From the ground up: LIMS design and implementation

With today's analytical laboratories generating seemingly endless flows of data, laboratory information management system (LIMS) has become indispensable to food and nutrition technologists

Throughout the supply chain, from ingredient suppliers to processors, the centre of action is located in the analytical testing laboratory. As part of a quality control testing programme, it is the first line of defence against the food-borne illness and contamination crises that make media headlines and erode consumer confidence. It is also the place where R&D experts verify what will – and will not – appear on their products' nutrition facts panels. All told, it is the central nervous system of any successful food or dietary supplement production operation.

As such, the analytical laboratory of today generates seemingly endless flows of data, both to support a company's programmes and processes and to shape its most important decisions. The challenge for food and nutrition technologists and industry decision makers becomes translating all that data into actionable intelligence – a task that has made laboratory information management systems (LIMS) indispensable. But just as the sheer mass of data that a 21st-century laboratory encounters presents an analytical challenge, so too does designing a LIMS infrastructure optimally suited to managing it.

Industry solutions

The utility of LIMS to the food or supplement laboratory is clear. The sophisticated capabilities of a LIMS can overcome the challenges the laboratory must face when dealing with the complex chemical composition of food samples. Whereas a pharmaceutical lab enjoys the luxury of focusing on a single active compound in a dosage form, food technologists deal with everything from canned spaghetti in tomato sauce to the filling in a jelly donut. The analytes of interest must be found from among the tens of thousands of other chemicals in the matrix – a daunting task given that most of these compounds are unknown and many may interfere with the analysis.

Consider the number of independent tests that a typical food testing programme might involve, such as quantifying protein via Kjeldahl analysis or Dumas combustion, or isolating free fatty acids using supercritical fluid extraction. A laboratory may conduct tests to distinguish between digestible carbohydrate and indigestible fibre. Quantifying a product's concentration of certain vitamins, minerals, and antioxidants – even the simple determination of its caloric content – may be the goal. Or a laboratory might need to measure the hardness of process water, look for heavy metal residues, or detect traces of pesticides and other contaminants. Microbial concerns ranging from *Salmonella* to *E. coli* also present themselves for investigation.

As each new development within the industry emerges – from stricter labelling regulations to a globalised supply chain to the potential for staff cutbacks in down economic times – LIMS programmes reinforce their value by bringing to the analytical lab the speed and accuracy that are the watchwords of the day.

Why are speed and accuracy so important? Because manufacturers and regulators face pressures that leave them little choice but to lean harder on the timelines they impose on labs. Gone are the days when turnaround time was calculated in months or weeks; today, what counts are days and hours. Imagine a scenario in which a shipment of milk powder awaits approval on the dock pending the quantification of melamine residues. With each tick of the clock, the supply chain creeps ever closer to paralysis.

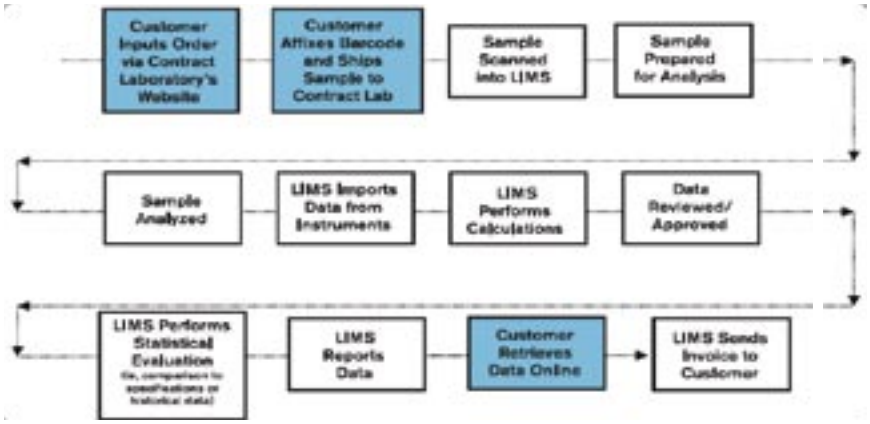
By using automation and accelerated throughput, today's LIMS captures and analyses data to meet the time and output demands imposed on them.

A smarter, speedier contract laboratory

At its most fundamental level, LIMS starts paying dividends at the moment of sample login. With a sophisticated LIMS, sample information is entered into LIMS before it arrives at the contract laboratory. Sample information includes everything from the client profile to special reporting requirements. As soon as the sample arrives, laboratory staff already has visibility to all of this information and can begin the sample analysis process.

When sample analysis begins, laboratory instruments used for detection – often a gas chromatograph (GC), high-performance liquid chromatograph (HPLC) or mass spectrometer (MS) – deliver readings into a data capture software system. The

Figure 1: Customer / contract laboratory interface of LIMS.



