Laboratory Information Management Systems (LIMS)

Antony J Williams, ChemZoo Inc., Wake Forest, NC, USA

Introduction

Modern laboratories providing analytical chemistry support have shifted from a staff of skilled experts acquiring and analyzing data just a few years ago to these staff dedicating a significant proportion of their time to the support and maintenance of open access or walk-up analytical instrumentation serving their user community. Organizations retain scientific expertise to be applied to the most challenging analyses, but rudimentary data acquisition and analysis is now in the hands of the general chemist. The need for Laboratory Information Management Systems (LIMS) has expanded from systems support for the processing of samples and requests in order to produce large numbers of test results and reports. Now LIMS have been expanded to support high-throughput generic and reproducible experiments for instrumentation with low downtime thus producing data outputs that will either provide canned paper reports or flow as data streams to the desktops of the chemists for processing and reporting. Today's laboratory workers are expected to be proficient in the utilization of highly automated spectrometer systems and their associated offline data processing suites and electronic notebooks for both data and knowledge management software. Analytical laboratories by default have had to computerize their sample tracking, tests, and results, especially in the Life Sciences industries where traceability for data is a necessary component of compliance. With this information accessible via a computer there are many benefits including methods management, test results, archive, calculation, comparison against specifications, control charting, and verification of instrument performance. The information is valuable for reference, problem solving, and modeling. While the management of complex spectroscopic data resulting from a heterogeneous environment of instrument types and vendors is hampered by a lack of standards and cooperation between instrument vendors and software developers, many companies at this point have successfully deployed analytical data management systems utilizing vendor software application programming interfaces. This allows them to query information contained within proprietary data formats and to build customized interfaces and data manipulation software. As the world has embraced the benefits of an Internet-based culture, the dramatic technical advances in the speed of data flow, the potential of data storage of enormous quantities of data, and the availability of flexible and intuitive desktop and Web-based user interfaces enable chemists to process, analyze, and increasingly integrate their data into electronic notebooks. Software platforms for integrated analytical sciences, specifically spectroscopy and chromatography, chemical structure handling software, and information systems are now the norm.

The Product of an Analytical Laboratory

The main products of an analytical laboratory are data and information. Some of this information is in the form of new analytical techniques or methods that extend a laboratory's ability to characterize new materials. Many laboratory settings today also act as hosts for 'walk-up' or 'open access' systems and have responsibility for the everyday operations of the hardware and software components of these systems the delivery of data to the desktops of the users, the training of users in the manipulation and interpretation of experimental data. These individual operations may be labeled as 'service' and 'support' roles where in the former case a laboratory acquires and interprets data while in the latter it is more responsible for providing an environment for data acquisition to the users.

In either case these measurements are the key to understanding and controlling either research or manufacturing processes, solving development and manufacturing problems, and developing novel materials. Preparing samples, making measurements, analyzing data, and generating reports are the common processes analytical laboratories, acting in a service role, use to generate information. Complex instrumentation has continued to become highly automated, and menu-driven interfaces allow access to measurements available only to skilled analytical scientists just a few years ago. The development of novel analytical techniques commonly migrates from the hands of skilled researchers to the general chemist very quickly as organizations are forced to improve productivity and the quality of their measurements. Analytical laboratories can now produce many terabytes of data in just a few days, and so data are generated in isolation from the analytical scientists; whose responsibility is now focused on studying the most problematic samples, ensuring the uptime, maintenance, and throughput of the instruments, and working with the IT group to ensure delivery of the data, selection and training in the processing software, and a higher level of general support. Properly managing this process and tracking the flow of work through the laboratory is critical to the efficient operation of a laboratory.

