

The Growing Role of Biobanking in Today's Medical Environment

by Jennifer Benner and Erik Koenig

For decades, biomaterials such as tissues, blood, and serum derived from clinical testing have played a critical role in drug development and academic research. The recent focus on molecular-based therapies, genomics, and biomarker discovery in today's medical research have dramatically transformed the way biotechnology and pharmaceutical organizations collect, transport, and store their biospecimens.

As the pharmaceutical industry shifts toward a more personalized approach to medicine, the need for high-quality, well-maintained biospecimens is at the forefront of medical research. But despite sophisticated protocols and strict regulations, organizations often overlook developing a strategy for long-term handling and storage of biological samples.

Such a lack of strategy could be detrimental because today's high-throughput molecular technologies allow researchers to implement a wide range of analyses on archived biospecimens that would not have been possible 20 (or even 10) years ago. These analyses have led to a better understanding of genetic and molecular changes involved in the progression of several complex diseases.

For example, advances in molecular and genetic epidemiology have enhanced the possibility of identifying individuals with genetic risk for certain cancers. Furthermore, the use of biomarkers is rapidly advancing, with applications now helping to



MILLENNIUM, THE TAKEDA ONCOLOGY COMPANY (WWW.MLNM.COM)

advance studies in cancer etiology, detection, treatment, and prognosis. The validity of results from biomarker studies using archived specimens, however, depends on the integrity of the specimens and the manner in which they are collected, processed, and stored.

For all those reasons, it is paramount that samples be maintained in the best possible condition and that a history of the samples' storage is kept in the greatest possible detail. For example, plasma samples should be stored at -70°C to -80°C with no freeze-thaw cycles (because they can damage sample integrity).

Given the pivotal role these materials play in pharmaceutical product development, long-term storage and handling of biomaterials is becoming an increasingly critical and strategic component of the worldwide drug development process. As such, companies must have

detailed business strategies when governing transportation, handling, and long-term storage of biosamples.

Organizations that explore biobanking solutions today have a number of options to choose from including storing on-site, off-site, or both. Nevertheless, due to the capital investment required to build a world-class biorepository, many pharmaceutical and biotechnology companies are increasingly outsourcing their sample management function to expert service providers.

A CASE FOR OUTSOURCING

To maximize margins and efficiency in a highly competitive and regulated environment, an increased number of biopharmaceutical companies are turning to specialized outsourcing providers to manage resource-intensive, noncore functions. Biomaterial storage, management, and logistics fall directly into this category. These services are particularly well-

suiting for outsourcing because of their required capital investments in equipment, facilities, trained personnel, technology, security, and transportation infrastructure.

A BIOMATERIAL STORAGE PROVIDER

Biomaterials generated during pharmaceutical R&D processes continue to grow exponentially in volume, type, and complexity. Even during the storage phase, clinical trial specimens represent substantial market value. For instance, pharmaceutical and biotech companies regularly conduct a range of testing, auditing, validation, and qualification processes on stored samples for different reasons.

Although of major importance, compliant storage is just one of many factors to take into consideration when considering an outsourced partner to manage your precious biomaterials. Because biotech drugs are made out of living cell cultures instead of the simple molecules used to create traditional pharmaceuticals, much of this development (as well as other research initiatives) relies on the safe, on-time, and compliant shipping of biomaterials.

COLD-CHAIN MANAGEMENT, TRACKING, AND MONITORING

As clinical research continues its migration toward globalization — expanding to such regions as Latin America, Eastern Europe, and East Asia — the process of transporting human clinical trial samples has become increasingly complex. As a result, the biomaterial cold chain has also become as critical as any other element in safeguarding valuable specimens throughout their lifecycles.

Cold chain management defines how temperature-sensitive products and biomaterials such as clinical trial samples, active pharmaceutical ingredients, and microbiological and viral samples are packaged, transported, and stored throughout research and development. Weakness or failure at any point in the cold chain can compromise product integrity, breach security, delay shipments, and ultimately result in financial loss or liability.

BIOREPOSITORY COSTS

A medium-sized biorepository could require an investment of more than US\$1 million for storage consumables and capital equipment such as ultralow-temperature freezers and liquid handlers. The energy costs alone to support such a biorepository can total as much as \$25,000/year, which only represents ~15–20% of the investment required to create a large biorepository. Additional hard costs and time are also incurred in

- Building specialized, secure facilities with dedicated, scalable storage space
- Purchasing state-of-the-art equipment (a single industrial freezer can cost >\$10,000)
- Developing or purchasing software for inventory and logistics management
- Establishing a sophisticated cold-chain logistics infrastructure that spans pick-up and delivery, handling, processing, and storage at exact temperatures and conditions
- Hiring skilled personnel with expertise in biomaterials storage, logistics, sample management, quality assurance, operations, and clinical laboratory management
- Maintaining staff training, certifications, and accreditations
- Validating equipment, technology, and processes
- Developing standard operating procedures (SOPs) and business continuity plans
- Ensuring “24/7” adherence to an expanding array of complex industry guidelines and regulations.

Consider what would happen if clinical trial samples thawed before they reached a testing laboratory. Such a compromise could cost the product sponsor hundreds of thousands of dollars to repeat a clinical study. Moreover, if samples are delayed by customs officials and don't reach their destinations on time, a ripple effect could result throughout the entire development process. Equally important is regulatory compliance. Lack of compliance can delay biologic shipments at inspection points or subject drug developers to fines ranging from a few hundred to thousands of dollars.