A responsive LIMS needs a degree of flexibility to react to changing regulatory requirements, as well. The industry has seen the importance of this flexibility recently, as concerns about melamine have changed the regulatory landscape.

data system captures the instrument raw data, calculates interim laboratory results, and delivers these results to LIMS. The LIMS then captures, records, and organises these test results. Finally, LIMS transforms raw data into finished reports.

The benefits go beyond simply automating and organising the process. LIMS relieves the tedium inherent to manual recordkeeping – freeing a sometimes limited workforce to perform the cognitive tasks it was trained to tackle and solving the complex problems that today's knowledge workers face. This ability of LIMS to maximise human resources pays back both in greater productivity and increased morale.

Equally important is the potential for error reduction that LIMS introduces. Even the most conscientious employee is not immune from making the occasional transcription error en route from reading an instrument display screen to logging a number in a notebook. By removing human fallibility from the equation and relegating data recording to the instrument architecture, LIMS bolsters the quality and accuracy of data – another benefit in today's high-stakes analytical and regulatory environments. By providing an audit trail of who recorded the data, and when, both regulatory compliance and data defensibility are extended to the data collection process.

Finally, LIMS moves us one step closer to the "paperless lab" that we have heard – or dreamt – of for years. Because LIMS gathers and organises data in one central location, laboratory personnel no longer need to maintain bulky files or a mounting collection of notebooks, chromatograms, printouts, and final reports. By storing critical information electronically, LIMS saves space, avoids loss and confusion, and archives data. The system brings transparency, traceability, and the capacity for automated total data reconstruction to the laboratory, client or regulator. When fielding requests from regulatory agencies and other concerned parties, anything less is unacceptable.

Paper trail of the future

Perhaps LIMS' highest-profile contributions to the paperless laboratory are electronic notebooks, electronic signatures, and barcodes. Regulatory agencies, including US Food and Drug Administration (FDA), have long prescribed extensive validation procedures that task laboratories with checking, reviewing, and effectively "locking down" records of their workflow structures, as well as their formulas, results, and communications. The introduction of electronic data collection and analysis technologies necessitated equally innovative methods for

authenticating them. Thus, in 1977 when FDA passed Part 11 as part of Title 21 of the Code of Federal Regulations (21CFR Part 11) – it outlined new requirements for electronic records and signatures and sparked a development boom in introducing these new functions to LIMS. A contract laboratory must ensure that all of their software programs, including LIMS, are 100% 21CFR Part 11-compliant.

Barcoding samples creates a "fingerprint" that identifies and characterises the sample, and uses the computer database to reliably track it through testing. In laboratories that shuffle among thousands of near-identical samples each day, any chance to eliminate potential confusion between Sample 123 and Sample XYZ is no small matter. Because barcodes can contain whatever data fields the laboratory requires – company of origin, key analytes, testing requirements – the information conveyed may expand or contract to meet changing data-tracking needs.

The principle value of barcodes and electronic signatures is that they give laboratories the ability to trace samples throughout their entire testing lifecycle and to assign accountability should a testing program encounter complications. Electronic signatures create a detailed, time-dated chain of custody to follow, enabling complete reconstruction of how a sample was treated. For example, an electronic signature would record when a sample left the freezer, who took it out, how long it remained out of storage, and when it was returned.

Anyone familiar with traditional laboratory recordkeeping can appreciate the advantages of the electronic notebook. Thanks to this technology, gone are the stained and smudged pages of paper predecessors, not to mention the illegible handwriting and lost notebooks. But as welcome as the convenience advantages of the electronic notebook may be, even more valuable is safeguard against inaccuracy and data loss by subtracting human error and storing quantitative readings in the database.

Although electronic notebooks assign the bulk of data recording responsibilities to the computer, they remain flexible enough to allow the analyst to note qualitative observations, like colour or textural changes. Properly configured LIMS allow analysts to do so using intuitive, handheld electronic devices that operate much like PDAs. Laboratory analysts make notations directly onto these e-notebooks with electronic pens and, rather than transcribe the information from the notebook into the computer, simply let wireless technology built into the notebook send the information directly to the database.

Tailor-made systems

By making laboratories smarter and speedier, LIMS amplifies their efficiencies exponentially. Beyond the progress that has already been made over the last three decades, the potential that future systems hold for creating even greater efficiencies promises the most excitement to those in the laboratory and in industry at large. New systems emerging on the horizon build upon their forerunners' benefits by merging leading-edge laboratory automation equipment – everything from highly sensitive robotic arms to advanced autosamplers and automated workstations – with web-based operability and enhancements to the precision numbers-crunching that earned LIMS their fame in the first place. That is exciting news to any food chemist, as the task of sorting through the tens of thousands of analytes in a typical large food ingredient study presents the kind of needle-in-a-haystack problem that only a next-gen LIMS can solve.