Analytical chemists and information specialists working to improve their own operations were the first to develop LIMS. They typically supported only one technique or small unit of a laboratory and did not communicate with other information systems. Over the years there have been dozens of LIMS vendors providing packages with varied capabilities and these have continued to adapt to keep up with the increasing demands for improved graphical user interfaces, ease of use, improved statistical analysis, and archival systems to name just a few standard selection criteria. Since 1993, the American Society for Testing and Materials has published a number of standard guides for anyone interested in LIMS, including users, developers, implementers, and laboratory managers. These guides define, appropriate to the time of release, standard terminology, a concept model, primary functions, an implementation guide, and a checklist. LIMS vendors have become experts in knowledge management and the provision of flexible software architectures to deliver a solution to meet the customers' needs rather than a solution that the customer must adjust their processes to.

Types of Laboratories

The information handling requirements of analytical laboratories vary from the research to manufacturing environments. A standard testing laboratory that supports manufacturing quality control and regulatory compliance uses analysis procedures that are well defined and strictly followed. These laboratories analyze relatively large numbers of samples and produce numerical or tabular results based on specific methods and protocols. Spectral analysis is usually used in this environment to determine concentration or verify identification relative to known reference spectra. Historically, such approaches were limited generally to the comparison of optical spectra; there has been an expansion into the use of both nuclear magnetic resonance and mass spectrometry–based techniques, especially by the life sciences, for example in their profiling of the metabolome and examination of biomarkers. The software analysis components of such approaches are complex in nature but have been automated to a large extent.

In contrast, a research analytical laboratory supporting the discovery of new materials uses analysis procedures that are defined in the mind of the analyst. While the analyst may use analytical techniques that are well defined, the process he/she chooses to apply to a particular sample is not predetermined, but is developed in response to the questions that need to be answered. These laboratories analyze fewer numbers of samples and regularly produce results that combine graphics and images with textual reports. In this environment, spectroscopy is also used to elucidate chemical structure and determine three-dimensional spatial relationships. The output of such studies can produce detailed mechanistic understanding, details of kinetics and any of a myriad of physical phenomena that can be exposed by modern spectroscopic techniques.

Other types of analytical laboratory environments vary between these two idealized cases. Process control environments model a fully automated standard testing laboratory. Development environments reflect the need to move research testing for understanding to standard testing for manufacturing. Problems arise when a LIMS vendor tries to sell one generalized solution, customized to fit all environments, and vendors have to deepen their understanding of an organization's knowledge management needs to supply a solution traversing all laboratories. Research laboratories, due to their diverse needs, remain a challenge in terms of delivering a LIMS solution, and only a few niche players with in-depth knowledge of spectral data handling have attempted to address the needs of spectroscopic data management in this environment. These include Advanced Chemistry Development (ACD/Labs), Thermo Fisher, and Waters.

Selecting a LIMS

Many factors drive analytical laboratories to implement LIMS. These include the need to demonstrate value, comply with detailed regulatory requirements, manage large amounts of samples and tests from automated analysis and screening systems, automate laboratory processes, improve accuracy, and deal with increased demands for efficiency and documentation. For successful implementation of a LIMS, it is important to know which factors are most important and where productivity will be impacted, both positively and negatively. While it may be appropriate to utilize a reengineering process to simplify a laboratory's workflow before implementing a LIMS, the majority of research laboratories require flexibility in their approach and may develop bespoke solutions rather than be constrained by a vendor's solution.

The installation of a LIMS is commonly a difficult and frustrating task for some laboratories. LIMS generally work best in laboratories where the operation is well understood and standardized and where the processes do not have to be changed to match the LIMS. This is generally not the case in research and development environments where microscopy and molecular spectroscopy laboratories usually reside. The need to manage images, various types of spectra, and chemical structures adds to the problem. The delivery of systems to manage integrated sample, workflow, structure, and spectroscopic data has been assumed by only a small number of niche vendors. Managers may still have a hard time finding a system that will work for their operations and meet the expectations of users, and the business case for buy and customize versus build can be unclear.

