The **LIMS** Effect

Trish Meek and Mark Murawski at Thermo Fisher Scientific discuss how LIMS can help to meet regulatory requirements and improve operational quality

The role of biobanks in today's research can be traced to the scientific progress made on the Human Genome project. Once the genome was characterised, science entered the 'genomic age' and researchers focused their efforts on understanding the mechanisms related to triggering a specific gene and the impact of that gene on the human body. The 'mapping' of the Human Genome gave scientists the ability to identify genes and their function, and to understand the role that genetics plays in the origin and progression of diseases. Biobanks grew out of the need to provide the biological samples, or biospecimens, that make this research possible. Today, these biospecimens serve as the basis for the novel research and development needed for the discovery of breakthrough drugs and medical treatments. Researchers investigate why some people develop particular diseases while others do not, and how each person's lifestyle, environment and genes affect the progression of particular illnesses. With the knowledge of how disease is triggered, scientists are better able to identify potential diagnosis and treatment strategies.

Another key development has been the use of biomarkers to help clinicians and drug manufacturers track the success of a drug in the clinic. Translational science or medicine connects the research lab to the patient (or 'bench to bedside') in order to help drive potential drug candidates through the drug development lifecycle. This increased focus on epidemiology and translational science has led to a surge in the number of samples generated for research and analysis. As a result, biospecimen management has become a key component of drug development organisations' research and clinical trial activities.

All of these advancements have led to the increasing importance of biobanks and repositories in a variety of organisations, to provide the samples and libraries necessary for the high-throughput laboratories engaged in drug discovery R&D. They can exist inside academic medical institutions as well as pharmaceutical and biotechnology companies, or they can operate as independent organisations delivering biological materials to researchers. Using the information stored in biobanks, scientists are able to drive towards the long term vision of truly personalised medicine.

DATA MANAGEMENT REQUIREMENTS

To facilitate the interplay between R&D and biospecimen management, pharmaceutical and biotechnology companies are increasingly turning to laboratory information management systems (LIMS) to manage the operational processes and workflow in biobanks and, because of the automation inherent in a LIMS, to facilitate the Food and Drug Administration (FDA) approval process for new drug applications (NDAs). Pharmaceutical companies use the latest LIMS solutions to help them integrate data in order to speed the drug development process, and to demonstrate auditable compliance to the FDA.

Biobanks offer unique solutions to research, assessment and documentation of important samples. With these advances, the growing need and focus on high quality sample yields and how they are accurately and efficiently managed is not a top concern for researchers, who are often charged with managing enormous volumes of both samples and their relevant data. The function of biobanks is quite diverse and can range from the storage of frozen cell aliquots intended for primary pharmaceutical screening; to tissue biopsies for disease research; to patient DNA samples used by government agencies; to large multi-sample population libraries for translational studies. LIMS can deliver purpose-built functionality to meet the unique needs of the biobanking industry, and are specifically designed to address the individual challenges of specimen collection, tracking and storage.

Along with the biological materials themselves, demographic information about the samples must be shared without

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violating the rights of the patient established by the Health Insurance Portability and Accountability Act (HIPAA) in 1996. The safe and secure transfer of this data is critical, so biobanks must have a comprehensive policy in place to ensure that they meet the needs of biomedical researchers without violating donors' rights. It is crucial that this information is associated with the primary sample and subsequent aliquots. The use of a LIMS can be used to address the needs of the organisation to manage donor information and sample tracking, data related to samples, security and regulatory protocols, as well as overall operational efficiency.

LIMS REQUIREMENTS FOR BIOBANKS

Pharmaceutical companies require biobanking for secure and traceable actions related to samples being archived, searched for and checked out, and ultimately destroyed. In addition, a solution is often needed which allows the company to have one central repository where samples are logged, archived and stored, shipped, verified and received back into the system.

