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Three Questions Mark W. Sawicki, Cryoport

CWWeekly *presents this feature as a spotlight on issues faced by executives in clinical research. This week, writer Karyn Korieth spoke with Mark W. Sawicki, Ph.D., chief commercial officer of Cryoport, which provides cold chain logistics and storage solutions to the life sciences industry.*

Q CenterWatch has reported that costs for supply chain logistics, which account for up to 25% of total R&D spend, are increasing primarily due to growth in therapies that require cold storage. Why are costs associated with cold chain logistics growing?

A With the advent of regenerative medicines and personalized therapies, many advanced cell and gene therapies are extremely sensitive to temperature. The vast majority of these materials must be transported cryogenically at liquid nitrogen temperatures, which require specialized packaging to ensure absolute stability in order to maintain viability.

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Temperature-controlled shipments also require a higher level of scrutiny. Condition and location data tracking is needed since, in almost all circumstances, a temperature excursion can reduce the long-term stability of the product or destroy it outright.

Batch size and the lack of economies of scale also drive up costs. Traditional, small-molecule therapeutics can be shipped in bulk quantities, stored in a warehouse or distribution center for an extended period of time and shipped via conventional methods. But the vast majority of these new regenerative therapies require a unique batch per patient, necessitating a more complex supply chain with individual, patient-specific shipments. These therapies have to be transported on a singular basis: one patient, one box, one sample.

Timelines are very, very tight. The minute that apheresis material or cells are obtained from the patient to go to manufacturing, the clock starts and materials have to be moved very quickly. It requires a specialty courier literally waiting at the procedure site for the product. In addition, almost everything is shipped via air with condition and location monitoring and managed from point of origin to the destination. Packaging, specialized equipment carriers, data monitoring and small shipment quantities all drive costs.

Q Do sponsor companies typically integrate cold chain logistics planning into their clinical trial designs?

A Traditionally, logistics was an afterthought. The scientists would develop a drug and, since a small-molecule drug or even a biologic was fairly stable in most conditions, they didn't have to worry much about temperature management and the condition of the final product. Now the entire work flow of these new therapies is centered on logistics.

The material has a critical logistics component with critical timing. Where previously there might have been a small-molecule drug with a single leg of transport, some of these new therapies will have six or seven different legs of transport in the manufacture of a single dose of product. The logistics are extremely complex and they can't be done through the traditional distribution processes.

Logistics should ideally be considered in preclinical planning. When we first started supporting clinical programs, companies would come to us in phase II and early phase III. Today, the vast majority of companies approach us during late preclinical studies, when we can sit down and help them design the engagement strategy for a phase I trial. Logistics planning is being pushed front and center. There have been examples of companies that did not think these strategies through in advance and it critically impacted their ability to market the product.

Q How can cold chain logistics planning and management affect data quality and the ultimate outcome of a clinical trial?

A Most of the newer drug targets have a series of biomarkers associated with them that are much more sensitive to temperature excursion than they were in the past. A temperature excursion on the material used for biomarker testing can destroy the clinical test

results or influence them to the point where they impair the clinical data and ultimately impact the clinical trial.

The choice of transportation for critical biomarker samples can have a significant impact on the quality of the data being used to determine the efficacy of a drug. Shipping temperatures have been shown to significantly affect the integrity of cell materials. Choosing the wrong transportation medium, or cutting corners, can put the clinical data integrity at risk.

If a company ships something on dry ice, for example, and it gets delayed in customs as it moves from one country to another and the dry ice can't be replenished, the material could be destroyed. Dry ice can also change the pH of samples that are being distributed. Even the process in which a scientist removes the product from the cryogenic shipping package and places it into a freezer will impact both the freeze/thaw rate and the product, and, therefore, will also affect the quality of the study data.

We advise all our clients conducting clinical trials to plan their logistics strategy as early as possible, complete a comprehensive risk assessment for each leg of the supply chain, confirm shipping lanes and train their staff and clinical teams. Not planning ahead and assessing risk may jeopardize the results of the clinical study.