



Limber Labs

The efficacy of LIMS in clinical trial laboratories has never been more important; Ed Krasovec at STARLIMS investigates the benefits



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Laboratories play a pivotal role in the clinical trial process. To begin with, laboratory data accounts for an estimated 60-80 per cent of the data generated during the entire clinical trial process. In addition, the clinical trial specimens managed by laboratories have high intrinsic value; lost, misplaced, or improperly stored trial specimens can endanger patients, disrupt trial execution, cause rework and delays, and lead to significant cost escalation.

THE IMPORTANCE OF CENTRAL LABS

Clinical trial specimen testing has evolved into a multi-billion dollar outsourced industry serviced by central laboratories. By tailoring their capabilities to the complex requirements associated with clinical trials, central laboratories have achieved economies of scale and improved data quality, shortened study timelines, and reduced costs. Central laboratories play an important role not only in creating and managing data that is important to the evaluation of the drug under study, but also in providing time-critical information to investigators, which helps protect patients.

THE ROLE OF LABORATORY INFORMATION MANAGEMENT SYSTEMS (LIMS)

The laboratory must manage sensitive information related to samples, tests and results. The laboratory work processes include sample identification/validation, work scheduling, data acquisition, data processing and reporting. Since the product of the laboratory is information, having appropriate information management solutions is crucial to the effective operations of the laboratory. To this end, the laboratory information management system (LIMS) serves as the central nervous system of the lab, responsible for: sample identification – barcode labelling and specimen attribute validation; work scheduling – test initiation and assignment; data acquisition – automated or manual entry of results generated by analytical instruments; data analysis – calculations, reference ranges, statistical analysis and QC; reporting – analytical test results, management summaries, *ad hoc* reporting and data extracts and lab management – sample/job tracking, invoicing, SOPs, training, certification and compliance.

THE SPECIAL NEEDS OF CENTRAL LABS

The aforementioned processes are needed in almost any lab, and they are important in central labs as well. However, clinical trials impose another layer of

special demands on the laboratory and the information systems utilised by the people in the lab. Any information management system aiming to meet the needs of clinical trial labs must address certain key issues.

High Volume

Phase III trials can involve managing specimen testing of thousands of patients. Large central labs can receive over a thousand samples per day, involving specimen from hundreds of different clinical trials.

Global Population

Clinical trials often involve patients from multiple geographic regions, operating in different time zones and languages.

Regulatory Compliance

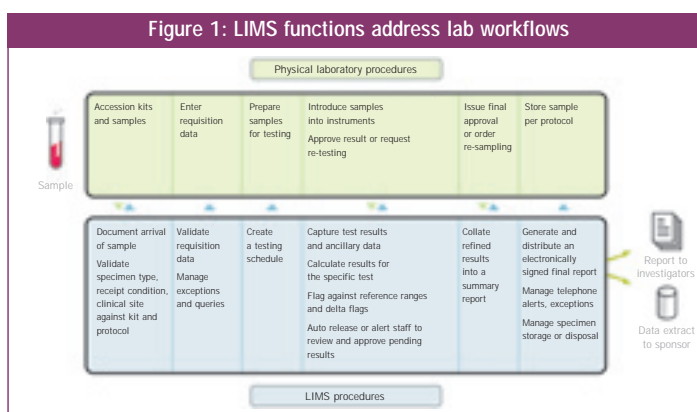
Clinical labs must adhere to a long series of regulatory standards: ICH, GCP, GLP, ISO 9001, CLIA, HIPAA, CAP, 21 CFR part 11.

Dynamic Business Rules

Each trial requires the enforcement of different laboratory business rules for accessioning validation schemes, reference ranges and the actions triggered by results outside of normal ranges, blinding and reporting rules. Some of these rules may vary within the visit schedule defined by the protocol. Furthermore, protocols can be amended whilst a trial is in progress.

Logistics

Central labs are often responsible for the preparation, distribution and management of pre-packaged protocol visit-specific



specimen collection kits. Each kit and its components are barcoded and specially prepared to meet the specimen handling and testing requirements imposed by the clinical protocol.

Rapid Turnaround Times

The central lab must not only deliver accurate results within the desired turnaround time, but must be able to support rapid protocol and site-initiation processes and prompt resolution of queries. A look at the Metrics Champion Consortium's Laboratory Performance Metrics illustrates the time-critical nature of the central laboratory's work. Protocol and site-initiation, resolution of queries, on-time reporting of panic values and on-time specimen shipments are all key metrics.

