Paperless Laboratories Are Designed Not Evolved

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Abstract

Paperless laboratories have been discussed for a number of years, however there is really no overall approach to the design and implementation of one. This article provides an overview to the design and implementation against an overall strategy.

1. Introduction

There is much talk about paperless laboratories, especially in the light of the FDA's 21 CFR 11 (Electronic Records and Electronic Signatures final rule) that allows the use of electronic signatures in place of handwritten ones. Modification of the enforcement discretion outlined in the FDA's Guidance for Industry on Part 11 Scope and Applicability has slowed the regulatory rationale for electronic ways of working. However, regardless of regulatory input, the main drivers for the paperless laboratory are speed of decision making, capacity increases, cost reduction and efficiency gains; preparation of regulatory dossiers. Regulatory compliance is becoming a side issue but nonetheless still important for those laboratories who want to work electronically.

1.1 Goals of the Paperless Laboratory

The main goals of a paperless laboratory are one or more of the following points:

- Reduction of paper work: Acquiring and manipulating data electronically is quicker and faster than using paper based processes.
- Increasing efficiency: Having data available electronically means that it can be shared between many people quickly and rapidly. Data and information can be delivered rapidly to those needing it and decisions can be made faster than on paper.
- Speeding throughput of samples: Sample analysis can be speeded up using electronic data acquisition and manipulation: work can be completed faster and goods released to market earlier or information used as part of a dossier preparation and submission.
- Automating regulatory compliance: Using systems that are technically compliant with 21 CFR 11 requirements e.g. ability to detect altered records and audit trail, the work can have the same if not better level of compliance but it is generated automatically not on paper.
- Reducing cost: Doing the same work with fewer resources or if capacity increases are required by an organization; doing more work with the same resources.

There may be other reasons for implementing a paperless laboratory. The promise of the Process Analytical Technology (PAT) will change analytical laboratories: taking the laboratory to the process rather than the sample to the laboratory. However, there will still need to be conventional analytical laboratories for the overwhelming number of current products that are tested before release. The expectation of healthcare providers of lowered costs due to PAT will take time to deliver but pressures to reduce the cost of manufactured products is already underway.

1.2 Business and Regulatory Drivers

The drivers for the paperless laboratory are two-fold: regulatory and business. From the regulatory perspective, we have:

- 21 CFR 11: The original request from the pharmaceutical industry was for a regulation to allow the use of electronic signatures to take advantage of technology. This regulation gives the legal basis for the use of electronic signatures but the issue is that the underlying process is still paper based.
- Electronic submissions (NDA. ANDA, IND plus also regulatory submission in the future of annual product reviews etc). To avoid Rockville MD disappearing towards the center of the earth under the weight of paper, electronic sumisssions are becoming mandatory.

With the publication of the Part 11 Scope and Applicability Guidance by the FDA, the regulatory pressure of 21 CFR 11 has abated somewhat. However, the business drivers for working electronic have if anything increased. The pressures are:

- Faster time to market with both R&D (faster dossier preparations and product licensing) and manufacturing (faster product release)
- Cost reduction: reducing time to release
- Efficiency and effectiveness of the analytical laboratory
- Speed of decision making

This needs to be delivered by effective and efficient data repositories, plus effective integration and data transfer between applications that constitute the paperless laboratory for an individual organization.

1.3 Reaching for Electronic Nirvana

However enticing that the prospect of an electronic nirvana appears; some of the main questions for consideration are:

- Can we use our existing paper based process electronically?
- How does a laboratory actually become paperless?
- Do we have the understanding necessary to design an electronic laboratory?
- Can we work electronically?

We will explore these themes in this article.

1.4 Can We Use Our Existing Paper Based Process?

The simple answer to this question is a resounding NO. I will explain this in more detail. The first stage in considering the paperless laboratory is to look at the basic processes and computerized systems: how they currently operate and how they integrate together. A laboratory may have many computerized systems such as chromatography data systems and data systems associated with the main analytical techniques such as MS, UV, NIR etc.

As such it can appear on the surface to be very effective but in practice these are islands of automation in an ocean of paper. The main way that data are transferred from system to system is via manual input using paper as the transport medium. Furthermore, the process will have evolved over time and may have additional tasks that do not add any value to the laboratory output and it becomes very slow and inefficient.

