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Pharma 4.0 and the Digital Regulated Laboratory

Part 3: Quick Wins and Implementing Projects

- Senior Management/ Organization Factors
- Cost Effective Validation
- Implementing Quick Wins
- Implementing Digitalization Projects

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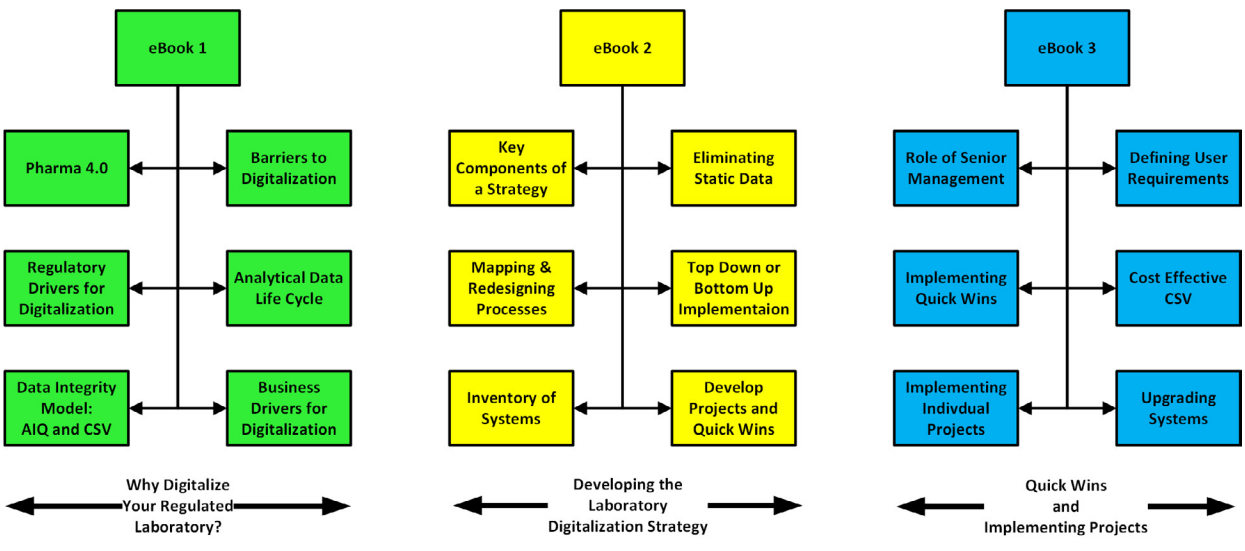
Introduction

Delivering Laboratory Digitalization

This is the last of three e-Books on planning and realizing a digitalized regulated laboratory. The series is aimed mainly at Good Manufacturing Practice (GMP), but the principles outlined here can also be used for laboratories working to Good Laboratory Practice (GLP). These three e-Books look at the journey from where your laboratory is now, through assessing systems and processes, planning how to automate your laboratory in stages and, finally, implementing quick wins and projects. The scope of the three eBooks is shown in FIGURE 1. The next sections provide an overview of the first two eBooks and, in more detail, the scope and contents of this eBook.

FIGURE 1: Overview of the contents of the three Laboratory Automation eBooks.



Introduction

eBook 1: Setting the Scene for Digitalization
The first eBook considered the current regulatory background, including why it is important to keep current with advances in technology, understanding the costs of compliance and non-compliance as well as some key FDA regulatory citations. Then, it discussed how critical Analytical Instrument Qualification (AIQ) and Computerized System Validation (CSV) were for ensuring both regulatory compliance and data integrity. However, the approach taken must be focused and risk based with a scientifically sound justification. Some of the barriers to digitalization were discussed, such as spreadsheets, hybrid systems, ultra conservative nature of the pharmaceutical industry and static data. This led into a discussion on a flexible analytical data life cycle and the elimination of static data. Finally, the business drivers for digitalization and the need for a strategy for the whole laboratory was recognized as essential for management support and resourcing.

eBook 2: Digital Laboratory Automation Strategy and Process Mapping
In the second eBook, the central question posed was: Where are you now and where do you want to be? The eBook started with a description of the "hidden factory," which hides in plain sight in most laboratories with paper printouts. This factory needs to be demolished and the paper printouts eliminated.

Mapping a laboratory's current or "***As Is***" processes is a crucial first step to digitalization. This identifies where the process bottlenecks and where problems are in each process. In addition, we need an inventory of current computerized systems, with information on how they are used now, what, if any, are their unused capabilities and if they can be used to further automate a process. It is likely that some systems will not be capable of automating the new ways of working and need to be replaced. The three rules of laboratory automation to digitalize a laboratory for more efficient and effective electronic working were described and demonstrated in the "***To Be***" process.

This requires resources, both human and monetary, to be available. Hence, the role of Senior Management is key to supporting the approach. A laboratory automation strategy that outlines projects with timescales and resources (with contingency for both) should be developed and is essential to achieve the digitalization strategy for a laboratory.

eBook 3: Quick Wins and Implementing Projects
This, the final eBook in the series, discusses turning a laboratory automation strategy that consists of digitalization projects and quick wins into business benefit, plus the demolition of the hidden factory described in eBook 2.

Introduction

First, we discuss the role of Senior and Line Management in ensuring the success of the digitalization strategy. Coupled with this is the need to change the organizational structure of the laboratory and prepare staff for different roles to match the new ways of working. This is a journey and not an event, and it must be handled sensitively.

Regulated laboratories must qualify and validate the analytical instruments and computerized systems prior to use and maintain the status throughout operational lives. Therefore, cost-effective approaches to these two related topics and a focused and risk-based approach is essential.

Leveraging the software development processes to reduce laboratory validation efforts is critical to ensuring rapid validation of systems, and supplier assessment plays a crucial role. Validation is a critical requirement in a regulated laboratory. But too often, companies take a conservative approach that delays a project. We need to leverage a supplier's software development, manage risk and apply sound science to focus scarce resources to where they are needed most.

Quick wins are small-scale improvements that can be implemented relatively quickly and inexpensively with some business benefits. These should be started first, as they give credibility and visibility to the overall automation strategy. It is crucial that Senior Management encourage the strategy from the first quick win implementation onwards.

Digitalization projects are larger, requiring more time and resource to implement but with the potential to return bigger business benefits. The first digitalization project is critical to the success of the laboratory and credibility of the strategy. This requires not only project risk, but regulatory and implementation risk as well, to be minimized to ensure success. Simpler projects with no custom software development are candidates to ensure success.

As the strategy progresses new technologies may emerge, requiring a revision of the overall strategy after implementation of a major system or every 12 to 18 months. This is normal and should be expected.

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Role of Senior Management and Organization Factors

In this chapter, we consider the critical role of Senior Management in supporting the laboratory digitalization strategy through personnel resourcing as well as informal means of supporting change in the organization. Digitalization not only impacts laboratory operations, but also the functional group(s) (e.g., process development or production) that provide the samples for analysis and use the information generated by the laboratory. This requires changes in the way the regulated laboratory is run as well as its interface with sample providers and information users.

Senior Management Support

In eBook 2, the finance for the overall digitalization strategy was agreed. Here, we focus on the proactive role of Senior Management in supporting and promoting the various initiatives and projects involved. This is the critical success factor in the

digitalization of a laboratory. As stated previously, this is a journey and not an event. You will need senior management approval initially and proactively throughout the program.

Initial support from Senior Management comes in various forms:

- **Acknowledgement** that the laboratory needs to improve and assurance that it remains *current* (as discussed in eBook 1) when looking at the cost of compliance versus the cost of non-compliance.
- **Support** of process mapping and redesign work by allowing it to take place. This is a critical first step, as the "**As Is"** process inefficiencies and bottlenecks are visualized, and the benefits and speed of an improved "**To Be"** process are calculated. This should convince sceptical senior management to invest in the laboratory digitalization strategy; an alternative is to receive warning letters such as those that have impacted Stason Pharmaceuticals [1] and Tender Corporation [2], as analyzed in detail in a separate article [3].
- **Review** of internal and external quick wins, implementation projects and associated budgets, including cost estimates and resource requirements.
- **Communication and co-ordination** between the laboratory and departments supplying samples and using the analytical data.

The major proactive support required from Senior Management comes when the quick wins and implementation projects start:

- **Visible and public support of all projects**, including supporting each one with finances and resources.
- **Formal and informal communication and support** from Senior Management, Line Management, Laboratory Management, project team members, laboratory staff, QA and IT.
- **Listening to and acting on feedback** from projects.
- **Oversight of projects** through regular reports from project managers.

If Gemba walks are used by Senior Management to see how an organization is functioning, such as part of a data integrity program, a similar approach can be used to leverage discussions about digitalization projects. In addition, informal visits to areas impacted by an implementation project to gauge how analysts are impacting the system can be implemented.

Line Management Support

Cascading down an organization chart from Senior Management, we come to Middle Management and Line Management of the regulated laboratory and the departments that interface with it. If Senior Management are in favor of the laboratory digitalization strategy, this group of managers must be as well. This is important, because if one of these managers does not support

the strategy, for whatever reason, they can subvert the aims, resulting in wasted resources and failed projects by adversely influencing the staff that report to them.

Therefore, to ensure that middle and department management support the strategy, changes to their job descriptions and objectives must be made. Any performance-related payments or benefits must be based on successful implementation of digitalization projects.

Redesigned Processes Require Changed Roles

In eBook 2, we explained that when processes were redesigned in the past, there was increased capacity and many organizations would be tempted to downsize staff. I cautioned that this was unwise. The rationale will be discussed in this eBook. Redesign of processes and digitalization results in automation and the elimination of paper using informatics applications. These systems do not run themselves. They require administration to ensure they keep operating and meet the user's needs. Administration comes in two forms:

1. **IT administration**, involving application configuration and user account management. This is seen as avoiding conflicts of interest and unauthorized changes to the application, such as turning the audit trail off and back on again to make deletions.
2. **Laboratory administration**, where staff are used as first-line support for users and have the ability to configure the application (e.g., workflows, incorporated calculations, configured reports etc.).

