WHITE PAPER

Simplifying life science processes: Connecting data assets for greater efficiency

$3 Billion

The average cost of the full product lifecycle of an approved drug.

12%

A drug's chance of FDA approval.

Document management is an opportunity zone for process and cost improvement inside the drug development lifecycle.

This executive brief presents models and products for the most efficient document handling and management available in today's market.

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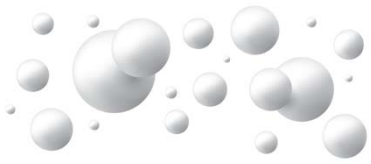
EMPOWERING DIGITAL TRANSFORMATION



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Automation changes everything

Developing a new prescription drug that gains marketing approval costs drug makers an estimated $2.6 billion according to a recent study by Tufts Center[1]. The average time to bring a drug through clinical trials has decreased, however, the rate of approval has dropped by nearly half—to just 12 percent.

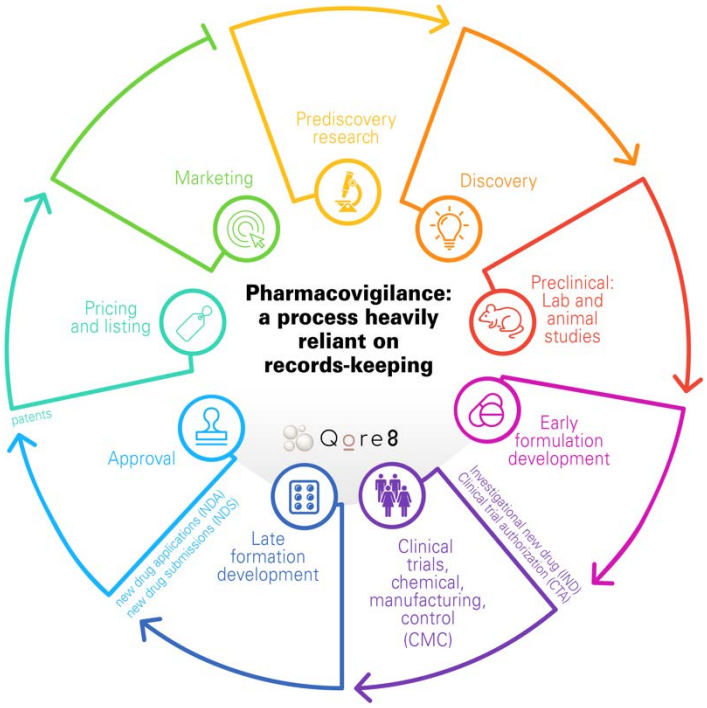
Add to that post-approval research and development, estimated at $312 million, bringing the full product lifecycle cost per approved drug to nearly $3 billion.

"New chemical entity" costs include discovery, Phase I to III clinical trials and approval, but also capital costs for the more than decade-long preclinical drug discovery.

Getting a drug to market—new or reclassified—is intentionally complicated. Each stage of development throughout the scientific process (systematic observation, experimentation, inductive and deductive reasoning, testing hypotheses and theories while recording all data, while operating in a secured environment)—is meant to be methodical, deliberate and searchable. Scientific process is a distinction given only to true science. **Record keeping is critical to achieving positive results.** Managing, maintaining and archiving those records is fundamental to scientific method, product workflow, on-going research and compliance.

Once a product is to market, manufacturing and testing records (and product retention samples) are all that remain as source information. Such data is invaluable and required for: legal disputes, compliance reviews, investigations, trending studies, product history, government audits, documenting the new product's safety and efficacy, and regulatory agency requirements.

The current U.S. good manufacturing practices (GMP) for finished pharmaceuticals are quite prescriptive about the creation, handling and distribution of documents. The general requirements are:



A 9-STEP LIFECYCLE A HIGHLY REGULATED ENVIRONMENT MAKES GOOD RECORDS MANAGEMENT CRITICAL IN THE PHARMA INDUSTRY.

- Good documentation constitutes an essential part of the quality assurance system. Clearly written procedures prevent errors resulting from spoken communication, and clear documentation permits tracing of activities performed.
- Documents must be designed, prepared, reviewed, and distributed with care.

