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Pharma IT journal

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Welcome!

Welcome to the first issue of the PITJ for 2008. In this issue we have some interesting papers for your compliance reading pleasure.

Vycky Lander discusses "The Applicability of the US National Institute of Standards and Technology's (NIST) "Engineering Principles for Information Technology (IT) Security" to Modern Corporate IT Security". The NIST Computer Security Laboratory publishes the special publication 800 series dealing with various aspects of computer security and Vycky has selected one of these to present in her article. You are also encouraged to have a look through the NIST web site and look at some of the other topics in this series.

It always strikes me as ironic that computerised system validation (CSV) is a manual and paper based process that is used to validate systems that should be designed to eliminate paper. In a welcome paper, Juan Perez takes a look at Validation Management Systems (VMS) and illustrates how these differ from document management and compliance management systems. The aim of a Validation Management System is to automate the process of computer validation. Juan lists the components that a VMS should do and lists (but does not compare) some of the current products on the market.

The myth of software validation is discussed by Tim Croft and looks at the emphasis on software validation and makes the point this is a misnomer when in reality we should consider system validation. The human factor or the controlled function is the missing part of the equation that must be put in place. Software components can be qualified within a wider computerised system validation effort - utilising a full life-cycle implementation of the V-Model. Vendors, internal technical groups and other third parties all have an important role to play, but ultimate responsibility lies with the end-user - as the "regulated user" of a computerised system they are ultimately responsible for the validation of a system.

The regulatory process does not stop, it may move slowly as a sloth, but does not stop. Recently there have been two new ICH quality publications published: these are Q8 (Pharmaceutical Development) and Q9 (Quality Risk Management) and Patricia Santos-Serrão discusses their scope and impact.

Kate Trainor, discusses how to leverage the benefits from a Clinical Trials Management System (CTMS) Technology for better data access and integration to ultimately reduce time to market for clinical studies. The major problem is that the pharmaceutical industry still relies on paper and moving to electronic data handling will result in dramatic time and cost savings as well as faster time to market.

And finally in Compliance Corner we look at the first modification to US GMP for finished pharmaceutical products (21 CFR 211) since they were published in 1978. In December 2007 the FDA issued a direct final rule that will become effective in April 2008 as it is anticipated that there will be no adverse comments about the changes. The main change of interest for Pharma IT compliance is the change of the regulations to allow only a single person to verify that a computerised system is working rather than the four eyes principle (two people) for comparable paper records.



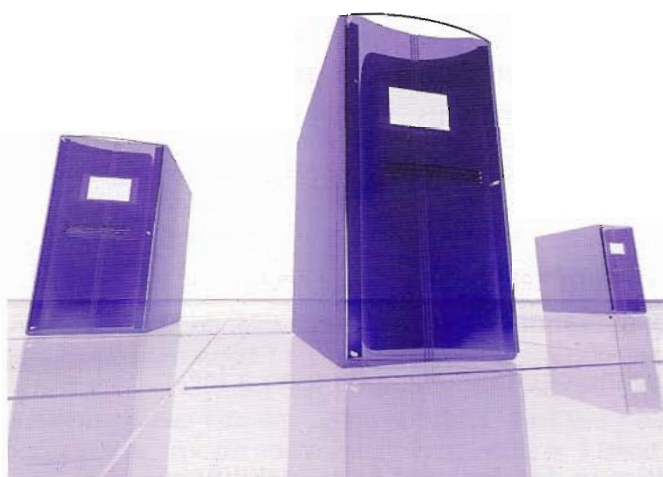
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Validation Management Systems: Time to Speed Up Validation

Validation has always been a conservative process within the life science industry. While almost every process in this industry already counts on a variety of Computerised Management Systems, the validation process is still a lengthy painful process that generates incredible amounts of paper based records, even when using computerised document management systems .

By Juan Oscar Pérez

Key Words: Validation, Quality, Good Practices, Quality System, Quality Audits, Computerised Systems, Risk Assessment, Computer System Validation, Validation Management Systems, Compliance Management Systems, Puerto Rico



Validation in the Industry

Validation, as defined by the FDA in their guidelines is *"establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."*

In order to establish that documented evidence, a validation process following a development model (e.g.VModel, Waterfall Model,etc.) is initiated to generate a list of document deliverables that will become a byproduct of the validation itself.

The typical way for the industry to establish the documented evidence is through paper, either by filling pre-determined forms contained in a protocol or by generating supporting documentation in the form of reports or screen captures.