Maintaining cold-chain integrity requires logistics and management expertise to ensure that temperature-sensitive materials are not compromised during packing, shipping, processing, and storage. Effective cold-chain practices incorporate continuous monitoring to ensure sample integrity at all stages. This requires expansive software that allows researchers to track and validate the storage temperature.

The US Department of Transportation's (DOT's) hazardous materials regulations (HMR) and the International Air Transportation Agency's (IATA's) dangerous goods provisions specify requirements for the safe transportation of hazardous materials by rail car, aircraft, shipping

vessel, and motor vehicle. These regulations dictate specifications for classification, packaging, hazard communication, shipping papers, incident reporting, handling, loading, unloading, segregation, and movement of hazardous materials. Fines and shipping delays often result from noncompliance and lack of awareness of HMR requirements.

Outsourcing such complex and specialized functions to biorepository experts helps biopharmaceutical companies mitigate risks and allows them to allocate capital and resources toward their primary mission of drug development.

A CASE STUDY IN SEAMLESS OUTSOURCING

Millennium: The Takeda Oncology Company (Millennium) is a worldwide pharmaceutical company specializing in the discovery, development, and commercialization of treatments for cancer and inflammatory diseases. It relies on a deep understanding of the human genome and disease biology to develop therapeutic products that target underlying elements of disease and the molecular profiles of specific patient populations.

The company pioneered VELCADE bortezomib for injection, a novel cancer therapeutic for treatment of relapsed and refractory multiple myeloma — an

incurable, but treatable cancer of blood plasma cells. The rapid clinical development of the VELCADE drug — with FDA approval granted in little more than 4.5 years after initiation of the first clinical trial — reflects the company's commitment to novel treatments for cancer patients.

Millennium's pipeline of product candidates in clinical development is targeted to several key disease molecular pathways that play crucial roles in underlying disease processes: the ubiquitin-proteasome pathway, leukocyte activation and migration, and kinase-mediated signaling. Expertise in these pathways and in many other aspects of disease biology has enabled Millennium to build a solid R&D program in oncology and inflammation.

With a growing pipeline of product candidates at varying phases of development, Millennium produces thousands of new samples per clinical trial. Each sample must be properly maintained throughout every phase of testing and for many years afterward.

The FDA requires that biological samples generated during clinical trials be maintained through a regulatory filing process. The agency can even request further analysis of drugs already on the market. Consequently, all clinical trial samples must remain stored in compliant conditions throughout the life cycle of a drug and be easily retrieved within hours if necessary.

As a result, this company stores a large portion of its biological samples at its on-site biorepository facility in Cambridge, MA, which includes thousands of discovery, nonclinical, and clinical samples. Additionally, thousands of clinical samples are stored at several off-site contract testing facilities and biorepositories.

Each clinical trial generates 10,000–20,000 samples. So sample storage, tracking, and invoicing is an arduous set of tasks, demanding excessive time and effort from personnel. Therefore, Millennium initiated efforts to find an outsourcing solution that would meet its clinical sample storage needs.

SAMPLE INTEGRITY

Because it can be years before samples are needed, they often must be maintained in highly specialized and consistent conditions. Standardized, secure, and compliant storage is critical to maintaining sample integrity for long periods of time. Features to look for when choosing an outsourced sample management provider include

- A facility capable of storing specimens at a wide range of temperatures including ambient (20–25 °C), cold room/refrigerated (2–8 °C), ultralow and ultracold (–20 to –95 °C), and vapor-phase nitrogen (–135 to –190 °C).
- Reliable, state-of-the-art, industrial-grade freezers and refrigerators with modern temperature monitoring equipment
- The ability to locate, retrieve, and ship one or many samples on demand
- Sophisticated, redundant power and data backup systems
- Secure facilities with sophisticated smoke detection and fire suppression systems
- Card-controlled access, video surveillance, burglar alarms, and other physical security measures
- Compliant, validated equipment, processes, and software systems that provide real-time access
- Business-continuity and disaster-response plans
- Service-level agreements with guaranteed sample retrieval and shipping response times
- A strategic geographic location away from natural disaster zones and close to convenient and cost-effective transportation and shipping options
- Dedicated, available storage space to accommodate growth and emergency storage needs.

The company searched to identify a partner with a specific focus on long-term sample storage and online sample tracking capabilities. A team thoroughly reviewed several market options, comparing services offered with the needs of their company. Millennium ultimately selected BioStorage Technologies (BST). Its compliance with good laboratory practices helps ensure high sample

integrity, security, and control with “24/7” visibility. The company's Web-based Intelligent Specimen Inventory Storage System (ISISS) tracks sample history and storage temperatures during every step of shipment and storage in real time and can be accessed from any computer with an Internet connection.

Administrative overhead was also reduced: Now only one set of invoices is managed rather than those from multiple vendors with differing invoice systems and contracts. This allows Millennium personnel to focus their efforts on their core competency, which is the discovery and development of new treatments. Through outsourcing, the company has been able to significantly decrease its staff, freezer size, and real estate. Millennium is fully confident that its samples are safe, secure, and can be accessed quickly when needed.

THE FUTURE OF BIOREPOSITORIES

The quantity of biomaterials produced from research and clinical trials continues to grow exponentially. By outsourcing these functions to experts in the field, drug manufacturers can mitigate risks and focus their resources on their core competencies. Strategic outsourcing obviates the need to invest capital and time into the development of specialized facilities and sample management software capable of handling large quantities of samples and associated documentation.

Whether stored onsite, outsourced to expert providers, or both, investments in a comprehensive strategy for archiving biospecimens and clinical trial samples that includes compliant collection and storage, proper tracking, and audit trails can provide significant value to an organization today and in the future. 🌐

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