Informatics in R&D

The roles for LIMS & ELN

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In an earlier article[1], we looked at the role laboratory information management systems (LIMS) played in manufacturing/production operations, as well as their relationship to other control/database systems. This article is going to shift the focus to the source of those manufactured/production operations: research and development.

Before we get into informatics, let's look at the working environment. Figure 1 shows the functions we need to consider. That model is based on the author's experience; however, it fits many applied research groups in different industries whose work is intended to lead to new/improved products. The names of the labs may change to include microbiology, toxicology, electronics, forensics, etc. but the functional behavior will be similar.

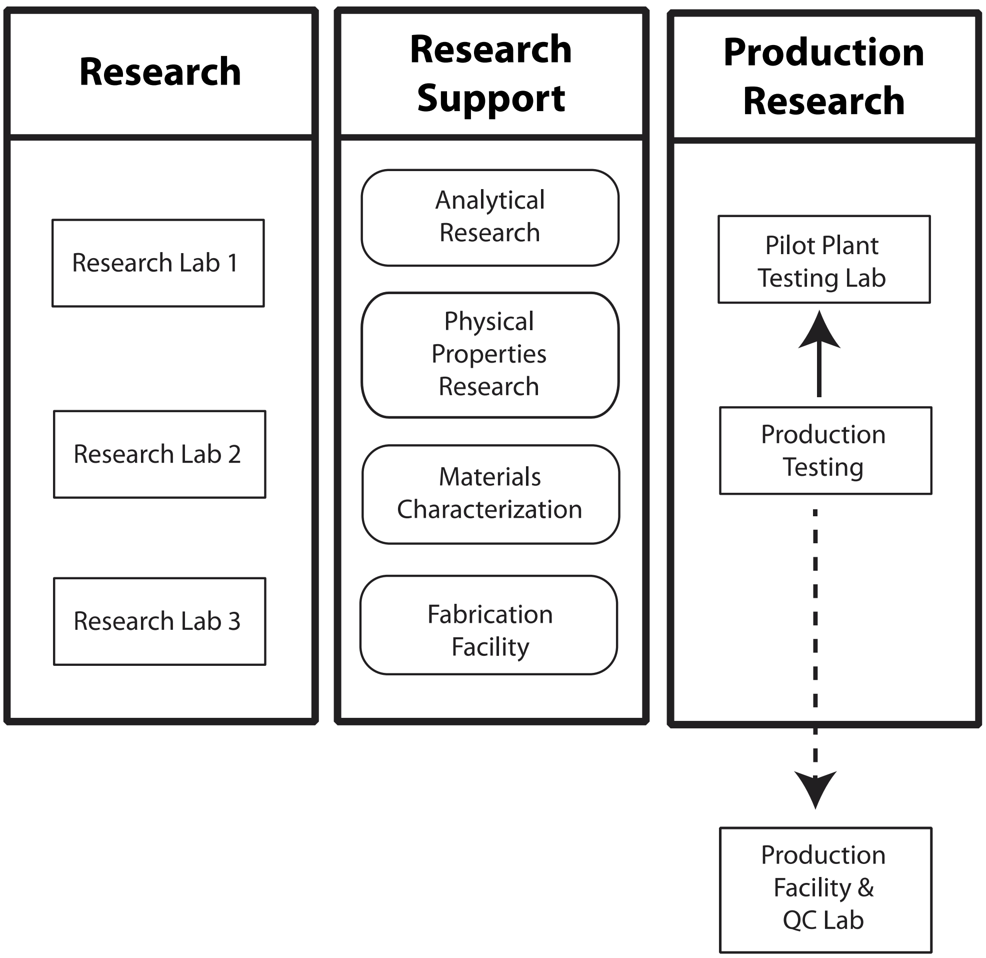

Figure 1 – An organizational structure of an R&D group

The labs I was working in supported R&D in polymers and pharmaceuticals – the overarching company had wide interests. The research labs (left column of Figure 1) were focused on those projects. The other facilities consisted of:

- Analytical research – this lab had four functions – routine chemical analysis in support of the research labs, new method development to support both research and production QC, non-routine analytical work to address special projects, and monitoring testing accuracy of the production QC labs (there were several production facilities making different products).

- Physical Properties Research – similar in function to the analytical lab but with an emphasis on measuring the physical properties of polymers instead of chemical analysis.
- Material Characterization – this group worked with research and special projects looking at the composition of polymers and their properties such as rheology, molecular weight distribution, and other characteristics.
- The fabrication facility processed experimental polymers into blends, films, and other components that could be further tested in the physical properties lab.

Once an experimental material reached a stage where it was ready for scale-up development, it entered the pilot plant where production processes were designed and tested to see if the material could be made in larger quantities and still retain its desirable properties. A dedicated testing lab supported the pilot plant to do raw materials, in-process, and post-production testing. If a product met its goals, it was moved to a production facility for larger-scale testing and eventually commercial production.