Given the size and scope of the data-analysis challenge, it should come as no surprise that designing a LIMS equal to the task is, in its own right, challenging. The linchpin to making any LIMS infrastructure truly effective lies in uniquely configuring the system to the data-processing needs and patterns of the

Table 1: Typical question to pose in LIMS design

• What is the test method reference?
• How much sample was weighed?
• What extraction method was used to obtain the sample?
• What type of detection system was used to measure the analyte of interest?
• What is the nature of the expected results?
• What units will those results carry?
• How many different tests does the sample go through?
• How many different samples are exposed to a particular test?
• Who will be privy to the results?
• How many sites within the laboratory or corporate network should have access to the results?

laboratory it serves. The level of data programming required to build a 21st-century LIMS should not be underestimated. Purchasing the most highly rated and advanced LIMS software off the shelf does not provide the optimisation advantages that make today's LIMS so revolutionary, without customising it to meet the laboratory's individual needs.

Of course, bringing an experienced programmer on board to create a custom-fit LIMS is one solution. The laboratory still needs to provide the programmer with a detailed roadmap of the workflow processes for which the LIMS configuration is responsible. That roadmap must take into account the differing processes and types of data that a laboratory generates, touching on every step in the sequence from the receipt of the sample to the release of the final reports for regulatory and internal review. For example, a supplement company QA/QC laboratory may have a predictable set of fixed tests to run on a fixed number of samples day in and out. By contrast, the typical food industry R&D laboratory might introduce more variability into its testing and analysis routine, with methods and samples matrices changing weekly depending on the current development project, analytes of interest, and the products in which those analytes appear. A large contract laboratory must be able to handle all of these testing variables within the scope of its LIMS. An effective LIMS configuration must reflect all of these differences.

Thus, in order to leave no detail behind, custom-configuration of LIMS requires that the programmer ask the right questions, defining the workflow variables and building them into the appropriate database fields.

It also pays to note that LIMS configuration must take into consideration departments and computer systems beyond the confines of the lab.

Multiple computer networks may operate different instruments and testing equipment in various locations throughout an organisation. Because the data in LIMS plays a role in accepting raw materials and releasing product for distribution, shipping and receiving needs to communicate with the system. Financial departments will have a part in determining the price of tests; human resources will track the performance of lab personnel; regulatory and production will need to know tests results and analyses; and even sales and marketing might want a place at the table. The participation of all these entities may mean that a system requires interoperability with a number of different databases and software platforms, and the most effective LIMS configuration will connect each one into seamless communication.

The existence of software platforms that communicate

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Table 2: Typical sample information needed to ensure prompt analysis

- Specifications
- Claims
- Customer profiles
- Requirements for TAT
- Final reports format
- Reporting units
- Report distribution
- Product specifications
- Fortification ranges
- Raw material information
- Detailed product description
- Invoicing requirements
- Information regarding regulatory compliance (DSHEA, etc.)
- Special analytical method requirements

this effectively is a relatively recent development, the result of a successful search for universal platforms by which the many nodes of a LIMS can speak a common language. Such interoperability has been a key theme in the evolution of LIMS over the past five to 10 years, and in 2002, the first completely *XML*-based LIMS was introduced to run on *Microsoft's .NET* platform. Yet while barriers to communication crumble by the day, tearing down those barriers entirely is still a challenge for enterprises attempting to build a LIMS network from scratch. Today's LIMS typically reside in relational databases, which makes compatibility with other software systems more straightforward. Since these types of communication are critical to the success of a LIMS, most of the software vendors have made their products more amenable to "outside" communication, and brand-specific barriers are found much less frequently.

Widening the communication network

With these capabilities in place, the barriers to information transfer between computer systems have significantly eroded. Whereas a client in the past had to wait for its contract laboratory to communicate test data and results via cumbersome faxes or even "snail mail", the network integration that characterises today's LIMS allows clients to access information without the direct involvement of the contract laboratory. Thanks to web-based access to LIMS, the client can go to a secured site and view test data and results in near real time, no matter where they are located or what their time zone. The relationship also benefits contract laboratories whose scientists can spend more time providing guidance on regulatory or technical testing requirements and not on administrative tasks.

