Validation Cost Reduction

Ivan Soto

Editor's Note:
This paper was originally submitted to the Journal of Validation Technology. We offer it to our JGXP readers for application in their quality and compliance organizations. Minimizing the cost of quality is an ongoing challenge in every GXP organization. Quality organizations are under continuing pressure to reduce headcount, lower costs, and increase efficiencies. The concepts proposed in this paper have been proven to be successful in several validation organizations. Its concepts should also have application to quality and compliance functions. The duplicative and inefficient practices cited in this paper are universal problems that must be continually evaluated and minimized whenever possible.

ABSTRACT

Traditional validation processes are not efficient and cost effective. These deficiencies are caused by excessive document reviews and approvals, duplicate roles and responsibilities, inconsistent practices, institutional silos, and other problems. These negatively impact project timelines, increase costs, and cause non-value-added work. Potential approaches to address these problems to reduce costs and increase efficiencies are proposed. Reduction of excessive numbers of personnel who approve validation documents offer potential cost reductions. Careful integration of commissioning and qualification activities eliminates duplication of activities. Implementing standardized and pre-approved forms for repetitive activities provides an alternative to creating protocols. Integrating equipment and automation qualification eliminates duplicative activities. Formalized procedures and assessment tools are efficient and eliminate endless debates, meetings, and discussions. Paperless validation documents have many benefits including global collaboration between sites and corporate teams, integration of traceability matrices with electronic protocols, electronic execution of protocols, real time validation status of any system and metrics, reduced cycle times, reduced errors, and other benefits.

INTRODUCTION

The cost of validation has become an important topic in the pharmaceutical industry in recent years. This is due to concepts introduced in guidance documents such as ASTM E-2500 and GAMP 5. These documents promote a risk based approach including integration and elimination of duplicate validation activities.

It is well know that the traditional validation process is not efficient and cost effective. This paper discusses ideas for reducing the cost of validation. These are intended to eliminate unnecessary duplication and provide efficiency without jeopardizing the intent of the validation.

WHAT IS THE PROBLEM?

The traditional validation process is not efficient and cost effective. The lack of efficiency is driven by a number of factors that include the following:

- Inconsistent practices
- Inconsistent objectives and expectations
- Duplicate roles and responsibilities
- Duplication of effort
- Excessive repetition and rework
- Excessive resource commitments
- Silo organizations and activities
- Excessive reviews and approvals of protocols and other documents
- Unnecessary handoffs.

The above have a negative impact on projects and create schedule delays, increased cost, duplication, and non-value-added work. These issues create delays on product approvals and equipment release for GMP manufacturing. It is critical to understand the inefficiencies of the process in order to reduce cost. Process-mapping is useful to identify the areas of improvement such as unnecessary waste and bottlenecks. The following discusses ideas for efficiency and cost reduction.

DOCUMENT APPROVALS AND NUMBERS OF APPROVERS

Excessive number of personnel required to approve validation documents are a potential cost reduction in the validation process. A traditional validation process typically requires five to ten approvers for each validation document. Approvals sometimes include two quality reviewers and two approvers from each functional area. Document approvals have a cost associated with the cycle time for each approval. Cost is based on the hourly cost of each headcount involved in the review and approval process.

Validation document approvals are a regulatory requirement. Regulations do not specify the required number of approv-

ers. At a minimum, the system owner and Quality Assurance should be represented in the approval group. Additional approvers can be added when they provide value and efficiency to the process. However, they should not exceed four approvers unless circumstances are unusually complex. Quality approvers and reviewers should be limited to one qualified resource with the appropriate skills for each document. Additional approvers are not cost effective. Excessive numbers of approvers sometimes create the issue of non-qualified resources reviewing document that they may not understand. Reducing the validation document approvers provides the following benefits:

- Reduced cycle times
- Faster turnaround
- Cost efficiency
- Reduced numbers of EDM users
- Lower license cost for document approvers.

In summary, reducing the number of validation document approvers provides potential for cost reduction and greater efficiency. Qualified resources provide the most value and efficiency in the process.

INTEGRATING COMMISSIONING AND QUALIFICATION

Careful integration of commissioning and qualification activities offers another opportunity for cost reduction. Duplication of activities is often observed is during commissioning and qualification of new or modified facilities. Activities performed during commissioning are often repeated during qualification. Duplication is sometimes driven by functional siloes and the lack of integration between commissioning and qualification. Commissioning activities that verify installation and functionality of the system can be used as qualification without the need to duplicate this work. Qualification work should be limited to critical items only – there is no need to retest trivial functionality.

The following should be considered to successfully integrate commissioning and qualification:

- Effective change management process
- Defining acceptable good documentation practices
- Defining an appropriate level of quality oversight
- Aligning key skills sets with the appropriate level of responsibilities.

