Laboratory Information Management Systems and Traceability of Quality Systems

by Zvi Grauer

Today's business environment places many demands on technical managers and corporate executives. At a time when global competition forces companies to introduce products at a faster pace with higher efficiency and productivity, quality systems like ISO and Six Sigma, stipulate rigorous testing documentation. Regulatory systems, such as Good Manufacturing Practices (GMPs) and Good Laboratory Practices (GLPs), require examination of manufacturing components—raw materials, production intermediates, and finished goods—together with meticulous records of every action and result. Customers routinely insist that manufacturers keep auditable schedules and thorough documentation as a condition of doing business.

These factors place strict guidelines on data management and document handling by manufacturing organizations and the testing laboratories that support them. Data archiving, retrieval, and auditing must provide traceability, accountability, and compliance with regulations.

LIMS is an excellent mechanism to meet these complex data management requirements and to facilitate the move to an electronic records environment in compliance with the electronic data integrity requirements of the U.S. FDA (21 CFR Part 11), U.S. EPA, OSHA (Occupational Safety & Health Administration), and their international counterparts.

Traceability, accountability, and quality

Traceability is defined as "the property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties."[1]

In a strict sense, traceability refers to results of measurements by scientific instruments. It is not the property of the instrument, the calibration report, or the originating laboratory. A traceable measurement is performed in a measurement system (i.e., analytical instrument) that is clearly understood and under control. Traceability implies that the instrument is subjected to a quality assurance program; is calibrated; is regularly tested against a standard reference before, during, and after sample measurement; and has established measurement uncertainty (commonly reported as variance or standard deviation)[2] for every step in the process.

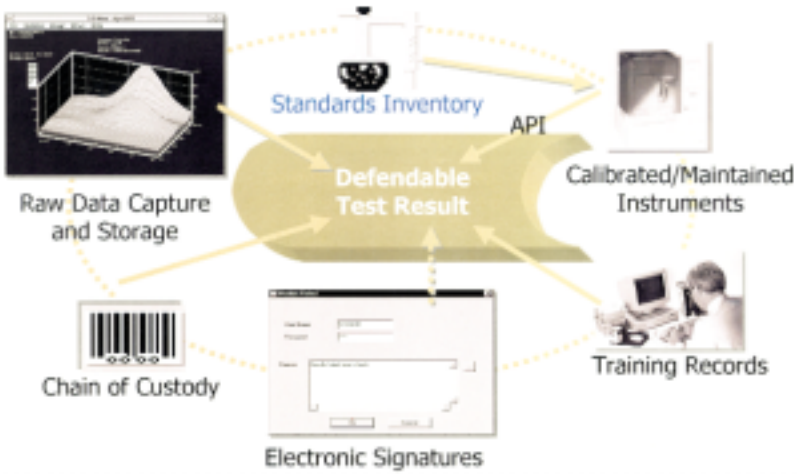

Figure 1 *StarLIMS traceability components.*

In a broader sense, traceability includes accountability to customers, regulatory agencies, and quality systems. It extends to record-keeping, sample tracking, staff training, certification maintenance, and more (*Figure 1*). A result would be con-

sidered traceable when documented procedures exist (supported by meticulous records) that demonstrate very low risk of error, which adds more items beyond equipment maintenance and calibration.

This article describes what it takes to establish traceability, accountability, and quality in a testing laboratory, and how a LIMS facilitates the process.

LIMS and traceability

A LIMS stores information in a relational database, such as Oracle (Oracle Corp., Redwood Shores, CA), DB2 (IBM, White Plains, NY), or MS SQL (Microsoft, Redmond, WA). Each table in the relational database is assigned a primary key, e.g., a column or set of columns, whose values uniquely identify every row (record) in the table. Tables are related to each other by using foreign keys. A foreign key in one table (the foreign table) contains a value corresponding to the primary key of another table (the primary table). This relates the information in the foreign table to that in the primary table.

The use of foreign keys allows the LIMS to establish links between samples, storage conditions, test dates, analyst certifications, instrument calibration, and testing parameters. Most LIMS provide an interface that takes the place of direct SQL queries to the database.

Maintaining a quality organization

For reliable data generation, each aspect of the laboratory performance must meet quality standards. Staff needs to be trained and certified in equipment use and sample handling. Training must be current and certified by an external organization. Equipment must be regularly inspected, maintained, and calibrated. Controls must be an integral part of the measurement cycle.

