



OPTIMIZING REGULATORY SUBMISSION PROCESSING TO
INCREASE REVENUE THROUGH IMPROVED SPEED-TO-MARKET

The Evolution of Regulatory Publishing Through Submission-Ready PDFs

By Scott Mackey

In the life sciences industry, time lost in the preparation of regulatory submissions represents money lost that will never be recovered. While the clock ticks down on patent protections, the tasks of formatting, organizing and performing quality control activities on huge volumes of documentation are consuming millions of dollars in profits.

The importance of submission preparation has never been more critical. With the U.S. Food and Drug Administration (FDA) and regulatory agencies around the world pressing forward requirements for electronic submission, the old days of preparing truckloads of paper documentation should soon be all but over. The efficiencies offered by electronic filings would seem to be a boon to all involved.

However, gaining these efficiencies can be a challenge. Most firms have established business and technology systems that are not designed to support the streamlined production that electronic submission makes possible. Standing in the way are information silos, heterogeneous systems creating source materials in various formats, the varying and stringent requirements of governing agencies, and the time and cost involved in major system overhauls.

However, there are good reasons to overcome these obstacles. Even beyond the competitive advantages and revenue gains of faster speed-to-market, the business advantages of standardized electronic formats and electronic delivery promise huge benefits for the entire enterprise. The benefits include the following:

- Improved document access across the enterprise
- Reduced work and costs through process efficiency
- Greater control over enterprise standards of document formatting
- Better service to internal and external customers

In fact, when the full range of benefits is considered, the only real obstacles could be the cost and disruption involved in streamlining the operational workflow to produce submission-ready documents more effectively. If those obstacles were overcome, huge advantages could be gained across the enterprise.

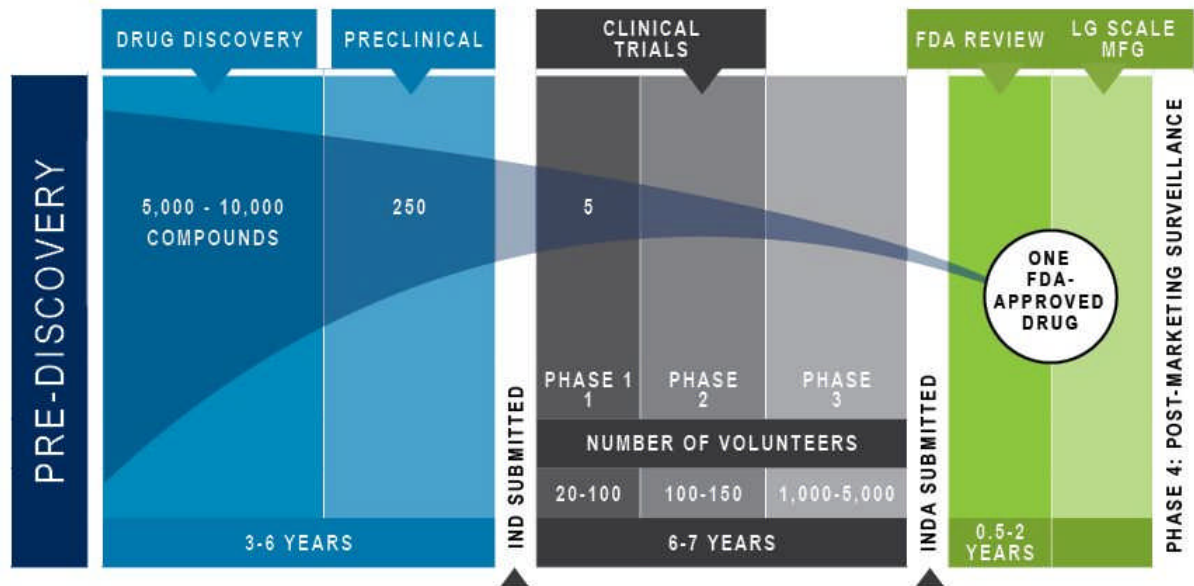
This white paper will explore the business and operational challenges facing life sciences firms in expediting the submissions process, offer an operational framework for radical reductions in submission costs and duration, and introduce Adlib Express as a uniquely attractive solution for firms facing these challenges.

Background

Few industries face record-keeping hurdles of the complexity and stringency faced by the life sciences industry. The need to confirm and document the safety and efficacy of a new product, the potential threats of litigation if problems arise after a product is launched, and the documentation requirements of the regulatory agencies add up to a perfect storm of record-keeping demands throughout the lifecycle of a product. This document lifecycle extends from the earliest stages of research and development to decades after the product is no longer marketed.