  Documents must be approved, signed, and dated by the appropriate competent and authorized persons.
- Documents must have unambiguous contents. The title, nature, and purpose should be clearly stated. They must be laid out in an orderly fashion and be easy to check. Reproduced documents must be clear and legible.
- Documents must be regularly reviewed and kept up to date. When a document has been revised, systems must be operated to prevent inadvertent use of superseded documents (e.g., only current documentation should be available for use).
- Documents must not be handwritten; however, where documents require the entry of data, these entries may be made in clear legible handwriting using a suitable indelible medium (i.e., not a pencil). Sufficient space must be provided for such entries.

- Any correction made to a document or record must be signed or initialed and dated; the correction must permit the reading of the original information. Where appropriate, the reason for the correction must be recorded.
- Record must be kept at the time each action is taken and in such a way that all activities concerning the conduct of preclinical studies, clinical trials, and the manufacture and control of products are traceable.
- Storage of critical records must at secure place, with access limited to authorized persons. The storage location must ensure adequate protection from loss, destruction, or falsification, and from damage due to fire, water, etc.
- Records which are critical to regulatory compliance or to support essential business activities must be duplicated on paper, microfilm, or electronically, and stored in a separate, secure location in a separate building from the originals.
- Data may be recorded by electromagnetic or photographic means, but detailed procedures relating to whatever system is adopted must be available. Accuracy of the record should be checked as per the defined procedure. If documentation is handled by electronic data processing methods, only authorized persons should be able to enter or modify data in the computer, access must be restricted by passwords or other means, and entry of critical data must be independently checked.
- It is particularly important that during the period of retention, the data can be rendered legible within an appropriate period of time.
- If data is modified, it must be traceable.

Good records management is as much the final product as the pharmacology itself. Millions of pages of documentation record a product lifecycle from discovery to marketing—and then capture more data decades after the product is off market. These documents must not only be digitized, but centralized, organized according to federal standards, secured and searchable. While a thorough documented history is essential to getting a product to market—a huge undertaking in itself—product lifecycle documentation also requires continual upkeep for a well-managed, optimized and controlled archive.

A single research study can consist of thousands of pages of data, annotations, formulas, charts, images and other disparate assets. Often content is compiled and maintained in unconnected Word documents, even including handwritten annotations. Disparate assets are only the beginning of the complexity. These files must then traverse multiple regulatory jurisdictions, different languages, patent laws, joint ventures, mergers and acquisitions. Product documents are also used to subcontract and outsource research, which adds another layer of disconnected and newly sourced/formatted trial and testing documentation. And through it all, every page of data, annotations, formulas, charts, images and more must coalesce as a single unit toward the unified goal of regulatory submission.

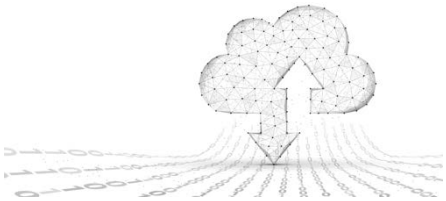
Changing economies, industry compression

Controlling costs is an ongoing goal of pharma, biotechnology, medical device firms, government institutions, foundations and universities. One significant way to control costs is to contract out tasks not inside a firm's core expertise. Such subcontractors, or "contract research organizations" (CROs), are in continual motion buying, selling, merging, and signing preferred partner deals.

This activity is further escalated by ever-changing economic conditions, a healthcare model focused on competitive pricing and a shifting market dynamic. The coronavirus is one example of how markets and suppliers must pivot quickly as supply chains are disrupted and market priorities reset. CROs are both operationally and cost efficient but create further complexity—and cost—with regard to document organization, control and management.

Through all market conditions, pharma will continue to outsource clinical trials, drug development and other tasks where the cost analysis identifies efficiency improvements. This creates and fortifies competitive market advantage, but it also places another stress point on document management. Throughout such partnerships—and there are many in a single product lifecycle—maintaining document control remains central to the movement of a product through a complex and multi-stage process, and perhaps even approval.

