Best Practices in Electronic Submission Management

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INTRODUCTION

The assumptions that guide the way industry approaches electronic submission management are changing. The common vocabulary of submission management is evolving and business processes are being redefined. Initiatives are underway to meet new submission management goals once thought impractical, or even impossible just a few years ago.

Driven by the onset of electronic submissions (eSUBs), the emerging needs of the electronic Common Technical Document (eCTD), and the goal of global simultaneous submissions, the practitioners of the art of submission management are realizing through painful experience that new approaches are needed to meet the goals of their organizations.

Since organizations began a more widespread adoption of eSUBs under the common standards set forth by the FDA in 1999, submission managers have looked to adapt paper-based publishing processes to meet the needs of electronic submissions. Inevitably, these managers learn some painful lessons. The first is that electronic submissions are not the digital equivalent of a paper submission. The second is that to produce submissions successfully, one has to focus on more than how to produce a PDF rendition intelligently.

There are larger issues at stake for submission managers. They must strive to overcome an organization's tendency to work within functional silos. They need to collect and analyze data related to their on-going submission process in order to manage resource needs. They face the challenge of identifying and working through issues. Above all, they must maintain a high degree of accountability for the work performed on the submission.

FUNCTIONAL ISOLATIONISM

Most organizations operate as a collection of functional areas loosely coupled together from a process perspective. Operationally, a project manager may have the responsibility of coordinating efforts between the team members or functional area representatives. However, this does not equate to an integrated approach. Each functional area operates under its own standard operating procedures (SOPs). Each defines standards, deliverables, and successful outcomes based on their own perspectives. These perspectives usually do not account for the needs of other functional areas. In fact, the resulting processes based on this single purpose viewpoint results in the output of one process being sub-optimal, or incompatible, as the input to other dependent processes. Additionally, the tendency of functional areas to operate within silos runs contrary to collaborative methods needed to produce a high quality submission. The impact of functional isolationism can be substantial. The impacts of functional isolationism may account for as much as forty percent of the time compiling a submission.

There are numerous examples of where functional isolationism hurts an organization. Consider the selection of an EDC solution. Clinical Operations recognizes the systems ability to streamline data cleaning. Unfortunately, it is discovered at submission time that its electronic case report forms are not submission ready, requiring extensive rework on hundreds or even thousands of documents. Another common example of functional isolationism relates to the presentation of data. While the clinical functional area may consider a project complete once data listings and tables have been generated for a report, the needs of the future submission are often left unsatisfied. Datasets that are often archived are not compatible with the standards for an electronic submission. Data definition files, required by the Agency to interpret the data, are not produced. Typically, these will

not be produced until late in the submission compilation process. By that time, it is often very difficult to generate them. Contracts with development partners may have expired, or subject matter experts with the historical background of the project may have departed the organization. Therefore, the same deliverable becomes twice as difficult and twice as expensive to produce than if it had been produced earlier.

Overcoming an organization's tendency to work in silos is challenging. It requires a change in process and a change in culture. In order to adopt a truly integrated approach, the organization must model and work from processes built with a cross-functional perspective. Accomplishing this objective requires several fundamental steps. It requires that the scope of the process definition cover all activities required by the stake holders to develop a drug. It further requires that the specifications for deliverables meet the strategic needs of the organization, and not just those of a single business unit. The resulting SOPs govern an overall *electronic research and development* process. This approach encourages the stakeholders to leverage the strengths of each department during the process. It also minimizes potential rework scenarios and leverages the strengths of each functional area resulting in a more collaborative process.

PROCESS OWNER

For the organization's new *electronic research and development* SOPs to be successful, they will require a process owner to overcome the cultural challenges, and facilitate the process across functional area boundaries. The process owner has several vital characteristics. The individual understands the continuum of drug development. They recognize that the desired end-state of the process is not the completion of an individual trial, or even just the filing date, but rather marketing approval. They understand the needs of each functional area and what each one needs to be successful. The process owner facilitates and coordinates exchanges across functional area boundaries. They further support upfront planning as well as cope with inevitable changes.

