



Thin LIMS, Thick LIMS — New IT Implementation Strategy for cGMP Quality Informatics

How to complete a QC/QA cGMP lab IT architecture with half the technical resources in half the time.



INTRODUCTION

The purchase and implementation of a compliant “Information Management System” for the QC/QA lab environment is a fundamental concern for modern 21st century life science companies. The critical issues in vendor selection and deployment processes often neglect the inherent short and long term “total cost of implementation and ownership” factors that impact the ultimate success or failure of the overall project. Those factors include:

- What capabilities of the IT system are “out of the box” and fully functional?
- How does the QC lab workflow affect the standard capabilities vs. the degree of customization needed for completion?
- How will I get the critical required cGMP metadata surrounding my test methods into the system?
- What other IT systems does the information management system need to interface with to complete the “informatics system”?
- What are the validation implications (and costs) on system changes on a short and long term basis?
- What resources will be needed for deployment — short term AND long term?

In practice, IT departments of most life science companies defer to the strategy of implementing a “LIMS” or laboratory information management system. Usually the LIMS strategy is for compliance management purposes with little attention to the lab-based productivity and documentation needs. From our research, LIMS deployments never totally automate all the lab data capture and critical cGMP documentation tasks but rely on human intervention to “key in” the data into LIMS results entry forms. The direct pedigree to all the lab tasks, supplies and compliance metadata is a paper-based process that consumes human resource costs on an on-going basis (log books and notebooks are used even after the LIMS deployment). The LIMS vendors and associated consultants fail to discuss the large level of custom coding that is needed to automate the lab tasks and required cGMP documentation needs. Often the company must hire an internal software development team for on-going LIMS work. The general deployment characterization of such a project is a “Thick LIMS” with the costs of the total deployment generally unknown to project management. Often referred to as “scope creep”, the overall LIMS costs can often be 2-5 times the original estimates. After running these projects for several years, the project managers often have no other recourse but to continue funding an almost never-ending project. Traditional LIMS deployments are projects, not products.

The “L” in LIMS stands for laboratory. Most commercial LIMS have a solid core capability whose primary function is for management, not lab analysts. The sample tracking and final results organization, reporting, specifications and trending is standard, however the lab execution tasks such as method viewing, data capture, instrument integration and calibration-state verification, method documentation, supplies logging, data reviewing and approving are still paper-based and manual processes requiring multi-levels of review and sign-offs by human resources. It is precisely here that LIMS projects fail to adequately automate lab operations and often take many years and millions of dollars to implement with on-going costs of ownership beyond the original plans.

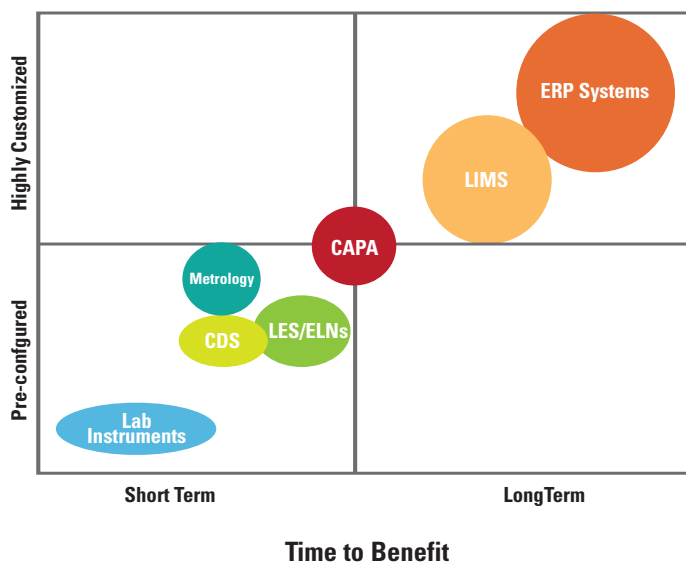
The solution to these issues is the new strategy of a “Thin LIMS” deployment. Over the last few years, this thin LIMS strategy, has been presented by major pharmaceutical, generic and biotech companies at the annual IMACS (International Meeting on Automated Compliance Systems) conference. In short, the “Thin LIMS” strategy is the implementation of a commercial LIMS in

combination with a GMP Lab Execution System. The LIMS functions are narrowly defined and fixed for quick implementation and are usually “supervisory functions” while the lab execution system is an off-the-shelf platform for lab “method functions” that include all data and metadata compliance documentation and instrument integration. Through this architecture, the cGMP lab operations are totally automated yielding productivity improvements of 25%+ and cycle time reductions in excess of 50%. The project cost considerations include a 50% resource liberation of traditional LIMS implementation requirements with project completion time frames cut in half.