INFORMATION MANAGEMENT IN CENTRAL LABS: MEETING THE CHALLENGE

Altogether, it is clear that central laboratories have a very demanding set of requirements for their information management systems. By and large, however, no single software has so far been able to meet the needs of such labs. In many cases, central laboratories have had no choice but to design their own information management software, or to heavily customise an existing system.

Traditionally, laboratory management software fell into two distinct categories: laboratory information systems (LIS), exclusively serving clinical laboratories, and laboratory information management systems (LIMS), serving analytical, manufacturing and R&D laboratories across many industries. Due to the wide variety of business requirements managed by LIMS across diverse industries, LIMS software is required to be inherently more flexible. However, LIMS software has traditionally lacked key clinical functionality such as reference ranges, patient/subject management, study management and delta checks. While LIS software has included some of these features, the solutions were often considered too inflexible to meet the demands of the central lab's requirements. Many clinical trial central labs have relied upon in-house software or heavily customised commercial LIS packages, which illustrates how poorly these labs have been served by commercial off-the-shelf LIS and LIMS offerings. In recent years, a number of these legacy systems have begun to reach the point of obsolescence, requiring significant reinvestment or replacement.

LIMS IN CENTRAL LABS

The good news is that commercial LIMS systems have evolved significantly over recent years, and can now provide a viable option to help a central lab address the complex requirements of clinical trial specimen testing. Most importantly, commercial-off-the-shelf (COTS) LIMS software is currently available that includes powerful tools tailored for clinical trials, such as protocol management and kit management.

A relevant example of a central laboratory using a COTS LIMS application can be found in HFL Ltd, a large contract lab that has implemented a commercial LIMS application to support clinical trial information management. The company has implemented STARLIMS to manage their clinical trial laboratory operations. The solution provided manages the study setup process including:

- ◆ Creation of client site and individual contact records for both the sponsor and other associated addresses such as clinics or couriers.
- ◆ Definition of the general conditions for the study. This includes parameters such as whether the system should prompt for a subject ID or subject initials, the definition of validation masks for subject ID and screening number fields, the default units system, the default report formats and the base price list.
- ◆ Definition of contact managers for the study. These represent the in-house staff that need access to samples logged as part of this study.
- ◆ Definition of the sites that will participate in the study. This can include such details as to whether dry ice is available and whether out-of-hours collection of samples is possible.
- ◆ Definition of the investigator, monitor and super-monitor hierarchy for the study.
- ◆ Definition of the time points (occasion codes) to be utilised, and the testing panels and procedures that are to be associated with each time point.
- ◆ Definition of the study-specific reference ranges to be utilised. Multiple sets of ranges can be defined, for instance corresponding to 'warning', 'alert' and 'panic' categories.
- ◆ Definition of the sampling kits required for the study. This involves specifying the components required for each kit, ensuring that sufficient stock is available, and managing expiry dates for items with limited shelf life.

As the study unfolds, the LIMS is used to manage accessioning, validation, testing, results capture, limit checks, QA/QC processes, reporting, and query resolution.

TOMORROW'S INFORMATION MANAGEMENT SYSTEM

For large organisations and central labs, the flexibility of LIMS is an important advantage. In addition, there are now advanced commercial solutions that directly address the specific needs of clinical labs. Taking all this into consideration, it is safe to assume that an increasing number of clinical labs will favour LIMS options – particularly if these systems can be easily deployed and used throughout the organisation.

In this regard, the new generation of web-based LIMS is particularly relevant. If it is based on a standard browser and offers a graphic user interface, such a system can offer a particularly short learning curve. A web-based solution lends itself well to global deployment, allowing multilingual, multizone operations with hundreds of users.

LIMS software must also evolve to better support the management of both structured and unstructured data, integrating features commonly found in scientific data management systems (SDMS) and electronic laboratory notebooks (ELN) to better meet the needs of research and text-centric histopathology applications.

Moreover, because a LIMS must exchange information with both internal and external enterprise information systems, tomorrow's LIMS must provide powerful interoperability capabilities with flexible interfacing tools including web services, HL7, file transfer, and database communication tools. ◆

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