Figure 1. Cross functional process map of laboratory and IT systems

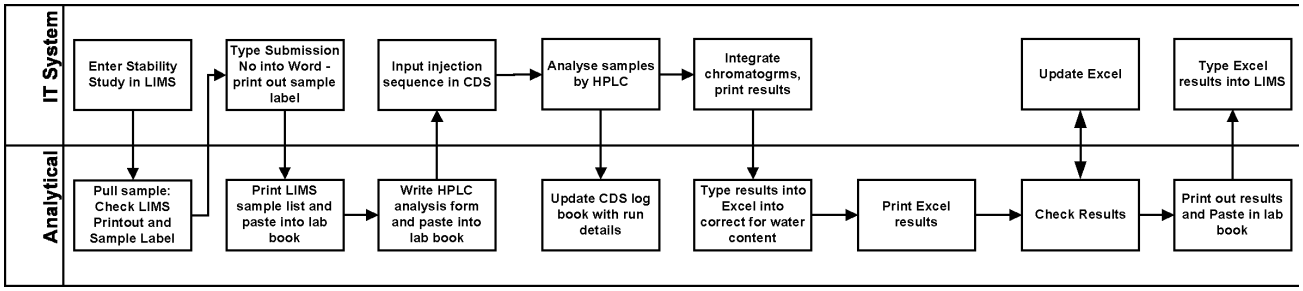
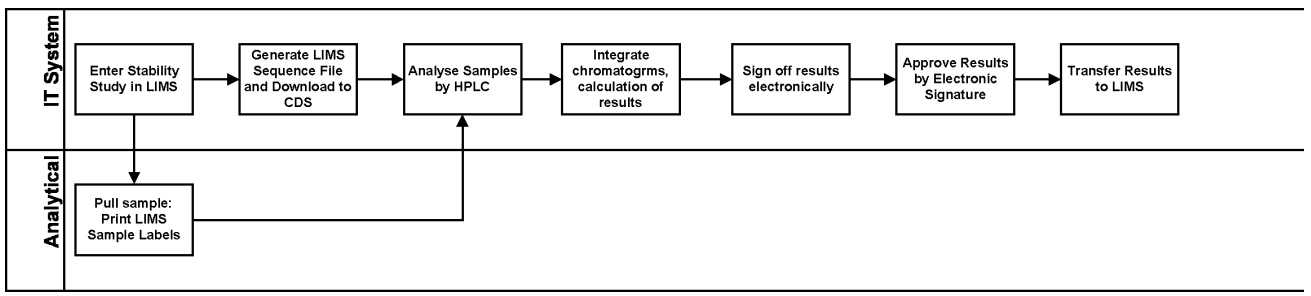


Figure 2. Cross functional process map improved electronic ways of working



For example, Figure 1 shows a cross-functional process map of the laboratory work and the IT systems used in part of the process. This is simply a way of process mapping workflows in an organization. The laboratory has a LIMS and a chromatography data system, but the whole process is manually based and there are multiple transcription error checks for all the manually entered data.

In essence, the existing systems are islands of automation in an ocean of paper and you cannot automate a mess.

1.5 The Way Forward

You need to map your current process and redesign and optimize your laboratory process to use IT systems effectively and efficiently to ensure that they deliver benefit.

Therefore, from the As-Is process maps, understand what you do and why you do it. In many instances it will be due to one or more of the following:

- Custom & practice (we have always worked this way)
- Evolution over time (we have had new projects or new tasks to do)
- Extensive quality control checks (FDA did not like our previous way of working)

In essence you will be looking at a paper driven process; unlike computer systems, this has infinite flexibility – if you need a few process new forms can be developed very rapidly and cheaply. However, the operating cost is very high.

The main aim is to understand where there are bottlenecks and issues in the process. Analyze and find the root causes of these bottlenecks as they will help you to challenge and improve the process. When the current process is redesigned and optimized, the aim must be to have as far as it is practicable:

- Electronic ways of working
- Effective hand-offs and transfers

This will enable a laboratory to get the process right. Figure 2 shows the improved cross-functional process flow. The key message is to ensure that once data are acquired they are not printed out or transcribed again but transferred electronically between systems.