This white paper will outline the key definitions, architecture and cost/benefit considerations for a “Thin LIMS” vs. “Thick LIMS” implementation strategy in cGMP quality operations.

THE cGMP IT PROJECT LANDSCAPE

The last decade has ushered in a host of IT infrastructures to meet the regulatory and productivity challenges of the life sciences industry. Projects include ERP, Chromatography Data Systems (CDS), PC-based Instrument workstations, CAPA, Document Management Systems, Electronic Notebooks, Chemical Inventory and Reagent Management etc. In general, these software platforms fall into a four quadrant matrix of degree of customization vs. deployment time frames. Typical cGMP lab and IT systems are seen in the following figure:



The desired quadrant is in the COTS (commercial, off-the-shelf) area where deployment timelines are quick with a small degree of configuration needed vs. custom implementations seen in the upper right quadrant. The relative investments (licenses and project resources) are indicated by the size of the circle.

Most traditional LIMS projects are characterized by a small degree of configured “out of the box” implementation and integration with the lab environment (instruments, reagents/chemicals and test methods). Typical LIMS have a high degree of custom coded workload before validation and use in the cGMP environment. In fact, many implementations have a full software development team on site made up of permanent employees and consulting groups. These on-going costs can dwarf the original project cost estimates and delay the “go live” automation benefits.

THE ENEMY — CUSTOM CODING

At the 2007 IMACS conference, a presentation by one of the top 20 pharma companies stated that during the due diligence in defining a harmonized IT architecture for their global QC/QA plant operations, the team stated their three top priorities. They were:

Priority #1 — No Custom Coding

Priority #2 — No Custom Coding

Priority #3 — If you custom code you're fired!

After the laughter stopped, they went on to outline a three tiered architecture comprised of an ERP system, a "thin LIMS" and a GMP Electronic Notebook System. This structure is currently being deployed to all global manufacturing sites. This "no custom coding" mantra is the key to rapid technology deployment and getting to the benefits of true lab automation from the analyst level up to operational management and product release to the supply chain.

The definition of Thick vs. Thin LIMS and the implication of custom coding is important to understand. In any LIMS implementation the key core LIMS functions are:

1. Sample Management and Stability Management
2. Specification Management
3. Results Management
4. Reporting and Trending

A "Thick LIMS" implementation deploys all 4 of the above core functions AND attempts to automate the capture and processing of lab data and required metadata, calculations, instrument integration and raw data capture and reporting. The additional lab-based functions are added to the "out of the box" core LIMS functions through significant data and workflow planning followed by custom coding, testing, validation and maintenance. This custom code requires all of the software requirements for cGMP compliance and therefore requires a software development team to be engaged. This team will be an on-going cost during the life time of the Thick LIMS deployment and represents over \$1 million/year for a typical 20-40 person cGMP QC/QA operation.

Case #1

During our research interviews, one biotechnology company that is deploying a "Thick LIMS" implementation outlined the number of resources needed (per site) for the project and after 4 years is still active. The resources are as follows:

- Citrix Administrator
- Oracle Database Administrator
- LIMS Expert Consultant
- Business Representative
- Business Manager
- Senior IT Manager
- IT Software Quality Assurance Resource
- Documentation Specialist
- Test Script Writer

- IT Crystal Report Writer
- Help Desk Support
- 3rd Party Validation Consultant(s)
- Site Representative

These 13 headcounts were on site, 5 days/week for over 4 years and the system is not completed. The significant on-going workload for these resources is derived from the customization of the analyst/lab infrastructure data/documentation and instrument integration tasks coupled to the “core” LIMS functions.

