LIMS as an Enabling Technology for the Pharmaceutical Industry

In the pharmaceutical industry, just as in many other industries, the purchase of a laboratory information management system (LIMS) is not a trivial exercise and requires a good deal of involvement from both the customer and the vendor. In view of this process, the resultant LIMS is frequently viewed as a ‘system’ that has been designed to meet the needs of the customer and is then set in stone. However, the range of potential applications for LIMS and the fast-moving pace of the pharmaceutical industry means that rather than having a ‘fixed system’ LIMS, pharmaceutical laboratories need to be highly agile and build flexibility into their systems to cope with change.

Change can come about for a multitude of reasons - new ideas surface, new departments are introduced to the system, overseas locations are added often through acquisitions or mergers, new business requirements emerge, new regulatory requirements are enforced etc. This article looks at how the wide-ranging opportunities for LIMS within pharmaceutical organisations such as QA/QC, stability studies, pre-clinical pathology, clinical trials, biobanking and environmental can benefit from a flexible approach to LIMS. In fact, it can be much more beneficial to view the LIMS as an ‘enabling technology’ which can evolve and adapt, often under direct control of the user, as the requirements change. For this to be the case, the front end of the LIMS has to be truly configurable, by the vendor and the end user alike. In fact, from a regulatory viewpoint configuration is actually preferred to custom coding according to the GAMP levels. Whilst most LIMS are configurable to some degree, depending on the particular system, a programmer or other IT person would need to write scripts or new custom programs to design new screens or link menus in different ways to support different workflows. Some LIMS, however, use exactly the same core program suite but feature a configurable ‘layer’, or set of configuration tools, that allows each system to be set up to exactly match user requirements. This makes the process of configuration much simpler and truly embraces the ‘enabling technology’ concept.

QA/QC
Pharmaceutical quality control laboratories have an important function in both raw material evaluation and production, and can significantly impact overall manufacturing performance. Enhancing laboratory productivity leads to improved manufacturing efficiency, and information management in laboratory operations is essential to improving laboratory efficiencies. Using a LIMS to control, manage, organise, document, analyse and report information leads to improved efficiency and functionality of data storage and manipulation. The system is likely to be required to manage data for a wide range of analytical techniques for both the raw materials and finished products. Raw materials and finished products have to conform to pharmacopoeia and relevant product licenses. The LIMS must be compliant with all of the relevant regulations and practices such as cGLPs and cGMPs, including audit trails, time- and date-stamping of all actions, version control of all reference data such as test definitions, and provide features to help with 21 CFR Part 11 compliance such as data entry authentication and comprehensive password management capability. The software could be used to generate certificates of analysis and monitor lab efficiencies whilst trending results for the finished products. A configurable LIMS solution can create a system that matches the specific requirements, such as customer-specific tables/modules and multiple screens for the same function (e.g. different login screens for different product classes, such as raw materials and finished products).

Stability Studies
Stability studies to measure the shelf life of a given product by testing a series of samples stored in environmental chambers to simulate accelerated testing is an essential part of the drug development process. The requirements for stability testing are described in 21 CFR 211.166 (Revised as of April 1, 2012). The application of LIMS to stability testing ensures that approved protocols are followed precisely, with “pulls” made on schedule and the appropriate tests completed, while providing the necessary security and audit trail to comply with FDA regulations, including 21 CFR Part 11. This requires change control, validation and audit trailing of changes to the system and the data that it holds. Yet today’s laboratories must be able to offer the flexibility to adapt and change their processes and workflows when necessary, and their LIMS must stay in step with these changes. Stability testing requires the management of significant amounts of data from a variety of sources. In addition, clear, cohesive reporting of stability testing results is required, both for dossier submission and for ongoing studies. The use of an appropriately configured LIMS can automate and control the entire operation of the stability study including:

- Protocol creation
- Study initiation and management
- Inventory management
- Sample login scheduling
- Future workload reporting
- Stability study reporting

This approach simplifies the whole study management process. While a LIMS can make a considerable contribution to managing stability studies, given the sheer range of studies that may be required, the system requires the flexibility to be configured to the particular application.

Pre-clinical Pathology
Pre-clinical pathology applications continue to be an important part of the pre-clinical evaluation of drugs to ensure that they are safe and effective before moving to the clinical phase of drug development. Pharmacokinetic studies are very important to reveal the safety and efficacy parameters in terms of absorption, distribution, metabolism and excretion. The implementation of a LIMS can create an almost completely paperless system for tracking laboratory samples and accounting for individuals performing the tasks (tests) on these samples. In multi-site organisations, this can require many users across multiple locations. A complex querying function, rapid registration of thousands of samples, and customised menus and options can all be created using a configurable LIMS. This allows saving
of cycle time, which is essential when
thousands of samples may be registered
per day.