Therefore, look at your basic laboratory process and design the electronic ways of working: see what changes could be made to your ways of working to remove inefficient tasks and improve the speed. Knowledge and interpretation of the GLP or GMP regulations that the laboratory works to is also very important: knowing which records need to be signed and when. However, trying to work electronically requires that any application used is technically compliant with 21 CFR 11.

Figure 3. Current high-level process for calculating chromatographic results in the LIMS

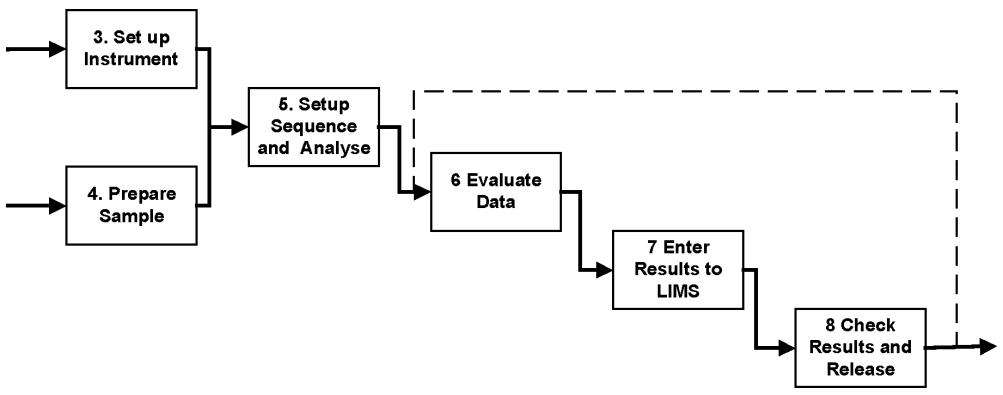
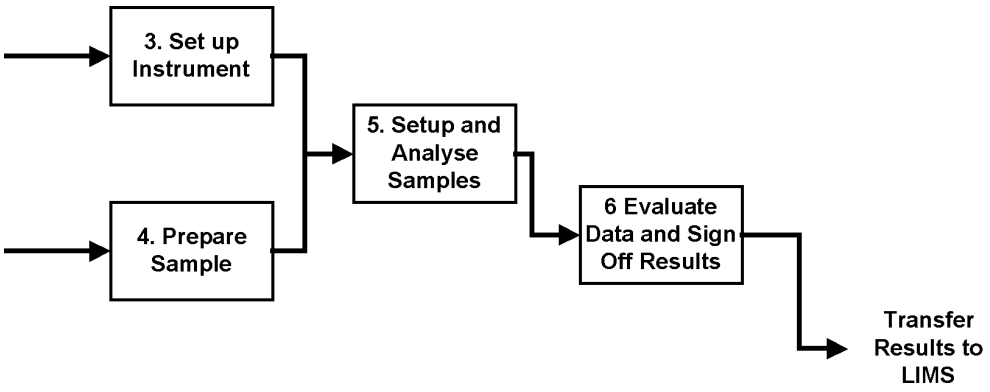


Figure 4. New process for calculating chromatographic results in the CDS



2. Overall Strategy and Pieces of the Jig-Saw

2.1 Paperless Laboratory Strategy

In designing a paperless laboratory it is important to realize that this will not happen overnight and will take several years to implement a fully paperless laboratory. Therefore it is important to have an overall automation strategy for the laboratory that is aligned with the overall business objectives of the organization. This strategy will need to be reviewed and revised on a regular basis for a number of reasons:

- Checking the alignment with the organization's business objectives
- Implementation of individual systems and their integration with the current ones
- Introduction of new technologies and systems that may impact the overall direction of the laboratory strategy

2.2 Individual Systems for Laboratory Automation

Within the overall scope of the strategy there will be a number of individual applications that will be implemented and integrated to the paperless operation. There are LIMS, CDS and other instrument data systems, electronic laboratory notebooks, scientific data management systems and experimental design applications.