Case #2

Another medium sized pharmaceutical company chose a traditional Thick LIMS implementation and after 4 years and \$3-4 million dollars the system went live. The live system is ONLY used in the Raw Materials testing area and not the entire QC operation. In addition, the validation implementation took 2 years and \$1.5M to complete. The custom coding process has no validation documents and as such needs to be defined, created, approved by QA and executed. Key lessons learned were as follows:

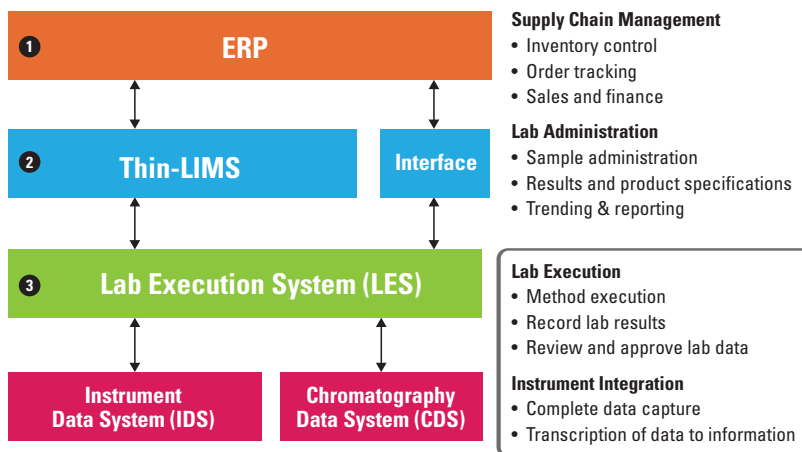
- Nothing available out of the box (even though LIMS vendor suggested it was a COTS solution).
- LIMS had to be custom built (time about one year).
- Scope started small but ended big.
- No validation documents were available.
- Entire validation package had to be created (2 years and \$1.5M).
- Resources for validation required (to run test scripts/consultants).
- Data is moved through environments as objects.
- PQ took months.
- Modifications require changes to custom code when business needs change.
- Time from concept to go live was 4 years (for raw materials only).
- Cost \$3-4M.

A “Thin LIMS” strategy contains the same four core functions as the thick LIMS implementation, however, the “in-laboratory tasks” are NOT custom coded into the project. Instead an off-the-shelf (COTS) platform is connected to the core LIMS via a simple XML-based data exchange facility. This platform, as defined by a top 10 pharmaceutical company that implemented this structure, is a GMP Lab Execution System. This technology automates the analyst’s day as follows:

- viewing test methods
- capturing all data from analytical instruments, CDS’s and devices (eg. Pipettes)
- capturing all reagent and supplies metadata and managing all expiration date requirements
- performs all calculations in a validated environment, automatically
- organizes all data in a dashboard for QA review and approvals
- alerts analysts should captured-data fall out of specifications at the method step level
- alerts reviewers with “compliance flags” on dashboard allowing approvals at-a-glance
- forwards the reviewed and approved data directly to reports, CofA’s, LIMS or ERP fields
- catalogs raw data sources for later viewing by management, auditors or regulatory personnel

In the Thin LIMS project the only configuration work that is needed is the transaction file-based communication (in and out) between the commercial LIMS and the GMP Lab Execution System. This configuration typically takes a few weeks to complete and validate.

At the IMACS conference, many multi-national pharmaceutical companies outlined their “Thin LIMS” architecture in a three tiered system — ERP, Thin LIMS, and LES as follows:



The significant deployment benefits that were consistently mentioned are:

- Reduction of the LIMS portion resources by 50% vs. traditional Thick LIMS staffing.
- Deployment of the Lab Execution Layer can be completed independent of the LIMS functions allowing lab benefits to occur in only a few months.
- There are NO custom coding requirements for laboratory task functions speeding up deployment timelines by 50%.
- All instruments and lab devices are fully integrated vs. only a few via the Thick LIMS process.

Case #3

A large international pharmaceutical company outlined their experiences with the new Thin LIMS strategy. The deployment is global for all their manufacturing plants. Within one and a half years, the system is deployed and operational in 7 sites (with dozens more to follow). All analytical instruments and the CDS is coupled to the lab execution system, data is electronically reviewed at the lab and QA levels and, with one “forward” button, the relevant QC data is parsed to the appropriate fields in the chosen LIMS.