It is critical that the second type of administration use laboratory rather than IT staff, as the former know the analytical processes and regulatory requirements better than the latter.

Before the digitalization project begins, plans must be made for how to support the various systems:

- Are there existing staff who could transition into a role of laboratory administrators?
  - A minimum of two administrators are required per system in case of absences.
- If a laboratory is large enough, should a Laboratory Support Group be established where all systems are administered?
- If a system is implemented across two or more sites, could a global support group be set up?
  - Recruit support staff from outside the laboratory or organization.

In managing this support, if a laboratory user is keen on a support role, then being on the project team or even being the project manager is one way to learn about the new application and forge relationships with IT and the supplier's staff. At the end of the

project, the individual transitions into the laboratory administration role.

If laboratory administration is not considered at the outset, a project may be delayed or fail.

Engaging the Users

User involvement is critical to success of any informatics project.

Although a digitalized laboratory process should have lower human input, computerized systems don't operate themselves. They need trained users. More specifically, they need trained *and* motivated users. As the old saying goes, "You can take a horse to water…." There is no point to having the best digitalized laboratory in the world if the users don't use it. Technology is only part of the solution. Winning and keeping the hearts and minds of users is equally important.

Although a digitalization project will be delivered by a project team (see Implementing Digitalization Projects, in this eBook), they must not work in a vacuum but involve the laboratory users to assess and comment on new ways of working as well as the look and feel of new working practices.

Communication is critical. Management can also help by supporting a project during meetings and via informal communication by walking about, talking and listing to the potential user base. Concerns raised by users is feedback to the project team.

Users and their involvement in the digitalization strategy and indivdual projects is critical. Users will be involved as subject matter experts in the following aspects of the program of work:

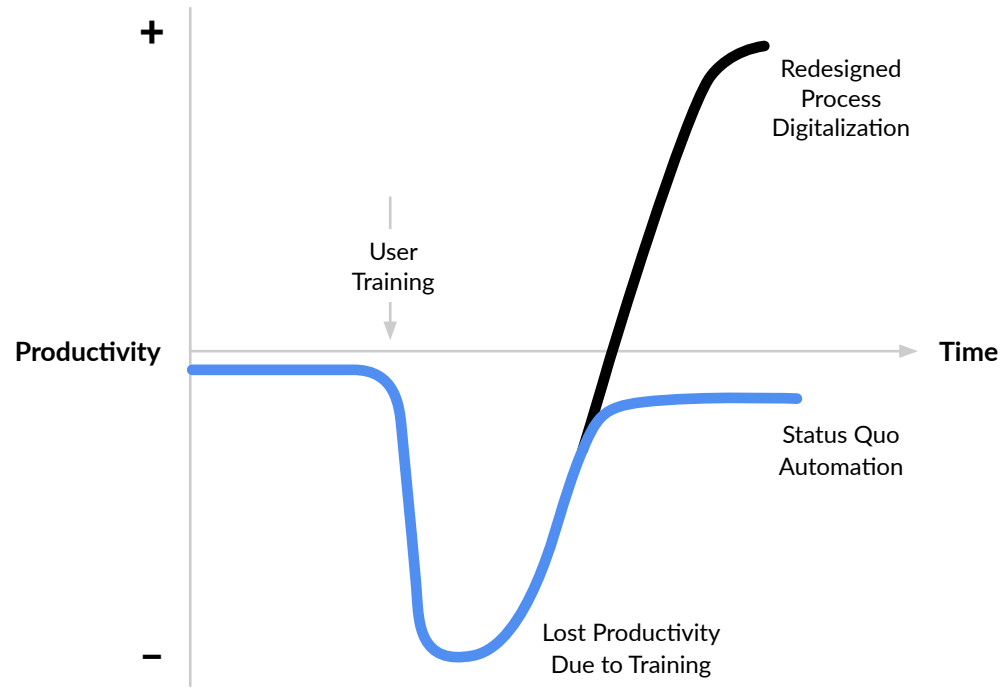
- Mapping and redesigning processes
- Specifying requirements
- Configuring and assessing prototypes
- Writing and executing validation testing
- Performing laboratory adminstrator functions for informatics applications

The key requirement for any system roll-out is adequate, effective training to use the system. Many systems will fail to deliver the business benefits at this point due to the lack of training. Why is this?

The Training Conundrum

Management wants to see a return on their investment in systems, so there is an impetus to train users rapidly and start using the new system immediately. However, for the reasons shown in FIGURE 1, this is wrong. On the left is the current productivity of the laboratory. If the rollout is a "Big Bang" approach, as shown in FIGURE 1, then productivity plummets because users cannot be working while training to use the system. After training concludes, there is a period of getting used to the system and putting learning into practice. Occasionally, users might read the training materials and applicable SOPs. Laboratory productivity is at rock bottom, then it slowly starts to rise. In this phase of the roll-out, management becomes agitated because they

FIGURE 1: Impact of training and new system design on laboratory productivity.



are receiving the, "Where are my results?" calls and e-mails.

Slowly, productivity starts to rise and we come to a fork in the diagram:

- If the laboratory has merely automated the status quo, you will end up with a computerized mess and lower productivity than when you started. You have a productivity gap, with a large hole in the company balance sheet.
- If laboratory processes have been redesigned and digitalized, productivity rises above the current productivity levels to generate the planned business benefits.

These two scenarios can reflect the organization maturity with informatics, as discussed latter in Implementing Digitalization Projects.

Managing the Productivity Gap

Of course, there is the productivity loss during training. How can this be managed? Little and often is the best way. Roll-out should be phased with small groups trained to use the system rather than a Big Bang approach. This reduces the productivity loss greatly and allows the laboratory administrators to provide help quickly while ironing out any teething problems with the system. It allows the credibility of the system

to be maintained. Then, a second group of users go through the roll-out. This way, the productivity gap is minimized and overall productivity rises earlier.

The question is, which users should be the first to be trained on the system? The answer to this is: know your user community and the different user types that there are.

A Gang and Continuum of Users

Within any laboratory there is the formal organization chart, but you also have to take into account the informal laboratory organization or, more appropriately, the Coffee Room Gang. Some of these users may not be particularly high in the organization, but through force of personality they can make or break a system by influencing other users. To counter this, management need to be proactive and reinforce the message that these systems will be used. Perhaps having performance objectives to use the new systems linked to pay would be an encouragement?

In addition, the laboratory has got to remember that there is a spectrum of users (FIGURE 2) within a laboratory. If we imagine a Gaussian distribution, there are four types of users shown in FIGURE 2.

- Hackers, shown on the far right of FIGURE 2. These are users who are extremely tech savvy and love working with computer systems, but they also know there are bugs in the software and will find them and show you. These users can be very involved in software evlaution and testing.
- Technophiles are the next group of users, to the left of the hackers. They like using applications but also understand the limitations, knowing that you're not always going to get it right. They can forgive minor software problems and can offer constructive options for improvement
- Next left in FIGURE 2 are the technophobes. Now we start to see some potential problem user groups. Technophobes don't like change, love paper and don't really like working with computer systems.
- Dinosaurs, on the far left, really don't want to work with computers, and you have to spend some time to train this group to work. Simple automated workflows that direct what the user should do next are essential.

This classification is important, as you can use the hackers and technophiles to evaluate new applications, check out prototypes and then write and execute validation test scripts. Members of these groups would also make good laboratory administrators. They will typically be the first users to operate a new system to show that it works successfully. In contrast, the technophobes and dinosaurs will be the last groups to use a new system. However, be careful not to ignore their views and inputs, as you may find many are fully paid-up members of the Coffee Room Gang.

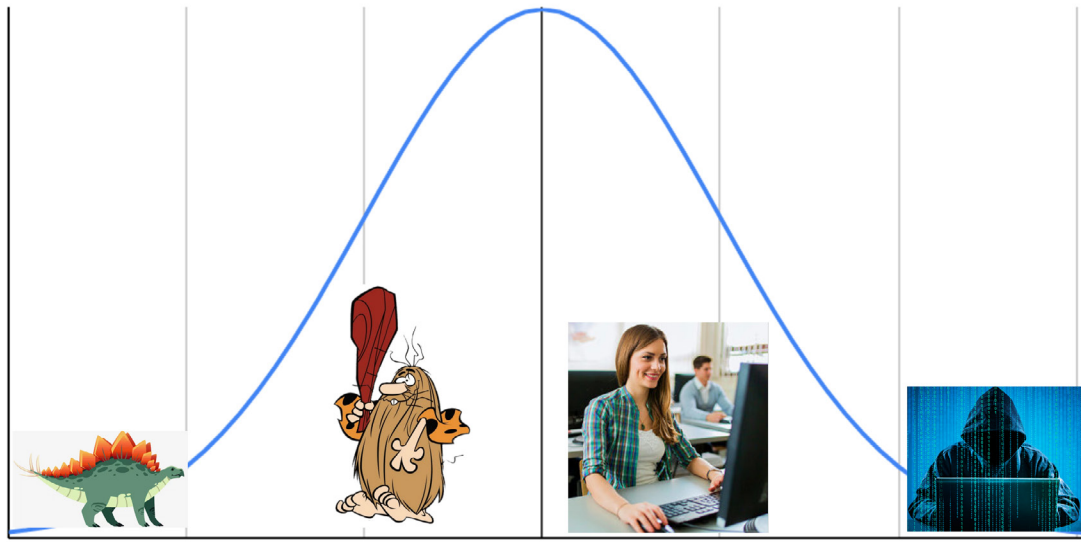
Targeted Training

One way to ensure successful roll-out of the system is to have a targeted training program so all user roles are trained appropriately. You will develop modules for laboratory administrators, reviewers, analysts, etc. However, you can go further. Using the user classification in FIGURE 2, you can identify the technically averse users in each user role and develop additional training and hands-on help for them, or allow more time for training.