This process, while lengthy, and in some cases painful, is crucial for compliance with cGxP's enforced by regulatory agencies. However, regulated companies had to become creative with the limited tools available to them in order to speed up this process while still ensuring process integrity.

Validation Management

The validation process was first managed as typical document files routed for review and approval. One person created the document and then sends it to the list of persons required (either sequentially or broadcast) for review and approval. Any comment would go back to the author for correction and start the process all over again since all responsible people need to be aware of changes. That process would start all over again for every deliverable to be covered in the validation procedure (Validation Plan, User Requirements, System Design, Protocols, Reports, etc.)

This "back and forth" process consumes a lot of time when you have several people (4 to 6) reviewing, commenting and approving what could be well over a dozen of validation documents depending the size and complexity of the validation process to be performed (e.g. computerised systems, process, cleaning, etc.). This is nothing short of effective, considering today's industry obsession with process excellence, effectiveness, on-time / on-budget trend. This process can be hard to measure and manage especially when the person responsible for this validation is also responsible for several other projects.

Another impact on timelines and budgets in a validations process is "Prioritisation". While the person responsible for the validation process has a priority, the people reviewing and approving the same documents will have a different feeling for the same project and in some cases it is not even a priority in their list. This leads to documents sitting in somebody's desk for days, weeks and even months.

If we fail to consider both the validation of documents and other variables such as training, SOP's, deviations, change control and audits, we end up with a sure recipe for delayed, over budget projects, faulty processes and in some cases non compliance issues.

Computers and Validation

The software industry has come up with several solutions to cope with document/project/compliance management issues. But validation is not a specific subject such as a

document, a project or a compliance issue. Validation goes beyond all of that and involves all three aspects together and adds one more: execution.

- **Document Management Systems:** As the name states, these kind of systems help with the creation of documents and how they are handled within an organisation. They provide a number of features like:
- **Document Number Control:** generate a number to identify the document based on your business for document ID nomenclature.
- **Version Control:** maintains controls of the documents and the changes made to such documents. It allows the reader to see the evolution of a document through time and ensure that only the current approved version is available for use.
- **Flow Control:** defines the list of people that can see the document and what can they do with it. It also allows for electronic approval and rejection (or comments) of the document once reviewed. A nice twist to this feature is that the author knows who has the document and for how long which means that reviewing process can be measured. People tend to be more effective when they are being "measured" for performance.
- **Format Enforcement:** The system enforces the use of established formats or templates to ensure a uniform look and feel of documents within an organisation.
- **Content Management:** This allows streamlining the capture, processing, and distribution of your company's digital information.

Typically these kind of Data Management systems are designed to allow companies to process and share information in ways that fundamentally improve how you manage information in order to do business.

- **Project Management System (PMS):** This kind of system has only one purpose in mind: if used correctly, it will help to deliver a project on time and on budget. That result will only depend on how good the project manager is doing his job.
- **Compliance Management Systems (CMS):** This is a versatile system that allows managing different subjects in order to ensure compliance with regulatory agencies. Compliance Management Systems (CMS) provide features to address compliance issues such as:
 - Corrective Action /Preventive Action (a.k.a. CAPA)
 - Complaints
 - Deviations / Non Conformances
 - Training
 - Audit Management and Remediation Plans
 - Change Control
 - Environmental Health & Safety
 - And even calibrations

These multifaceted systems are widely used in the life science industry because of the many roles they can deliver.

It is true that with all these systems (properly implemented and used) you can establish control of many processes, ensure compliance according to pre-established business / regulatory rules, increase collaboration among people and reduce costs. When it comes to managing validation, you still need the use of these three systems together with the other all important element: execution.

Validation Management Systems

Validation Managements Systems are designed to help companies overcome problematic validation pitfalls such as over-time/over budget validation projects, handling of paper-



based validation deliverables and supporting documentation, test deviation management, incomplete user requirements testing, re-validation schedules, risk assessments, completeness verification and collaboration.

For example, in Puerto Rico, that comprises of a 100 X 35 mile territorial extension:

- 16 of 20 "blockbuster" drugs of Life Sciences industry are manufactured
- Over 50% of defibrillators and pacemakers sold in the USA are manufactured
- Largest concentration of Life Sciences industries per sq. ft in the world
- Over 60 Pharmaceutical /Biotech plants established
- Over 50 Medical Device plants established

With this amount of regulated companies, validation management costs can be measured in hundreds of million dollars each year. Validation is so intensive in this market that hundreds of companies (local and foreign) are created around this process alone. Imagine the amount of money saved by implementing a computerised system that helps you manage and maintain in control your validation projects increase your compliance levels and reduce the amount of paperwork and paper management functions. That is the purpose of these systems and they can fulfill it.

