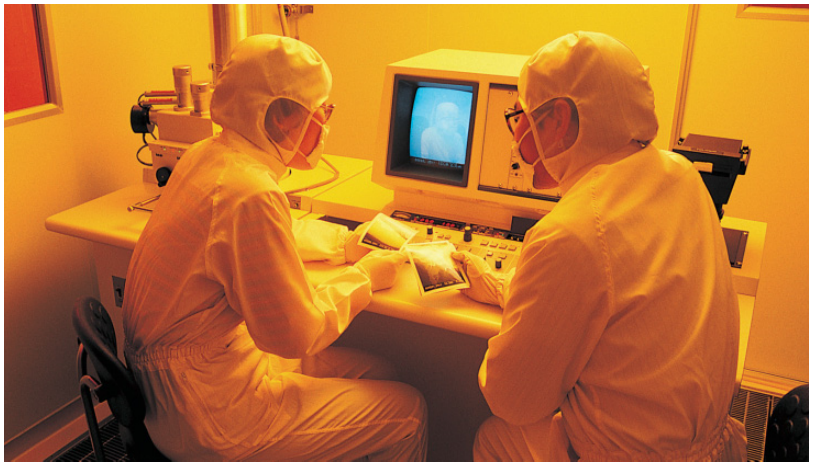


An Overview of LIMS in the Pharmaceutical Industry

The pharmaceutical industry is in many ways unique. The challenges facing pharmaceutical companies, including large pharma, biotech and generics manufacturers are sometimes overwhelming. Diverse laboratories, regulatory constraints, complex batch management and testing needs all demand sophisticated, enterprise-level informatics solutions.

Richard Wagner

This article will review the challenges facing pharmaceutical laboratories, and examine the three most common alternatives available to pharmaceutical companies evaluating laboratory informatics systems in the context of the above-mentioned challenges. These include in-house developed systems, 'generic' laboratory information management systems (LIMS), and commercial off-the-shelf (COTS) solutions. We will also discuss some of the new trends in the capabilities of LIMS, and in the use of LIMS in the pharmaceutical enterprise.

Challenges in pharma laboratories

One of the controversial challenges in selecting a LIMS in pharma is the wide diversity of laboratories in a company. Combinatorial chemistry, screening, preclinical and clinical bioanalysis, analytical chemistry, manufacturing R&D and production quality control (QC) all have unique needs and workflows. However, end users seeking a solution to their business needs are often challenged by upper management to somehow 'make do' with a system already used in another part of the company. In some cases it can work, but more often than not the result is a failed implementation, and a lot of unhappy (and potentially unproductive) users. In general, the industry is rapidly acknowledging that one tool cannot possibly meet the needs of these diverse users. True solutions must solve the business pain of the end users. Complex test methods with multiple-

stage acceptance criteria must be automated as much as possible. Pharmaceutical product testing is highly batch-oriented, therefore, any potential solution for the manufacturing area must include batch management capabilities. Preclinical and clinical bioanalysis is very protocol-driven, therefore, solutions for these laboratories should be designed with an understanding of the study protocol.

Some may interpret this approach as contrary to the industry-wide trend of standardization. The fact is, one should only standardize where it is advantageous to do so. If a company has 25 manufacturing facilities worldwide, with a QC laboratory in each, standardization can have great benefit in harmonizing processes, and in reducing deployment and validation costs across those 25 sites. However, it doesn't make sense to try to apply a tool designed for QC testing to a protocol-driven clinical bioanalysis laboratory. That is not standardization, and for end users it is akin to abuse.

It is also widely recognized that the industry faces more intense regulatory scrutiny than any other, except perhaps the nuclear energy industry. Any potential solution must satisfy the concerns of both internal and external auditors. This includes the flexibility to support widely varying review and approval workflows for both static data, such as product specifications or study protocols, and dynamic data, such as test results and batch disposition.

Finally, the vast majority of pharmaceutical companies are being challenged to become more efficient. The massive profits of the blockbuster drugs are quickly becoming history, and pharmaceutical companies are facing the same pressures to streamline, become more efficient, and focus on core businesses that faced the petrochemical industry in the 1970s and 1980s. Big IT projects have felt this pressure acutely and no major project is able to proceed without clearly demonstrated cost justifications.

LIMS trends

LIMS were introduced to the pharmaceutical industry approximately 20 years ago. At that time, most were implemented to serve solely as a final repository for completed, approved data. Data collection, calculations, and, in most cases, evaluation were performed outside the scope of the LIMS in a paper-based environment. 'Interfacing' with other systems meant putting all the paper printouts into the same binder!