It's not only important to optimize this workflow for time and cost efficiency, but to assure that proper document control measures are in place to meet compliance. Missing, incomplete and mishandled archives are known for causing multi-year delays and even denials from regulatory agencies. Documentation in the highly regulated environment of pharma is a significant part of the product value. Good document management affords project managers the ability to more efficiently traverse the many legal requirements and demands for faster approvals.



Regulatory agencies go digital

A study by McKinsey found that the world's governments would save $3.5 trillion per year by 2021 if they matched the productivity gains that leading countries have made in four functions, of which one is digital technology. Digital technology gives federal and state governments the means to fulfill their missions with greatly increased productivity. Through digital transformations, agencies can integrate cutting-edge technologies (such as cloud computing, mobile apps, artificial intelligence, and automation) and modern management practices (for instance, agile software development) to dramatically improve services and outcomes for their constituents.[4]

It's not a coincidence that U.S. government agencies have been instructed to keep paperless records, switching completely to digital formats by the end of 2022. The Office of Management and Budget (OMB), announced the deadline after the National Archives and Records Administration (NARA), which stores data from across federal agencies, stopped accepting paper files in 2019. "The Federal Government spends hundreds of millions of taxpayer dollars and thousands of hours annually to create, use, and store federal records in analog, paper and other non-electronic formats. Maintaining large volumes of analog records requires dedicated resources, management attention, and security investments that should be applied to more effectively managing electronic records," OMB said in a statement.[3]

The OMB directed agencies to "transition record-keeping to a fully electronic environment that complies with all records management laws and regulations." It also called for agencies to "develop plans to close agency-operated storage facilities for paper and other analog records," asking for those records to be transferred to NARA centers or commercial storage facilities by December 31, 2022.

The practice of recording data on paper, said the agency, increases the "burden on citizens by requiring them to conduct business with the government in person or by mail, rather than online." The process also traps "valuable federal data in paper records where it can only be extracted manually and at great expense. And so, digitization is now, and officially, widely adopted by federal government agencies.

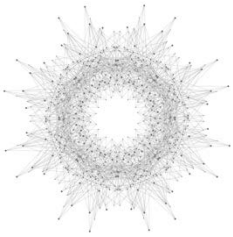
It's been a long and winding road. The Federal Drug Administration (FDA) piloted electronic submissions to its agency in the 1980s with word processed documents that included hyperlinks to supporting data. Files were generated on proprietary systems that often required the delivery of both hardware and software to the FDA, as well as the training of reviewers to read the submission. Literally truckloads of paper were eliminated, but the cost and time to prepare submissions increased dramatically. Nevertheless, the path was laid for the age of digitization.

Then Adobe Systems' portable document format standard (PDF) introduced in the 1990s changed everything again. PDFs, an ISO standard file format, revolutionized document creation, submission preparation and electronic transmission. PDFs are now the global standard for converting and electronically transmitting files over the internet. eCTD (electronic common technical documents), an XML-based structure for high-quality PDF documents, is in development.

While the problem of establishing a universal file structure is solved, systematizing, securing, tracking and finalizing document content to comply with agency standards remains the challenge. A single broken hyperlink buried within thousands of pages is a cause for rejection. And the rate of human error runs especially high when assembling large, complex regulatory documents manually. Federal agencies have zero tolerance for clerical mistakes. There exist a number of technologies that will build and maintain the most common submission formats; eCTD is just one. Even with these format creators, the document must still be created according to regulatory standards. Therein lies the challenge.

Those working on digital projects for U.S. federal government agencies such as the FDA, face formidable technical challenges. The complexity of government submission packages, the difficulty of coordinating them across CROs, and the scarcity of digital talent and software make digital projects costlier and slower than necessary. Issues and delays in process or noncompliant work can also prevent digitization efforts from having a transformative effect on results.

The reason is that process is typically designed around traditional workflows: highly sequential waterfall-based methodologies, on-premise architecture, and closed-source technologies. Conversely, the development world is shifting toward agile development, cloud-based architecture, and open-source. Many have attempted to alter these controls to add flexibility, but few have succeeded in fully capitalizing on the potential of digital at a significant scale.



