

Authoring Practices for Submission Documents

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Authoring of submission documents is not an easy task. It has become a more complex task as new submission standards and supporting electronic processes have emerged. Changes in submission requirements and formats have left many authors trying to discern what good authoring practices really are.

With so many variables affecting the process, it is important to start with the basics to ensure that your submission documents are created with minimal pain and maximum efficiency. There are several basic principles at the core of submission document authoring. If you develop your authoring practices with these principles in mind, the individual task of submission authoring will be improved but subsequent tasks such as electronic publishing and review will also be facilitated. In this manner, a ripple effect may occur through your organization whereby good authoring practices will enable automation of publishing tasks, quality checks and reviews.

1. Understand the submission model

It is important to have a clear understanding of what submission model your organization will use. There are multiple submission formats that are currently being accepted by global regulatory agencies. Two of the more common formats in the U.S. include submitting electronically in a hybrid format (CTD content in eNDA folder structures) or submitting in eCTD (electronic Common Technical Document) format.

There are pros and cons to submitting in either format. It is important to note that whatever format you choose, you must understand how it impacts authoring processes. For example, the eCTD format requires that documentation be presented in a "granular" format. This means that content is broken into more, smaller documents throughout the submission. Drug substance and drug product are good examples of documents that had historically been submitted as single documents and now are submitted in multiple files to support the necessary granularity. As authors begin to create documents and distribute for review, it may be necessary to make other relevant documents available to internal reviewers so they can understand the content in the context of the larger submission. This requirement may change internal review and approval processes. Adding complexity, if one of the granular documents is later modified or updated in some way, internal reviewers must again see it in the context of the larger submission. This scenario illustrates how individual document lifecycles begin to converge and highlights dependencies between documents and the need to understand the details of the submission model that you will be using.

2. Employ authoring standards

Once you understand the submission model, it is important to employ appropriate authoring standards across the organization. Since many authors from multiple disciplines will contribute to the submission, it is important to train all contributors on submission document standards. The most important standard with the greatest impact on the process is the utilization of some type of authoring template. Templates can automate commonly used tasks for authors such as inserting landscape pages or applying heading styles. Some templates provide content assistance based on agency regulations and guidances as well as company-specific boilerplate text. Templates are most frequently used to allow authors to focus on developing content, rather than format of a document. By providing predefined styles, templates also facilitate electronic publishing tasks. As heading styles in a document are rendered to PDF (Portable Document Format), those styles can be automatically translated into bookmarks that are used for navigation of the final submission document. This automatic translation of navigational information can save a great deal of time and manual effort in the electronic publishing step.

As the organization develops standards, a guidance interpretation will also assist authors to develop content in a consistent format. A guidance interpretation is a document that records the organization's accepted understanding of regulatory guidance requirements. It provides a common foundation for all contributors and combined with other authoring standards, facilitates consistent formatting and content development.

Consider additional internal standards as you develop your authoring capabilities. Documented reference strategies and style guides provide additional consistency across authors, documents and functional areas. These types of standards enable automation of other tasks, provide a degree of consistency across the regulatory application and facilitate QA/QC procedures.

Before cross-functional resources begin to generate submission documentation, it is also important to agree on one specific term: "*eSub ready*". This term means different things to different people. As an organization, you must define this term very clearly so that you can limit the amount of rework that is needed once a submission document is finalized. Once you agree on a definition, the requirements should be incorporated into your other authoring standards.

3. Design appropriate QA/QC procedures

As submission models evolve, QA/QC procedures must also change. The content of submission documents is outlined in regulations and guidances. As these guidances are updated, content and format requirements may shift. These changes have a direct impact on the design of quality procedures.

For example, consistency checks across documents may require finalization of dependent documents prior to completing a thorough quality checking process.

When defining document-specific roles, a "technical" resource should be assigned to monitor document formatting. A printed document may look well formatted but if a user did not apply heading styles properly, electronic publishing tasks will be more complex and navigation of the final submission document will be affected. These types of errors can be reduced through adequate training and awareness of the larger submission process.

Submission models also affect what should be checked in a QA/QC process. The eCTD submission model includes documents, data and metadata. The metadata is a new component to the submission. It is located in an XML (eXtensible Mark up Language) file and includes information about each individual component of the submission. Traditionally, this information was strictly used for internal search and retrieval purposes. But as part of the formal submission, it must now be included in quality checking procedures. Depending on your authoring environment, you must determine when and how this information should be confirmed.

4. Define and control access

When developing good authoring practices, it is important to control access to submission documents throughout their lifecycle. Pharmaceutical and biotechnology organizations have implemented various electronic document management systems (eDMS) to manage access to documents and provide other functionality such as version control. Whether you have an eDMS or are implementing control through procedural methods, it is important to recognize how quickly errors can be introduced into a document when someone incorrectly updates a file or inadvertently updates the wrong version of a file. If you have experienced this scenario, you can understand how one document, one author and a reviewer can very

quickly get mired in confusion trying to figure out which version of a document should be used in a final submission.

It is also important to identify who owns a document, who contributes to the development of a document, who reviews the document and who approves it. These roles will vary depending on the type of document and the internal expertise required to finalize content. However, access to the document can be codified through these roles and incorporated into an eDMS or procedural methodology. Role-based access rules can be used to determine what level of access (read, write) an individual has to any document.

Access to final documents (ready for submission or previously submitted) should be carefully limited. At most, "read-only" access is usually appropriate, depending on the user and their role on the team.

5. Document the process

As solid authoring processes evolve, documentation of the process becomes essential. This documentation is typically a combination of SOPs (Standard Operating Procedures) and Work Practice documents. This is important from a consistency perspective but it is also a huge asset from a training perspective. New employees, partners or contractors should be trained on the processes and associated authoring standards to minimize rework and redundancies. In fact, authoring standards should be included in any discussion with external medical writers. As you implement standards internally, you can also enforce use of those standards externally by including them as requirements in contracts.

Documented processes also help to set expectations across functional areas. Often, submission authors never see the final compiled submission. They may not appreciate the importance of good authoring practices and standards and how they impact publishing and reuse of documents throughout the organization.

6. Train the organization

Good authoring processes evolve over time. However, in order for standards and processes to remain scalable and sustainable, the organization must develop a solid training program. Global standards have a tendency to morph over time and eventually aren't global or standard if they are not conveyed consistently to cross-functional teams. This usually requires a formal program that is reinforced through refresher training and updated training sessions as standards and processes evolve.