As the business, IT and regulatory environments have evolved, so too have LIMS, and more importantly, their role in the pharmaceutical organization. LIMS often store final data and all data collected to produce the final result. They are expected to apply business logic to evaluate results and trigger events in real-time, and enforce regulatory compliance according to cGxP. They are expected to communicate directly with other enterprise systems and to generate true submission-ready output. Ultimately, LIMS are assuming a pivotal role in the evolution towards paperless laboratories. To meet these lofty expectations, solutions must integrate logic based on industry standards, such as those supplied by the International Conference on Harmonization, national formularies, such as the United States Pharmacopeia and European Pharmacopoeia, and various guidances issued by regulatory agencies.

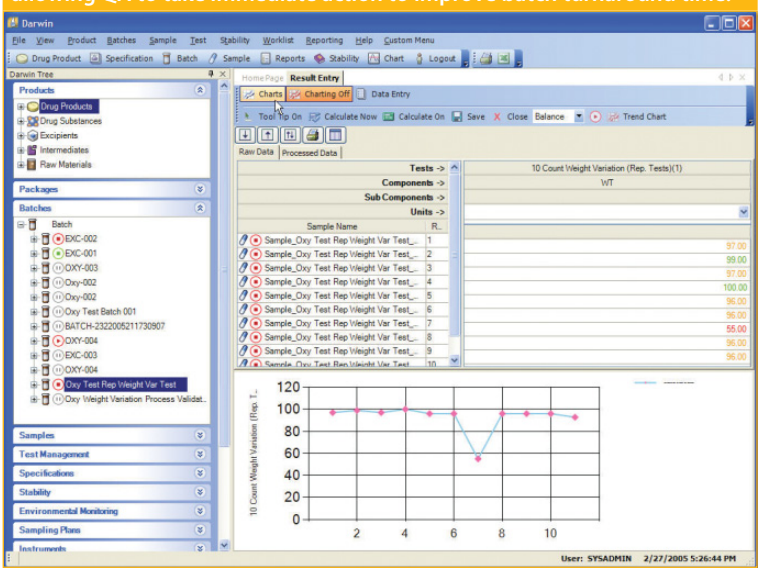
LIMS options

There are several potential solutions available to meet the challenges and trends identified above. However, these solutions do not all offer equal appeal.

Custom solutions. For many years, custom solutions were very popular in the pharmaceutical industry. Many of the challenges identified here have been constant in the pharmaceutical industry for the past three decades, particularly the regulatory constraints and the complexity of the testing performed. With no commercial product available that met the specific needs of the pharma business process, and with no pressure to limit the scope or budget of large-scale IT projects, many companies built custom solutions in-house, or contracted with custom software development firms to have custom systems built for them.

In many ways, it is still possible that a custom system could meet the needs of an individual pharmaceutical company better than any commercial offering. However, the cost of such a system can be prohibitive. The project development cost is monumental in terms of cash and time, and the cost of ownership

Figure 1 This example shows how collected data is compared to specifications and charted in real-time, and any limit violations automatically cascade up from the test level to the drug product batch, allowing QA to take immediate action to improve batch turnaround time.



becomes an annually recurring nightmare. In addition, software development projects distract from a pharmaceutical company's core business of developing and marketing therapeutics.

'Generic' LIMS. Commercially available LIMS began appearing during the 1980s. Some of these systems endure, and have expanded their scope to address many varied areas of laboratory management, including equipment inventories and training management. Over the course of their evolution, these systems have been designed to be industry independent. In many cases, they were also designed to be somewhat platform independent, supporting various database platforms and operating systems. Because of this, they have frequently been referred to as 'generic' LIMS.

Generic LIMS systems are almost universally sample-oriented and laboratory-centric. This means that the central entity around which the system revolves is a sample, and the actions and functions available are designed from the laboratory's point of view. Samples are received in the laboratory; results are entered against the samples; and each sample is reviewed and/or approved. Generic systems are delivered with basic sample-oriented functionality, and with guidelines and sometimes tools to enable the customer or implementation consultants to extend the basic functionality of the generic system to meet customer needs.

In many industries, generic LIMS can be successfully used without excessive customization. Because they have been under development for many years, there are several generic LIMS that have proven to be very robust, however, there can be limitations to the functionality achievable through customization because of the legacy architecture and technology used to build the generic LIMS.