Building cohesion of many

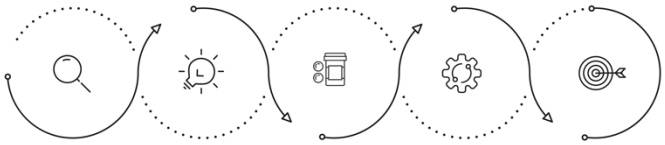
With the patent clock running, many firms are under immense pressure to locate, organize and digitize old, archived files in order to re-file patent documents. This labor intense procedure adds great cost and risk to a process that should otherwise be an abbreviated version of the last submission. Files must be scanned, manually converted to a submission-standard format, electronically connected, quality checked, edited, then updated to current agency standards using desktop software. Once complete, any additions or revisions mean cycling back through the process.

This time-consuming scope of work is further exacerbated by the fact that the process injects another layer of error-prone human interaction—heightening the risk of regulatory rejection.

Then there's file processing. Building a submission package involves processing documents arriving to an organization from multiple sources, including CROs. Many, if not all, incoming files must be manually converted to PDF. During PDF conversion, inadequate rendering solutions often fail to support source file structure. The means bad conversions with serious problems—such as the loss of key navigational information. Unless these errors are caught during the quality assurance (QA) process, they can make it to the final submission creating delays, even returns during FDA reviews. Not surprisingly, such a QA process is time-consuming, again prone to human error, and expensive.

Further complicating matters, requirements for eCTD-compliant submissions apply to living documents. As an investigational new drug (IND) or new drug application (NDA) is prepared, the document package is under a constant state of review: regular annotation and revisions by internal and external audit are made to package submissions. These changes increase the risk of error and inject inaccuracies in post-production re-rendering.

Better technology created this issue. Better technology is also the solution. Multiple agencies contribute to different parts of end-to-end drug development. The fact that the lifecycle is digitized in piecemeal fashion makes the overall experience, without a unifying translator—a Rosetta stone of sorts—frustrating and inefficient.



Rendering software innovates workflows

How do we create a single stream from a disparate flow of documents? What's needed is a simple solution that ensures compliant upstream document workflows without disrupting existing processes. It must also integrate easily into existing applications and platforms. From an engineering and investment standpoint, it should offer low maintenance with a price point that delivers rapid return on investment.

Qore8 automates the conversion and assembly of high value, high volume documents into accurate, high-fidelity and searchable PDFs across life sciences enterprises. It simplifies processing, removes internal barriers and allows workflows to operate at full digital speed.

Project timelines compress and content retains the full accuracy and fidelity of its original form, while also conforming to U.S. GMP. Although time and accuracy pressures can create expensive burdens on systems and personnel, Qore8 eCTD software and other information management tools allow businesses to better manage information and streamline document workflows.

Qore8's high-level function transcends traditional document management. It automates the rendering and creation of accurate, high-fidelity PDFs that comply with the detailed formatting standards required by the regulatory agencies.

Qore8 users can:

- Record file change dates electromagnetically or photographically
- Reduce time and cost through intelligent conversion and assembly of submission-ready documents
- Automatic compliance with enterprise document format standards, while enabling job controls for scheduling, custom formatting and rendering
- Deliver a superior experience to users, stakeholders and customers through the conversion and compilation process

Server-based Qore8 expedites workflows and reduces cost. Because it operates in the background, it's invisible to end users. Documents are automatically converted to submission-ready formats as they are created or received. Qore8 then aggregates and archives PDF documents into organized directories. Documents are converted to formats compliant with regulatory formatting requirements. In the case of FDA submissions, tables of contents, functional bookmarks and accurate hyperlinks transfer beautifully. Qore8-processed documents may also be locked, prohibiting changes, except by authorized users or by creating new versions. Watermarks or time stamps may also be added to documents for state-of-the-art version control and document security.

Automated submission-ready conversion means improved speed-to-market. Qore8 decreases the time required to manually rework documents and perform quality assurance. With Qore8, content additions and changes are automatically converted according to the user's pre-sets. Rendering integrity remains constant through all incoming and ongoing document versions.