Functions of a LIMS

Whether they support manufacturing, research, or problem solving, all analytical laboratories receive and prepare samples, make measurements, analyze data, and report results and information. A simplified illustration of the analytical support process is shown in **Figure 1**. Improving the overall efficiency of this process is the primary function of a LIMS. The most common and perhaps most important use of a LIMS is to maintain proper records on samples and the tests requested on them. This electronic logbook or sample management type function assigns sample numbers or bar codes and records administrative information, often including an indication of the work requested. Most LIMS also allow numerical and tabular results to be entered for tests performed on the samples. Once data have been collected and properly recorded, the LIMS may be used for data manipulation and automated report generation. Significant productivity enhancements are usually obtained from this last step. The following sections describe how a LIMS is used to support the steps in **Figure 1**.

Definition of Problem or Job

For the laboratory supporting research, problem solving, or method development, the definition of a problem or job is the first step of the analysis process. Job requests could include determining what is happening to a material as it degrades, how the properties of a material might be improved, or if a fabrication process is producing devices with the desired composition and geometry. When a new chemical is to be commercialized, the request may be to develop tests and fitness-for-use criteria needed for production monitoring. The job usually defines the context for investigative analytical work performed on many samples. When the work is

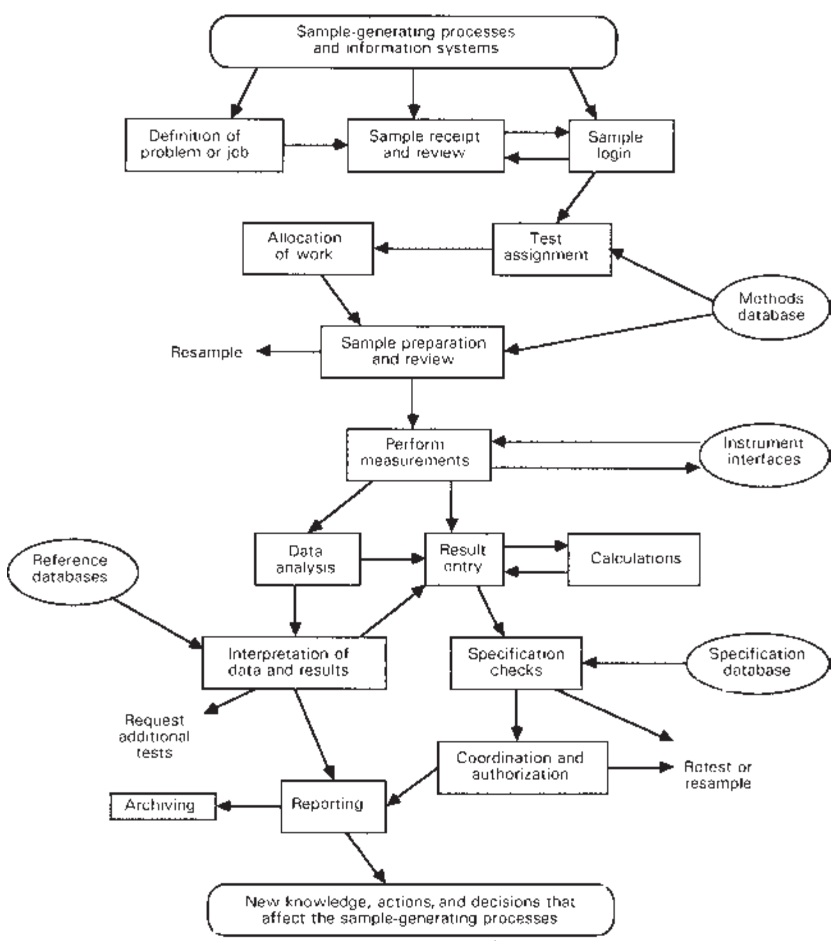

Figure 1 Generic analytical laboratory workflow supported by LIMS.

complete and a report is written, this information may be made available in an electronic library.

In a standard testing laboratory, the problems or jobs are predefined by the time materials are analyzed. Given a type of material and its point-in-process, the suite of required tests, testing methods, specification limits, and resulting actions and reports are clearly defined.

