Collaborative Models for Managing Research Samples in China

Lori Ball¹ and Terrence Fisher²
¹Chief Operating Officer, BioStorage Technologies
²General Manager, Research Models & Services, Charles River China

Introduction

While China represents a number of advantages and a strong environment for clinical research, including vast patient populations and fast patient recruitment, there are still a number of obstacles that present significant challenges to pharmaceutical companies conducting research in the region. Particularly, the collection and management of human samples and associated data has become a complex landscape to navigate for drug developers in the region. As a result, many study sponsors are increasingly searching for companies with expertise in global comprehensive sample and data management within China. An innovative service approach is the use of a Contract Research Organization (CRO), which offers an established infrastructure and experience conducting research activities in the region combined with a global sample management solutions company whose singular focus is on global best practices for managing research samples and data in the region.

This article will examine the growth of research activity in China, the challenges associated with sample and data management, and present best practices for adhering to the strict policies set forth by regulatory bodies for collecting samples and the transmission of related data.

China as a Leading Player in Research

Over recent years, major pharmaceutical companies have faced the challenge of developing new products and new markets in order to replace the significant revenues threatened by the loss of blockbuster patents. A strategic response to this challenge has been a shift towards rapidly developing geographies that offer efficient clinical development and the potential for enhanced revenue growth.

One particular country that has experienced extreme growth in clinical research activity over the past decade is China. There are a number of driving factors that make China very attractive for conducting clinical trials. While saddled with many of the common western patterns of illness, China offers potential advantages over its western counterparts, including vast patient populations, access to treatment-naïve patients, fast recruitment and high-quality sites, as well as the potential for significant cost savings. China is fast becoming the world’s second largest economy and third largest R&D market. In fact, industry leaders believe that the overall Asian market will overtake the US by 2020.

Further adding to China’s appeal is that the local government has taken drastic steps to help foster an environment that spurs efficient drug development. The formation of the Chinese State Food and Drug Administration (SFDA) eliminated conflicting standards between provincial government agencies, and resulted in a centralized Chinese healthcare regulatory system with increased transparency. While regulatory reforms have improved the consistency of the clinical trial process in China, clinical trial process and drug application timelines are still a challenge as it takes longer to gain approvals than in many other countries around the world. China implements strong control over samples and data for Chinese patients enrolled in clinical studies. A highly complex regulatory checks and balances system is in place which is the primary cause of long approval timelines.

Growth of Outsourcing in China

While continuing to build core research facilities and staffing in China, drug developers are increasingly seeking innovative ways to
As China’s clinical research landscape continues to shape itself with new areas of opportunity emerging, the region will continue to be an integral part of major drug developers’ global programs.

outsource their non-core competencies such as clinical trial and sample management to local service providers who can bring best-practices, expertise, and cost-efficiencies in these areas. This approach has become a highly effective way for major pharmaceutical companies to streamline operations and invest more in core activities. In just a few years, the dynamics of outsourcing in China have changed dramatically, with CROs emerging as strategic drug development partners rather than transactional headcount providers facilitating recruitment, site management, or data analysis tasks. Reinforcing this fact is that recent estimates indicate that outsourcing to CROs has grown by 31% and in 2012 represented a $1.5 billion market in China.

Sample Management Regulations in China

Collecting and managing human genetic materials is closely regulated in China. In late 2012, the Chinese government set forth the “Human Genetic Resources Regulations,” which implemented a system for qualifying, examining, and approving activities where human genetic materials are collected. The regulation defines human genetic materials as “resources and materials, such as human organs, tissue, cells, nucleic acid, or nucleic acid products that contain human genome, genes, or gene products, as well as any information derived from such resources and materials [1].” Simply stated, “human genetic resources” includes physical materials and any genetic information derived from them, including data. This, of course, has had a great impact on clinical trials and research in China.

The regulation looks to accomplish four main goals:

1. Establish management procedures governing the collection, research, development, trade, and export of genetic material.
2. Define liability and punishment for those who violate the provisions.
3. Further standardize the administrative procedures and licensing laws.
4. Improve coordination with existing laws governing clinical trials and other medical procedures.

The regulation also defines procedures for collection and preservation of genetic material. It states that anyone collecting human genetic material must be a legal entity in China with reasons to collect the information, and must meet the requirements of an ethics committee (China’s equivalent to an institutional review board) [2]. Prior to sample collection, the science and technology administrative department at the provincial level must approve documentation related to informed consent and ethics committee approval, and other mandated regulatory documents. The regulation also gives administrative departments the authority to:

1. Enter facilities for on-site inspection [2]
2. Inspect and copy relevant information [2]
3. Question any persons concerned [2]
4. Seize and detain any illegally collected or preserved human genetic resources or materials [2]

The regulation goes on to detail set parameters on the transmission of genetic data and materials; stating that all entities must guarantee that any cooperative research and development activities with groups outside of China have been approved [2]. Only organizations that have been preapproved to receive data or materials outside of China are eligible to do so. Each applicant for review must include:

1. An administrative license certificate from the institution [2]
2. A description of the cooperative research and development activities [2]
3. A copy of the contract between institutions [2]
4. A defined period of use and the method of disposal of the remaining samples [2]
5. An agreement from the overseas organization to provide verification of receipt [2]

Clearly, adhering to regulations is of utmost importance; however, just as critical are the methods employed to collect and manage samples and their associated data. After all, achieving regulatory compliance could be a non-factor if samples are rendered useless due to unsophisticated, ad hoc processes for collection and long-term sample management.

