Cryoport Systems Inc.
www.cryoport.com

cryoport
SCIENCE. LOGISTICS. CERTAINTY.

Building an unbreakable Chain of Compliance

Cryoport's experience in cold chain logistics is now facing its biggest challenge yet—keeping patients' therapies safe from damage in the revolutionary new field of cell therapy.

Regenerative medicine advanced therapies (RMATs) in the form of cell and gene therapies are breaking new ground, providing patients the potential of treatment, reversal or even cure of serious and life-threatening conditions, including genetic disorders and cancer. The logistics and supply chains for these therapies, particularly those that involve the manipulation of autologous cells, can be complex, and there are many points in the chain in which the cells are vulnerable to accidental diversion or temperature deviation.

Cryoport provides cold chain logistics for temperature-sensitive life sciences materials to biopharmaceutical, in vitro fertilization and surrogacy, and animal health organizations around the world. Materials are shipped in proprietary Cryoport Express liquid nitrogen dry vapor shippers, and their condition and location are monitored constantly.

The importance of the Chain of Compliance

For any therapeutic, and particularly for a personalized therapeutic, it's important to know that the treatment that leaves the manufacturer is the same drug, in the same condition, as when it reaches the patient, and that it hasn't been interfered with or damaged in any way, whether accidentally or intentionally. Bioinformatics and serialization play an increasingly important role in the therapeutic supply chain, ensuring the chain of custody, the chain of condition, the chain of identity, and now the Chain of Compliance.

The Chain of Compliance can be defined as the traceability of the equipment, processes and logistics handling of a therapeutic, which together ensure the best possible management of the environmental control of the drug or product in transit.

"We already had a focus on custody, condition and identity, but the real significance of the Chain of Compliance only struck us when we received feedback from a physician, who would not take custody of our Cryoport Express shipper containing a cell therapy until we could assure them that the shipper had never held any animal-derived products," said Mark W. Sawicki, chief commercial officer at Cryoport.

After further investigation, the Cryoport team discovered that health-care professionals wanted assurance not just of the history of the shipments themselves, but of the historical use, performance, handling, and cleaning of the equipment as well. This has its roots in 'traditional' biologics manufacturing, in which manufacturers have to prove the absence of any contaminants such as animal-derived products in the manufacturing process, as well as provide assurance over cleaning protocols.

Fig. 1 | Cryoport's proprietary and dedicated human-use-only fleet for RMAT products. RMAT, regenerative medicine advanced therapies.

Making changes to improve compliance

Cryoport is creating its own Chain of Compliance, throughout the entire equipment, processes, and logistics route.

"This is going to become increasingly important very quickly," said Sawicki.

All products shipped by Cryoport are tracked from loading, through storage and fulfilment, to delivery at their destination site. The tracking parameters during travel include location, pressure, temperature, orientation, shock, light, and humidity. After emptying, the cryogenic shippers, which combine advanced packaging with cryogenic and vacuum technologies, are cleaned and reused. Cryoport holds an information archive for each vessel and its components and accessories, including its contents, performance, and maintenance and refurbishment history.

Examples of changes implemented in-house specifically for the RMAT products include ensuring the traceability of the contents of each tank from inception, and the tanks' cleaning and requalification. This level of tracking and monitoring will require additional informatics, but Cryoport is confident that these changes are already in place. Cryoport has also committed that the tanks used for RMAT products will be dedicated to human use only (**Fig. 1**).

Developing standardization in the Chain of Compliance

As the RMAT arena is relatively new, standardization is still a process in development. Currently, regulatory authorities, including the US Food and Drug Administration (FDA) under the 21st Century Cures Act, only consider the recovery, isolation, and delivery of RMATs, but are likely to extend their view to the supply chain as the industry becomes more established.

"We spoke with the FDA about the concept of the Chain of Compliance, and the agency recognized how important it could be," said Sawicki. "We are also working with our suppliers to ensure that they commit to these levels of compliance."

Two nonprofit bodies, the Alliance for Regenerative Medicine and the Foundation for the Accreditation for Cellular Therapy, are analyzing all aspects of the collection, manufacture, transportation, and administration of regenerative medicines, and this will include the development of a standard for the Chain of Compliance. Cryoport is working with the two organizations to have input into what could become a common industry requirement.

Risk management in the field

One of the biggest challenges that Cryoport and RMATs face is risk management in logistics—while Cryoport can control the handling and environment while the shipper is in-house, once the package leaves the company and enters the field where it will be handled by untrained personnel such as couriers and baggage handlers, there is less control.

"There is no latitude for failure with these products as human life and health is at stake," said Sawicki. "If we can't control the environment, we need to minimize the risks."

To do this, Cryoport continues to work to understand the risks better, including bringing real-time track and trace online. The company is also developing its Cryoport Express shipper construction to ensure better protection and traceability for the contents.

contact
Mark W. Sawicki,
Chief Commercial Officer
Cryoport Systems Inc.
Irvine, CA, USA
Tel: +1-949-232-1900
Email: msawicki@cryoport.com