BioServices:

Advanced Solutions for Cell and Gene Therapy Material Management

Cryoport Systems

Americas • EMEA • APAC
info@cryoport.com | +1 949.232.1900
cryoport.com

MKT-164 Rev. B IQS-3235 Effective Date: 4/22/2024

Introduction to BioServices

The global cell and gene therapy (CGT) manufacturing market continues to rapidly advance. The Alliance for Regenerative Medicine reported that as of the end of Q3 in 2023, there were 1,804 clinical trials being conducted worldwide which had garnered a total of $2.2B in investments.[1] With so much growth in such a short amount of time, efficiency and compliance throughout each phase must be top of mind for manufacturers to stay on track with the desired approval timelines. But to keep with these standards, the burden of cost for facilities and resource management largely takes capital away from budgets.

However, because the cell and gene therapy field is quickly evolving, there has been parallel growth in supply chain solutions to meet the exacting needs of this industry. Integrated BioServices offers a range of supply chain solutions to support the management of biological materials. Utilizing BioServices solutions offers manufacturers and sponsors a way to create and sustain a stronger supply chain for the cell and gene therapy market. When manufacturers and sponsors take advantage of BioServices, they are actively mitigating risk to their overall supply chain while saving valuable capital for the research of their lifesaving therapies.

> “The average cost of a single dose of a specialized therapy starts at $1 Million.”
>
> - As stated in an analysis by ICER

The Need for BioServices

As cell and gene therapy manufacturing processes mature, it’s essential for the industry to grow alongside and correspondingly develop systems to support commercial scale production.[2] The growth in this specialized field starts with establishing specialized facilities. Many developers seek to build a facility that can manufacture these cell and gene therapies that also contains distribution solutions all in-house. However, building this type of facility is time consuming and expensive.

A study published in the Journal of Health Economics found that total capitalized costs of cell and gene therapy research and development were shown to have increased at an annual rate of 8.5% above general price inflation.[3] This year-over-year increase has added pressure on manufacturers to find ways to save money, but there are few areas of expense where cutbacks are possible. Organizations are required to comply with the federal regulations imposed by their country (for example, FDA CFR 21[4] for the United States and EudraLex Vol. 4[5] for Europe). These stringent standards coupled with the cost of building and maintaining proper facilities for the production and preparation of distribution places a high burden of cost on manufacturers.

Additionally, adhering to GMP practices throughout each development and trial stage is extremely important. Proper documentation for all conducted processes is critical to ensuring the validity of all activities and operations. If the necessary standard operating procedures (SOPs) that show how the materials were handled are not completed correctly, then the therapy product is considered non-compliant[6], which could result in the rejection of the therapy and subsequent waste of expensive resources as well as the potential inability to treat a patient.

In summary, the combination of complex manufacturing processes, high facility costs, and stringent regulatory requirements puts strain on the entire therapy manufacturing process. BioServices is focused on addressing these strains through high-quality, compliant support services and a network of integrated facilities. By outsourcing material management with BioServices solutions, manufacturers and sponsors can focus more of their attention on their research and developmental efforts.

Cryoport Systems' Integrated BioServices Capabilities

Cryoport Systems is an industry-leading provider of supply chain management solutions for the life sciences. We have extended our platform to include our own integrated BioServices solutions to support the manufacturing and distribution of cell and gene therapies.

Our unified BioServices offerings provide developers with an outsourced solution for the support of their cell and gene materials without requiring all services be conducted in their facilities. The scope of BioServices' materials management is aimed to help developers cut back on facility costs while easing the growing pains of market scaling through flexible and custom solutions. Cryoport Systems' integrated BioServices materials management fulfills those capabilities and goes beyond with our risk-mitigating solutions.

Cryoport Systems' BioServices solutions offer global reach through our facilities located both within the U.S. in Houston, TX, Morris Plains, NJ, and within Europe in Clermont-Ferrand and Pont-du-Château, France. The following offerings encompass our integrated BioServices capabilities.