The issue at hand, however, is the challenge of deploying a generic LIMS in the pharmaceutical industry. Virtually none of the many laboratories in pharma are sample-oriented. Screening laboratories are product- or molecule-oriented. Preclinical and clinical bioanalysis laboratories are study- and subject/patient-oriented. Analytical development is product-oriented, and manufacturing QC is product/batch-oriented. In each of these examples, a generic LIMS would require extensive customization. It is important to note the definition of customization used here: ANY manually written code designed to alter the functionality of the core product. Whether the LIMS embeds a scripting language or requires custom functionality to be written in an external tool or environment, any written instructions to enable or create functionality represents customization. This would include manually creating XML or HTML, or stored routines or procedures to automate workflow or routine processes. In many cases the magnitude of the customization required can result in a system with such expensive maintenance, validation and upgrade costs that there is little difference in expense between the customized generic system and a completely custom built one.

Commercial off-the-shelf solutions. Because of the high cost of deploying either custom-built systems or highly customized generic systems within the pharmaceutical domain, there is a rapidly growing trend towards employing COTS software wherever possible. While these may have a higher initial purchase price than a generic system, the costs of deployment, training, validation, maintenance and upgrades can be dramatically lowered, making the overall cost of ownership a fraction of that of a customized solution.

There are other significant advantages to seeking COTS solutions when evaluating LIMS for pharma. To produce an application or solution for a specific domain, a vendor must demonstrate a thorough understanding of the domain and its specific challenges. In the pharma domain, this includes awareness of the existing and evolving regulatory environment, and of new developments in testing and QC. Such expertise can allow a vendor to ensure that future releases of their solution can introduce new functionality and business logic as required to ensure support for the most recent regulatory requirements and industry trends (Figure 1).

When using COTS solutions with highly developed functionality, there is often a trade-off between configuring the system to be aligned with existing business processes and adjusting existing processes to be aligned with existing functionality. However, the internal analysis required during this phase can be beneficial in identifying outdated processes and optimizing inefficient ones. From a standardization perspective, COTS can also prove useful in establishing standard practices across multiple installations.

It is important to note that even a so-called COTS solution is unlikely to truly satisfy 100% of the requirements of a pharmaceutical laboratory. Assessing industry or application-specific solutions is an effort to maximize the level of out-of-the-box functionality and minimize the amount of customization required. Once the assessment is complete, there may be some extension of the system required, so it is important to have a complete understanding of any COTS vendor's strategy for closing the functional gaps. Tools to extend the software must be available; the vendor should

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KEY POINTS

- Sample-oriented, generic systems can require extensive customization
- Customizations carry a high price in validation, deployment, training, maintenance and upgrade costs.
- The trend is towards off-the-shelf solutions
- A true COTS vendor should have a thorough understanding of the pharma domain
- Even a COTS solution may not be a perfect fit

be able to provide experienced analysts to assist in deployment; and the technology platform should use modern architecture and open standards to facilitate the required extensions. Likewise, a COTS solution does not eliminate the burden of responsibility on the part of the user. While the validation effort may be greatly reduced, there will still be some effort required to provide reassurance that the system, as configured, is functioning according to expectations.

It is also important to assess the levels of compliance and flexibility inherent in the COTS solution. Historically, despite extensively customizing generic systems, pharma companies have been unable to implement one solution to concurrently meet the needs of the less-regulated users, such as analytical R&D and the tightly monitored production laboratories. The configuration of the system should include the definition of compliance rules based on the type of data being manipulated.

Conclusion

The pharmaceutical industry faces a number of unique challenges, including intense regulatory scrutiny, complex testing methods and mounting financial pressure as the market grows increasingly competitive.

For companies choosing a LIMS, there are three primary alternatives: a custom-built system, a customized generic system, or a COTS solution. While it is possible to build a custom system that could meet a company's needs exactly, the cost of the effort and the overall cost of ownership once deployed are astronomical and prohibitive. Because of the extent of requirements that are unique to the pharmaceutical domain, many of the generic commercially available LIMS often undergo extensive customization to satisfy pharmaceutical business requirements.

This extensive customization has the effect of dramatically elevating the cost of deploying the system and the ongoing overhead to keep it in place. In contrast, a COTS solution can meet a large portion of the needs of the pharmaceutical domain without customization. Because it is unlikely that even a COTS solution could meet 100% of a company's needs, it is important to ensure that the selected one can still be extended when required. Provided that the vendor offers this support, it is clear that COTS solutions are the preferred choice by a wide margin.

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