validated to maintain a stable temperature below -150°C for an average 10-day dynamic shipment. The stable system virtually eliminates sample and cell loss that occurs with temperature excursions.

Combined with our proprietary logistics management technology platform, Cryoport actively manages the chain of custody and chain of condition throughout the shipment (Figure 2). The system sends automated alerts should temperatures or conditions change, allowing Cryoport to intervene if necessary to protect the commodity. Additionally, the intelligent logistics platform integrates all logistics, conditions, and regulatory data in a single data stream for each shipment, enabling manufacturers the ability to directly correlate external events to the condition of the commodity and its impact on the holding time of the equipment. The platform includes portal-accessible dashboards and validation documentation for every shipment. It records temperature (internal and external) along with other crucial data such as humidity, opening to light, orientation, etc. Consequently, every shipment using the condition monitoring system has a full chain-of-custody and chain-of-condition.

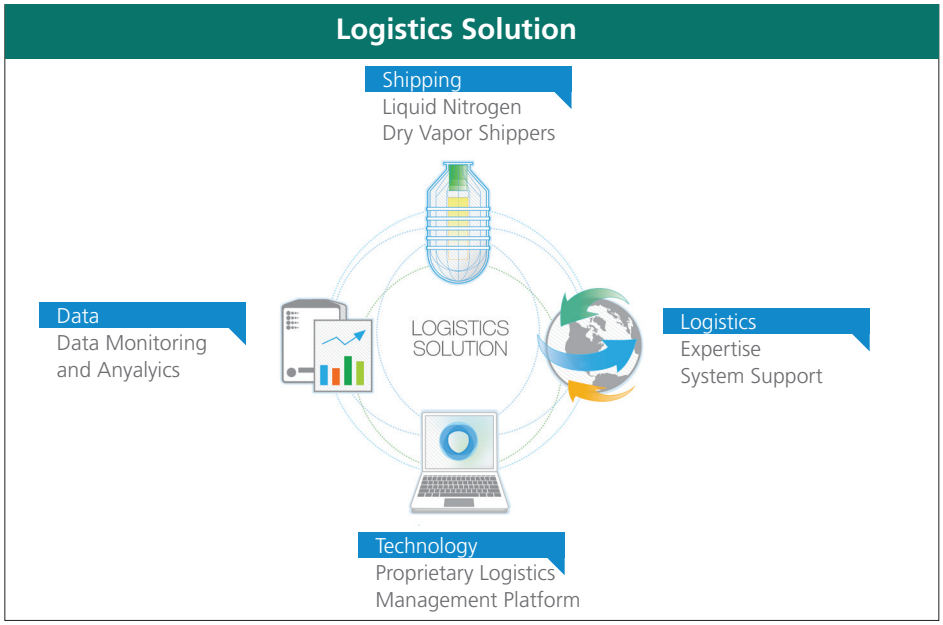

Figure 2 Source: Cryoport

Mark Sawicki, Ph.D., Chief Commercial Officer of Cryoport, stated, "Regulatory bodies are starting to take notice and establish specific criteria related to the storage and distribution of these types of therapies."

The International Organization for Standardization ("ISO") is currently reviewing guidelines for the storage and distribution of these types of therapies. ISO /TC 212 and ISO/TC 276 will be the standards by which all regulations are likely to be established. ISO 212 specifically outlines the testing requirements that must be met and maintained when evaluating the quality and potency of these therapies. ISO 276 will define the standards for storage and distribution of these therapies including storage and packaging validation, comparability, and metrology.

It is anticipated that part of these standards will dictate the limits of environmental excursions acceptable during distribution of these therapies and the level of detail required for the packaging qualification and validation. Dr. Sawicki further stated, "Current phase change and dry ice solutions do not support the criteria required for the safe and efficacious transportation of these products. Phase change materials can be adversely impacted by the external environment unfavorably shortening holding time and are highly susceptible to delays. Any intervention would require opening the package and potentially impacting the commodity being shipped. Dry ice options usually only have a three-day window for temperature hold time and have a tendency to have volatile temperature control issues that are highly dependent on packaging and can subject the commodity to temperature fluctuation of up to 60 degrees C. This can negatively impact the commodity shipped by changing the pH."

Cryoport, with headquarters in Irvine, California, and operations in Rotterdam and Singapore, currently supports 68 clinical trials in the regenerative medicine space, and 11 of those 68 are in phase III. Additionally, Cryoport supports eight of the top 10 CAR T-Cell therapies.

Cryoport's deep frozen shipping expertise has been developed in supporting programs for everything from vaccines and biologics to semen and embryos. They offer programs and solutions for the biopharmaceutical, animal health and reproductive medicine (IVF) industries. ■

Tamie Joeckel, Senior Vice President of Client Services, leads Cryoport Temperature Controlled Logistics' Consulting Division. She has 25+ years of experience in pharmaceutical industry logistics, commercialization strategies, distribution, and manufacturing, and has participated in launch strategies for over 20 biopharmaceutical therapies.