Additional benefits are available with the enterprise and end-user versions, but the highest value of Qore8 is keeping users on task. Users can concentrate on core competency work product, rather than derailing to repair formatting issues. Document formatting is only the beginning of Qore8's value model. Documents from various locations, sources and native file formats can be made available to other departments, or across the enterprise, as specified in the owner's control panel.

By eliminating manual assembly and QA, and by accelerating of submission preparation workflow, Qore8 can pay for itself in a matter of months. With all needed documents rendered to exact agency specifications, both organizational and quality control tasks are dramatically reduced. The new product submission goes through the regulatory review process expeditiously and market launch times are compressed. Qore8 is a no-brainer when solving workflow issues related to prepping regulatory submissions, as well as when creating searchable digitalized files for future access.

Advancements where basic rendering software stops

Qore8 is the de facto standard for document rendering solutions. It accelerates document rendering into a submission-ready PDF, or into other formats such as PDF/A, TIFF or HTML. Qore8's full range of features meet the many requirements of local and global regulatory agencies. Deployed in a matter of days, the software integrates with all applications to transform any document into high-fidelity PDF formats for submissions, archiving, text search, aggregation and publishing.

FDA submissions guidelines are rigorous. Some include:

- Hypertext links must be designated by rectangles using thin lines or by blue text, and must open the correct page enabling reviewers to access all data
- All pages must have a ¾" margin on the left side (so if the document is printed and bound, no information is cut off)
- All text must be searchable
- Scanned images and documents must be subject to accurate Optical Character Recognition (OCR) so reviewers may copy and paste content when discussing items in context
- Non-standard fonts must be embedded (so special characters such as mathematical or chemical formulas are not misrepresented
- Page orientation must be correct, so reviewers don't have to manually rotate documents
- The PDF must be an exact representation of the original document, which is usually a Microsoft Word file so that no content is missing or distorted

Qore8 automates these formatting requirements allowing users to focus on the quality of the content. By rendering submission-ready PDFs, QA and manual correction are reduced to a fraction of the time required by any other rendering software. Qore8 saves pharma developers time and money, by eliminating submission delays due to formatting issues.

Qore8 has partnered with pharma companies for nearly two decades and is proud to have brought needed efficiency to the industry, and perhaps faster and greater innovation to the world.

Qore8's price point is priced highly competitive, especially when compared to the many native software licensing costs of desktop PDF rendering solutions. Perhaps its greatest advantage is the reduction of burden on IT departments to maintain and train for multiple desktop software platforms. Even when deployed alongside other user choices rather than as a pure background service, Qore8 enables conformity with enterprise standards through centralized controls.

Qore8 partners include global firms with submission materials flowing to and from offices around the world, heterogeneous platforms and software systems, as well as multiple submission standards for regulatory agencies in countries around the world. Qore8 meets those challenges and supports international document conversion and assembly.

QORE8 COST ANALYSIS

NUMBER OF DOCUMENTS PER WEEK	HOURS SAVED PER WEEK	WEEKLY COST SAVINGS (BASED ON $60/HOUR)	ANNUAL COST SAVINGS
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

In the business of pharma development where revenue 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 revenue, if the proper systems are in place to expedite time-to-market workflows.

Addressing the challenge with symphonic beauty

Like a perfectly orchestrated symphony, Qore8 creates harmony from many different instruments, and many different musicians. The complexity of performing this feat is found in the invisible: programming with vision. Simple and intuitive commands deliver the power to render and assemble high value documents as fully functioning PDFs which are submission ready.

Qore8 simultaneously harmonizes both the technical and business sides of an operation, as well. A technical marvel, Qore8 integrates seamlessly into existing platforms, applications and workflows with minimal organizational disruption. And Qore8 makes business brilliant: it's a functional and cost-effective solution for regulatory submission but leverages assets to gain maximum benefit across an enterprise.

From small to large organizations, Qore8 is already saving time and decreasing costs for many life sciences firms with its superior enterprise rendering, OCR and publishing.