The volume of biological samples and the associated medical records stored in biobanks requires a powerful data management system to gather, store, sort and retrieve data in a useable format. Samples and the associated patient information can be collected as a single donation or over time, depending on the sample type and the goals of biobanks. This clinical information must be linked to biological samples in a secure way. When researchers make a sample request, they need to be able to query the patient information to select the correct samples without violating the patient's privacy.

Biobanks have special considerations in deploying a laboratory information management system: they need to deploy LIMS that contain built-in capabilities and targeted analytical tools to help them serve the varying needs of the different laboratories they support. The LIMS of choice must be capable of gathering, analysing and storing large volumes of data for both standard and complex studies. In addition, data must be reviewed, summarised and presented in compatible report formats to facilitate seamless communication and data transfer between pharmaceutical companies and the FDA, allowing rapid review and approval.

Investing in a LIMS to manage the entire process from sample receipt through to analytical report provides a number of benefits, including improvements in sample throughput, more efficient use of laboratory equipment and limited downtime for instruments. In addition, powerful LIMS solutions are specifically designed to comply with Good Laboratory Practices (GLP) and 21 CFR Part 11 regulations.

A LIMS can provide secure and efficient management of all donor samples as they are submitted and as they are sent out for research purposes. The LIMS maintains the full history of each sample from collection to destruction, and provides a secure environment for the private donor information related to those samples. Because the LIMS automates the processes related to sample tracking, the historical information related to those samples is free of any errors that may have been made by any former manual transcription processes, guaranteeing the integrity of the information being provided to researchers. Finally, the automated tracking capabilities of the LIMS also provide the biobank with the ability to assemble and transfer requested samples to researchers in a fraction of the time that would be required if these processes were conducted via manual methods. This automation also provides the biobank with the ability not only to provide timely electronic reporting to the FDA, but also to respond very quickly to any request that may come from an auditor or regulatory authority to sample information.

COMPLEX SAMPLE MANAGEMENT

In addition to storing biospecimens and their related patient demographics, researchers need to be able to search for a particular disease state, race and age range for targeted studies. A LIMS designed for a biobanking environment provides a central location where this information can be stored and managed without violating patient confidentiality.

Once the potential samples have been identified, the LIMS also needs to support organisation-wide inventory control so that the biobank can easily determine whether the samples are available to fulfil an order. A LIMS with a configurable laboratory workflow allows individual laboratories to tailor the definitions of samples and parent/child relationships, along with the extent to which each physical item and related information are tracked by the LIMS. This can include as-needed sample locations, amount tracking, associated testing, patient information, and any other complex information needed to verify and fulfil biobank customer requests. Sophisticated tracking of samples is required to manage biospecimens, including the ability to locate samples geographically, down to their specific freezer location.

SUPPLIER MANAGEMENT

A unique challenge faced by most pharmaceutical companies is the fact that samples do not always come from an internal source. Pharmaceutical companies receive samples from CROs, each with their own paperwork format, often in the form of an electronic manifest. A LIMS can assist in the development of an electronic process to standardise all incoming documentation into a single standard format that registers automatically. It is important that all samples coming into a company are handled and stored effectively and communication between all laboratories within the company is efficient, quick and simple. The timely and accurate flow of information and samples across all laboratories is essential.

EFFICIENCY BENEFITS

LIMS automate and simplify existing processes as well as helping laboratories to improve efficiency and good laboratory practice (GLP) compliance. Investing in a state-of-the-art LIMS to manage all incoming samples is imperative once the drug reaches late stage R&D activities, such as bioanalysis. The handover from the biobank to the bioanalytical laboratory and back needs to be managed in a compliant way. In addition to facilitating the exchange between biobanks and R&D laboratories, a powerful, fully integrated LIMS also helps scientists to manage their vast workloads, and provides a platform to support growth and achieve the objective of optimum efficiency. Further immediate

benefits include improvements in sample throughput, more efficient use of laboratory equipment and limited downtime for instruments.

