Implementing eCTD Through Outsourcing

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Background

The FDA has mandated that all regulatory submissions be in the eCTD format in the near future. For small bio-pharmaceutical companies, the fastest and most efficient way to transition from paper-based submissions to eCTD submissions is outsourcing. In as much time as it takes to select a new vendor and sign the contract, companies can say goodbye to boxing up press-board binders and say hello to eCTD. Although making the decision to switch really is this easy, companies still need to develop a submission and document management strategy that will address both short-term and long-term goals. The business should evaluate options for eCTD outsourcing, implementing eCTD submission capability in-house, and solutions for electronic document management.

Transitioning to eCTD inevitably requires change. To plan the transition, you must determine your short and long-term objectives, how document control will be handled, and what process changes are needed.

Submission Goals: Short-term vs. Long-term

A good example of a short-term business goal to transition to eCTD format is starting with an original IND submission. Starting to submit in eCTD format with the original IND submission will maximize the benefits of the eCTD format and lifecycle throughout the development phases of the project. If the business decides to use this short-term goal as the opportunity to start submitting in eCTD format, then eCTD outsourcing makes a lot of sense. The decision to go eCTD can be made in as little as 12 weeks before the submission is scheduled to go out the door (or later, though it may not be fun). The business can focus on implementing process changes that impact submission contributors in the short-term, and leave the larger task of implementing eCTD software and building a department of regulatory operations staff to be addressed as pending long-term business goals.

In the long-term, the business will need to evaluate if the investment in eCTD infrastructure, which includes software, hardware, and personnel in IT, QA, and regulatory operations is aligned with the direction of the company. eCTD applications provided through a Software as a Service (SaaS) model should also be evaluated as a potential solution to bring the capability in-house without large capital expense and minimal impact on IT and QA personnel. If there are multiple products in the pipeline and at least one marketing application planned within the next two years, then it's a good time to start evaluating and potentially implementing an option to support generating eCTDs in-house.

The long-term evaluation should also consider the total volume of submissions. The business can compare the expense of eCTD outsourcing over two or three years versus the expense of acquiring eCTD infrastructure to see which solution has the lowest total cost of ownership and financial impact on the company. When doing these analyses, one important thing to keep in mind is realistically predicting the personnel requirements to do submissions in-house. The business will need to figure out how to manage workload peaks and valleys juxtaposed to finding (and hiring) talented, experienced, and available personnel to both maintain the infrastructure and publish eCTD submissions. The business may also explore a hybrid solution that combines outsourcing and generating submissions in-house. For example, a company may choose to outsource original IND, NDA, or BLA submissions, and submit all serial sequences utilizing in-house infrastructure and resources.

Document Management

Electronic submissions require a sound document management system to facilitate both version control and electronic review, approval, and archival of files. Businesses that have not made an investment in an electronic document management system (EDMS) and are focused on achieving the short-term goal of submitting in eCTD format do not necessarily need to invest in an EDMS right away. If the decision is made to wait on investing in an EDMS, strict manual processes and permissions need to be put in place to ensure integrity and control over final versions of documents, files, and the folder structure. Authors and reviewers must follow manual processes for document drafting and reviewing.

In the long-term, more complex document management systems should be evaluated to determine if, and when, it makes sense for the business to make such an investment in infrastructure, and which system most closely meets the business' user requirements. Implementing document management systems can take anywhere from six months to two years depending on the level of customization required and the complexity of the deployment itself. Even for a small implementation with little-to-no customization, document management systems usually require at least one full-time dedicated administrator to maintain the system over time.

Although there are benefits to implementing an EDMS prior to submitting in eCTD format, there is no real risk in starting to submit in eCTD format without having an EDMS in place. The business may choose to start submitting in eCTD format through outsourcing to achieve a short-term goal, and evaluate the various EDMS options as part of determining the business' long-term submission and document management strategy.

Business Processes

Once the decision is made to submit in eCTD format, there are three main business process changes to implement.

Business Process Change #1: Track, Plan, and Deliver.

The goal of tracking and planning submissions is to ensure submissions are sent on or before the company's target date. Regulatory will need to deploy a system for submission tracking to identify each component intended for submission, the due date for each piece, the content owner, and the overall submission due date. The tracker should be maintained as a live document and updated regularly to keep a clear vision of submission priorities.

