Computerised LIMS

In today's modern analytical laboratory such as a contract research organisation (CRO), a laboratory information management system (LIMS) is no longer a luxury but a necessity, critical to the management and control of laboratory data and information. Due to the rising cost in R&D and biotechnology, many companies are looking at ways to maximise efficiency and profitability in order to remain competitive

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Approaches to achieve these goals include implementing LIMS and automation, deploying Six Sigma, extending facilities to the Asia-Pacific region, and increasing the amount of outsourcing to CROs. This article will focus on ways to leverage automation with LIMS and method validation software as a means to increase operational efficiency, enhance data quality and facilitate regulatory compliance.

The majority of US laboratories face the challenge of doing more with fewer resources, at lower prices, in a complex regulatory landscape, and with a constantly evolving global economy. Organisations often do not invest in automation infrastructure, instead, relying on outdated manual systems that are prime targets for audits. Not only can negative audit findings prove to be costly, but they can damage the organisation's reputation and result in a loss of business.

One Integrated System

It is common to see CROs managing significant workloads with a series of home-grown database applications, Excel spreadsheets and logbooks. These solutions tend to be piecemeal; they often lack security, do not scale, do not integrate across steps, do not have any documentation (relying on institutional memory that can walk out the door), and are not subject to standard backup and recovery methods. The total time required for all data entry and verification tasks is rarely justified at any level of the organisation, and the lack of standardisation introduces significant flaws that audits are guaranteed to find. These manual systems are frequently plagued with transcription errors, large Excel sheets that are prone to corruption, as well as a lack of an audit trail and accountability. In addition, there is often no quick or easy way to view trends in data, extract any business intelligence or have the ability to automatically generate reports, such as a Certificate of Analysis (CoA). Often these organisations lack integration with the instrumentation; analysts can spend hours cutting and pasting or re-entering data into Excel sheets or Microsoft Word report templates. Usually, the management team is not even aware of how many hours are wasted with these manual systems. Gap analysis by an external laboratory automation consultant provides the management team with an objective assessment of the current automation status and will suggest one or more blueprints for improvements. In most cases, implementation of these methods will result in immediate efficiency gains simply by the elimination of repetitive tasks and error-prone duplications. A laboratory should produce data of clear provenance, known and traceable accuracy and precision, securely housed and unambiguously reported.

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The goal of a LIMS is to consolidate the information and data in the laboratory, from bar-coded labels and specimens, to chemical inventory and resource management (employee training records). These, as well as method validation software, help to promote the management of data, facilitate regulatory compliance and enhance collaborations. As the business expands, a good LIMS will integrate more readily

Table 1: Key benefits of LIMS and method validation software

LIMS (feature)	Benefit	Method validation (feature)	Benefit
Each sample is provided a unique identifier	Compliance with good automated laboratory practice (GALP)	Ensuring calculations comply with regulation and guidelines	Regulatory compliance (GAMP 5 and 21 CFR Part 11)
Linked chain of custody (COC)	Track/view testing request throughout workflow	Ability to electronically import test data from instrument to MV software to LIMS	Eliminate transcription errors, enhanced data quality
Efficient sample tracking/ chain of custody	Enhances collaboration throughout the laboratory	Ensuring that operation procedures must be reviewed and approved	Regulatory compliance (GAMP 5 and 21 CFR Part 11)
Electronic Signatures	Compliance with 21 CFR Part 11	Regulatory report created automatically	Confidence that the report contains required regulatory information
Linked SOPs	On-line readily available to assist in compliance	Determining which statistics are relevant	According to ISO/ ICH/FDA
Notification of chemicals and reagents approaching expiration	Better utilisation of laboratory resources	Provides complete electronic audit trail	21 CFR Part 11 Compliance
Notification of instruments requiring calibration	Facilitate regulatory compliance (ISO 17025)	Instrument integration to establish workflow	Secure and efficient data management
Notification of employees that required certification training or re-training	Facilitate regulatory compliance (ISO 17025)	Built-in critical checkpoints such as precision, linearity, accuracy, stability and more	Regulatory compliance (GAMP 5 and 21 CFR Part 11)
Automated, emailed reports, CoA, final analysis, and so on	Enhanced TAT and efficiency	Secure data exchange in Oracle and MS SQL server	Centralised data storage
Can enforce permissions, access, data review, validation and approval with date and time stamps	Facilitate regulatory compliance	Leverage workflows and templates to accelerate method validation	Eliminate manual steps, reduce time and costs

with enterprise-level systems, which in turn promotes partnerships. However, possibly the most important aspect from a business perspective is the significant cost, time and efficiency savings that LIMS and laboratory automation offers the organisation. Laboratories face constant change – in sources, methods and personnel – and the LIMS must be able to adapt quickly, meaning that it needs to be easy to reconfigure workflows and reports. Continual improvement can be achieved by monitoring statistical data, regularly evaluating metrics and looking for ways to be more efficient from laboratory turnaround times (TAT) to integration with enterprise systems such as SAP or accounting packages.