At sample intake, LIMS can improve the efficiency and security of data entry and can greatly assist sample identification and tracking by printed and automated label generation. As laboratory data is recorded in a single electronic database, the LIMS can provide biobanks with a means to retrieve, analyse and report samples in a way that would not be possible with a paper-based system.

REGULATORY CHALLENGES

The most important challenges facing biobanks are strict regulatory requirements: safety and security of donor information, patient privacy and sample integrity. Worldwide regulatory bodies increasingly require more detailed safety control of drug candidates to ensure the safety of final products and avoid potential product recalls.

Pharmaceutical products are subject to rigorous preclinical, nonclinical and clinical testing and other approval requirements by the FDA in the US under the Federal Food, Drug and Cosmetic Act, and by comparable agencies in most other countries. Prior to a new drug being marketed or distributed, there are rigorous regulatory requirements related to the full life cycle of the drug, including documentation and audit trails from research, development, and testing, to manufacturing and quality control. Additionally, prior to any regulatory approval, there are strict regulations pertaining to proper labelling as well as promotion and advertising. Finally, the record-keeping related to storage and distribution of the new drug is highly regulated. One of the ways to address these challenges is to implement market-specific, high-performance LIMS that improve sample management and data tracking. The LIMS will also help to facilitate seamless transmission of data between laboratories, researchers and regulatory authorities.

CONCLUSION

Implementing a market-specific LIMS solution provides many immediate benefits to the pharmaceutical, biotechnology and biobanking industries. LIMS can address the challenges of stringent regulatory scrutiny and pharmaceutical consolidation while improving sample management and facilitating flawless transmission of data between laboratories and the FDA. Deploying a LIMS can enable secure storing and efficient management of samples while also ensuring uninterrupted, dependable transmission of information between the laboratories within a company. A purpose-built laboratory information management system can help management to make better decisions more quickly, increase overall productivity across laboratory operations, lower operating costs and improve quality and integrity of data, all while enabling compliance with strict regulatory requirements, and improving sample traceability.

Data management for regulatory submission

FDA approval process

As an initial step in the FDA regulatory review process, toxicity studies in animals and other nonclinical studies are typically conducted to help identify potential safety problems that might be associated with administration of the drug candidate being tested. For certain diseases, animal models exist that are believed to be predictive of efficacy in humans. For such diseases, a drug candidate is typically tested for efficacy in that animal model. The results of these initial animal safety and disease model studies are submitted to the FDA as a part of the Investigational New Drug (IND) submission, prior to commencement of human clinical trials in the US.

For clinical trials in the US, each protocol must be submitted to the FDA to supplement the original IND application. Furthermore, each clinical trial must be evaluated by an independent Institutional Review Board (IRB), which evaluates clinical research at each institution at which the trial will be conducted. The IRBs will consider, among other things, ethical factors and the safety of human subjects in the proposed trials. Data from nonclinical testing and all clinical trials, along with descriptions of the manufacturing process, analytical tests, proposed labelling and other relevant information, are submitted to the FDA as part of the process of requesting approval to market the drug in the New Drug Application (NDA).

NDA process

Preparing an NDA involves extensive data collection, verification, analysis and expense, and there can be no assurance that approval of the drug candidate that is the subject of a particular NDA will be granted on a timely basis, if at all. The FDA reviews all NDAs to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The approval process is affected by a number of factors, including the severity of the targeted disease, the availability of alternative treatments and the risks and benefits demonstrated in clinical trials. The FDA may deny an NDA if applicable regulatory criteria are not satisfied, or may require additional testing or information. Among the conditions for marketing approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to the FDA's GLP regulations, which must be followed at all times. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money and effort in the area of production and quality control to ensure full compliance. Manufacturing facilities, both foreign and domestic, are also subject to inspections by the FDA and by other federal, state, local agencies or foreign authorities. The process of completing nonclinical and clinical testing, submitting the NDA and obtaining FDA approval for a new drug is likely to take a number of years and require the expenditure of substantial resources.

About the authors

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