Once the initial training is over, you should not stop training users. If the budget allows follow-up training, this should be offered either from the experienced laboratory administrators or from the software supplier about 3 months after roll-out. For technically averse users, the training would be refresher training to reinforce the initial training and to offer personalized training for specific areas for which these users have problems with the application. For more experienced users, advanced system training could be performed to allow them to use the system more efficiently.

An alternative approach could be to use training videos from the supplier, either in-house, if allowed, or accessible via their website. If time permits, training videos could be made in-house for heavily configured applications. The latter could be available as either on-demand or via a Learning Management System (LMS).

FIGURE 2: The continuum of users.



The overall aim is to ensure that the whole user base has sufficient skills to ensure there is a good return on the company's investment.

Summary

Senior Management and Line Management Support is essential to ensure that the overall laboratory digitalization strategy is successful. Management should encourage users to engage with the various projects for input into requirements and assessment of candidate systems. Automating a process will result in lower human involvement, but it is essential that the organization and laboratory create roles for staff to support the system (e.g., development of custom reports or input of calculations, etc.). Laboratory administrators are crucial to ensure success of each implemented system.

Training the whole user base is critical to ensure that the company investment in any system is successful. Training modules need to be developed for all user roles, but also bear in mind the continuum of users with different abilities. It is highly recommended that updates and advanced training should be available 3 to 6 months after roll-out of a system.

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Cost Effective Computerized System Validation

Before starting a discussion on cost effective Computerized System Validation (CSV), it is important to understand that it is a regulatory requirement to validate computerized systems. However, if approached right it is no more than good software implementation practice. Knowing the redesigned process and the business benefits will enable the validated system to deliver as we shall see now.

This chapter is not intended to be an all-encompassing guide to CSV, but suggests ways to improve and speed up the validation of any laboratory computerized system through documented and justified risk management.

CSV: Generating Business Efficiencies or a Document Boat Anchor?

CSV has a reputation for being a slow, non-added value activity with interest solely in generating great mountains of paper, thus giving "GMP" a new meaning. As somebody who has been involved in CSV for over 35 years and as an auditor for merely a quarter of a century, I would say it depends. Here are two CSV examples of the sublime to ridiculous approaches that I have seen:

- **Sublime**: Map and improve your processes from which your intended use requirements are written. Then, apply effective risk management and scientifically sound logic to leverage supplier software development and application configuration to focus testing. The documented rationale for why you don't test one function is just as important as why you should test another. This approach is an example of managing the cost of compliance versus the cost of non-compliance, as discussed in eBook 1.
- **Ridiculous**: An organization has a one-size-fits-all approach to CSV. You know you are wasting effort when the corporate CSV SOP states that you must write three specification documents (user requirements specification, functional specification and a design specification) but the intended use for a UV spectrometer is measuring absorbance of samples at one or two wavelengths, or a scan over a wavelength range. A detailed risk assessment adds fuel to the non-added value fire. This is followed by a demand for detailed test instructions accompanied by copious screen shots to demonstrate that each step of each test had been executed.

A one-size-fits-all validation approach lacks the flexibility to tailor each validation based on intended use and condemns any regulated laboratory to great mountains of paper. You can see why CSV gets a bad reputation: Instead of applying a healthy dose of common sense and analysis (the current buzz phrase is *critical thinking*) that then results in business benefit generated by the system, an inflexible approach coupled with the ultra-conservative nature of the pharmaceutical industry consigns CSV to the paper dustbin of last century.

You must have:

- Redesigned process for digitalization, as discussed in eBook 2
- Defined the intended use of the system in a URS and configuration specification
- Information regarding the impact of the records created by the system and on patient safety (e.g., product development or release or supporting records such as calibration, validation or training)
- An understanding of a supplier's development and testing activities

to leverage this into your validation efforts
- Defined, accurately, the application GAMP software category. The higher GAMP software category, the greater the risk that the system poses. So, no cheating by placing it in a lower category, please.

This will enable a laboratory to focus CSV efforts where they are needed most. Flexibility is the name of the game.

Impact of the FDA Computer Software Assurance (CSA) Guidance

In September 2022 we saw the release of the FDA's long awaited and overdue guidance for industry on Computer Software Assurance for Production and Quality System Software [1]. Far from being a new paradigm and a universal replacement for CSV, it turns out that when finalized this guidance will replace Section 6 in the existing 2002 FDA guidance on General Principles of Software Validation [2].

What CSA does bring to the table is some guidance and increased emphasis on risk-based approaches to CSV and testing depending on risk posed by the system and records generated. However, I maintain that CSA is not needed [3], as there is already sufficient guidance in place, such as GAMP 5 Second Edition [4]. But even with this, there are companies that are too risk averse to understand a risk-based approach.

Of the scripted and unscripted testing options in the guidance, only robust scripted testing [1] appears to be applicable to a pharmaceutical validation. There is a requirement in EU GMP clause 4.4 for traceability of requirements throughout the life cycle [5]. There is also the potential for inspectors and auditors to not accept CSA unscripted testing and continue to rely, instead, on printouts and screen shots.

However, the best part of the CSA guidance is:

> *As a least burdensome method, FDA recommends the use of electronic records, such as system logs, audit trails, and other data generated by the software, as opposed to paper documentation and screenshots, in establishing the record associated with the assurance activities* [1].

This is using the system to self-document user acceptance testing and has been in GAMP 5 since 2008 [6]. Why do more?

Lifecycles for Different GAMP Software Categories

Cost effective CSV requires an appropriate life cycle model. Since 2008, GAMP 5 has had flexible system life cycle models for different classes of software which has continued into GAMP 5 Second edition [4, 6].

To recap, the GAMP software categories for applications are:

- **Category 3**: Commercially available non-configured products. The business process automated by the software cannot be changed, as the application is only able to perform tasks it was designed for. A typical example would be a spectrophotometer that is only able to measure absorbances at a single wavelength or scan over a user-defined range.
- **Category 4**: Commercially available configurable products. Here, the application can be configured using a variety of means, such as switches to turn a function on or off or a graphical workflow builder. To take a simple example using the spectrophotometer above, if the application had electronic signature capability a laboratory could make the decision to use the system as either a hybrid or an electronic system.
- **Category 4 with Category 5 modules**: Commercially available configurable products with the ability to link standard functions together into a macro to perform repetitive tasks. This category also includes an application with a supplier language that is used to "configure" new functionality (GAMP 5 notes that this should be treated as Category 5 [4]) or a computer language to extend functions of the application.
- **Category 5**: Custom applications. This is the highest risk software. Don't even think about this option. Your organization makes pharmaceutical products and is not a software development company.

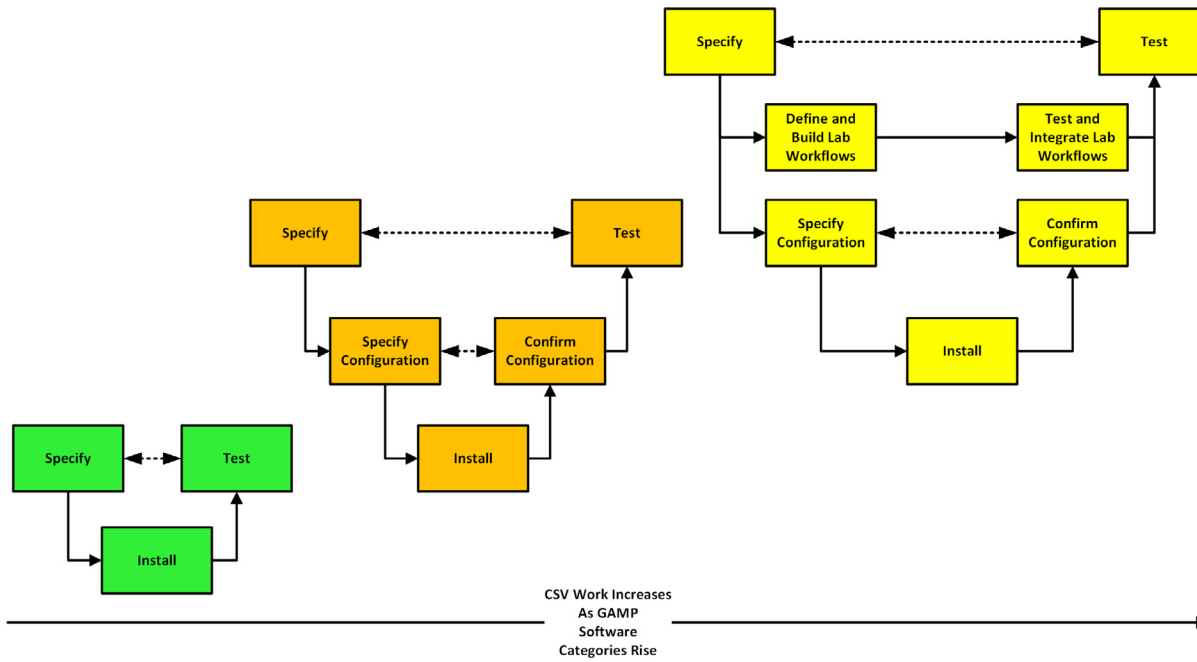
The life cycle models adapted from GAMP 5 are shown in FIGURE 1. As demonstrated, the amount of validation work rises with increasing GAMP software category.

Shown in FIGURE 1 on the left is a GAMP category 3 life cycle. The cycle is very simple and consists of specify, install, and test. EU GMP Annex 15 clause 2.5 states, "Qualification documents may be combined together, where appropriate, e.g. installation qualification (IQ) and operational qualification (OQ)" [7]. Using this and EU GMP Annex 11 clause 1, when applying risk management throughout the life cycle [5] all phases of such a life cycle can be combined into an integrated validation document to streamline the validation process [8].