What benefits does a Validation Management Systems offer to manage validation projects and cut costs, improve compliance and meet delivery schedules?

• **Document Management Features:** these systems can communicate with your current document management systems or serve the purpose by themselves. They can assign document numbers, manage version control, use

control flows to allow review by specific users, and to approve/reject a document. The systems can help enforce consistency through the use of templates and allow content management features for digital content.

- **Project Management Features:** these systems allow you to find real time validation status as well as to determine who is reviewing or has not reviewed a document or is still developing a test script required to closely follow up the approval process to meet deadlines. Also, these systems provide dashboards to track validation project status in real time.
- **Compliance Management Features:** these systems provide features to manage compliance issues like deviations, change control and risk management. Also a collaborative approach can be used with these systems since they allow for several people to work on validation protocols such as having Subject Matter Experts to develop specific test scripts to be used on the validation protocol.

Other features that these systems provide include:

- Track Validation Inventory – this feature facilitates drilling down validation packages looking for specific documents or components.
- Re-Validation Scheduler – companies have a periodic assessment to guarantee that validated systems or processes are still in the required state, this tool helps validation departments to plan such activity ahead of time.
- Automatic Traceability Matrix – ensures that all user requirements are automatically covered throughout the validation process.





- Automatic Change Impact – any change in any section in any document will reference which other documents/sections are impacted within the same validation package as well as company documents such as SOP's.
- Automatic Risk Assessment – the system will automatically generate a risk assessment based on the risk factor established for each requirement documented even for methodologies like FMEA.
- Compliance segregation – not only capable of ensuring compliance with FDA but also with other regulations or policies such as SOX or ISO
- Test Management – provides the user with the ability to assign the development of individual test script to specific people and maintain change/version control over such scripts.
- Test Scripts Reusability – You can use test scripts for future validations instead of creating a new one.
- Configuration management - with Baseline tracking and reporting for Instruments, Equipments and IT Systems maintaining validation status and supporting re-qualification or/and calibration schedules.
- Paperless Execution – the execution of the validation protocols can be performed on line (or on paper). Results are recorded within the system including time stamps of the person who executed each step of the test script. When doing paperless execution, the amount of paper and the time associated with the paper management process is greatly reduced.
- Digital Supporting Documentation – Supporting documentation generated during the validation through digital/electronic means may be attached to the executed protocol.

- Deviation Management – if a step fails during the execution of the test, the system automatically starts a deviation management process linked to a workflow to determine the cause and the remediation to be followed. Severity levels can be assigned to such deviations which will determine the level of information to collect from the deviation event.
- Deviation Warning – If a test has associated deviations, when that test is reused, the system indicates the deviation to allow for proper re-design instead of using the faulty script.
- Reporting tools – Reports can be obtained from these systems.

Validation Management Systems will become a crucial tool for companies looking to maintain a competitive edge by reducing validation costs, delivering on-time validated systems or processes and increase compliance levels.

Benefits

It is clear that VMS will be able deliver their promises, however, many companies are reluctant to implement this kind of tool. They still have a conservative approach that paper based systems are the way to go at least when it comes to validations.

In Puerto Rico, even with the numbers presented earlier, not one company has implemented a Validation Management System, so I do not have specific numbers by how much can costs be reduced with the implementation of a VMS, but during a discussion thread in the 21 CFR Part 11 forum, one of the participants who shared the experience of implementing such kind of system alleged benefits of as much as a 50% reduction in review and approval cycles. Another participant stated that he was impressed with the system's ability to generate complete traceability matrixes on the fly, something that normally takes a lot of time using Word or Excel.

Conclusion

Regulated companies are still second guessing the benefits of a Validation Management System. Not many companies have calculated the real costs of validation beyond hiring consultants/contractors and equipment acquisition. When companies do decide to calculate costs on time spent in approving validation documentation, deviation management, paper costs, and records management; that is when they will really appreciate understand the need to speed up validation. ■

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http://www.pridco.com/english/industry_groups/pharmaceutical/5.10ind_group_ps_pharma.html

² Some Validation Management Systems available in the market:

³ Clarmon's QA Valid (www.clarmon.com)

⁴ Valgenesis (www.valgenesis.com)

⁵ Compliance Associate's Validator (www.complianceassociates.com)

⁶ ThinQ Compliance Manager (www.thinqcompliance.com)