GMP-Compliant Storage

We have a range of storage options that offer secure, GMP-compliant, and controlled-temperature storage of biological materials. Our storage equipment is validated with full temperature monitoring, redundant infrastructure, backup storage units, and on-call technicians. We can store materials for long or short periods at the following temperatures:

- Controlled Room Temperature (15-20°C)
- Refrigerated (2-8°C)
- Frozen (-20°C)
- Ultra-cold (-80°C)
- Cryogenic (<-150°C)

> The Cryoport Systems' team not only knows BioServices, but we know supply chain management. When you utilize our BioServices offerings, you're gaining opportunities to actively mitigate risk to your supply chain through our expert knowledge and solutions specifically designed to keep your materials safe throughout each phase.
>
> - Mark Sawicki
> President and CEO
> Cryoport Systems

Kit Production

We can handle the specifics of distribution with our kit production services. Our expertise extends to all types of kits such as apheresis, blood/tissue collection, manufacturing, drug administration, etc. This service encompasses:

- Kit design services
- Component procurement
- Inventory management
- Labeling
- Distribution

Secondary Packaging & Labeling

Our packaging and labeling services take care of the packaging and labeling of drug products and other materials. Conducted by a team of experts, this service includes:

- Carton and label design
- Validated translations
- Tamper-evident seals
- Labeling down to Ultra Low temperatures
- Packaging down to Cryogenic temperatures

Regulatory & QP Services

The EU Clinical Trials Directive 2001/20/EC[7] and Annex 13 of EU GMP Guide[8] requires all manufactured drugs be certified by a Qualified Person (QP). Our EU locations offer this service as well as the following:

- Confirmation and certification of clinical and commercial products
- Pass-through depot for urgent shipment requests
- Consulting services concerning regulatory requirements
- EU QP audits of manufacturing/testing facilities
- Issuance of EU QP declaration to support CTA submissions
- Trade compliance guidance

Drug Return & Destruction

Our BioServices offerings extend to post-production. With our drug return and destruction capabilities, we handle all aspects of the return process including:

- All required services concerning returns, reconciliation, and destruction by GMP/GCP compliant procedures
- Coordination with the investigational site and study team
- Temporary quarantine storage
- Destruction certificates
- Temperature-controlled returned shipments when required

Clinical Sample Management

Our EU facility offers clinical sample management and central laboratory services for pharmaceutical and biotechnology companies. We provide centralized administration of clinical sample logistics flows, including those not routed to our facilities. We specialize in providing:

- Innovative material documentation and processes
- Dedicated project management
- Remote-accessible business intelligence tools connected to our Clinical Trial Management System (CTMS), Laboratory Information Management System (LIMS), and Enterprise Resource Planning (ERP)
- Real-time monitoring, review of indicators, and data report generation

BioBanking

Our comprehensive and adaptable solutions extend to the management of biological and chemical resources. Our biobanking services provide the support required to centralize and store client research collections while adhering to the proper compliance protocols. We can support a range of storage options and accommodate the needs of various:

- Sample origins (human, animal, plant, etc.)
- Settings (R&D, clinical trials, scientific cohorts, etc.)
- Types (blood, serum, cells, bacteria, etc.)

BioServices & Broader Capabilities

The addition of our BioServices offerings fits with Cryoport Systems' established network of solutions and extends our expertise beyond logistics. Our BioServices solutions integrate seamlessly into our existing Cryoport Systems platform, otherwise known as our network of solutions and services that support robust supply chain management. This integrated approach means that Cryoport Systems can take care of both an organization's BioServices needs and its broader supply chain management requirements throughout each step in the process.

Additionally, Cryoport Systems has strategically established its BioServices facilities under the same roof as our logistics centers. The centralization of our logistics and BioServices activities reduces risk and the number of legs required to transport material from our centers, thus cutting the overall cost and the needed oversight.

Our singular outsourced method is poised to save time through our streamlined services and add additional safety measures with our instituted SOPs and compliance procedures. This approach allows our clients' critical therapies to reach patients within a reduced amount of time in comparison to utilizing multiple providers.