The other two life cycle models shown in FIGURE 1 are for GAMP software category 4 and are modifications of the category 4 model in GAMP 5 [4]. The model in the center of FIGURE 1 is for simple category 4 systems where the business process can be modified by configuration of the application (e.g., turning electronic signatures on to change a hybrid system into an electronic one, as noted above). This requires the addition of a configuration specification and confirmation that the settings have been turned on correctly.

The right-hand life cycle in FIGURE 1 is for a more complex category 4 system for which, in addition to application configuration, specific laboratory workflows can be set up. This may be via a graphical drag and

FIGURE 1: System Life Cycle models for GAMP software Category 3 and simple and complex Category 4 (adapted from GAMP 5SE [4]).



drop mechanism or a language provided by the supplier. Either way, this requires an additional layer of specification, build and test before integrating each workflow into operational use.

Just In Case User Requirements

Just in case user requirements add insult to the injury of testing them. Adding additional complexity and time to any validation is to include additional requirements in the system's URS *just in case* they might be used in the future. If tested, these requirements result in extra work for zero value if they are never used. A better way is to focus on just the current requirements in the initial validation.

If required later, other software features can be evaluated but not used for regulated work in either a development environment or even in the production environment, itself. If you want to use them, raise a change request, include the requirements in an updated URS and verify that they work as expected. This is a practical way of adding new functionality to a validated system with minimal validation effort.

Leveraging a Supplier's Software Development

Both the first and second editions of GAMP 5 discuss leveraging the supplier's software development and testing in sections 2.1.5, 7 and 8.3 plus Appendix M2 for supplier

assessments [4, 6]. To do this and reduce your validation effort, you must do more than just send a supplier a questionnaire to complete and have QA stick it in a filing cabinet or document management system. This requires a pro-active assessment that reviews the procedures and practice of software development for Software Category 4 applications. For example,

- What software development life cycle is used?
- What software development tools are used?
- How are requirements for the system specified and understood?
- How extensive and accurate are software code reviews, and are they acted upon?
- How are software builds and configurations managed?
- Is regression testing systematically performed and accurately reported?
- How extensive is the formal testing?
- How are software errors identified, classified and resolved?
- What is the release process?

This type of assessment is not suitable for a questionnaire but, rather, an on-site or remote audit. It will require at least 1 day to perform. You are looking for a robust software development process. You should identify two or three requirements and trace them through the supplier's development process. How extensive is the work to specify, write, test and integrate the new code into the main build? Does this give you confidence in the supplier? This assessment must be documented in a report, as it is the foundation upon which you leverage the supplier's development into your validation project to reduce the amount of work.

Where Agile development is used, the GAMP Good Practice Guide on Enabling Innovation or a shorter chapter in the second edition of GAMP 5 [4] are strongly recommended before any audit. This is to understand the Agile software development process, how user stories are the basis of developing requirements that are managed with software engineering tools such as Jira and Team Foundation Services. There is typically no URS or equivalent document. Rather, there is a backlog of user stories and epics for software development.

This information can be used as follows:

- The application assessed is a configurable software product (GAMP Category 4).
- Although classified as category 4 at the system level, for laboratory applications there are many functions that are category 3.
- The requirements in the URS can be assessed and compared to the application and then used to classify each one as either category 4 (configured) or 3 (parameterized, see the discussion below).
- Providing the assessment report is positive, all category 3 requirements considered as validated by the supplier are implicitly tested in the user acceptance testing phase [9].

It is important to understand the use of the word *parameterization* in the section above. A Category 4 application can be configured to change the business process. Within the Category 4 application there are often many functions that are Category 3. The business process does not change. It remains the same when a value is changed (e.g., select a wavelength to measure a sample absorbance, input a temperature for an oven or adjust HPLC mobile phase flow rate). This is parameterization and is discussed in the Category 4 section of GAMP 5 Appendix M4 [4].

Therefore, a small investment in time can reduce the amount and extent of user acceptance testing of any laboratory informatics system.

Critical Thinking

Rather than a *test everything regardless* approach, critical thinking (otherwise known as common sense, logic and scientific soundness) should focus on demonstrating intended use of the system and the associated compliance functions to support product development or release.

Consider a simple case of password expiry set at 90 days. Apart from confirming that the expiry has been configured in the application, what are you going to do now?

- One system that I audited had a test script that started in November and finished in February of the next year. Why did it take so long to run the script? "We were waiting for the password to expire," was the answer!
- An alternative approach is to reset the password expiry to one day to test it, have it expire and then reset it to 90 days. This is not the best way to demonstrate that you can change configuration settings easily in the current data integrity climate.
- How about thinking this through? How is password expiry measured? A computer uses a system clock that is synchronized to a network time server that should be synchronized to a trusted time source. The clock is a vibrating quartz crystal of known frequency that the computer counts and then converts the number into time. All you are doing is checking that a computer can count. This is how every computer tells time. Why are you testing this?
- Alternatively, if password expiry fails and passwords are still valid after 90 days, what is the risk? Low. If expiry fails in use, it is readily detectable. Furthermore, allowing passwords to go to 91 days before discovery does little to put a product at risk. Roles and passwords are still in place and work.

Testing Assumptions, Exclusions and Limitations

Barry Boehm illustrated that it is impossible to test software exhaustively in a 1970 report for the US Military [10]. We see this in everyday use of computers with security updates, patches, minor versions, quick fixes or whatever name is applied to fix bugs.

The purpose of validation testing is to demonstrate intended use efficiently and effectively against user requirements. It is not to find software errors. That is the job of the supplier. The key to reducing the amount of effort in testing, in addition to leveraging supplier development, is to document what assumptions, exclusions and limitations you are making in your test approach. Just because you have a requirement does not mean that you must test it blindly. Think objectively.

The key to reducing the amount of effort in testing, in addition to leveraging supplier development, is to document what assumptions, exclusions and limitations you are making in your test approach.

For example, if an application has 100 different access privileges and you want five different user roles, this is 500 different combinations. Hopefully you won't test all of them, but if you do, please contact me as you need some expensive consultancy. But how many combinations will you test? How will you justify your approach? This is the role of documented assumptions, exclusions and limitations of your test approach, which can be linked to the supplier assessment report. This documents any rationale for what, how, extent of your testing and how you will leverage supplier development. If you are going to exclude specific user requirements from testing, state why you are doing this [9].

Death by Test Instructions

A bane of CSV is test documentation. At what level of detail will you document? This is a focus of the new CSA guidance from the FDA. However, given the nature of laboratory systems in product release that you will be undertaking, it is unlikely that unscripted testing will be used, especially as there is no mention of laboratory systems in the guidance [1].

Will you be using trained users or drag someone off the street to test your software? Using the former approach, you can reduce the instruction detail required compared to the latter. Don't treat testers as if they are naïve people with mind numbing detailed instructions. Testers are educated and trained. Treat them as adults.

TABLE 1 compares test instructions for risk-averse and trained users. In general, with risk-averse instructions shown in the left-hand column, each instruction needs to be documented with observed results, dated with initials. If you are really unlucky, you'll have a screen shot to take at each step.

In contrast, a better way is to give a trained user a simpler instruction, shown in the right column of TABLE 1. Simpler, easier to write and faster to execute and document, a trained user will know how to execute

TABLE 1: Comparison of test instructions for risk averse and trained users.

Risk Averse Test Instructions	Test Instructions for Trained Testers
1. Access *file* on the top ribbon of the application 2. On the dropdown menu select *open file* 3. Select *browse* option 4. Open the *validation* folder 5. Select the file *validation.dat* 6. Open the file	1. Open the *validation.dat* file in the *validation* folder

this instruction consistently. Note that the quality of test instructions is dependent on the knowledge of the software by both the test writer and the tester.

- The more training and experience with the system, the easier it will be to write simpler instructions and execute them.
- Instead of dating and initialing each test step, why not just allow the tester and reviewer to sign and date the bottom of each page, just as you do for a laboratory notebook?
- Some test instructions may tell a tester to move to a different function of the application. If so, why do expected and observed results need to be documented?

Screen Shot at Dawn

One sacred cow lined up for slaughter. Screen shots are the bane of CSV. They are overused and, in most cases, of zero value. If used for documenting every step in a test, it is indicative of an over cautious and risk-averse approach to computer validation and an absolute waste of resources required to execute, collate, review and retain information. If used sparingly, a screen shot can add value to document a transient message on the screen where there is no other recording of it.

However, if a transient message on the screen also generates in an audit trail entry, why take a screen shot? Use the audit trail entry to automatically self-document the activity. In this way, you can save time by not just testing analytical functions but simultaneously verifying audit trail functionality. This way increases the testing elegance as well as reduces the time to test. This approach to self-documentation is in the draft CSA guidance and is quoted earlier in this article [1].

An alternative approach to documenting your testing could be to use screen video that records all that is being done. If properly described in the test plan and outline test instructions, this is a perfect way to document the evidence. Reviewers can randomly select passages to review [Siegfried Schmitt, personal communication].

Upgrade Systems More Frequently

Once a system is validated, the mantra of most pharmaceutical companies is "DON'T TOUCH IT!" No changes unless absolutely necessary. And certainly, no upgrades, as the dreaded R word is uttered: *Revalidation*. This risk-averse and, quite frankly, irrational mindset must be changed. Any laboratory that has implemented a SaaS application knows there is a continual release of new versions every three months (if you are really unlucky) or annually (phew!). It is a validation treadmill, but it is manageable. According to the contract you have signed with the SaaS provider, you will be required to accept these upgrades regardless, especially if the installation is multi-tenant, as all users are upgraded simultaneously.

It is simpler, cheaper and more efficient to upgrade an application regularly rather than wait until a "Dear Esteemed Customer" letter or e-mail drops in your lap. The latter is a trigger for Defcon 2 status, as the application version you are using goes out of support in six months. Let us look at the problem rationally.

The application will not stop running in six months, but it may be unsupported. Instead of panicking and trying to upgrade or, worse, looking at alternative suppliers and systems, just think it through and keep current.