Functional isolationism greatly impacts an organization's ability to achieve their goals of producing electronic submissions that will benefit the regulatory authority, as well as the sponsor organization. Process Owners facilitating a high-level, cross-functional, drug development process can break organizations out of their silos.

PROCESS CONTROL

Organizations are under increasing internal pressure to take greater control of their processes. The ability to manage the process in real time significantly enhances an organization's ability to manage its deliverables. As data moves through an organization (for example captured in an EDC system, then cleaned by data managers, analyzed by statisticians and report writers and formatted for electronic submission), the price tag associated with the data increases as each resource touches it. This means that there is an intrinsic value in managing these critical and costly assets, not only to reap the rewards of faster approval times but also to minimize risk of losing information that costs so much to produce. Managers now require solutions that facilitate the marshalling of content towards a compiled submission. They must operate along project timelines that may span months to years as opposed to days and weeks. Currently, many submission managers are attempting to shepherd the hundreds to thousands of unique components with the limited tools they have today. It is a complex process to coordinate, especially when conducted with multiple development partners across widespread geographic locations. Managers face

constraints on resources, time, and often, visibility on how the process is being executed. Often, problems or bottlenecks are identified too late to avoid a crisis. Iterative project management meetings provide limited, and often shallow views of the complex collection of related workflows that must be executed. The tools managers have available today such as Microsoft Excel or Project are inadequate to the task of managing submissions due to the volume, complexity and level of details required to support submission development.. Managers should begin to evaluate business process management solutions that will help them take control of their processes.

Through implementing a Process Management Solution, those responsible for delivering electronic submissions are provided considerably greater awareness of their current progress, risks, bottlenecks, and production rates. Managers are thereby enabled with the tools they need to proactively manage their submissions, rather than reacting to each crisis point along the way.

PROCESS ANALYTICS

Planning an on-going submission is an enormous challenge. It is characterized by the plight of submission managers who often must set expectations for senior managers based on incomplete information. For example, submission managers are routinely called on to determine the level of effort required to compile a submission, even as the content plan is changing, incomplete, or entirely absent. Even if a content plan is accessible, there is usually very little hard data available to generate estimates. Moreover, the plan will likely change frequently during the course of the project making maintenance of the plan a full time occupation.

The key to scheduling and planning submission development activities relies heavily on the availability of process metrics. Accurate process metrics are difficult to obtain manually, especially during peak periods of activity. Therefore, organizations should look to unobtrusive methods of gaining these metrics. Their solution should capture metrics behind the scenes and make the data available for real-time analysis. Process analytics then allow managers to leverage this data to improve process performance and measure whether current processes are supporting key business goals.

In a successful scenario, a manager given a content plan describing factors such as the number of studies, submission patients, and other content items, should be able to provide a reasonable estimate of the time required to complete anticipated publishing tasks. As an organization's body of metrics builds, additional specifications can be built into the production rates. For example, the time required to bookmark an image-based document varies significantly from a text-based document. The type of content and expected method of operating on that content also play a role in planning.

Production metrics that serve as benchmarks for the execution of publishing processes provide managers a powerful tool to monitor the on-going progress of their projects. Solutions that incorporate benchmarks into their workflow support a manager's ability to adjust to the changes in the plan without an enormous manual effort calculating the effects.

RESOURCE MANAGEMENT

Managers have difficult choices with regard to aligning their resources to meet their business needs. Headcount is often static, but submission compilation workloads are characterized in many organizations by an ebb and flow. Teams are overwhelmed at one

point, and looking for work the next. Senior managers are less inclined to offset the painful peak times by introducing additional headcount while the less active periods persist. Managers are faced with making predictions on when the peaks will hit in a timeline in order to ensure they have additional support as required. The level of support is often just as great a question as when they will require it.

Managers can address this issue by utilizing business process solutions that provide the necessary foresight to determine where the peaks and valleys in activity will occur via scheduling functionality. This enables "just-in-time" staffing plans that senior managers are more ready to support. Managers are able to identify the types of tasks and roles necessary to meet a quantifiable need. They may then use this quantifiable data to articulate to senior management the need to supplement staff via outsourcing for critical periods. Over time, staffing data and utilization rates can support the determination of an optimal level of staffing.