Factsheet

Qore8 value model

Qore8 delivers enterprise-ready, compliant document transformation for life sciences organizations, including pharmaceutical, biotechnology and medical device manufacturers. Qore8 creates high level efficiencies in document lifecycle workflows by integrating accelerated rendering and archiving technology into enterprise content management (ECM), product lifecycle management (PLM) and other business applications.

Accelerated rendering for life sciences

Qore8 is mission critical for organizations with high-volume environments and multi-site installations where accurate, scalable, highly available and regulatory-compliant document-to-PDF conversion and transformation services are shared across the enterprise.

Qore8's PDF accelerator delivers efficiency:

- Garner efficiencies in the regulatory approval process
- Streamline workflows that meet regulatory requirements
- Eliminate reliance on native applications
- Increase accuracy and reduce risks of human error associated with manual document transformation processes
- Ensure long-term access to archived information
- Deliver high-volume advanced rendering benefits

Easy to deploy, simply to use

- Enterprise-wide deployment
    - Deploy as a shared service across multiple enterprise applications, business departments or geographic locations
- Fully scalable
- Scale easily for added capacity to meet growing conversion and transformation job volumes
- Widely available
    - Maintain high reliability and availability with intelligent redundancy to ensure no single point of failure and to maximize uptime
- Integrates with EMC Documentum, IBM FileNet, OpenText ECM Suite, Microsoft SharePoint, Nintex and Dassault ENOVIA
- Performance-oriented load balancing

Qore8 core competencies

- Job management
    - Intelligent job routing to appropriate resources based on resource availability, job priority, and proximity to content
    - Job monitoring to ensure successful job completion

- Web-based management
    - Monitoring, reporting and troubleshooting via web-based management console
- Lower total cost of ownership
    - Enterprise server-based solution provides lower licensing, IT, administrative and training costs
- Increased efficiency
    - Accelerates delivery of special library associations (SLA) through enhanced efficiency and reliability where client workstations remain unaffected by document workflows, updates or add-ons
    - Qore8 automates document-to-PDF conversion function within ECM systems or SharePoint
    - Improved productivity by reducing risk of manual error
- Comprehensive rules engine that configures metadata-driven document workflows that reliably automate processes and apply specific instructions at the document level on how to merge various documents into a PDF, add enhancements, assign priorities and more
- Integration with other ECM, workflow and business processing management systems including EMC Documentum, IBM FileNet, OpenText ECM Suite, Microsoft SharePoint, Nintex and Dassault ENOVIA. Other integrations are possible through Qore8's connector framework via the Professional Services team, through a web services interface between Adlib and any external client application or business process, and through a simple Folder Connector integration that monitors folders for content
- Managed configuration, reporting and system health monitoring in a centralized fashion for optimal business continuity
    - Powerful, intuitive centralized management features reduce IT costs by simplifying system management and provide early warning of potential problems, enabling proactive response
- High-fidelity conversion and document-level publishing with automated rendering of 400+ file types—including Microsoft Office, Lotus Notes, CAD drawings, images, faxes, scans, emails, maps, forms, charts and other types of content—ensuring output exactly matches source content, regardless of original source
- Automated, regulatory-compliant and submission-ready PDF content through metadata-driven rendering for document workflows that automate document processes and parameters such as margin size, font and version controls, security features and more
- Enhanced search capabilities through conversion of images into fully-searchable PDFs—including JPG, CAD and vector graphics— through advanced Optical Character Recognition (OCR)

- Archived content for long-term access across all devices via automated publishing to PDF or PDF/A which also eliminates reliance on native applications
- Intelligent and automated document assembly and merging with application of tables of contents, headers/footers, watermarks, active hyperlinks and security settings
- Support for digital and electronic signatures to reduce reliance on paper-based processes for archiving and submissions
- Rendering of documents as thumbnail images, enabling previewing of document contents before selecting and downloading full document
- Automating the collection, merging and enhancement of diverse documents into platform-agnostic PDFs makes them more shareable promoting collaboration
- International support for rendering in multiple languages to ensure content is in compliance with global internal and external regulatory requirements

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