> "Cryoport Systems' integrated BioServices solutions is the link that connects the manufacturing of advanced therapies from its initial trial phases to a commercial, life-saving product in one consistent process."
>
> - Robert Jones
> Vice President of Global BioServices
> Cryoport Systems

Network of Compliant Solutions

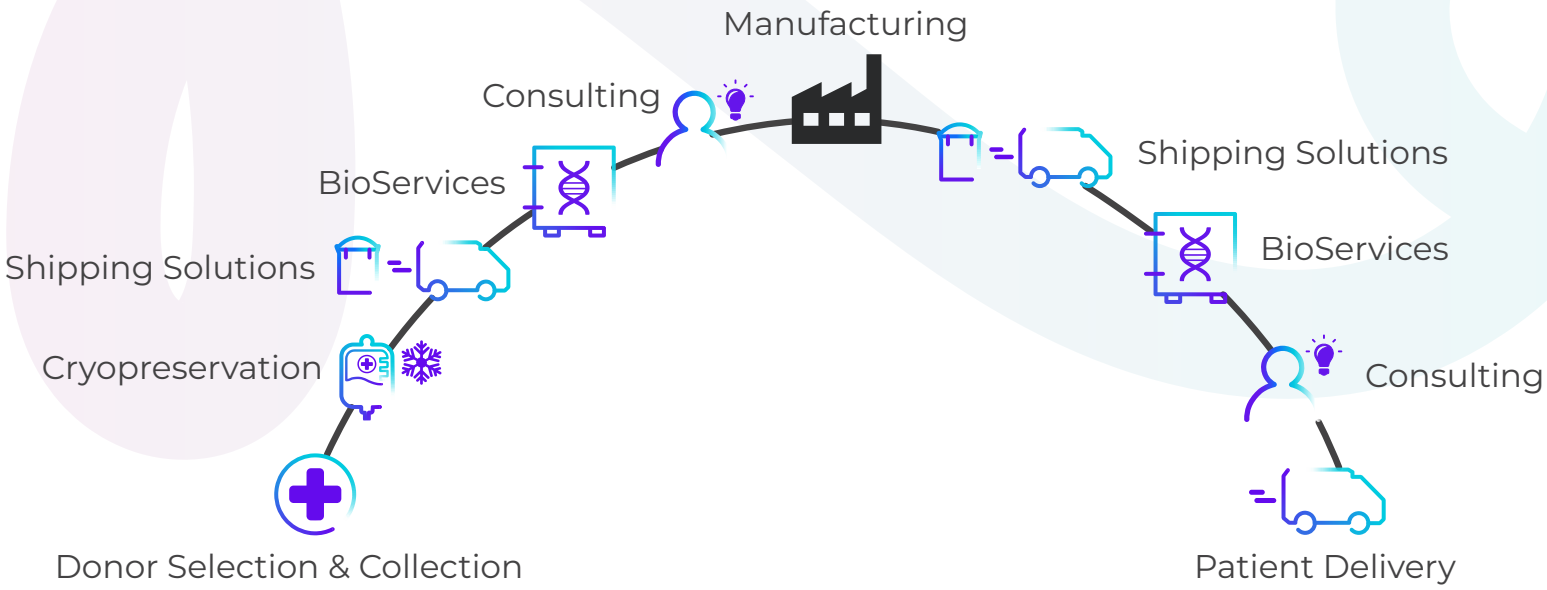
When you trust Cryoport Systems with your BioServices requirements, you are backed by a network of compliant supply chain management solutions across global facilities. We possess ISO 9001:2015 certifications, adhere to ISO 21973 "General Requirements for Transportation of Cells for Therapeutic Use," and are registered with the FDA for HCT/Ps per CFR 1271. Our supply chain expertise has supported 775,000+ shipments, 650+ clinical trials, and 10+ commercial products. We work with manufacturers and sponsors throughout all trial stages and can scale our services to meet clients' growing needs.