Sample Login

A primary function of the LIMS is to track the samples of materials to be analyzed by a laboratory. This can be as simple as tracking when a sample enters and leaves a laboratory or as detailed as tracking every action that is performed on the sample while it is in the laboratory. The process normally begins with the client or analyst recording general descriptive information about each new sample or batch of samples and the work request. Typical information includes the name of the requester of the work, an account number to be charged for the work, the date the request is made, the client's identifier for the sample, the date the sample is received, the job or project to which this sample belongs, the priority, and the hazard information. Test requests vary from a general description of the problem to be solved to a suite of specific point-in-process tests using very specific methods.

Sample Receipt and Review

Samples may be logged into a LIMS before they arrive in the laboratory. Good-quality operating procedures dictate that when a sample arrives, it should be reviewed to ensure it is suitable for analysis, the requested work is appropriate, and it has not visually degraded. The LIMS sample receipt function allows the time a sample arrives and any anomalies to be recorded. If anomalies are observed in the sample, then a decision to proceed, resample, or request other tests is made, often after consultation with the client.

Test Assignment

The client may request a specific collection of tests when the sample is logged in. In a standard testing environment, the suite of tests is often assigned automatically by the LIMS. If a general test is requested or the request is for some problem to be solved or investigated, then the appropriate specific tests or course of investigation is selected by the analyst.

Allocation of Work

Work may be allocated among specific instruments, analysts, or support groups. This is done to match the test requirements to appropriately skilled analysts and equipment and ensure the best utilization of resources. If samples are received in a laboratory with different priority levels, it can be accounted for here. When work is allocated, it is recorded in LIMS so that it can generate work lists for the analysis and instruments. In other cases, analysts simply check out the next pending sample from the queue in LIMS. In a research or problem-solving area, this may not be recorded in a LIMS until the results are entered.

Method Management

Methods are the procedures and protocols by which materials are analyzed. LIMS designed for standard testing laboratories often provide some support for managing methods. This can allow complete automation of the analytical process, as exemplified by online analysis.

Sample Preparation

Most samples and analysis techniques require some preparation such as dissolving, diluting, or mounting before measurements can be made. This step and the subsequent measurement step are a typical focus for laboratory automation using robotics. Such systems follow detailed procedures that may vary for every sample. Most automated sample preparation and measurement systems were initially isolated, performing very focused tasks and requiring manual data transfer at the beginning and end of a run. This has changed as automation and LIMS have matured and computer-controlled balances, integrated bar coding, and wireless transmission of measurements have developed.

Perform Measurements

Measurements are performed using instruments. In an automated laboratory, the LIMS can download data acquisition instructions to the instruments and receive data and analysis results for entry into its database. Nowadays LIMS utilize standard computer protocols to interface with instruments. This has been particularly successful in chromatography where good standards have been developed and followed by both LIMS and instrument vendors, but due to the explosive growth in hyphenated chromatography-mass spectrometry techniques, this integration has also been applied to LC-MS technology.

Result Entry

After the tests have been performed, the results are often entered into the LIMS. While this used to be primarily a manual process, generally data are now streamed directly into the LIMS or the raw data are moved into an archival system and a reduced form of the processed data is moved into the LIMS. These can be simple yes or no phrase results to tables of amounts of various materials.

Usually these tables have to be predefined by the method that is used to perform the analysis. Efforts in spectroscopy were previously limited partly by the lack of widely accepted standard spectral formats and partly by the lower demand for general spectroscopy applications in standard testing areas. As spectroscopic analyses have become crucial in the life sciences for genomics, proteomics, metabolomics, and metabonomics measurements, the results of analysis extracted from the raw data by complex software processing are assembled into tables and fed to a LIMS for review.

Calculations and Data Analysis

Most LIMS provide simple capabilities to perform calculation on the results that are entered. These calculations may simply be transformations into standard units or the generation of averages. More sophisticated analysis is generally performed using instrument vendor data systems or specialized data analysis software, and increasingly available open source software tools, such as the R statistical platform, are integrated into the LIMS for analysis purposes. Most LIMS provide customization functions to facilitate entry of these results.