When I walk though many laboratories as either a consultant or auditor it is like visiting a science museum. There are old, unsupported and cyber-insecure operating systems, and creaking out-of-date applications keep soldiering on. The best advice is to stay current or upgrade more often.

Summary

Computer validation is a fact of life in GMP regulated laboratories. However, it must be conducted in an efficient and effective way. As mentioned in eBook 2, redesign the process and then configure the selected application to automate it. User requirements and configuration settings must be updated and documented respectively and, if possible, should avoid custom software. Assess the supplier's software development to reduce the amount of user acceptance/Performance Qualification (PQ) testing undertaken. Test instructions should be written for experienced users. Any assumptions, exclusions or limitations to your testing should be identified at the same time and you should self-document the testing where there is an audit trail. Screen shots should be kept to an absolute minimum, only used when they add value. Finally, upgrade the application to keep current.

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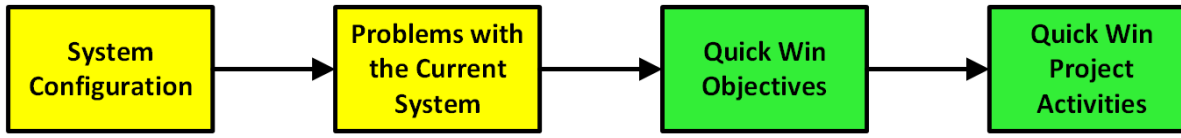
Trusted Answers

Implementing Quick Wins

Quick wins are small projects that generate benefit, can be implemented quickly and are inexpensive. They are implemented in advance of main digitalization projects to provide proof of principle of approach but, above all, to demonstrate the viability of an overall digitalization strategy and support of management.

We will discuss quick wins for two computerized systems that improve data integrity and are steps towards digitalization. We have discussed these two systems briefly in eBook 2. Here, we will look at them in more detail.

FIGURE 1: Discussion of quick win projects.



The format of these two quick wins in is demonstrated via four stages in FIGURE 1. The time scale of each project must be short to qualify to be a quick win – ideally 4 to 6 weeks. Shorter is better.

EXAMPLE 1: AUTOMATED DISSOLUTION SYSTEM

System Configuration

This automated dissolution system consists of the following items:

- Dissolution bath with six vessels
- Auto-sipper to sample each dissolution vessel and transfer the sample to the UV spectrophotometer for measurement
- UV-Vis spectrophotometer with multicell changer
- PC with controlling software for the bath, auto-sipper and spectrophotometer

When an automated procedure is used, the analyst is only required to drop the tablet or capsule into each vessel when prompted by the system. During the time course of the experiment, the software controls sampling from each vessel. The spectrophotometer is used to analyze the sample with a multicell changer to keep the individual vessel measurements discrete. At the end of the analysis, the system calculates the reportable result with a determination of pass or fail against the acceptance criteria of the method.

Problems With the Current System

Of 49 dissolution analytical procedures that use this system, only one uses the system in its fully automated intended use: tablet or capsule is dropped in each vessel and calculated results come out of the data system at the end of the procedure.

The problem is that the system is used as a hybrid even though there is electronic signature capability for both the performer of the test and the reviewer.

The remaining 48 procedures use the system as separate items of instrumentation: dissolution bath, where an analyst drops the tablet or capsule in and records the time manually on an analytical batch record. Then each vessel is sampled manually at specified time points and the sample is transferred to a test tube. The sample time is recorded on

the batch record. When the dissolution is complete, the samples are measured manually, with the spectrophotometer and absorbance values printed out. Then, the piece de la resistance of the procedure: the results are manually entered into a spreadsheet for the final result to be calculated, printed and signed. Inefficiency personified!

Quick Win Objectives

There were two objectives for this quick win project:

1. To ensure that the remaining analytical 48 procedures (currently manual) use the system in fully automatic mode.
2. In addition, the electronic signature capability of the system will be implemented for all procedures.

This aim is to eliminate the spreadsheet, transcription error checking and speed up analysis and review.

Quick Win Project Activities

The quick win objectives were achieved by the following activities:

- Change request was raised, describing the project activities including prototyping the new ways of working.
- Prototyping was put in a specific folder of the system and included statements that the changes in configuration settings and data generated were part of the change control. Configuration settings were changed to enable electronic signatures.
- When the new process was understood, the URS and configuration specification were updated and a test script was modified to accommodate electronic signature by the performer and tester.
- No further testing was undertaken, as the system was already validated. This was simply a modification of two configuration settings.
- At the end, the change control was approved.
- Manual methods were migrated to the new process as samples became available.

The objectives were achieved within a four-week time frame, including the prototyping work. This enabled the system to eliminate paper records. The only output was the electronically-signed summary report for each batch dissolution test.

EXAMPLE 2: FT-IR SPECTROMETER USED FOR IDENTITY TESTING

System Configuration

The system consisted of the following items:

- Fourier Transform Infra-Red (FT-IR) spectrometer
- PC with software that controls the instrument, acquires the data and prints the results
- An ATR (Attenuated Total Reflectance) accessory, which is preferred over making nujol mulls. This is a quicker way to analyze samples.
- The system was used as a hybrid system

Problems With the Current System

There are a few problems with the current ways of working with this system:

- There was no check performed by the laboratory to ensure the spectrometer was fit for use on the day, either by using the polystyrene film from the supplier to perform an ASTM Level 0 test or an EP check built into the software.
- Comparison of the spectra from the reference standard and sample was performed manually and subjectively, even though there is a Compare function in the software.
- As mentioned above, the system was used as a hybrid. However, there is an extensive electronic signature workflow, including signing and rejecting results.

Quick Win Objectives

There were three main objectives from this quick win project:

1. Ensure that a System Suitability Test (SST) check was carried out to ensure the instrument was fit for use on the day to analyze samples.
2. Implement the Compare function in the software to provide a scientifically sound basis for identification of a sample.
3. Implement the electronic signature capability function for the performance of a test and the QC reviewer. The rationale for this is that US GMP in 21 CFR 211.194(a) clauses 7 and 8 only require two individuals to sign the record: performer and reviewer [1].

Like the dissolution system above, the aim was to remove paper from the process, only printing a summary report of the identification results. Another objective was to enhance the scientific soundness of the process by removing the subjectivity from the identification.

Quick Win Project Activities

The quick win objectives were achieved by the following activities:

- Change request raised, describing the project activities including prototyping the new ways of working.
- Prototyping of the instrument checks, using the Compare function and evaluating the electronic signature capability were carried out. Data were identified by reference to the change control number. Once the prototyping was completed, like the dissolution system the URS and Configuration settings were updated. Owing to the complexity of the electronic signature configuration, no rejection signatures were implemented.
- A new test script was written to test instrument checks, setting up and using the Compare function and signing the test outcome.
- When the new process was understood, the URS and configuration specification were updated and a test

script was modified to accommodate electronic signature by the performer and tester.
- No further testing was undertaken, as the system was already validated.
- Finally, the change control was approved.
- Over time, as samples became available, reference spectra were incorporated in the Compare function and the wavenumbers of peaks for identification Manual methods were migrated to the new process.

The objectives were achieved within a five-week time frame. The end result was better science and less paper, with only an electronically signed summary report printed.

SUMMARY

Quick wins provide the overall laboratory digitalization strategy with credibility in a short time (circa 2 to 3 months) and with little cost. For the first quick win example, the business benefit was fully utilizing the system for fully automated dissolution testing with electronic signatures. This approach also eliminated printing the spectrophotometer output, entering the absorbance values into a spreadsheet with associated transcription error checking. The second quick win enhanced the scientific soundness of testing by eliminating the subjective confirmation of identity. It also used the electronic signature capability in the current software to eliminate paper printouts.

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Implementing Digitalization Projects

Unfortunately, laboratory informatics applications do not come with an ON button. Implementing a digitalization project requires two items: the first is effective project management and the second is ensuring the project that you implement provides good business benefit and has a high probability of success. The rationale is that success means the overall digitalization strategy has enhanced credibility. Get it wrong and you have a mountain to climb.

ORGANIZATIONAL INFORMATICS MATURITY

The first question to ask is, how well can your organization specify, implement and use informatics applications?

There are two ends of the spectrum:

- **Sublime**: Every system is implemented on time and on-budget, and the business benefits promised are realized.
- **Ridiculous**: Implementation is over budget, requirements are changing, current business process are automated, there is a hybrid system and little business benefit.

The organizational maturity for implementing informatics applications will have a major impact on how the digitalization strategy will be implemented and how the first project needs to be scoped and managed:

- Is an experienced project manager required?
- Should a safety-first approach be used: start small and expand outwards?
- Bottom up: data acquisition first?
- Top down: interface the laboratory to sample suppliers and information users but ignore automating analytical processes?

In this chapter we will explore these questions and provide answers that can be adapted to individual organizations and laboratories.

PROJECT MANAGEMENT

Before charging off into the distance implementing a project from the laboratory strategy, one factor that is usually overlooked is project management. This is a critical success factor to delivering any project on time and on budget. To quote the old saying, "Failing to plan is planning to fail."

Project Management has two key facets:

1. **The Project Manager**: The single point of integrated responsibility for the entire project.
2. **Integrated Planning and Control**: There is integrated planning and control of the project. Ideally this should use a Work Breakdown Structure (WBS) to deconvolute the project down into individual tasks and deliverables.

The Project Manager

As mentioned above, the project manager is the single point of contact for the project. This person will delegate tasks to members of the project team and be responsible for regular updates to Senior Management and other stakeholders involved with the project.

A project manager should have leadership skills, be flexible and adaptable to change with effective communication skills to liaise with management, laboratory staff, QA, IT and suppliers. He or she should be able to balance any technical solutions that are required with the time, cost and human factor. Depending on the size of the project, a project manager can work either full time or part time.