A key IT challenge was eliminated with this architecture. This company deployed the LIMS as an enterprise solution at 3 locations around the world with ties to the individual plants. By implementing the lab execution system at all plants, the raw lab data are maintained at the local level and only final approved data is transmitted to the LIMS. This strategy helps the bandwidth issues in dealing with remote sites sending data (particularly large file types such as HPLC/CDS data) across the pipe.

An estimate of savings by going “Thin” are reducing LIMS implementation technical resources by 50% and significantly shortening the “go live” dates at each plant.

Case #4

The mid-sized company in Case #2 abandoned the further deployment of the Thick LIMS implementation and implemented the off-the-shelf Lab Execution System. The title of their paper at the 2008 IMACS conference was:

“Deploying [a LES] at [Pharma company]: From Vision to Reality in Months.”

This title outlines the timeline (and cost) benefits when changing to a Thin LIMS strategy. Going live in months vs. many years tells the story.

THE CHROMATOGRAPHY DATA SYSTEM (CDS) ANALOGY

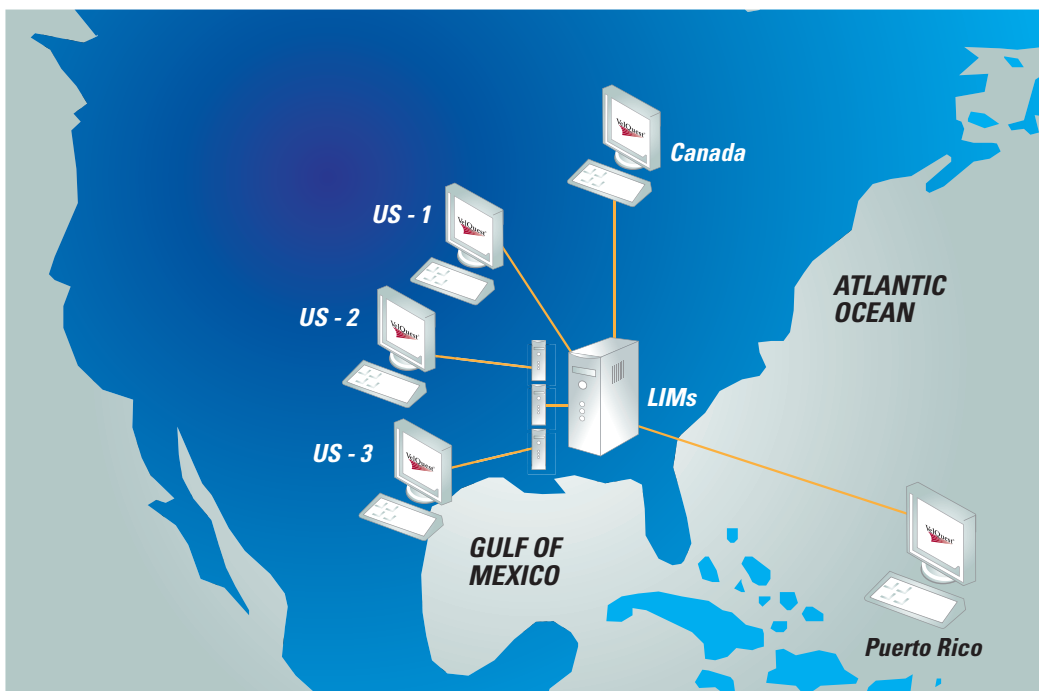
Why do many companies buy a separate CDS (Chromatography Data System) instead of building one with a traditional LIMS custom coding processes?

To effectively automate the QC lab workflows, ALL analytical instruments must be integrated into the platform. This automation allows direct to database capture of critical QC data and metadata for cGMP operations. How instrument data is captured and documented is very important in meeting cGMP compliance mandates. When looking at the entire lab, virtually 100% of lab and IT managers agree to purchase a CDS (Chromatography Data System) to manage all the HPLC analytical work. In the context of “instrument integration” and LIMS technology, a question that should be considered is “why is it that labs buy a CDS vs. custom code the workflow directly using the LIMS platform”? The answer is that HPLC has a large percentage of analytical and system suitability data and the LIMS custom integration would be too involved, costly and would take months, if not years, to complete and validate. The CDS is a good example of an “off the shelf” data platform. The same is true for ALL the other instruments in your lab. The Lab Execution System in a Thin LIMS deployment can be thought of as the CDS for all the other instruments (balances, pH meters, titrators, particle size analyzers, spectrophotometers etc.) and a method execution and documentation engine. Just like a CDS, the LES provides compliant data capture (direct to database), with all the metadata needed for cGMP work. The system includes a “compliance state” check before data is captured, thus ensuring regulatory oversight in an all electronic system. This functionality often is referred to as “Right First Time” thus eliminating rework loops in the lab.