Specification Checking

Many standard testing laboratories run analyses to determine if a material is within manufacturing specification limits. The manufacturing process and analysis method usually define these limits. Most LIMS provide a mechanism for these specifications to be stored or retrieved and compared to the results. The specifications are often stored in a database controlled by the clients of the analytical laboratory. Materials that are within specifications can be automatically released. Those that are not can be flagged or operators can be automatically notified regarding the test results.

Coordination and Authorization

In some environments, it is important to validate results before they are released. This usually involves a person other than the analysts checking the results and verifying the procedures. The LIMS can enforce such rules to help ensure that the business processes are followed. In environments where several tests are performed on one material, this role may be to coordinate reporting to the client and to identify and resolve inconsistencies.

Interpretation of Data and Results

The result of research processes is new knowledge. This is generally in the form of written documents with graphics and images that may involve many samples. A LIMS that supports analytical research needs to support the storage of these kinds of results as well as numerical and tabular results. These documents may be HTML-based documents or more commonly PDF-based reports but the support of a plethora of formats provides the inherent flexibility required for flexible data management and communication.

Report Generation

The output of an analytical laboratory is information that is reported to the client and often affects further actions and decisions. A major function of a LIMS is to improve the efficiency of report generation. To facilitate this process, report templates can be established that are automatically triggered when a step in the workflow is completed. Reports of analysis results, billing, turnaround time, instrument calibration and control charts, justification, and inventory are just a few of the common ones. Because of the variety of clients that analytical laboratories interact with, report generation is an area where there is significant investment in customization to make a LIMS effective.

Archival

The results and reports from an analytical laboratory can be of great economic value. Reference information, historical understanding of processes, solutions to problems, and assigned spectra from structure elucidation efforts represent a few of the valuable resources that need to be maintained, sometimes indefinitely. This information is usually best stored in a knowledge management system specifically designed for this purpose. Organizations may be required to save this information for many years. Archival of this data is generally supported by LIMS.

Summary

The analytical support process exists to aid and enhance the sample generation process. If it cannot be measured, it is hard to improve it. Making the information produced by this process available electronically can significantly enhance its value to an organization. Having measurements available and logically organized is required for any material or process modeling. Quick and easy access avoids duplication of work and speeds up research and problem solving. Computerization of the process requires consideration of interfaces to other information storing or generating systems. These include methods management, manufacturing resource planning and control, electronic laboratory notebooks, instrument interfaces, and reference databases.

LIMS for Spectroscopy

Ever since computers became of a practical size to fit in a spectroscopy laboratory, they have had an ever more intimate relationship with the spectrometers themselves. Spectrometer vendors have applied them to instrument control, data collection, library searching, and information management. The information management functions of these systems could be considered a LIMS with a focus limited to a particular type of testing. With the exception of chromatography, these systems were limited in scope and did not interface well with laboratory-wide LIMS. Vendors of spectral analysis packages have enhanced their software packages to provide some LIMS functions such as sample and workflow management. While not as flexible overall as the majority of modern LIMS, these niche systems are focused on managing complex data types including chemical structures, and analytical data of various forms.

To aid in sharing spectra obtained using equipment from different vendors, a number of efforts have been made to establish standard exchange formats. In the late 1980s the Joint Committee on Atomic and Molecular Physical Data (JCAMP) published the JCAMP-DX format as a standard for exchange of infrared spectra. This general format was subsequently extended to include mass and NMR spectra. Although JCAMP-DX files are created with small variations from vendor to vendor, this format is supported as an export format by most infrared instrument vendors. The Analytical Instrument Association (AIA) created a netCDF-based Analytical Data Interchange (ANDI) format for chromatography, which received widespread acceptance. After this success, the AIA adopted a standard for mass spectroscopy and began definitions for infrared and NMR. Since that type there have been multiple efforts to develop 'markup languages' compatible with Web-based technologies, which include AnIML (Analytical Information Markup Language) and mzXML and mzData (both for the interchange of mass spectrometry data).