In my opinion, for any major informatics project the manager role must be a full-time role. The assumption that the project

manager can do the work required in a part time role is false. This is a recipe for failure and can potentially limit the career for the unlucky individual. It also sends a message from management that a major project is being done cheaply. Lack of an organization's commitment is the root cause of many failed projects. Attendees at some of my laboratory informatics training courses have often explained that they were repeating their LIMS projects not just twice but, on one occasion, three times due to the company failing to commit enough project management and laboratory resources to the project.

The same approach should be taken with project team members: full time versus part time. Major projects require at least some of the members to work full time, otherwise they can get pulled away at key times for urgent analytical roles. Actions like this will delay any project.

A project manager's role is a transitional position because at the completion of a project, the individual is redundant. If using a professional project manager, this is not a problem. He or she can be redeployed to another project. Or if the person is a contactor, he or she can move to another company. However, if the project manager comes from the laboratory, a career development path is an important consideration. One option is that the project manager become the power user of the application or a member of the automation group responsible for managing the laboratory side of the informatics applications.

A project manager is unusual, as the individual has no management responsibility and no authority over other people. And so, he or she must earn authority and respect. This person should be able to resolve conflict easily and amenably, and will earn authority by being right. However, a project is a matrix taking project team members from the line organization. The problem occurs when there is an issue in a functional area that requires a project member to resolve. The project may suddenly lose staffing. In a line versus matrix discussion, the line inevitably wins. Therefore, measures such as changing the job descriptions of project team members to allocate a specific percentage of time on the project, backfilling staff or allocating staff full time to the project are options to consider.

Integrated Planning and Control

A key item in any project is a comprehensive plan, which must be sufficiently detailed with tasks and deliverables outlined and allocated to responsible people. A good project plan requires the following:

- Defines the scope of the project and its boundaries, including interfaces with other project and existing informatics applications.
- Defines key milestones throughout the project.
- Defines realistic limits of each milestone.
- Breaks down each milestone into manageable tasks that allow control and visibility.
- Defines deliverables, timescales and personnel responsibilities for each task.

- Where work involves other departments and external providers, obtains commitment to do the work and documents how they will be held accountable for project work that they will be undertaking.
- Documents what each milestone requires in time and cost, then identifies how these relate to overall resources and budget.
- Identifies project risks and potential problem areas.
- Allows time for contingency, especially if there are external factors to consider or something has been omitted from the plan. Also considers the impact of national and staff holidays. This is especially important with multinational projects.

The key message is to plan but not be frightened to revise the plan, considering events and project progress.

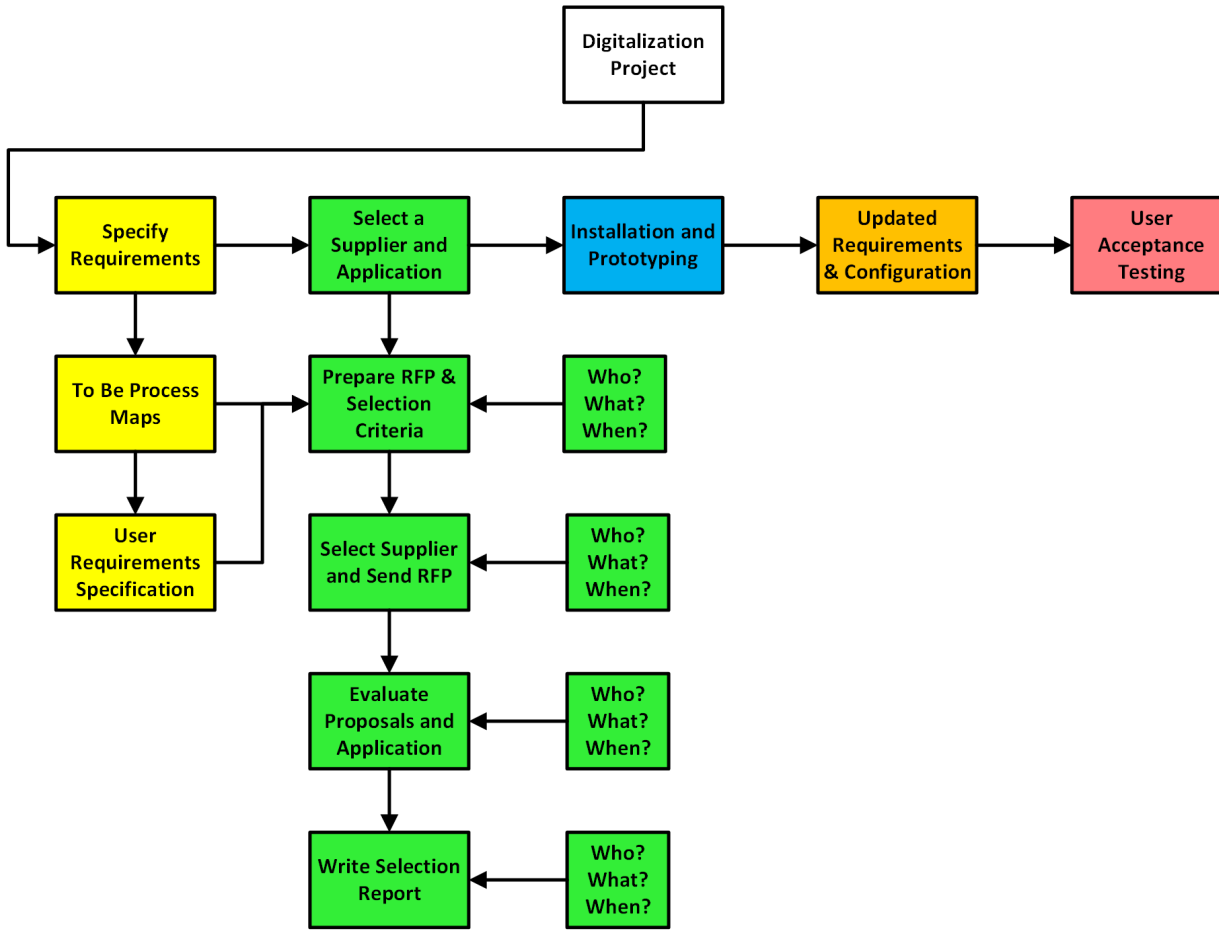
One way to present and visualize a project plan is via a WBS, which is a decomposition of a project into deliverable tasks. This process is like IDEF, presented in eBook 2, to map processes in the laboratory. However, most projects gravitate to that well known project management application: Excel.

UNDERSTANDING A WORK BREAKDOWN STRUCTURE

FIGURE 1 demonstrates a simplified WBS for a portion of a project for system selection. The inputs to the first stage of the process are the "***To Be***" process maps and the current version of the URS, which form the inputs to the first stage of system selection. The overall activity for system selection has been broken down in this example to four tasks:

1. **Prepare a Request for Proposal (RFP) and Selection Criteria**: From the URS and process maps, a document knows as an RFP is generated. This asks a supplier to clarify if they can meet the user requirements. Any prioritization in the URS should not be included in the RFP, as this will bias the response. At the same time, the selection criteria must be identified and documented. The selection criteria may also include tests to apply to the application based on the way the laboratory wants to work in the future. The person or team responsible for preparing both the RFP and the selection criteria should be identified, and the deadline for return should be documented.
2. **Select Suppliers and Send the RFP**: The RFP is sent to a list of pre-selected suppliers with a deadline for return stated. An individual is allocated to field any questions from suppliers and to ensure that responses are received within the deadline.
3. **Evaluate the Proposals and Application**: Using the selection criteria generated earlier, a specified evaluation team will evaluate the supplier responses. I would advise reducing the number of suppliers

FIGURE 1: A simplified example of a Work Breakdown Structure (WBS).



based on the responses before seeing the applications. The reason is that after a while you find it difficult to remember which application a specific function was from. Try and keep it simple. Use the selection criteria to identify which application you want for the laboratory. Ensure the team has the time to do the evaluation properly, as you must manage not just internal resources but also the supplier's system and staff availability.

4. **Write the Selection Report:** An individual will be assigned to write the selection report to justify a particular application was chosen. Don't forget to include the tasks for review, revision, and approval as well as the individuals allocated to these tasks in the Who and When sections.

DEFINE THE SCOPE OF THE PROJECT

Without a proper definition of the scope of a project as well as the boundaries, it will be impossible to define an accurate project plan (TABLE 1). Failure to define the scope of the project means that it will be easily susceptible to scope creep, resulting in delivery failure and cost overruns.

WHICH PROJECT GOES FIRST?

As mentioned previously, selection of the first project is critical. The reason is that the credibility of the whole digitalization strategy depends on it being seen to be a success, providing business benefit to the organization and laboratory as well as delivering a simpler working strategy to users.

TABLE 1: The main criteria for defining a laboratory digitalization project.

Criterion	Details Required
Title	Project title and a single paragraph describing it
Objectives	What will be achieved at the end of the project
Strategy Link	How this project fits into the overall laboratory automation strategy
Project Owner	Name of the individual in the business who will be the process owner when the project is complete
Project Manager	Name of the individual who will manage the project
Justification	State the outline business justification State the outline regulatory justification
Location(s)	Site(s) and Department(s) that will use the system when operational
Start & End Dates	Anticipated dates for beginning and end of the project
Outline Milestones	List the main milestones of the project (e.g., define requirements, select supplier, etc.)
Project Risks	List any known risks
Budget	How is the project financed?

TOP DOWN OR BOTTOM UP?