The weight of this task can be measured in the sheer volume of documentation required in regulatory submissions for new product approvals. Documentation for a single research study can be tens of

thousands of pages with a full submission typically including multiple study results. Though cutting edge research is conducted using the latest technology, often the key results are compiled and maintained on unconnected MS Word documents, image files and even handwritten notes. Extend this complexity over multiple regulatory jurisdictions, different languages, patent laws, joint ventures, subcontracted and outsourced research, and it is no surprise that paper submissions were often delivered by the truckload.



REGULATORY SUBMISSIONS CONTINUE THROUGH THE LIFE CYCLE OF A PRODUCT, INCLUDING SURVEILLANCE AND RECORDKEEPING FOR DECADES AFTER THE PRODUCT IS NO LONGER MARKETED.

SOURCE: PHRMA

It is also not surprising that the transition from paper to electronic documentation has been spearheaded by the regulatory agencies. The US Food and Drug Administration (FDA), has been piloting increasingly sophisticated and standardized approaches to electronic submissions since the late 1980s. Early efforts focused on the delivery of word processing documents with hyperlinks to supporting data. These files were generated on proprietary systems that often required delivery of hardware and software to the FDA, as well as training of reviewers to enable them to read the submission. While this may have eliminated the truckloads of paper, it both increased costs and slowed delivery of submissions for sponsor firms.

The introduction of the Adobe Systems' Portable Document Format standard (PDF) in the early 1990s revolutionized document creation, submission preparation and electronic transmission, offering a standard based on commercial software that was portable, readable without major software investments, customizable to agency standards and easily transmitted electronically. Around the globe the move to eCTD (electronic common technical documents), an XML-based structure for high-quality PDF documents, is underway. The percentage of pharmaceutical companies still using paper submissions is gradually falling.

While the logic of providing standardized electronic documents submitted through agency portals seems obvious, the preparation of these finished documents still presents many of the same challenges faced in the paper era. Organizing and formatting documents to meet agency standards continues to be a daunting task, and given the risk of submission rejections from the agency because of formatting failures, a task with zero-tolerance for errors.

The Submission Challenge

With the patent clock running, many firms still face the challenges of physically locating and organizing files, manually converting them to submission-standard format using desktop software, editing, quality-checking and revising them to conform to detailed agency standards, and cycling back through the formatting and editing process whenever additions or changes are made. This is a highly iterative process that is critical to successful submissions.

With documents originating from many sources, including disparate third-party firms handling research segments, many of the documents that make up the submission need to be manually reworked into consistent formats. During conversion to PDF, inadequate rendering solutions cannot honor the structure of the source files, thus creating imperfect renditions with problems, such as the loss of key navigation information. Unless these errors are caught during the QA process, they can create delays or even returns during FDA reviews. Not surprisingly this QA work is time-consuming, prone to error and very expensive.

The requirements for eCTD-compliant submissions are unique and must be applied to documents that are constantly evolving. As an Investigational New Drug Application (IND) or New Drug Application (NDA) submission is prepared, the incorporated documents are continuously under review, endlessly annotated and changing through internal and external improvements. These improvements increase the risk of corrupting the submission, creating errors in post-production re-rendering.

In sum, the competing stresses of time pressure and the need for total accuracy create expensive burdens on systems and human resources. Enterprise Content Management applications, eCTD software and other information management tools all provide benefits that are designed to better manage information and streamline document workflows. As much as these applications assist companies in dealing with the basic challenges of document management, there are critical requirements in the preparation of regulatory submission documents that these general applications fail to automate – specifically the automated rendering of creation of PDFs that comply with the detailed formatting standards required by the regulatory agencies.

An Ideal Solution Framework

The solution to this costly and time-consuming activity requires a means to streamline document workflows without disrupting existing processes. Such a solution would ideally be simple to integrate into current applications and platforms. Additionally, it would be low maintenance and priced at a level that would produce extremely rapid return on investment.

On a business level, the fundamental characteristics of this solution would be the following:

- Reduced time and cost associated with organizing and formatting of submission documents
- Automatic compliance with enterprise document format standards, while also enabling job controls for custom formatting and rendering
- Enhanced satisfaction for users and customers (internal and external) of the document production

The straightest path to these outcomes is a server-based PDF rendering solution that operates in the background, automatically creating renditions of all documents in submission-ready formats as they are created or received from outside parties. The solution would archive these PDF documents in submission directories from which they could easily be gathered and aggregated. Crucial to this ideal solution would be the ability to produce the precise formatting requirements of the regulatory agencies. In the case of

FDA submissions, these details include tables of contents, with functional bookmarks and accurate hyperlinks that match FDA standards. The documents could also be secure and locked against changes, except for those users authorized to access them or create new versions. Elements such as watermarks or time stamps could enhance document identification and controls.