Intra-lab workflows

Let's look at each of these support lab groups more closely and examine how their workflows relate.

Analytical research

The workflows in this lab fall into two categories: routine testing (i.e., the service lab model) and research. In the routine testing portion, samples can come from the research labs, production facilities, and the pilot plant testing lab. The research work can come from salespeople (e.g., "we found this in a sample of a competitive product, what is it?", "our customer asked us to analyze this", etc.), customer support trying to solve customer issues, and researchers developing test methods to support research. The methods used for analysis can come from a variety of sources depending on the industry, e.g., ASTM[2], journals, vendors, and intraorganizational sources.

Physical properties research

The work here is predominately routine testing (e.g., the service lab model). Although samples can come from a variety of sources, as with analytical research, the test methods are standardized and come from groups like the ASTM and in some cases the customers of the company's products. Standardized methods are used so that results can be compared to testing by other organizations including potential customers. Labs like this will be found in a variety of industries including pharmaceuticals where the lab might be responsible for tablet uniformity testing among other things.

Materials characterization

As noted, this lab performed work that fell between the analytical and physical properties labs. While their test protocols were standardized within the labs, the nature of the materials they worked on involved individual considerations on how the analysis should be approached and the results interpreted. At one level they were a service lab and followed that behavior, and on another, the execution of testing required more than "just another sample" thinking.

Fabrication

The fabrication facility processed materials from a variety of sources: evaluation samples from both the production facility and pilot plant, competitive material evaluation, and the research labs. They also did parts fabrication for testing in the physical properties lab. Some physical tests required plastic materials formed into special shapes, take for example tensile bars for tensile strength testing. The sample sizes they worked with ranged from a few pounds to thousands of pounds (e.g., film production).

The pilot plant testing lab did evaluations on scaled-up processing materials. They had to be located within the pilot plant to do fast turn-around testing, including some on-demand work in addition to routine analysis. They also serviced process chromatographs for in-line testing. Their test procedures came from both the chemical and physical labs as they were responsible for a variety of tests on small samples, anything larger was sent to the analytical research labs. The pilot plant testing lab follows a service lab model.

On the service lab model and research in general

The service lab model noted a few times, is common in most industries. The details of sample types and testing will vary, but the operational behavior will be the same and will work like this:

- Samples are submitted for testing. In many labs, these are done on paper forms listing sample type, testing to be done, whom to bill, and a description of the sample and any special concerns or issues. In labs with a LIMS, this can be done online by lab personnel or the sample submitter.
- The work is logged in (with LIMS electronically, paper systems manually), and rush samples are brought to management's attention. Note: in the pilot plant test lab, everything is a rush as the next steps in the plant's work may depend upon the results.
- Analysts generate worklists and perform the analysis required, and results are recorded in the LIMS or in lab notebooks.
- The work is reviewed and approved for release and, in paper systems, recorded on the submission forms.
- Reports are sent to whoever submitted the work, either electronically or via the method the submitter requested.

Work from non-routine samples may be logged in under “special projects”, though it may create the need for additional testing.

There is no similar common model for research work aside from project descriptions, initial project outlines, etc. The nature of the work will change as the project progresses and more is learned. Recording results, observations, plans, etc. requires a flexible medium capable of maintaining notes, printouts, charts, and other forms of information.

The role of laboratory informatics

Lab informatics has several tiers of systems that can be applied to lab work to make it more effective and efficient.

- The top tier consists of electronic laboratory notebooks (ELNs) and (LIMS)[3]
- Supporting those are scientific data management systems (SDMS) and laboratory execution systems (LES)
- Below that are instrument data systems (IDS) which are a combination of instruments and computer systems. Common examples are chromatographic data systems (CDS) connected to one or more chromatographs, mass spectrometers, and almost any major instrument.
- At the lower level are devices like pH meters, balances, and other devices that have no databases associated with them and have to be programmed to be used with upper-tier systems. Their data output can be manually entered into a LIMS, ELN or LES, but in regulated labs, the input has to be verified by a second individual.

Our initial concern will be with the top-tier systems. The primary interaction between a service lab and someone requesting their services is shown in Figure 2.

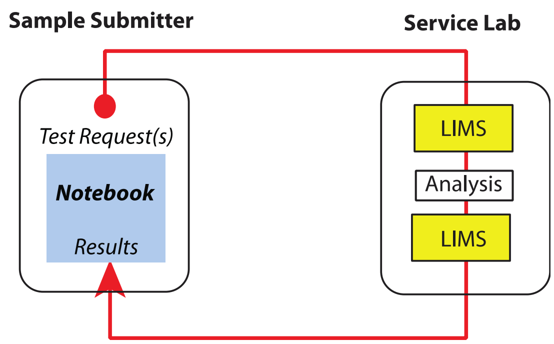

Figure 2 – Sample request/results flow

Samples are submitted by the research group or other groups, and the request proceeds through the system as described above. The split between the LIMS in Figure 2 is there to illustrate the separation between logging samples in, the analysis process, and using the LIMS as an administrative tool for completing the work request and returning results to the submitter.