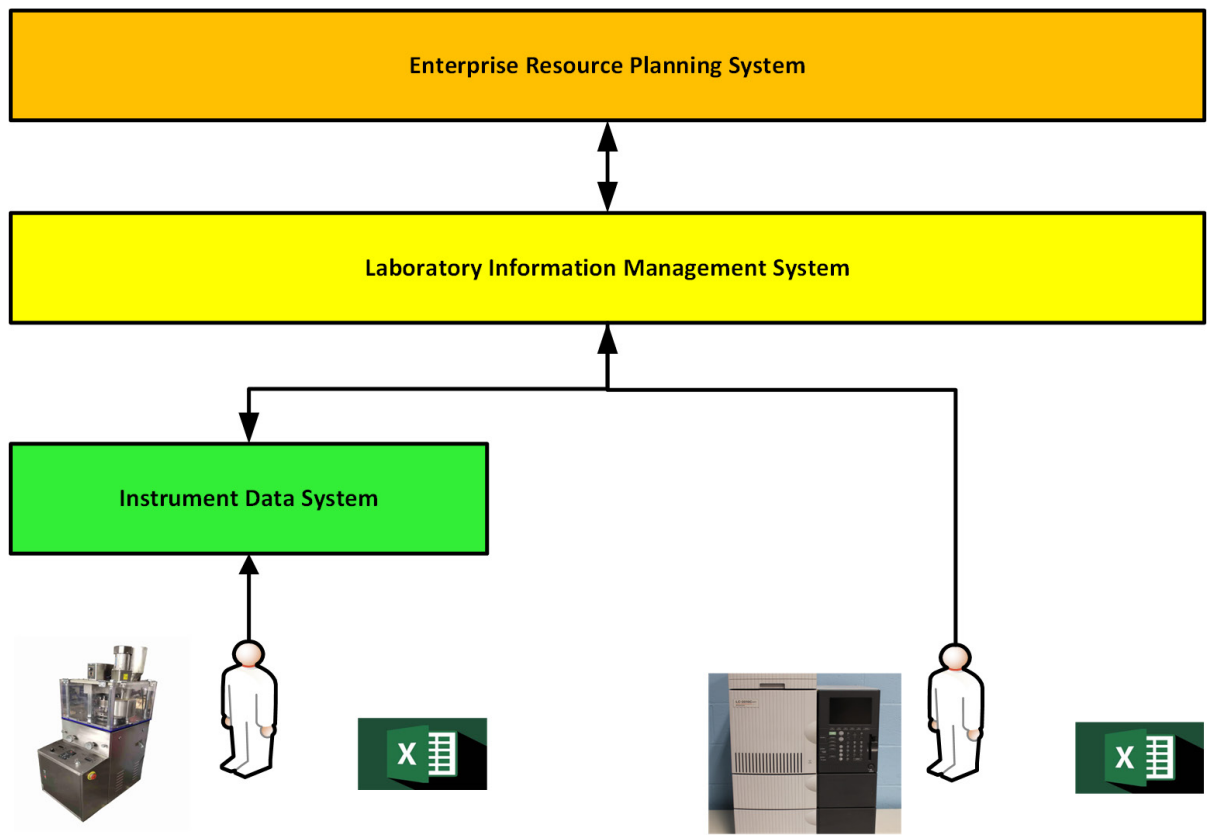
One of the questions about a program of digitalization is, should informatics solutions be built from the top down or bottom up?

FIGURE 2 shows an informatics landscape that could be built consisting of:

- A Corporate Enterprise Resource Planning (ERP) system
- A Laboratory Information Management System (LIMS)
- An Instrument Data System that controls an instrument used as a hybrid, and results are calculated in a spreadsheet.
- Manual activities recorded on paper with spreadsheet calculations

The question is, should this landscape be built from the top down (starting with the ERP), or from the bottom up (digitalizing the laboratory operations)?

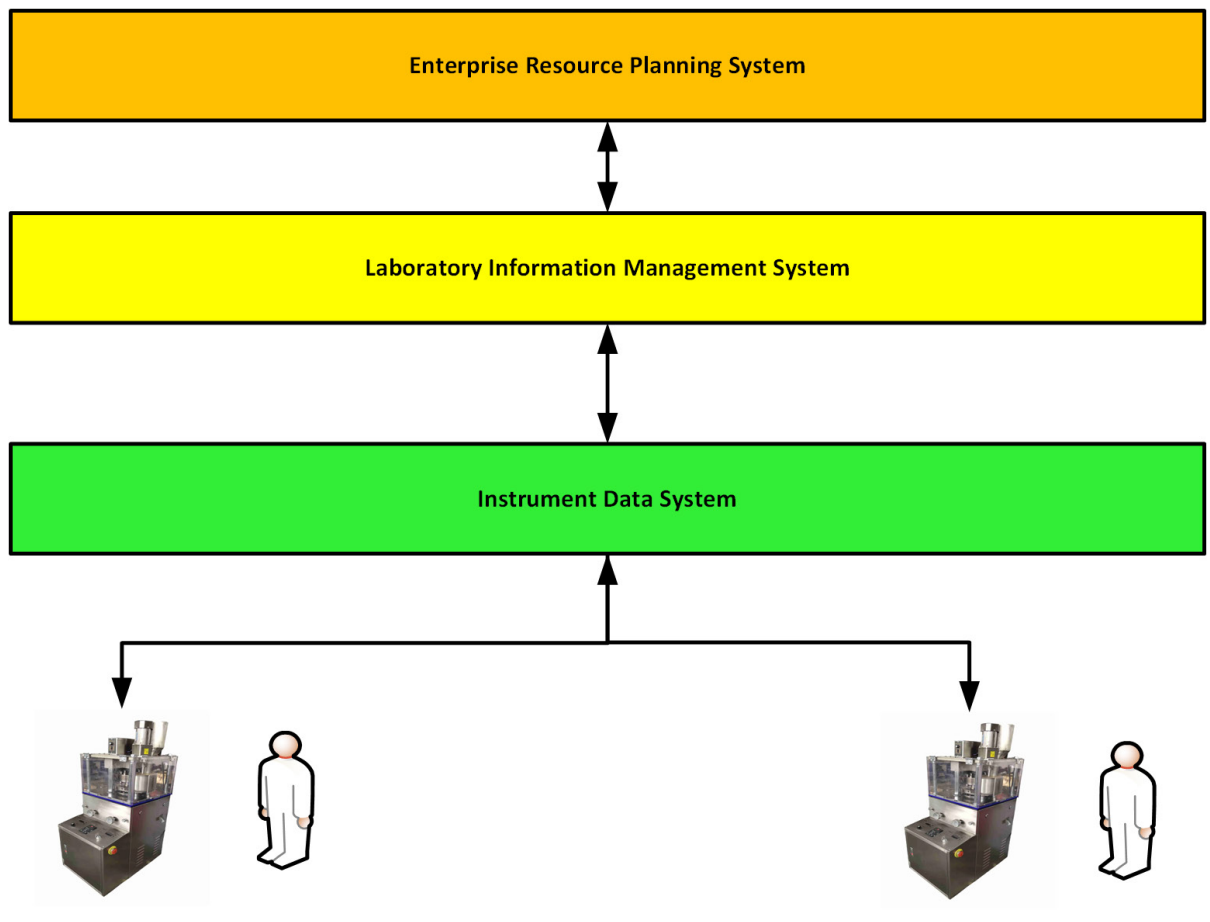
FIGURE 2: A laboratory informatics landscape.



From a personal perspective, I have seen major informatics implementations that make great strategic sense but leave the laboratory in the Stone Age, using paper and spreadsheets followed by manual data entry. Therefore, don't think top down but bottom up. Ensure that the analytical engine room is firing on all cylinders first.

FIGURE 3 reveals the way forward: harmonize working practices in the laboratory to ensure that workflows are just built once, validated and used in multiple locations and laboratories. Harmonize further by using the same instruments and computerized systems to save on analytical instrument qualification and computerized system validation costs. If validated in one location, subsequent

FIGURE 3: Data capture project to harmonize working practices and leverage benefits of a single system.



validation effort of the same software in different locations can be greatly reduced.

LEVERAGING EXISTING DIGITALIZED SYSTEMS

As the strategy roll-out progresses, digitalized systems will be operational. To leverage even more business benefit from them, new systems should be interfaced with existing ones. This brings in some interesting conundrums that each laboratory needs to resolve, in designing electronic workflows. Take, for example, a chromatographic analysis. The CDS can be configured to work on its own as an electronic system, but with manual input of sample identities, weights, factors and calculation of the individual aliquot results and the reportable result for the test. The individual results and the reportable result are manually entered into a LIMS, which compares the reportable result with the specification, collates all test results and generates a Certificate of Analysis.

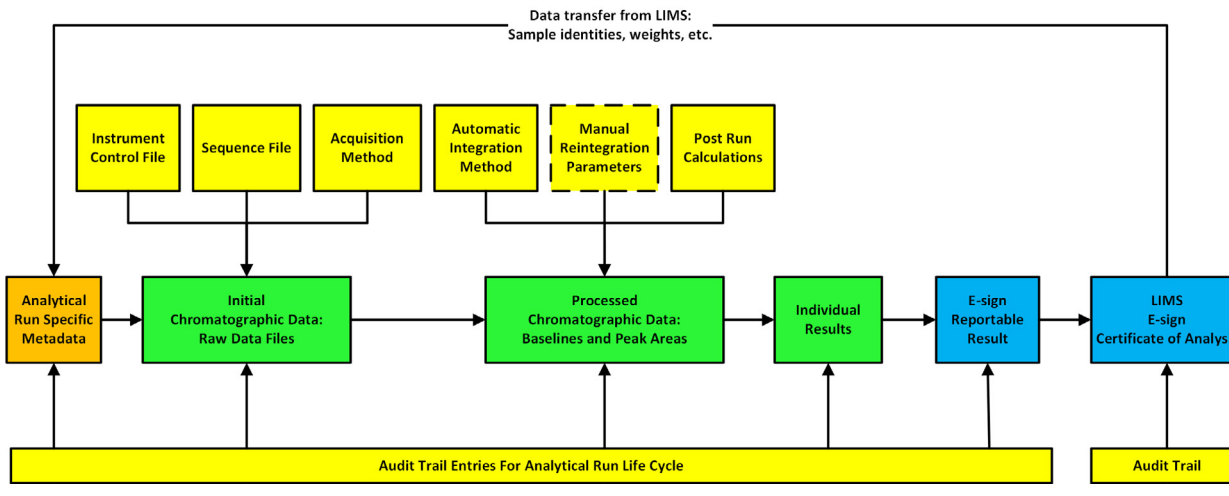
If the CDS is interfaced to the LIMS, as illustrated in FIGURE 4, there is an immediate benefit, with data from the LIMS being downloaded to the CDS. Manual entry and transcription error checking is avoided. The results can be uploaded into the LIMS from the CDS. All is good with the world.