The key benefit of this automated submission-ready rendering solution would be improved speed-to-market as a result of a quantum decrease in the time required for reworking documents and quality assurance. In addition, it would guarantee that additions or changes to the submission documents would be automatically converted using the same standards, ensuring that the rendering integrity survives through ongoing versions of the documents.

Additional benefits would be found at both the enterprise and user level. Desktop users, freed from responsibility to know or execute the finer points of submission PDF formatting, would be able to concentrate on knowledge work, rather than technical details. Depending on how the solution is implemented, the benefits could extend far beyond submissions processing, making documents from a variety of locations, sources and originating software tools easily accessible across the enterprise.

From a financial perspective, this solution would pay for itself in months or even weeks, depending on the amount of time eliminated from the QA processes and the resulting acceleration of the entire submission preparation process. With all relevant documents rendered to exact agency requirements, both the organizational and quality control tasks are dramatically reduced. The new product submission goes through the regulatory review process successfully and market launches are made that much faster.

The Real-World Solution

NUMBER OF DOCUMENTS PER WEEK	HOURS SAVED PER WEEK	COST SAVINGS PER WEEK (BASES ON \$60/HR)	COST SAVINGS PER YEAR
100	183	\$ 11,000	\$ 572,000
500	917	\$ 55,000	\$ 2,860,000
1000	1833	\$ 110,000	\$ 5,720,000
1500	2750	\$ 165,000	\$ 8,580,000

Today Adlib Express is the de facto standard for document rendering solutions in the life sciences industry. Dramatically simplifying and accelerating document rendering to submission-ready PDF format, as well as a variety of other formats such as PDF/A, TIFF and HTML, Adlib Express offers a full range of features to meet the requirements of local and global regulatory submissions. A server-based solution, Adlib Express can be deployed in a matter of hours, integrating with applications and automating workflows to capture documents of any type and transform them into quality PDF formats for submissions, archiving, text search, aggregation and publishing. Its extensive options for submissions include the following:

- Linked tables of contents, hyperlinks and bookmarks to meet any format standard
- Controls to ensure consistent results from

- inconsistent source documents
- Headers, footers, time stamps and watermarks for identification and security
- Forms support for progressive processes, such as electronic signatures
- High-quality optical character recognition for scanned documents

Designed to render submission-ready PDFs with stringent adherence to agency standards, Adlib Express reduces QA and manual correction to a fraction of the time required by any other document transformation solutions. Adlib customers in the life sciences industries have saved millions of dollars in submission PDF review time, and have virtually eliminated submission delays from regulatory agencies, due to formatting errors. In the largest firms, Adlib Express has paid for itself in days. In mid-sized firms, the complete payback typically takes only a few months.

Compared to desktop PDF rendering solutions, Adlib dramatically slashes licensing costs, while simultaneously reducing the burden on IT to maintain desktop software and train users. Express cuts the risk associated with manual processing errors and formatting inconsistencies. Even when deployed with user choices, rather than as a pure background service, Adlib enables conformity with enterprise standards through centralized controls.

Adlib customers include global firms with submission materials flowing from offices around the world, heterogeneous platforms and software systems, as well as multiple submission standards for regulatory agencies in various countries. Express meets those challenges, and centrally supports international rendering and print scheduling, all from a single, scalable server-based system.

Conclusion

In a business environment where the revenue window is linked to the patent clock, speed of submission processing can add millions to the bottom line. Electronic submission processing creates an opportunity to capture those revenues, but only if the systems are in place to take advantage of the potential for faster time-to-market.

The operational challenge is to streamline the process of document capture, rendering to submission-ready standards, and creation of organized archives that simplify document assembly. The technical challenge is to integrate a solution seamlessly into existing platforms, applications and workflows with minimal organizational disruption. The business challenge is not just to identify a functional and cost-effective solution for regulatory submission, but to leverage that solution to gain maximum benefit across the enterprise.

For a growing number of life sciences firms, including the largest in the world, Adlib Express is helping to meet these challenges. A highly cost-effective solution to departmental challenges, Express rapidly proves itself as an enterprise rendering, OCR and publishing solution that vaporizes wasted time and effort, while optimizing existing systems and human resources.

For more information about Adlib's software, partners and the many ways our customer are using Adlib Express, please visit our website at www.adlibsoftware.com. Or contact us at info@adlibsoftware.com to discuss your firm's regulatory submission challenges and explore how Adlib can help speed your products to market.