ENTERPRISE-SCALE DEPLOYMENT ISSUES – REMOTE LIMS, LOCAL SMARTLAB

Another critical factor in deploying a LIMS project on a multi-site or multi-national basis is the bandwidth issue involved with moving all the supporting cGMP data across large areas. This is particularly the case with HPLC and instrument data files. Since the LIMS functional design strategy is to “manage” the final results for product release purposes, it is important to only populate the LIMS structure with final, approved QC lab data and not all the metadata (instrument IDs, Calibration Dates, Solutions used, Expiration Dates, ...). It is best to maintain the metadata and all source documentation at the local level and only send the final information to LIMS for higher order decision support purposes. This “tiered architecture” eliminates the bandwidth bottlenecks in attempting to use the LIMS technology for all data, metadata and documentation capture purposes. Keep the LIMS thin and deploy a few instances while using the off the shelf GMP LES for all local plant instrument & method data and document capture.

The following graphic depicts one company's multi-site structure:



LESSONS LEARNED FROM INDUSTRY RESEARCH — THE TOP 10 CHALLENGES IN LIMS DEPLOYMENTS

Over the last year, VelQuest's senior management interviewed companies that have experienced a LIMS deployment in cGMP operations. The top 10 challenges found are as follows:

- Typical initial cost is more than \$1M and average LIMS deployments continue beyond 3 years with deployment costs of \$1M/year (for a 20-50 person quality group).
- Workflow definition (results entry, rework loops etc.) and data migration have significant pressure to customize.
- Many LIMS stretch capabilities beyond what it was designed to do (i.e., bolting on functionality can actually hurt core functionality).
- cGMP metadata requirements on results cause LIMS deployment to customize result entry forms by adding reagent pedigree, expiration dates, standards, instrument calibration etc.
- Calculation requirements create complexity for "out-of-the-box" LIMS systems.
- Lab user interface experience is poor, causing customization.
- Validation requirements are significant efforts, further complicated with custom code.
- Instrument integration including: raw instrument data mapping to result entry is complex, customization of data tables and coding is complex, PC's are generally needed on every instrument and validation of these processes requires custom documentation and is long to execute.
- Reporting requirements begin with results and trends and then expand to track lab level details, causing significant customization.
- Validation and QA requirements grow exponentially when systems are not off-the-shelf.

In their Thick LIMS implementation, three IT leaders stated...

“when migrating an “off-the-shelf” LIMS from Results-centric to Test-centric, the project experienced a “chain reaction” in custom coding and validation workload!”

“...just the QA validation cost was 2 years and \$1.5M.”

“...it works to some degree, but I would never do it again”

A summary of the key Thick vs. Thin total cost of ownership success factors are as follows:

Critical Success Factors	THICK LIMS	THIN LIMS
Out of the box functionality	NO	YES
Build & Configuration Time	Very Long	Short
Documentation Requirements	Complex and Custom Created	Simple
Testing Requirements	Difficult	Simple
Validation Requirements	Difficult	Simple
QA Requirements	Long	Short
Training Requirements	Complex	Simple
Support Requirements	Large Team	Small Team
Upgrade Requirements	Very Difficult (custom code issue)	Simple

THE BUSINESS OF A CGMP IT INFORMATICS ARCHITECTURE

The Thin LIMS approach combines the core LIMS functions outlined above with a COTS Lab Execution System. The apparent incremental costs of the LES system are quickly paid for by the overall project economics. The resultant cGMP IT architecture will need 50% less resources to implement and will be completed in 50% of the time. In addition the LES layer improves lab productivity by 25% and reduces review and approval cycle times by 50-75% (ref: IMACS reporting companies). These factors impact on the lab to plant business dynamics by:

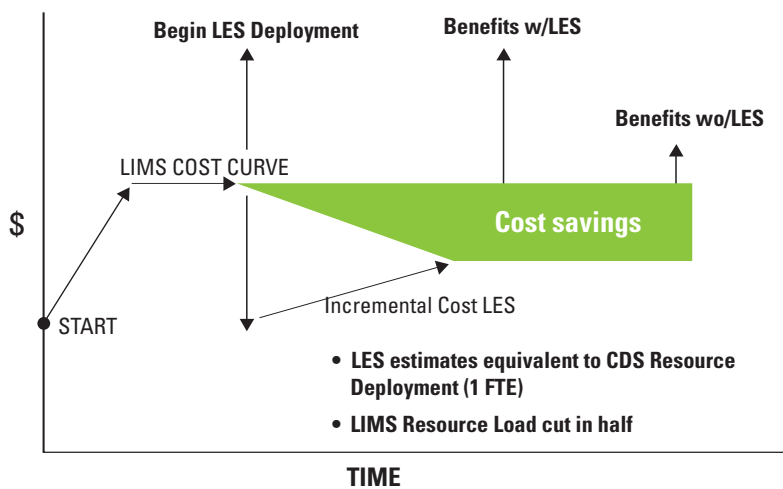
- reducing the overall headcount needed for QC and QA operations
- enhancing the cash conversion cycle on materials to product shipments to your customers (i.e., finished product is shipped “just in time”)
- overall production cycle time reductions vs. manual paper-based processes

The following figure outlines these issues (for a typical 20-40 person QC/QA operation):

	THICK LIMS	THIN LIMS
Average Resources to Deploy	12 FTEs	6 FTEs
Average # Yrs to significant benefit	5	2
Total investment to Significant Benefit	60 FTE Years	12 FTE Years
Total Cost — using \$100k per FTE	\$6,000,000	\$1,200,000

The overall total cost of ownership and time to benefit is significantly impacted by implementing a Thin-LIMS architecture. The following figure outlines a typical 5 year deployment scenario yielding major benefits in about 4-5 years for a traditional Thick-LIMS implementation. The additional cost of the Lab Execution System (LES) is offset by the cost reductions from the LIMS investment. The resultant benefits are in the reduction in time to going live as well as the additional 25-30% head-count reduction in QC/QA due to the reduced need to manually review every piece of data, metadata and calculations for samples from each lot. In addition, the 50-75% cycle time reductions in laboratory review and approval times will impact the production delivery cycles saving on quarantined materials and improving the financial cash conversion cycle for operations. These dynamics are outlined in the following figure:

Cost Savings with LES as part of a LIMS Project



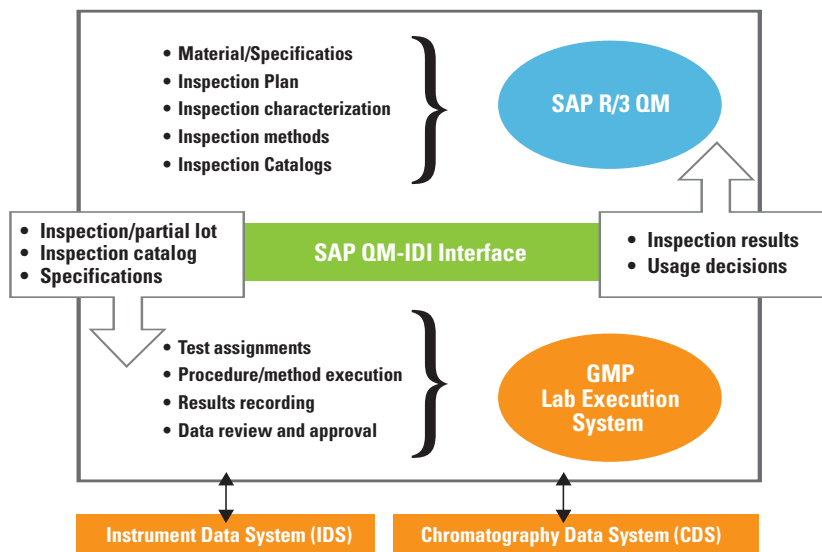
The initial LIMS cost/resource curve is steep and will continue at significant levels as customization at the lab level occurs. By deploying a GMP ELN at some point in the process, it actually reduces the LIMS cost/resource demands along with an incremental ELN cost/resource demand. The total LIMS project is then completed in months (due to the off-the-shelf GMP ELN) with the benefits realized quickly vs. a multi-year total cost of ownership drain when attempting to complete the LIMS project without the GMP ELN.