Benefits of LIMS

As the laboratory environment continues to evolve and integration with other systems becomes more important, there has been a movement towards promoting open standards that will allow disparate systems to communicate easily and exchange data. In the past there were multiple islands or silos of information; there was a LIMS, a chemical inventory database, SAP, SCADA, a QA/QC database, with little or no scope for integration. This has changed with the promotion of open standards. The adoption of common data models, ontologies and exchange standards (mark-up languages, for example) in the public sector and by professional groups, as well as real-time web access to much of the data, has changed customer expectations. This instant access has provided a competitive advantage to laboratories as they can meet their customers' expectations for on-demand data, as well as the convenience of 24/7 data access to sample status, preliminary results and final reports. Instead of laboratories spending time on the manual creation of reports, mailing, faxing or emailing these reports to clients, the secure LIMS/web portal can automate this process so that reports are created automatically, converted to a pdf (following validation and approval), and linked to the web portal for client access and download. Staff that were dedicated to 'pushing' reports to clients and fielding sample status calls can now be re-allocated because the web portal will provide the ability for clients to 'pull' their data from a secure portal – where they can only see their own data – and print out their own reports when they need them. This offers a competitive advantage over other companies in the same market. Table 1 lists a few of the features and benefits that are provided with commercial LIMS.

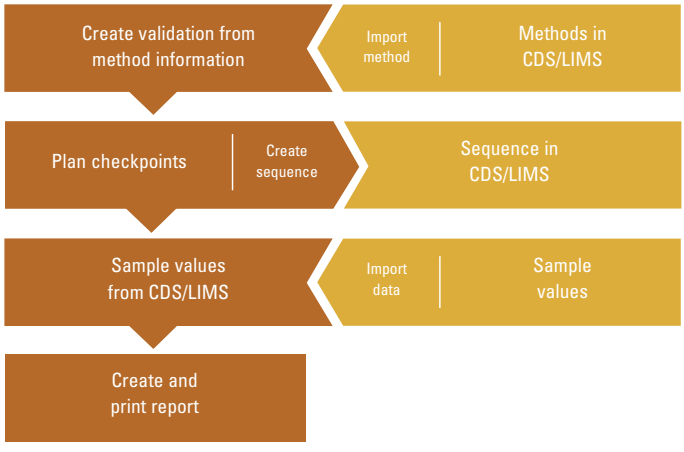

Figure 1: An overview of method validation workflow

The method validation software parlays a variety of guidelines and regulations translated into system checkpoints, ensuring that no steps are being forgotten or missed. Validation workflow is guided by wizards to ensure that no steps are skipped; once the data is generated, a direct link is created to import the data from chromatography data systems (CDS) to LIMS or data system ensuring a reduction in transcription errors, enhanced productivity and resource savings. Figure 1 describes the

key steps followed in commercial method validation software.

Instrument Integration and Open Standards

Integration of instrument data to LIMS is cost-effective, with a typical ROI of six to 10 months, which can be faster based on sample volume. Not only will it increase throughput (a worklist can be sent from the LIMS to the instrument and once the run is complete the worklist is sent back to the LIMS for import), it also reduces errors and increases productivity. Integration is also important when working with method validation software as it helps to streamline and prevent errors in the pipeline. By leveraging commercial automation packages, much of the planning has been integrated into the software with wizards that walk users through the various required steps in setting up a method validation, and final report creation greatly facilitating regulatory compliance.

Unfortunately, many instrument companies cling to their proprietary standards, which they believe provides them a competitive advantage. In instrument integration, for example, there is no universal standard, therefore each instrument has a user-configurable output format; that is, each integration must be a custom interface. There have been many proposals for a standard format; the last was called analytical information mark-up language (AnIML), which provides a generic data container – the AnIML Core – permitting the storage of arbitrary analytical data. This includes:

- Sample information
- Method information
- Measurement results
- Instruments and software used

Workflow information that ties experiments and samples together is also captured. AnIML is XML-based for several reasons. First, there are many tools for XML manipulation readily available and as it is a text-based format, which is human readable, it is an important tool for long-term data storage. Many instruments export data in a format that can only be read using the proprietary instrument software that was supplied with the original instrument; for example, many older instruments require operating systems, such as Windows NT or Windows 98, which are no longer supported. Therefore, for a laboratory to access historical data, they would have to have the historical software loaded on hardware or a virtual machine that could support the application and proprietary output. This further goes to emphasise the need for standardisation. There are two types of XML data standards: open (those that are publicly available); and closed (those that are proprietary). The popular option is the open standard because it promotes interoperability. XML is also used in web services applications, created in many different languages to enhance communication. Web services utilise HTTP – a basic transport protocol that is fairly ubiquitous on the web. Another group, SAFE-BioPharma Association, is also promoting standardisation in biotechnology and pharmaceutical markets (1). To date, standardisation remains a lofty goal, although progress is being made.

Conclusion

In addition to data management benefits, computerised LIMS improve regulatory compliance, business growth and survival rates. With mounting regulatory requirements, organisations that attempt to master compliance with manual systems do so for higher labour costs, audit vulnerability and potential impact on the final data quality. The same automation enhancements that are provided by a LIMS are also seen with automated method validation software, which can save up to 70 per cent in labour costs. Laboratories that embrace automation are able to optimise their resources with more efficient reporting, regulatory compliance and better quality data. In the end, the data is the final product of the analytical laboratory, and it is important that it is as accurate as possible. Computerised LIMS and method validation systems can provide significant costs savings to labs, while providing enhanced collaboration across the organisation that integrate enterprise systems.

Reference

1. SAFE-BioPharma Associations, www.safe-biopharma.org

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