Assembling eCTD submissions requires more processing time than assembling paper submissions. Companies can still meet aggressive target submission dates if documents are provided for eCTD processing on a rolling basis. Plan to finalize and approve documents based on when the data is available as opposed to working backwards from the target submission date. Once documents are approved, they should be sent for eCTD processing. The fewer files left for processing nearing the target submission date, the faster eCTD compilation activities will be completed, and the probability of hitting the company's target date (or beating it) will increase dramatically.

Business Process Change #2: Define the term "submission-ready."

The term "submission-ready" should be defined as a complete, data quality controlled (QC'd), content-approved, properly formatted, text-based document that has been rendered to PDF. Submission-ready documents should also adhere to eCTD granularity requirements.

Generating submission-ready PDFs starts with high-quality Word documents. Companies should use a standardized set of content templates correctly to get to this end. Templates will guide authors to generate documents to meet content and granularity requirements, as well as be technically sound for publishing (generating bookmarks and hyperlinks). Consistent use of Word styles and accurate cross-referencing techniques are essential for generating submission-ready documents.

Legacy reports often require custom tailored PDF-level processing. Clinical and non-clinical reports generated from long-ago and far-away origins will require more intensive processing than files initiated in content templates. The key is consistency. All files, regardless of their origin, should have the same level and style of publishing standards (no compromise).

Business Process Change #3: eCTD Review, Publishing QC, and Validation prior to submission.

After all submission-ready files have been transferred and fully processed, the business should perform a quality review of the eCTD prior to submission. The quality review should consist of the business ensuring all documents are present, any version updates to content have been incorporated, and the publishing is adequate and correct. Leaf titles should also be reviewed to ensure they are descriptive and take into account the eCTD lifecycle implications over time. Lastly, the complete submission should be validated ensuring a clean technical validation report and technical acceptance upon receipt at FDA.

Conclusion

Cliché as it may be, change is certain. The question is not "will we start submitting in eCTD format," but when and how will we do it? The transition to eCTD involves many changes that will inevitably affect many people within your organization, particularly those in the business units within drug development

The three business process changes discussed above need to occur regardless of whether eCTD submissions are outsourced or published and submitted in-house. These changes enable the company to transition from paper to eCTD format as well as improve the overall quality of submission documents. Improved quality and submitting in eCTD format should lead to more efficient reviews and more effective interactions with the Agency throughout the development and marketing lifecycle for the business' products.

Lastly, outsourcing eCTDs is always available as an option, and can either replace or compliment the business' ability to submit eCTDs in-house. Outsourcing is a great way to transition from paper to eCTD format since it allows for the business to gradually implement systems and process changes needed to support long-term goals associated with developing multiple products and submitting marketing applications. Outsourcing as the single solution also allows the business to gain experience in generating submission-ready documents and submitting and reviewing eCTD applications. Outsourcing as a complimentary solution allows the business to leverage internal staff and infrastructure for maintaining INDs and NDAs, and manage workload peaks associated with large original marketing applications with a reliable and knowledgeable service provider.

The bottom line is that at some point (sooner v. later) you will be making the switch to eCTD. The transition to eCTD involves many choices that will inevitably affect many people within the organization. Transitions can be difficult, but experienced partners, such as Synchrogenix, can help fill the knowledge gaps and share industry best practices, while also helping you achieve submission success simply, quickly, and cost-effectively.

Beyond eCTD Publishing

While finding the right eCTD Publishing vendor provides tremendous value to an organization short on internal resources, pairing with a vendor that can offer extensive Regulatory Strategy, Regulatory Affairs, Regulatory and Medical Writing experience brings numerous synergies. The understanding that a vendor can be well versed in a program and quickly provide services as needed across a multitude of potential needs can provide higher quality submissions at expedited speeds, all while accommodating the numerous curveballs that will inevitably be thrown your way.

Want to know more?

For more information on the regulatory and communications strategy, science, and services available through Synchrogenix, please contact us at contactus@synchrogenix.com or call 302-892-4800. A schedule of upcoming product demonstrations is available at www.globalsubmit.com/events/

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