Good engineering practices are needed to support an integrated approach to commissioning and qualification. Integrating these activities can significantly reduce cost and increase efficiency.

PRE-APPROVED VALIDATION FORMS

Implementing standardized and pre-approved validation forms are another potential cost reduction. Utilizing these forms provides an alternative to creating protocols. These may be applied to repetitive activities that do not change. The lifecycle of the forms must be controlled by an SOP that describes the process for creating, reviewing, approving, implementing and executing documents. The forms are pre-approved individually as they are created but do not require additional approvals prior to execution. The form can include several applications that are created from previously created protocols, requirements, functional specifications, and other documents. These are an efficient tool to qualify changes to existing systems.

The following are examples of pre-approved verification forms:

- Security verification
- Recipe parameter verification
- Audit trail verification
- Parameter verification
- P&ID verification
- Loop check verification
- Pump verification
- Alarm/interlock verification
- Valve and miscellaneous equipment verification
- Agitator verification

The implementation of pre-approved forms potentially provides a significant amount of efficiency and cost reduction. The following benefits are realized by implementing pre-approved verification forms:

- Cycle time reduction
- Faster turnaround time
- Only one approval cycle
- Cost reduction: ~ $ 750 per form and $ 5,000 per protocol

INTEGRATED EQUIPMENT AND AUTOMATION VERIFICATION

Another area of opportunity for efficiency is the integration of equipment and automation qualification. Due to the shift of the industry to validate computer systems in the late 1980's, the industry started verifying the equipment and automation as separate systems. These created an environment over the years of excessive duplication of activities. The duplication was driven by the copying and pasting from the automation protocol into the equipment qualification documents. The equipment protocol became an exact duplicate of the automation documentation. This created the issue of not testing the equipment adequately and failing to verify that it meets the intent of the process. The integration of these activities can be accomplished by using installation and functional verification forms that can be used in the automation protocols. Another approach is to leverage the calibration data as equipment verifications; this eliminates the duplicate verification activities that are performed in calibration and the equipment protocols. The benefits of this integration are reduction of capital cost, efficiency, and faster release of systems for GMP manufacturing.

ASSESSMENT TOOLS

Some companies have very informal processes for assessing systems for GxP impact, Part 11, direct and indirect system impact, and system level risk assessments. The lack of formality, procedures, and assessment tools create the perfect environment for inefficiency. This deficiency creates endless debates, meetings, and discussions that sometimes take days or months to resolve and to bring to closure. This all can be avoided with the creation of standardized assessment procedures and tools. A simple procedure that describes how to perform the assessment using standard tools is all that is needed to

make the process more efficient. Standard tools should be created using regulations, industry guidances, and best practices. The standard tools are intended to provide objectivity and consistency on the results.

The following are example of standard tools that can be created:

- GxP Assessment
- Part 11 Assessment
- System Level Risk Assessment
- System Impact – Direct or Indirect.

Assessment tool should have the following attributes to provide efficiency

- Short (cycle time – hours vs. days)
- Simple (5 pages or less).

The benefit of implementing these tools is efficiency, cycle time reduction, and elimination of endless debates and meetings.

PAPERLESS VALIDATION

One of the major drivers of cost for validation is paper-based manual documentation and execution. Paper-based validation documents create a significant amount of inefficiencies related to the creation, issuance, and control of validation documents. In some companies, the validation team dedicates a significant amount of their time performing document management tasks instead of executing validation activities. Paperless validation systems provide the following benefits:

- Eliminates paper validation documentation and system specifications
- Integrates electronic deviations to protocols
- Enables global collaboration between sites and corporate teams
- Integrates the creation of traceability matrices with electronic protocols
- Enables electronic execution of protocols
- Electronic review and approval of protocols and system specifications
- Automates and manages the validation life cycle
- Provides real time validation status of any system and metrics
- Expedites the validation process and removes the inefficiencies that plague paper-based processes
- Provides a holistic view of project status and validation deliverables for internal and external auditors, with real time status
- Significant cycle time reduction
- Significant error reduction
- Enables faster release of equipment to support GMP operations
- Return of investment of less than 12 months

Paperless validation technology is emerging as an efficient solution to the cumbersome and time-consuming paper-based validation processes. Several implementations have been successfully completed in the industry. This is a cost effective solution to manage the increased demands of the business without adding a significant amount of headcount.

SUMMARY

The validation process can be more efficient and cost effective. Opportunities for efficiency can be found in all traditional validation processes. Efficiency improvements such as reducing the document approvers, implementing assessment tools, and paperless validation reduce cycle times, minimize costs, and increase efficiency. All improvements require a concurrent assessment to ensure that there is no unexpected negative impact associated with their implementation.

About the Author

Ivan Soto is the Associate Director of Quality Validation at Alexion Pharmaceuticals. His team provides QA Validation oversight and strategy for all validation activities at the Rhode Island manufacturing facility.