Figure 2 shows the classical assignment of informatics products to labs; LIMS in service labs and notebooks, usually ELNs, to research labs. That assignment is an oversimplification, the systems have broader usage in both types of laboratory workflows.

In the research labs, it is possible that work will generate a large amount of testing that has to be done quickly so that the next steps in the experiments can be determined. The demand may be great enough that it would swamp the service labs and they wouldn't be able to provide the turn-around time needed for research. In these cases, a LIMS would be added to the research lab's range of informatics tools so that high-demand testing would be done within those labs, and other, less demanding testing would be submitted to the service labs. The research lab LIMS could be an entirely independent installation or work with the same core system as the service labs. The choice would depend on the locations of the labs, the need for instrument connections, how cooperative they are, and corporate politics.

The analytical research and materials characterization labs in Figure 1 could justify an ELN on the basis of research associated with method development work. In addition to providing a means of detailing the research needed to create a new procedure, the ELN would need access to a variety of databases and tools including chemical reaction modeling, molecular structure representation, published methods retrieval, etc., as well as any corporate research databases that could exist in a large organization.

The fabrication facility could use an ELN to record the progress of any non-routine work that was being done. Equipment operating conditions, problems encountered and solved, and the results of their processing would be noted. This could be coordinated with the pilot plant or product development group's work.

Table 1 summarizes the likely application of upper-tier informatics to the elements in Figure 1.

Facility	Expected Upper Tier Informatics	Additional Upper Tier Informatics
Research	ELN	LIMS
Analytical Research	LIMS	ELN
Physical Properties Research	LIMS	None, as there is usually no development work; if there is an ELN would be used
Materials Characterization	LIMS	ELN
Fabrication	Work order management system[4]	ELN
Pilot Plant Testing	LIMS	None, no development work.

Table 1: Upper-level tier informatics and their use in R&D

Now we'll begin moving down to the lower tiers of lab informatics. SDMS is designed to manage documents and files that don't neatly fit into ELNs or LIMS. It may be a matter of size or formatting. LIMS are looking for numeric or short alphanumeric entries in the database and not images, spectra, etc.; references to those items would be placed in the LIMS with pointers to an SDMS or possibly an IDS.

The primary purpose of an LES is to guide the analyst through each step of a procedure and along the way gather information about its execution including:

- Who the analyst is and their qualifications for doing the analysis;
- Certifications that all equipment used is calibrated, maintained, and suitable for use.
- Certification that all reagents used are current and that any standards used are recently shown to be within specifications for the procedure;
- Any measurements made during the course of the analysis (e.g., weighing of samples or materials, instrument measurements, etc.) whether they are manually entered (with verification) or programmed to be entered electronically;
- Any files generated during the procedure, their identification and where they are located; and
- Sign-off by the analysis that the work was completed.

The results of an LES executed procedure may result in a stand-alone file or be directly connected to a LIMS or ELN. The rigor involved in its use is intended for compliance with regulatory agencies' requirements and as a result, it's primarily used in labs that are under FDA, EPA, and ISO 9000 purview. An LES would not be expected in a pilot plant test lab or a lab conducting early-stage research work.

The last tier above the device level consists of one or more instruments coupled with computer systems. The instruments provide the measuring tool, and the computer controls the instrument and any attached equipment (e.g., an autosampler), collects and analyzes data, and then provides local storage. It communicates with a LIMS or ELN over a network, exchanging worklists, results, and any data files needed. Depending on the information handling demands of the instrument, the computer can also

support one or more devices. Note that single instrument-computer combinations represent an old but workable computing model, whereas modern computers should be able to easily handle multiple instruments providing an option for a simpler network design and reducing maintenance costs.

Laboratory informatics plays a major role in R&D, to the point that it would be sensible to install the appropriate software as soon as the lab is put in place. The standard evolution of paper-based notebooks, followed by spreadsheets before implementing a LIMS or ELN is a false economy. The deferred expenses will be overwhelmed in the long term by the need to manage "the old way of doing things" alongside modern informatics. By starting with less capable system's you can frustrate productivity through difficulties with shared access, lost data, an inability to search your entire lab's data structures, and the eventual need to merge the old data into a new system which will need to include verification of data entries. However, modern informatics solutions provide a strong basis for building a lab's data systems architecture and demonstrating that lab operations are on a solid footing.

Footnotes

[1] https://www.lablynx.com/library/articles/lims-in-manufacturing/

[2] ASTM at one time stood for American Society for Testing Materials but has shortened the name as it's breadth of work increased. Its primary role was developing standardized testing procedures that were used industry-wide.

[3] For more information on the software noted see: https://www.lablynx.com/news-events/what-is-a-lims-eln/

[4] This would be a separate system possibly built around an enterprise resource planning package rather than lab informatics