Despite the existence of these standard formats, spectrometer vendors have been slow to include them as export options. This has been a hurdle for spectral analysis and database software vendors who have been required to deliver format converters.

The Dominance of Web-Based Technologies

Since the mid-1990s the world has experienced an explosive growth of the Internet. This growth has primarily been caused by the introduction of graphical Web browsers that provide a simple and intuitive point-and-click environment for access to information. The Web is based on widely accepted and robust standards that are open and simple enough that everyone can participate. It supports most kinds of information (text, graphics, audio, video, binary, etc.) and provides a simple mechanism for adding specialized support. Browsers are now available on all computer platforms and have provided the paradigm shift to a Web-based world for navigation. LIMS vendors who have not embraced Web-based technologies have, in general, left the market.

Scientists in many analytical research laboratories now use browser-based systems to provide analytical data support for their chemists. Spectroscopic data handling has proliferated in recent years, and commercial solutions have delivered intuitive environments for the viewing and manipulation of sample information, chemical structures, and spectra of various forms, including hyphenated MS spectra and 2D NMR spectra. Data can be searched in a variety of ways including, of course, alphanumeric text but additionally by chemical structure, substructure, and spectral features.

Web-based technologies continue to develop at a breathtaking pace. Text-based searches can easily be conducted in a matter of seconds. Cheminformatics software vendors have fully migrated their technologies to the Web and can perform chemical structure- and substructure-based searches at speeds similar to that for text searches. It is also possible to search vibrational and optical spectra online using many of the standard search algorithms; mass spectra can be searched using basic mass searches, and even 1D and higher-dimensional NMR spectra can be searched by spectral features. The Web is now a standard platform for searching, and while it lags behind in terms of real-time data processing of analytical data, this too will come.

Conclusions

When selecting or developing a LIMS, a laboratory should be clear on why the system is needed and what workflow and business functions it must support. Keeping the installation simple in scope, design, and, most importantly, user interface will help ensure success. As the laboratory's business changes over time, so must its LIMS, and continued investment in information management must be expected. With most companies generally now having competent software developers on staff and more flexible programming environments to develop applications, it is generally more productive for a company to license a series of software components and build unique workflows and a bespoke solution for their laboratory rather than be frustrated at trying to force their processes into an out-of-the-box solution. Nevertheless, in recent years increased vendor competence in the delivery of knowledge management and electronic notebooks systems have produced better systems for research environments. Web-based technologies allow information system interfaces to be developed more quickly, and users familiar with browser technology expect intuitive workflows and graphical user interfaces. With these technology improvements and the necessity for many laboratory heads to control the flow of information LIMS with better integration and simpler interfaces for spectroscopy have been developed. While they are yet to become ubiquitous in research laboratories, the increasing demands for managing data will drive further development of LIMS in the research environment and certainly in the spectroscopic laboratories.

See also: Analytical Methodology Standards for Metabolomics, Calibration and Reference Systems (Regulatory Authorities), Chromatography-MS, Methods, MS Based Metabonomics, Multivariate Statistical Methods, Overview of NMR-Based Metabonomics, Spectroscopic Methods in Drug Quality Control and Development, Spectroscopy for Process Analytical Technology (PAT).

Further Reading

ASTM (2007) *E1578-06 Standard Guide for Laboratory Information Management Systems (LIMS)*. West Conshohocken, PA: American Society for Testing and Materials.

Hinton MD (1995) *Laboratory Information Management Systems: Development and Implementation for a Quality Assurance Laboratory*. New York: Marcel Dekker, Inc.

Mahaffey RR (1990) *LIMS: Applied Information Technology for the Laboratory*. New York: Van Nostrand Reinhold.

McDowall RD (ed.) (1987) *Laboratory Information Management Systems, Concepts, Integration, Implementation*. Wilmslow, UK: Sigma Press.

Nakagawa AS (1994) *LIMS: Implementation and Management*. Cambridge, UK: The Royal Society of Chemistry.

Stafford J (ed.) (2007) *Advanced LIMS Technology: Case Studies and Business Opportunities*. New York: Springer.