BUT....

What happens when an Out Of Specification (OOS) result is generated?

In the "***As Is***" world, the analyst and their supervisor will reach for a uniquely numbered OOS form to begin the laboratory

FIGURE 4: Interfacing a CDS with a LIMS.

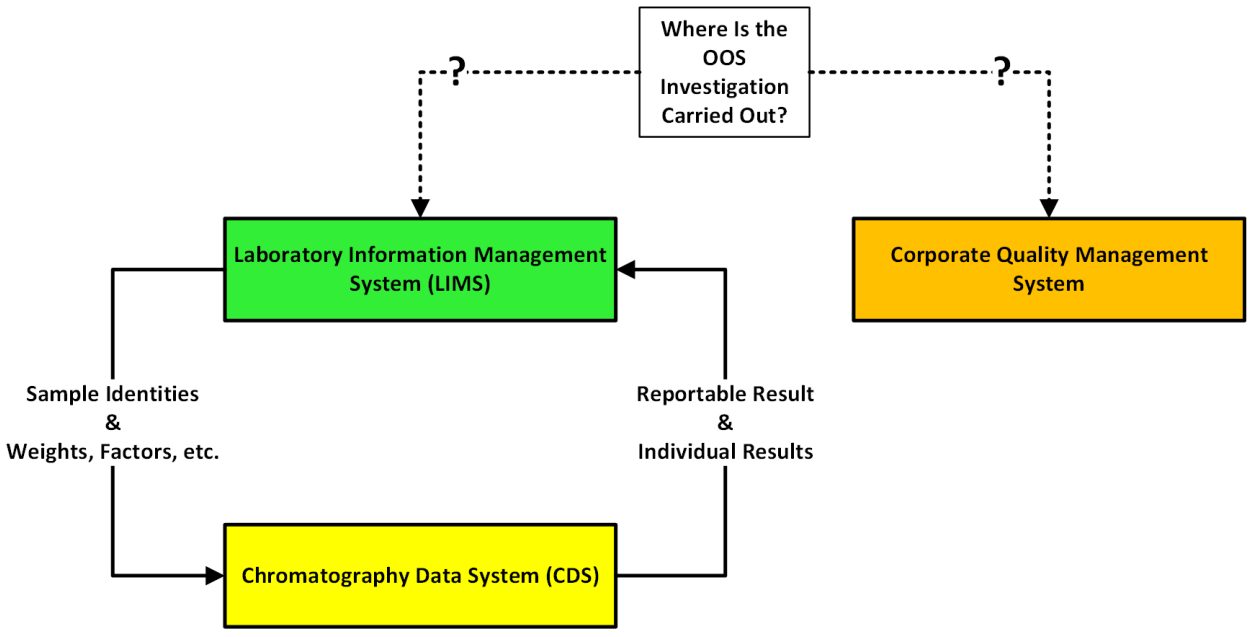


investigation. In many organizations, these investigations and deviations are managed in a corporate Quality Management System application outside of the laboratory's control. This is fine in a hybrid world, but there could be a problem in the digitalized world.

What happens in the "***To Be***" world? Here, things can be interesting, as shown in FIGURE 5.

- Where is the OOS result identified? If an experienced analyst is running the samples, they will have a good idea that there is an OOS. However, the CDS will only generate the results of the aliquot injections plus the reportable result. There are no specifications for the aliquot or reportable results in the CDS.
- All these values are uploaded to the LIMS, which contains the specification and the means to identify the OOS either with the reportable result alone or the results of the individual aliquots, which will have wider acceptance criteria [1].
- After the OOS is identified, the laboratory investigation begins. Where is this to be documented and managed? Some LIMS have a deviation or laboratory investigation module that can manage the

FIGURE 5: How should a laboratory OOS result be handled in an electronic environment?



on-line documentation of the investigation and may be configured to follow a checklist contained in the laboratory investigation SOP. From the laboratory's perspective, the investigation is close to the data.
- However, Corporate Quality are apoplectic, as the investigation is not in the corporate QMS application!

Should the LIMS be interfaced to the Corporate QMS application, and should the investigation occur in the QMS alone?

Could the LIMS conduct the investigation and then transfer the data to the corporate QMS? In this case, how does the clock for the 28-day investigation operate?

Specific guidance cannot be given, but this is one example of how a problem that is relatively simple to resolve in the paper or hybrid world needs thought and discussion with colleagues outside of the immediate laboratory environment.

METRICS OF THE NEW AND OLD PROCESS

In eBook 2, the metrics of the current process were measured. This provides the baseline of the "***As Is***" process, for which business benefits of the faster "***To Be***" process were calculated and the justification of the digitalization strategy was based upon.

About 6 months after the implementation of any new informatics project, when any problems have been ironed out and the users are using the system effectively, the same metrics should be generated to demonstrate tangible improvements.

One suggested metric could be the sample transit time of the "***As Is***" and "***To Be***" processes. Note that this is not the sample turnaround time, which would encompass the time from sample receipt to reporting, but a subset of it. Another metric could be the number of errors identified in the two processes as a measure of the overall quality of the new process. The metrics of the new process can be compared and assessed to see if the promised business benefits were obtained or not. Meeting or even exceeding the promised benefits should convince senior management to continue funding the strategy. The article by Newton and McDowall should help define more metrics for monitoring laboratory performance [2].

SUMMARY

Implementing a laboratory informatics solution of the digitalization strategy requires two components. The first is effective project management for control and direction of the work. The second is selecting the first project with a high probability of success and tangible business benefits to enhance the credibility of the overall strategy.

Effective project management requires a project manager as the single point of responsibility for the project. For large digitalization projects, a full-time project manager is a critical success factor to

ensure that the project remains on time and within budget. The control and direction of the project requires a plan, and a work breakdown structure is the best way to identify tasks, deliverables and responsibilities, as well as visualize the whole project.

Selecting a suitable first project for implementation would be typically focused on the data acquisition and processing. The aim is to eliminate paper, manual or spreadsheet calculations and the use of electronic processing and electronic signatures. Measuring the metrics of the "***As Is***" and "***To Be***" process should provide senior management with evidence that the strategy is working and ensures their continued backing.

References

1. FDA Guidance for Industry, Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production. Food and Drug Administration: Silver Spring. MD (2022).
2. M.E. Newton and R.D. McDowall. Data Integrity Metrics for Chromatography. *LCGC Europe*. **30** (12) 679–685 (2017).

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Pharma 4.0 and the Digital Regulated Laboratory: Overall Summary

EBook 1, eBook 2, and eBook3 have outlined the journey from your current laboratory processes that are manual, paper records and hybrid systems, not forgetting the occasional spreadsheet or even a handheld calculator, to reach a digitalized future.

This is a journey and not an event.

Knowing, understanding and interpreting applicable GMP regulations and guidance, including those for data integrity, is a critical success factor for the strategy, as the overall compliance of systems will be ensured and effective risk management applied during the validation of each system.

It requires long-term commitment from Senior Management, down throughout an organization, plus the time, planning and resources to carry out the work of the strategy. This is essential if a laboratory is to keep current to comply with both FDA and EU expectations.

A laboratory digitalization strategy is developed from several strands of work:

- An assessment of the age and capability of current systems.
  Do they have additional functions that can be used to digitalize a process? Are they obsolete and need to be replaced with up-to-date instruments and software?
- A list of instruments and systems that will be retained, and a list of instruments that will be replaced over time.
- A map of the current process to identify bottlenecks, paper records, spreadsheet use, manual entries into computerized systems and data vulnerabilities.
- A redesign and digitalized process to eliminate the items in the bullet point above to provide improvements in speed, efficiency and compliance.
- A portfolio of quick wins and improvement projects that form the digitalization strategy.
- The strategy must be reviewed and updated as new technologies are available and regulatory interpretation and guidance changes.

Overall Summary

Quick win projects provide an early taste of benefits and build credibility in the overall digitalization strategy. As the name suggests, they are quick and inexpensive to implement and provide good business benefits.

Implementation of the laboratory informatics project should aim for digitalization of a main analytical process with a high probability of success. To support this, project management with someone working as a full-time project manager and a detailed project plan are essential. This should be coupled with a cost effective and risk-based approach to computerized system validation. There is little point having a great system if the roll-out is bogged down with slow and risk-averse computerized system validation.

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Bob McDowall is an analytical chemist with 50 years of experience, including 15 years working in the pharmaceutical industry, followed by 29 years working for the industry as a consultant. He has over 35 years' experience in automating laboratories and computerized systems, mainly involving analytical systems and laboratory informatics. Bob edited the first book on Laboratory Information Management Systems (LIMS) in 1987 and he is the 1997 LIMS Awardee from the LIMS Institute presented for advances and training in the subject.

He was a co-author of the revision of USP <1058> on Analytical Instrument Qualification that integrated instrument qualification and computerized system validation that was updated in 2017. Bob has also been involved with the validation of computerized systems for over 30 years and is the author of Validation of Chromatography Data Systems, 2nd Edition published in 2017. His latest book is Data Integrity and Data Governance: Practical Implementation for Regulated Laboratories was published in 2019 by the Royal Society of Chemistry.

He is a member of the GAMP Data Integrity Special Interest Group, contributing to the Records and Data Integrity Guide in 2017 and two Good Practice Guides on Data Integrity Key Concepts and Data Integrity by Design. Bob is a lso the author of the "Questions of Quality" and "Focus on Quality" columns in LCGC Europe and Spectroscopy magazines, respectively.

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