Clinical Trials
The development of novel pharmaceuticals
requires rigidly regulated clinical trials.
Competent authorities (those tasked with
enforcing legislation) need to be able to
verify that all analyses during the trial
were carried out without bias. This means
that each step must be securely recorded
at the time and there must be evidence
that these records have not been
tampered with after the event. For each
sample, the audit trail may extend to
hundreds or even thousands of entries;
starting with the nature of sample
collection and storage, which may
dramatically alter the results of analyses,
potentially ending with complex data sets
such as those from next generation DNA
sequencing or mass spectroscopy. A trial
may involve many thousands of samples,
so handling of these records in
accordance with the regulatory
requirements is challenging. Conducting
clinical trials in the EU is tightly regulated.
This is to uphold the rights and ensure the
safety of clinical trial participants, as well
as the reliability and robustness of the
data generated. A LIMS is capable of
tracking clinical trial collection kits/
supplies, managing and tracking
specimens, managing laboratory testing
workflows and recording quality
performance, creating laboratory reports
and managing study-specific documents.
A configurable LIMS can log each step in
the workflows for each trial and store the
log in a readily accessible format that
allows audit in minutes rather than days.
The database can be created and
updated, with audit points for each
sample being added from workflows in
the LIMS that mimic the wet lab processes
used in the trials. A configurable LIMS
means that the system can be readily
modified in the event of any future
changes to the official statutes.

Biobanking
Biobanks play an important role in
biotechnology, pharmaceutical and
medical research. The ability to manage
an ever increasing number of bio-
samples (blood, tissue, DNA etc.) and to
comply with the regulatory requirements,
such as HTA, GCLP, MHRA, FDA 21 CFR
Part 11 and other similar requirements,
is a high priority for all organisations
working in this area. One of the
challenges faced when implementing a
biobank management system is how the
system can evolve with time. A LIMS that
can offer flexible configurability can keep
the system in step with user requirements
and regulatory change moving forward.
This both extends system life and reduces
overall cost of ownership of the system.
Samples need to be tracked at all
times and it is essential to be able to
record the complete genealogy for all
samples and track the aliquots, pooled
samples and derivatives of each sample.
Typical requirements that a biobank
management system should be capable
of handling include management of the
documents, study plan and standard
operating procedures (SOPs) with change
control. Since samples could easily be
taken at distributed sampling points,
patient consent forms, sample collection,
tracking and inventories for sampling
kits, local sample storage and sample
delivery will all need to be considered.
Once the samples are received at the
central facility, accessioning, sample storage, and sample distribution, transfer and return all need to be handled. With regard to sample testing, consideration must be given to screening tests, results entry, storage, aliquots, derivatives and sample processing. At the end of the testing, final sample disposition may be required and, of course, reports must be produced. Biobank management systems therefore need to be configured to deliver a solution that meets the specific requirements in a clearly understandable way.

**Environmental**

Environmental monitoring is an essential part of any pharmaceutical manufacturing process. It is essential to show that the microbial and particulate content of all cleanroom air and work surfaces is within acceptable levels. Any utilities used in product manufacture, such as purified water or compressed air, must also be shown to be free of contamination. Implementation of an effective EM programme allows corrective action to be taken to ensure that the manufacturing process remains in control and safe from dangerous contaminants. Testing includes air sampling, settling plates, surface sampling, water monitoring (USP <1231> (TOC & conductivity)), and heterotrophic plate counts (microbial levels). A configurable LIMS can be used to define a complete environmental monitoring protocol, including sampling plan and testing schedule. The collected samples can be associated with particular analysts, control samples, instrumentation and in/out of incubation dates. In addition, observational monitoring documentation can be associated with testing of a particular controlled environment. Trend plots and summary reports can be produced. The user can optionally associate morphology data with the batch of collected samples.

**Contract Laboratory Testing**

Away from the pharmaceutical manufacturing sector, there are also opportunities for flexible LIMS usage in business contract laboratory testing. Here the opportunities for a configurable system are even greater as, in addition to laboratory information management, there is the possibility of extending the system to handle an extensive range of management functions, from invoicing to consumable inventory control. In the traditional laboratory environment, the configurable LIMS offers all the capabilities needed to capture, store and report on a very wide range of materials and tests for small or large contract laboratories, and introduce new protocols and tests as demanded by individual customers. A freely configurable LIMS could also provide the functionality for management of a variety of activities essential to running the actual business, such as the creation of quotations, order booking, allocation of appropriate prices, generation of results and customer reports and the production of invoices, either directly or in conjunction with a corporate accounts system. By having a fully configurable pricing capability, business profitability can be monitored right down to the test level.

With such an extensive range of applications within the pharmaceutical industry, the concept of LIMS as an ‘enabling technology’ is an important one. The rich and diverse requirements from organisations both large and small make it essential that the LIMS can be adapted to the needs of the laboratory, rather than laboratory workflows being adapted to fit into a restrictive LIMS structure.

---

John Boother, Managing Director at Autoscribe Ltd, has had involvement in around 5000 LIMS projects. Autoscribe is a UK-based, global supplier of LIMS to both the laboratory and the wider business markets with distributors in every continent offering localised technical support. Visit [www.autoscribeinformatics.com](http://www.autoscribeinformatics.com) for more information. E-mail: john.boother@autoscribe.co.uk.