Best Practices for Sample Management

Growing in parallel with the influx of clinical research taking place in China is the burgeoning need to have localized partners who are experts in sample management. Due to the aforementioned regulations, coupled with the intrinsic scientific value of properly preserved samples, it has become critical for sponsors to have specialists who are well-versed in local regulations, regional and global transportation guidelines, and who have processes and technologies that ensure consistent sample quality and regulatory adherence.

Best practices for standardized methods for collecting and managing samples have been published by several industry entities, including the International Society of Biological and Environmental Repositories (ISBER) and the U.S. National Cancer Institute (NCI). Most recently, the College of American Pathologists (CAP) developed a gold-standard biorepository accreditation program that focuses on quality, accuracy, and procedural consistency in sample management and transportation [3]. While this CAP accreditation program is not yet available in China, the tenets of this program are being referenced as best-in-class processes for managing a biorepository.

Best Practices for Obtaining Informed Consent

Planning for sample availability to support future research begins with obtaining the proper patient consent prior to sample collection. In addition, irrespective of sample type, source, or the assay being performed by the researcher, it is essential that the unique information associated
with each sample be determined prior to collection and documented at time of collection. Research protocols should be explicit regarding consent, collection and processing requirements (i.e., consent form, collection process, centrifuge time, defined temperature requirements, and the manner in which the specimen should be processed and shipped). Providing sites with a specific sample management section within their investigator manual can help improve compliance of site processes and reduce the impact of pre-analytical variables on sample integrity prior to laboratory processing. In China, the Human Genetic Resources Administration must approve any sample collection prior to initiation.

Good Storage Practices for Long-term Sample Storage

Good Storage Practices (GSP) are best practice guidelines for managing research samples and are part of GxP quality and compliance guidelines for research organizations. While not a regulatory mandate, GSP requires discipline and attention to critical details, such as regulatory and industry compliance, process standardization, data management, logistics and business continuity planning. Processes should be integrated into an organization’s Standard Operating Procedure (SOPs) to ensure methodologies are widely recognized and constantly met by personnel. All staff that manage samples need to be trained on these best practices and SOPs should be regularly updated to guarantee compliance to an expanding array of regulatory requirements from a number of entities. Factors to consider when establishing SOPs for good storage practices in China include:

- Secure facilities and redundant measures to ensure specimens are kept in compliant conditions at all times when in storage
- Expert staff that has been trained specifically in global sample storage and transportation guidelines
- Unique sample bar-coding and chain of custody tracking to support regulatory audits
- Storage technologies capable of monitoring and reporting sample temperature variations
- US FDA 21 CFR Part 11 compliant data systems for managing sample inventories
- Business continuity plans and redundant systems to protect sample integrity during emergencies

Sample Transport

Companies conducting research in China will find it difficult to transport samples outside of the country due to complex regulations and even find barriers to sample movement within the country. Because of these limitations, an on-site presence is often required to support and serve the market. Foreign entities seeking to transport samples from China must work with a Chinese cooperating unit, which go through formal reporting and approval formalities.

Sample Management Models

From an outsourcing perspective, specialized service providers with a core expertise in sample management provide flexible solutions that allow partnering research organizations to scale and customize storage as research needs evolve. These solutions can include:

- Offsite storage – Entire sample inventories are stored at a specialized central biorepository or standard regionalized biorepositories for future studies. This approach is often utilized by mid- to large pharma companies with large volumes of samples, as this strategy lowers cost and optimizes resources while delivering improved economies of scale.
- Onsite – Samples are stored onsite at the client’s location for fast access by researchers, but external people, processes, and technology are brought onsite by a company with sample management expertise. This method is often used by academic centers, hospitals, and research companies with pre-existing investment in facilities who lack the expertise and tools necessary to employ best-practices in sample management.
- Hybrid – Samples are stored both onsite and offsite. This scenario offers a flexible avenue for research organizations to keep aliquots of samples close while protecting parent samples for future research. This strategy enables fast access to active trial samples combined with improved economies of scale for long-term storage samples.

Conclusion

As China’s clinical research landscape continues to shape itself with new areas of opportunity emerging, the region will continue to be an integral part of major drug developers’ global programs. Reciprocally, we can expect that the growth of outsourcing in the region will continue to grow to support the demand for expanded expertise in navigating the complex regulatory landscape and increased interest in the utilization of best-practices. However, new regulations introduce an added layer of intricacies that companies must factor into any clinical trial strategy in China. In no area is this more important than sample and data management. As such, it is imperative that research organizations seeking to capitalize on the benefits presented by this region find trusted partners that not only ensure regulatory compliance, but also provide sample management best practice techniques that ensure the integrity of biological samples.

References


Lori Ball is the Chief Operating Officer of BioStorage Technologies. She leads the successful development and execution of BioStorage Technologies global biorepository operations and logistics expansion strategies, comprehensive sample management solutions, global strategic marketing and business development, and the design and delivery of innovative technology solutions. She has 25 years of consumer products, CRO, and pharmaceutical services industry experience.

Terrence Fisher is the General Manager of Research Models and Services for Charles River China. He is familiar with the drug development life cycle requirements, from discovery research through clinical trials, affording the knowledge needed to support the strategic initiatives of Charles River and BioStorage in China to provide world-class sample storage capabilities.

This article was printed in the July/August 2014 issue of Pharmaceutical Outsourcing, Volume 15, Issue 4. Copyright rests with the publisher. For more information about Pharmaceutical Outsourcing and to read similar articles, visit www.pharmoutsourcing.com and subscribe for free.