The customer also holds the reins when it comes to setting up testing requirements. For example, a client may, via the secured site, schedule a series of tests for a set of samples. They can inform the laboratory about the nature of the samples, what analytes to look for, which tests to run, and the requested date for receipt of results. Then the client can send the samples to the lab via overnight delivery for placement in the testing queue the following morning. When the laboratory receives the samples, the client will get an automated notification of receipt, as well as a confirmation that the results and analysis will be complete on the specific date. In the meantime, the client can check the status of the samples' progress, which of the prescribed tests has run to completion, and whether any preliminary data are available – all via the website.


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How large can these communication networks grow? As yet, there is no limit to the number of location nodes that can be built into a system. If a client has multiple production sites, they have the option of installing a master database at a head office for centralised management, or they can spread that management among a diffuse community of operational locations.

Defining data delivery

Each client has their own unique needs for data. Defining parameters for reporting the data – assay by assay as it emerges, at the sample testing conclusion, at a project conclusion or according to some other schedule – allows clients to shape the LIMS reporting to fit their timing and format needs. What is more, with all the information stored securely on a relational database, the client can sort and collate that data via any number of criteria. Even when conducting dozens of tests at once on a single sample, a properly configured LIMS can select and provide information of a specified result.

For example, the customer can direct the system to view a sample's fibre content in comparison to some other nutritional attribute. It could compare that same sample's complete nutritional profile with the profiles of samples tested over the past 12 months. An intelligent LIMS knows how to create tables displaying these results by sample, by time of test, numerically, graphically, or in any other format desired. All the system need do is assign a unique identification tag to each test within the workflow context, and to locate the test within the appropriate data fields for the capture of information and calculation of results. Again, because the idea is to manage data rather than simply to churn it out, these capabilities for contextualising information help researchers turn data into knowledge.

Clients can also work with the contract laboratory to incorporate check-and-balance functions into the LIMS configuration. For instance, a test may be looking for the amount of protein in a sample of wheat gluten. By building windows of acceptability or product specifications – say, between 74.9% to 75.3% protein – into the detection system, the LIMS can send an automatic e-mail alert to the client with suggestions for corrective action if a sample falls outside the specifications. The system both initiates the communication and gets the ball rolling on remediation, while still letting the client choose the proper next steps. By providing the electronic equivalent of "shutting down the line", this capability has proven indispensable in QA/QC situations.

A responsive LIMS needs a degree of flexibility to react to changing regulatory requirements, as well. The industry has seen the importance of this flexibility recently, as concerns

about melamine have changed the regulatory landscape. While action limits had been set at 10 parts per million (ppm), FDA has recently ratcheted the acceptable amount down to 2.5 ppm. For manufacturers with business dealings abroad, the limit may be even lower, as it is in Thailand, where it now stands at 1 ppm. But the system needs to have this nimbleness built in from the start, which is a programming feat that requires a dedicated staff available to maintain the database.

Safe and secure

Regardless of the size of the network, a critical feature for its success is that it ensures security and confidentiality. When a client communicates with its contract laboratory via web-based channels, there must be no doubt that the information exchanged is for those eyes only. Usually a customer will access the LIMS data at the contract laboratory through a secure website. This web access will give them access to their data, and only their data, through a series of password-protected firewalls. In order to provide an effective web access the architecture of LIMS must be able to "isolate" secure files sorted by a defined customer access.

While it is desirable to keep access flexible and user friendly, the communication must remain 100% secure at all times. Modern relational databases have the ability to restrict this access if the system is programmed correctly. A contract laboratory with a proven track record in building and securing LIMS from the ground up can make sure that it is.

To build or not to build

Of course, in addition to bringing its custom-configured LIMS into operation, a food or supplement manufacturer must keep with its day-to-day responsibilities of production, marketing, packaging, regulation, human resources, and more. Add to these tasks the significant time and financial outlays involved in independently setting up a LIMS – estimates place the cost of implementing a fully integrated, "tailored" system at US$1 million to US$3 million and two to five years of work – and full LIMS design, implementation, maintenance may be a larger project than any enterprise cares to handle on its own.

Increasingly, companies are finding that they can achieve a better return on investment by working with contract laboratories whose testing and analysis experience gives them an edge in setting up highly complex LIMS networks for clients in a variety of industry segments facing any number of data analysis needs. What is more, because their laboratory and computer networks are well-established and their staff include dedicated software programmers, contract laboratories enjoy a head start in tackling the nuanced task of custom LIMS configuration. In essence, when the relationship is right, a contract laboratory can serve as a virtual offsite annex of its clients' analytical testing departments.

The client-contract laboratory relationship continues to improve with the introduction of wireless computing capabilities as well as with the entry of global-positioning satellite (GPS) technologies for geo-locating samples from the time of collection onward. The advent of electronic notebooks, paperless laboratories, relational databases, and web access to data has resulted in the creation of industry partners able to tackle the 21st-century challenges that 21st-century data provide. **FBA**

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Reference

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