The Cryoport Systems platform delivers unparalleled supply chain services for biological materials and therapies that need specialized temperature-controlled management. In addition to our BioServices offerings, these solutions include:

- A specially designed Advanced Therapy Shipper™ (ATS) fleet exclusively dedicated for the shipment of cell and gene therapy materials
- Full transparency regarding equipment performance, commodity history, equipment requalification, calibration history, and the correlation of in-field events with our exclusive Chain of Compliance®
- The industry's first and only validated shipper cleaning and disinfection process, Veri-Clean®
- IntegriCell™, a standardized cryopreservation and distribution solution for the global cell therapy market
- Consulting support with expert services to accommodate specific material management needs through personalized shipping risk assessments, shipping lane validations, packaging validations, and many other critical solutions

> The combination of our integrated BioServices solutions and our broader supply chain services is a natural capability and function of what we offer to our clients. We fulfill our clients' BioServices needs at a single location that also houses our logistics capabilities. Our experts can, for example, move a therapy from storage into a fully validated shipper and to the patients within a few hours. It's truly incredible how we're able to help support our clients in their life-saving work in this way.
>
> - Robert Jones
> Vice President of Global BioServices
> Cryoport Systems

Comprehensive Supply Chain Management



Conclusion

In the rapidly evolving world of cell and gene therapy development, the complexity and cost of manufacturing plus maintaining a succinct supply chain can drain operations of capital before therapies have the chance to reach patients. Outsourcing material management to a partner who can provide integrated BioServices solutions allows manufacturers and sponsors to focus their capital and efforts on their important research while also saving time and adding additional security measures to their processes. Cryoport Systems' integrated BioServices offerings include clinical sample management, temperature-controlled storage, biobanking, kit production, packaging and labeling, regulatory and QP services, and drug return and destruction. These services combine directly into our platform of intelligent logistic solutions, allowing Cryoport Systems to be the single vendor for supply chain management and BioServices solutions backed by over two decades of industry-informed expertise.

> In the dynamic world of life sciences where the tiniest fluctuations in environment could render valuable biological materials ineffective, Cryoport Systems stands as a steadfast enabler. We are client-centric, and at the heart of our mission lies an unwavering commitment to supporting life and the health of humanity.
>
> - Jerrell Shelton
> President and CEO
> Cryoport, Inc.

References

1. The sector snapshot: December 2023. Alliance for Regenerative Medicine. (2023, December). https://alliancerm.org/sector-snapshot-december-2023/
2. Pigeau, G. M., Csaszar, E., & Dulgar-Tulloch, A. (2018, July 31). Commercial scale manufacturing of allogeneic cell therapy. Frontiers in Medicine. https://www.frontiersin.org/articles/10.3389/fmed.2018.00233/full
3. DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016, February 12). Innovation in the pharmaceutical industry: New estimates of R&D costs. ScienceDirect. https://www.sciencedirect.com/science/article/abs/pii/S0167629616000291?via%3Dihub
4. Title 21 of the CFR. Code of Federal Regulations. (n.d.). https://www.ecfr.gov/current/title-21
5. European Commission. (2022, February 16). The rules governing medicinal products in the European union volume 4 EU guidelines for good manufacturing practice for medicinal products for human and veterinary use. Health.eu. https://health.ec.europa.eu/system/files/2022-03/vol4_annex21_en.pdf
6. Denault Agnes Coquet Vincent Dodelet, J.-F. (2008, June 11). Construction and start-up costs for Biomanufacturing plants. BioProcess International. https://bioprocessintl.com/manufacturing/facility-design-engineering/construction-and-start-up-costs-for-biomanufacturing-plants-182238/
7. Clinical trials - Directive 2001/20/EC. (n.d.). Health.ec.europa.eu. https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-directive-200120ec_en
8. EudraLex: the rules governing medicinal products in the European Union. (2010). In Health EC (Annex 13). European Commission. https://health.ec.europa.eu/system/files/2016-11/2009_06_annex13_0.pdf

About Us

Cryoport Systems is a comprehensive supply chain partner for the life sciences industry focused on meeting the challenges of the global cell and gene therapy market. We excel in the specialized management of the biopharma supply chain through our comprehensive offerings in logistics, BioServices, cryopreservation, and consulting. With our expansive platform and decades of temperature-controlled supply chain expertise, Cryoport Systems helps Enable the Outcome for advanced therapies programs, safely and securely guiding critical therapies to patients in need.

Cryoport Systems

Americas • EMEA • APAC
info@cryoport.com | +1 949.232.1900
cryoport.com