Large multi-national vs. medium to small company infrastructures — a No LIMS strategy

For many companies the absolute need for a traditional/commercial LIMS installation can be questioned. Often times the conventional approach of “I want a LIMS” is the issue vs. “I need a LIMS”. Again, the L in LIMS is for Laboratory. The operating costs for typical quality operations are predominately from human resources (analysts, reviewers and approvers). Automating their workflows provides significant tangible cost reductions, as presented by the IMACS reporting companies.

During IMACS, several medium size companies presented an IT infrastructure that was comprised of an ERP system (SAP) and the Lab Execution System platform. The key to this implementation is the use of SAP’s QM (Quality Module) combined with the LES’s ability to use a sample administration “method” to perform many of the traditional LIMS administration functions. This two-tiered architecture eliminates the initial cost and on-going maintenance requirements of the LIMS technology. This reduction of “platforms” and vendors is in-line with many IT strategic initiatives to reduce the number of systems in their lab IT landscape where possible.

Two-tiered cGMP Informatics Platform ERP and GMP Electronic Notebook, no LIMS



Determining the absolute need for a LIMS technology deployment is often dependent on the depth and breadth of the products, formulations and distribution needs of the plant. For some medium to small pharma companies the LIMS layer can be eliminated all together. For those needing the core LIMS functionality a “Thin LIMS” approach will prove to be the most cost effective and timely implementation.

CONCLUSION

Traditional LIMS deployment initiatives in cGMP operations are “Thick LIMS” implementations. The Thick LIMS is a result of the enormous amount of custom coding and the cGMP compliance requirements associated with any customization, in tying the information management system to lab operational tasks. Key to the issue is the compliance metadata for instruments, supplies and analysts that must be associated to the sample, lot and facility. Often the customization tasks become an on-going project vs. what was thought of as a “product” purchase on day one.

Today, many innovative pharma, generics and biotech companies are implementing a “Thin LIMS” strategy by coupling a CDS-like, off-the-shelf Lab Execution System (LES) to the core LIMS functions (sample administration, specifications, reporting and trending). This coupling will reduce the total number of LIMS resources needed by ½ and provide a configured platform that can “go live” in only a few months vs. the years it takes to custom code and validate using traditional LIMS technology.

This system architecture is currently implemented in pharmaceutical companies, generic companies and biotechnology companies as well as CRO’s on a global basis. The architecture minimizes the bandwidth requirements for enterprise scale LIMS deployments and provides full cGMP compliance documentation in an automated system.

It’s important to note that leading LIMS vendors are already deploying the thin LIMS strategy in combination with GMP electronic notebook systems globally at several of the top pharmaceutical companies.

Thick LIMS, Thin LIMS or No LIMS. For additional information on a LIMS Tool Kit to convert your Thick LIMS project to a Thin LIMS implementation contact VelQuest Corporation.

About VelQuest Corporation

VelQuest Corporation was founded in 1999 to address a critical requirement of the life science industry: *How to leverage scientific resources to meet compliance regulations while increasing the productivity of people, reduce operational costs, and move finished product off the shipping dock faster than ever before.*

We remain committed to this mission, with GxP data management our ONLY business. Our flagship product is the award-winning SmartLab GMP Electronic Notebook System.

The VelQuest SmartLab GMP Electronic Notebook System is an innovative software platform designed to provide the foundation for compliance-based activities in the life science markets. The core software embraces the ICH Q-10 initiatives, as well as the FDA's "cGMPs for the 21st Century: A Risk Based Approach", and "Quality by Design (QbD) initiatives, and supports the company's SmartLab™ Applications for a fully compliant electronic laboratory and SmartBatch™ manufacturing batch record system.

This patented technology eliminates compliance bottlenecks from paper-based processes in regulated development and quality operations. It captures all lab data at the source in real time, and seamlessly links procedures and SOPs with the data capture process. So not only does it reduce your compliance risk, it virtually eliminates tedious paperwork and dramatically simplifies reviews and audits.

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