PROCESS INTELLIGENCE

Submission managers are usually at a disadvantage when they must react to change. Often they must determine the impacts of a delayed study, late deliverable, or a deviation from the expected specification of a deliverable. When change occurs, managers are faced with the challenge of assessing the impact and determining what actions are required to manage that change.

Managers must utilize solutions that will enable them to assess the effects that a change has on the overall project. Beyond tools such as Microsoft Project, business solutions exist that will leverage process metrics and scheduling data to provide managers with immediate feedback on the impact of a change. Most importantly, these solutions permit the manager to play out the "what-if" scenarios to determine a prudent course of action.

For example, an ISS fails a quality assurance check resulting in a push back of the expected delivery date to the submission compilation team. The project is in the late stages of the submission compilation process. An effective business process management solution provides that manager with a determination of the impact the change has on the overall project based on current assumptions. In this example, the submission manager determines that the change has a two day impact on the submission timeline. The submission manager however, examines how changes in resource levels can match the workload with the available time. Once realized, the submission manager is able to report that they have adjusted their plan to meet the needs of the change in plan.

FULL CYCLE ISSUE TRACKING

Those individuals compiling submissions are in a unique position to identify inconsistencies, discrepancies, and omissions in a submission that can result in serious consequences during the regulatory authority's review. Organizations often do not capitalize on this opportunity, instead leaving submission personnel to do little more than "operate the machinery." Organizations that take advantage of this additional perspective may encourage the collection of issues, but lack an effective methodology for handling them.

Current methodologies for issue identification and resolution are diverse. They range from attaching sticky notes to monitors, to ad hoc emails, to creating running lists that are discussed at project management meetings. Each of these methods is suboptimal for a

several reasons. First, as common as sticky notes are, they should never be observed to being part of, or having an impact on a regulated process. They are easily lost or discarded, and provide no means of ensuring the issue is resolved. Emails have the benefit of being immediate, and can be effective. However, it becomes difficult to assemble any audit trail of the changes that were implemented based on them. Discussing issues at a project meeting provides for a dialogue, but introduces the bottleneck associated with setting up the meeting, or waiting for the next regularly scheduled meeting to occur.

Submission managers should drive their organizations to formalize their process for identifying and resolving issues. This process should provide the organization the capability to electronically identify issues, route them to the appropriate point of contact, determine a resolution, and implement the resolution. The process should standardize the acceptable time allowed for responding to assigned issues. Visibility on the entire process should be accessible by quality assurance representatives. On demand, reports that provide the current status of all issues should be available.

ACCOUNTABILITY

The submission compilation team is usually the last group to touch the submission. There is an implied, if not direct responsibility that the submission manager inherits by the fact that they are the last to work on any submission component. For example, datasets are delivered to the submission team immediately before filing to replace the existing datasets. The change is never documented. Following the submission, someone realizes that the wrong datasets were included in the submission. One of the first people contacted for an explanation will likely be the submission manager.

Submission managers must retain the confidence of the teams they support in order to maintain their effectiveness in the organization. To achieve this, a submission manager must be able to account for every piece of content that is destined for a submission from the time that it enters their control, until it is delivered to the regulatory authority. This accountability must also provide details of every processing step that occurred to that content. A time-stamped, auditable log of the decisions, actions, and most importantly, changes in the submission must be available to the manager.

CONCLUSION

The process of submission management may be viewed as an exercise in choreographing the people and events from across the enterprise towards the common goal of preparing the organization's case for market approval by a regulatory authority. All of the critical paths lead to the submission manager's doorstep. With inflexible deadlines before them, managers continue to require the capability to manage their projects more effectively. Beyond the basic mechanics of publishing lay significant challenges that effective submission managers must deal with. Breaking through functional barriers, maintaining a high degree of awareness of current and future obstacles, aligning resources to meet the needs of a dynamic situation, while always maintaining quality and accountability are the challenges that must be overcome to be successful.