The approach that should be taken for the overall strategy must be:

- Each application must be self-justified
- Automates the underlying analytical process efficiently
- Interface with existing systems to leverage bigger business benefits

However, implementing steps towards the paperless laboratory require the active involvement and co-operation of the analytical scientists, quality assurance and laboratory management. A paperless laboratory requires radical changes in working practices not only within the laboratory but also outside of it - this requires communication, effective management support and effective change management.

3. Designing Paperless Operations

To illustrate the principles we have discussed in the previous sections, here is an example of moving from paper-based operation to an electronic way of working.

3.1 Electronic Signatures in a Chromatography Data System

3.1.1 High Level Process and Its Improvement

The following examples are taken from a chromatography data system that is being implemented with electronic signatures. Figure 3 shows the current high-level process; here calculations of the system suitability test (SST) results and the calculation of the chromatographic results are performed in the LIMS after manual transfer of the peak area data from the CDS. Note this work is done post analytical run; if there are any issues with the results, then there is the need to go back to the CDS and chromatograph to investigate and when resolved rerun the samples. This is slow and inefficient.

In the redesigned process, shown in Figure 4, the CDS system has been set up to automatically calculate the SST results immediately after the individual SST injection has finished. The results from all SST injections are averaged immediately once the last injection has finished to see if the chromatograph is suitable for analysis. The system will continue if the result meets predefined criteria; however, if the SST fails, the samples are not committed for analysis. This means that valuable sample is not lost if the chromatographic system is not fit for purpose and also the issue preventing analysis can be resolved quicker than with the old process.

Figure 5. Existing paper based process for signing and approving chromatographic results

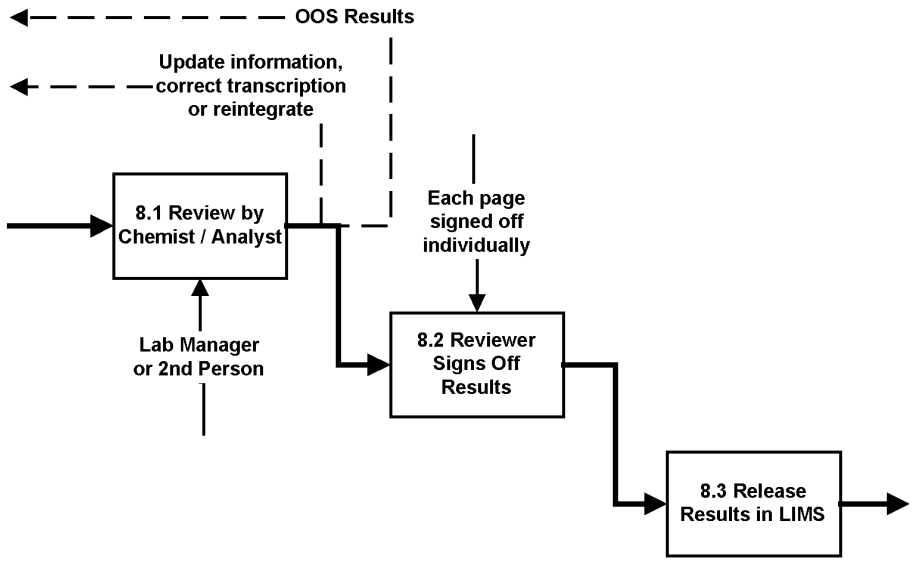
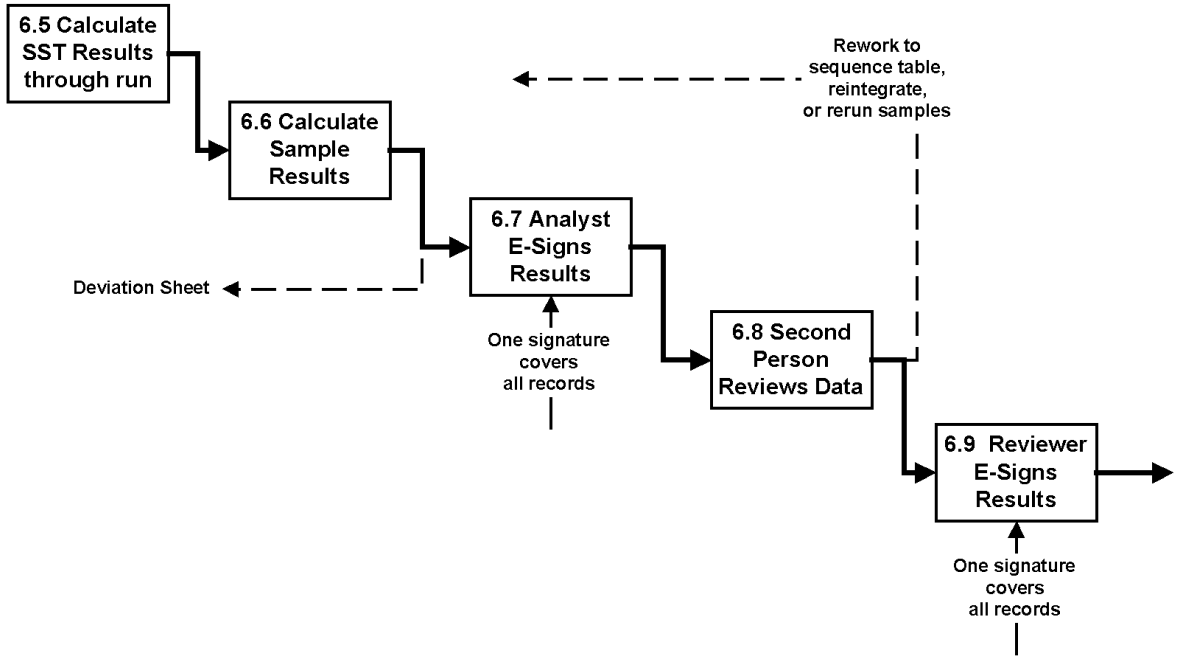