To prove chain of custody, samples require tracking from receipt through analysis, through data entry and approvals up to the final report. Every action must be logged, and every record properly signed and archived for future retrieval.

A compliant LIMS follows the laboratory workflow at every step. It accepts manual sample and data entries, uploaded documents, and computer file attachments (faxes and word processor and spreadsheet files) and stores them in a database. It communicates with analytical equipment. It schedules laboratory work, equipment maintenance, and staff training, and updates staff, managers, and customers with the latest information. A compliant LIMS product makes policy enforcement, data integrity, and traceability an easy reality.

LIMS and electronic record-keeping

Modern scientific instruments, such as spectrometers, chromatographs, and microscopes, generate data in electronic formats using integrated or external data acquisition and processing systems. Older equipment has (or can be retrofitted with) serial ports to transfer data to external computers. Modern LIMS software can interface with scientific equipment through the network to automatically retrieve and store the information in a database without the need for human intervention.

The data fields provided by analytical instruments often include technician and sample details, operational parameters, and analyst's comments, in addition to the technical data (e.g., spectrum, chromatogram, and image). The LIMS collects and processes the instrument data for archiving and retrieval. For increased security and performance, the data are stored in an external database server running Oracle or MS SQL. These database servers offer redundancy, high availability, fault tolerance, and strong security.

A good LIMS is flexible and configurable, and allows automated entry of additional fields. With such flexibility, a single data archive format can be generated by different instruments, and data collection is easily updated when the instruments or their software are upgraded.

StarLIMS from L.I.M.S. (USA) Inc. (Hollywood, FL) has a Data Capture Utility (DCU) that automates numerical data entry from all principal laboratory instruments. Data are

collected through the network, allowing simultaneous access to multiple instruments without requiring direct connection or even physical proximity. The full automation of results entry reduces technician workload and eliminates transcription errors.

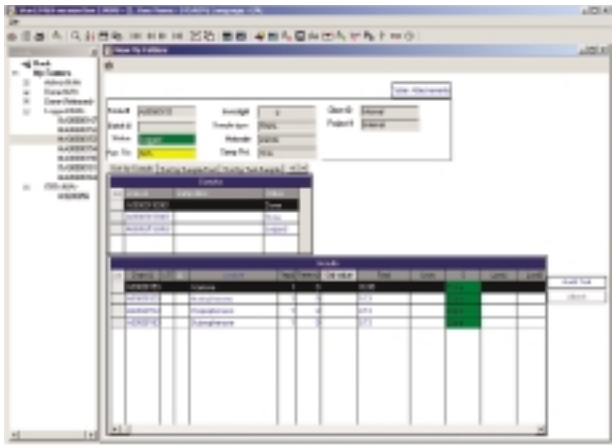

Figure 2 Sample tracking.

StarDOC, a StarLIMS module, captures and archives unstructured data (spectra, photos, and other documents) in accordance with 21 CFR Part 11. A unique ID number is created for each data file. This ID, sample information, and raw data are all stored together as a single entity, as required by GLP. These data are easily tracked, sorted, and retrieved at any time. It is possible to view the data using the StarDOC utility, the original applications that generated the data, and a special viewer such as the ACD spectral viewer.

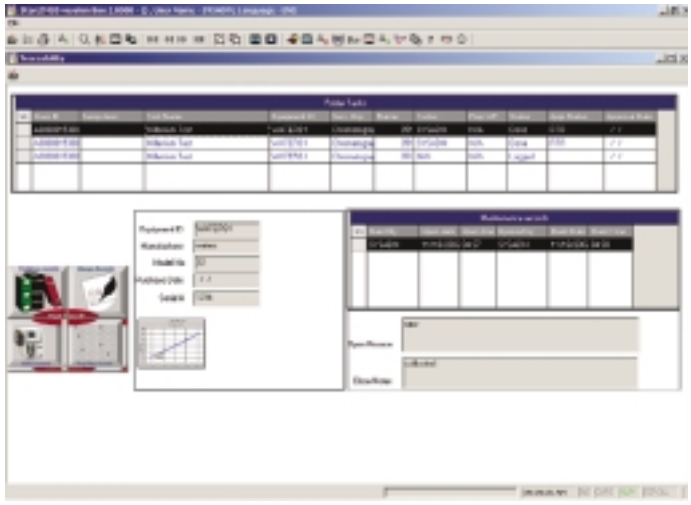

Figure 3 Audit trail.

Sample tracking

An important part of traceability is keeping track of samples from the moment they arrive at the laboratory to the time results are reported (*Figure 2*). At a minimum, this means maintaining a relational database containing lot numbers, specifications, operator names, time stamps, and authorizer information, as well as electronic signatures for each sample. A majority of companies impose much stricter tracking requirements on laboratory data. This may be done to comply with regulations, to prevent litigation, or to protect intellectual property rights. StarLIMS' automated electronic record-keeping goes far beyond that minimum. It includes test results and equipment settings that cover all sample movements, conforming to 21 CFR Part 11, which is becoming a model for global traceability standards. An integrated electronic record management module produces a completely auditable track record of all laboratory resources taking part in a specific analysis (scientists, instruments, standards, and standard operating procedures [SOPs]).

The role of a LIMS in a GLP/GMP environment is to help ease documentation of regulation compliance. StarLIMS has extensive features to aid in this process. Modules facilitate maintaining versions of test methods, training certifications for analysts, log books for instrument maintenance, instrument standards and control charts, MSDS (Material Safety Data Sheets), and general material management and tracking. These modules are integrated into the StarLIMS workflow process. For example, when assigning a test to a selected analyst, it is possible to automatically compare the certifications of the analyst to those required, and assign qualified analysts only to perform the test. StarLIMS also combines the ability to maintain schedules, content, and review questions for each certification course.

Data safeguarding

To produce data that will withstand even the closest scrutiny, a laboratory needs to implement strict controls. Critical elements to be included in a secure electronic data management system are monitors such as strict user access rules, document and data change con-

trol, transactional or silent audit trails, and password security.

StarLIMS supports peer review (requiring a peer to evaluate and approve testing data, thus preventing individuals from signing off on their own tests), auditable data change policy (requiring recorded explanation and authorization to change recorded data), report release hierarchy (mandatory manager review and signatures), and data security policy (password-protected individual computer accounts).

StarLIMS' integrated auditing tool links each sample to records on technician training and certifications, equipment maintenance, equipment control standards and calibration, and sample testing history (*Figure 3*).

Policy enforcement

Traceability requires auditable, recorded equipment maintenance and calibration schedules and regular equipment testing routines (daily, weekly, and monthly performance testing against known standards), but records do not guarantee compliance. For instance, keeping records of equipment calibration does not prevent personnel from using noncalibrated equipment, or failing to use proper controls and standards.

LIMS can be used to enforce policies. For example, StarLIMS can be set to allow only authorized personnel to run specific tests. The work is automatically assigned, and unauthorized staff members are unable to run or sign the test. Tests would not even show up in an analyst's personal console unless he/she is authorized to run them. Likewise, it is possible to tie the use of equipment to completion of scheduled maintenance, and to require that a QC standard be run before using the instrument to measure samples. All requirements have to be met for the instrument to run and log the samples.

The results of calibration and standardization runs can be used to determine measurement uncertainty and to clear the instrument for use in testing (if it passes specifications). An integrated scheduling tool facilitates creating and keeping track of equipment maintenance and personnel training schedules.

Conclusion

The right LIMS is an essential tool in improving the data quality and operational efficiency of technical organizations and testing laboratories. A LIMS logs every action and every record, enforces signatures, archives for future retrieval, and provides data integrity and traceability. It establishes sample chain of custody from receipt to final report. A LIMS can be used to monitor and enforce staff training and certification, equipment inspection, calibration, and maintenance by denying data entry unless all equipment maintenance and training requirements are met.

The use of LIMS electronic databases means that data can be easily tracked, sorted, and retrieved. Computerized records reduce paper use and lower the costs associated with manual filing, copying, and storerooms, while reducing handling errors and improving response times.

A LIMS is an excellent means of meeting complex data archiving, retrieval, and auditing needs, and for complying with electronic data integrity requirements of U.S. and international regulatory bodies.

References

1. *http://www.nist.gov/traceability/suppl_matls_for_nist_policy_rev.htm.*
2. *http://physics.nist.gov/cuu/Uncertainty/index.html.*

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