Figure 6. Improved electronic process for signing results in the CDS



3.1.2 Signing and Approving Records

When looking in more detail at the review and approval of results in the existing process (Figure 5), the chromatographer and the supervisor sign off results manually: each page is signed and dated by both individuals. This is a very slow, laborious and tedious process.

In contrast, the redesigned process (Figure 6) uses electronic signatures and the ability of the data system to highlight potential issues for the analyst and the supervisor to investigate before approval and release of the results. For example, if there has been manual integration of a sample, the database view-filters highlight the fact in the review screens and this enables a user to focus on a specific event or events. Similarly, setting the view filters up to highlight manual integration means that the placement of baselines in those chromatograms can be assessed and reviewed more easily than on paper.

Signing results electronically is streamlined over the existing process. Instead of signing every paper page, a report is generated electronically and signed by the analyst who did the work and then by the supervisor who reviewed the work. As per the GMP requirements under §211.194, only two signatures are required for these results. Following electronic approval, the results are transferred to the LIMS electronically.

The ways of working with the CDS have been transformed from a paper-based to an electronic process with tangible time and cost savings. The promise of the paperless laboratory is there to be exploited for those who plan and implement carefully.

4. Can We Work Electronically?

There are the applications available to enable the paperless laboratory; the main issue is the human one: can we work electronically? In principle, the answer is yes, but it needs to be managed carefully. Change management is the critical component that will take us from the paper domain to an electronic one. The issues are summarized as:

- We are used to working with paper; it is a known and tangible medium that has been used for 2000 years.
- We are moving to an intangible magnetic and optical medium that has been widely available for 30 years at best.
- The way to sell this to the users and overcome resistance and inertial is to design the system to eliminate the boring and repetitive jobs such as transcription error checking and allow analysts to focus on value added scientific activities.
- However electronic workflows for laboratory systems are in their infancy (notification of work pending etc.) and need to be enhanced to entice users.
- The role of senior management and management in this process is key; without their support and encouragement over the long-term, then it is not worth considering the project.

Dr. McDowall is a consultant specializing amongst others, with computerized system validation and electronic records and electronic signatures. Dr. McDowall has published many articles on these and other subjects. He received his undergraduate degree in Biochemistry from Newcastle University and received his Ph.D. in Toxicology from London Medical College. Author correspondence should be addressed to: R_D_McDowall@compuserve.com