



Streamlining the drug development lifecycle with Adobe® LiveCycle® enterprise solutions

Using intelligent PDF documents to optimize collaboration, data integrity, authentication, and reuse

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For life sciences companies, drug development is a tremendously complex process involving many hundreds of people, lengthy cycle times, and a high level of financial risk. The Tufts Center for the Study of Drug Development estimates that to bring a new therapy to market costs between US\$0.8 and US\$1.7 billion. The time to market for a new product is estimated to be between 12 and 16 years, leaving a relatively short period of time for an organization to recoup development costs. This high level of business risk is a major barrier to investment in new and innovative therapies.

Life sciences organizations are faced with a delicate balancing act: On one side are stockholder interests to maintain market share and provide an acceptable return on investment; on the other side are customers requiring products that are safe, effective, and affordable. Adding even greater complexity are the government and regulatory agencies around the world, whose diverse requirements are never negotiable. Life sciences organizations must demonstrate to these agencies that they have complied with the many and varied regulations.

The operating model for a life sciences company can be viewed as a manufacturing process, with the input being agency regulations and the output being safe, effective, and affordable products for customers. Success depends on an organization's ability to move critical information and data along the "assembly line," from basic research through clinical development to manufacturing and finally sales, in a secure, efficient, and timely manner. Life sciences organizations create, use, and exchange a variety of documents and data based on information captured using paper forms, electronic forms, and other sources. Depending on the media, the method of information transfer can vary from mail, courier service, and faxing for paper documents to e-mail, removable media, system-to-system interfaces, and web services for electronic information. Regardless of the media and transfer method, at certain points in the process, information is repurposed.

This white paper focuses on data exchange throughout the drug development process. It describes how Adobe PDF documents integrating industry standards can help organizations avoid duplication in acquiring, keying, validating, and authenticating data and/or sources. The paper also describes how organizations can use intelligent PDF documents in concert with Adobe LiveCycle enterprise solutions to provide the foundation for scalable, repeatable, automated processes that are secure and manageable.

The drug development process involves myriad information that must be:

- Captured from many sources
- Extracted from many formats
- Combined into new documents
- Transferred to business partners
- Appropriately protected at every stage of the process

Challenges of the drug development process

Data volume

A significant challenge in the lifecycle of a biomedical product is the collection and preservation of development data. With such a lengthy development process, typically 12 to 16 years, the supporting data and documents are voluminous. When a life sciences organization submits an application seeking regulatory approval for a new drug, the documentation can consist of hundreds of thousands of pages. And all this information must be preserved for the life of the product, which can exceed 80 years.

Data use

Development data is used for a variety of purposes, including:

- Compliance with agency regulations
- Product labels listing the chemistry, manufacturing process, efficacy, and safety of the product
- Applications to varying regulatory authorities for approval to manufacture and market the product
- Monitoring ongoing safety once the product is on the market
- Defense of product liability claims

Data sources

Some examples of information contributors to the drug development process are:

- **Regulatory authorities**—These bodies have the power to regulate and include the authorities that review submitted clinical data and those that conduct site inspections (trial sites, manufacturing sites, and so on).
- **Sponsors**—These companies, institutions, or organizations are engaged in the development, manufacture, and/or sale of biomedical products.
- **Product project team**—These individuals are identified by a sponsor as being responsible for the successful development of a product. Project teams are comprised of hundreds of individuals across an organization, from scientists in basic research responsible for early compound development to professionals in regulatory affairs responsible for the successful submission of applications to regulatory agencies. The project manager is responsible for tracking the development activities across the timeline of the project.
- **Investigators**—These individuals are responsible for the conduct of clinical trials at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.
- **Patients**—These include the individuals who consume product(s) in an effort to eliminate or alleviate the effects of illness or disease.
- **Subjects/trial subjects**—These include the individuals who participate in a clinical trial, either as a recipient of the investigational product(s) or as a control.
- **Scientific experts**—These individuals, identified by peers as experts in one or more scientific area, provide input during the development lifecycle.
- **Contract research organizations**—These include individuals and or organizations (commercial, academic, or other) contracted by the sponsor to perform one or more trial-related duties and functions.

Data in many formats

A further complication in gathering information from these disparate sources is the wide variety of formats in which the data is provided. In addition to information entered on paper documents, there is also electronic data captured directly from multiple sources. Organizations with previously coordinated partnerships may have defined system-to-system interfaces. In many instances, however, data from one source must be moved to another medium and mapped to another format many times for transfer or data authentication.

Data reacquisition

In some cases, multiple organizations requiring the same information may be forced to reacquire the data directly from the source because the integrity and authenticity of the originally supplied information cannot be validated. Reacquisition of information may incur additional costs and cause versioning issues, since the majority of the data involved is dynamic.

Obstacles to an effective drug development process

The following list summarizes the major challenges of the current drug development process:

- Multiple regulatory agencies have different requirements for product applications.
- Various information providers, consumers, and maintainers use differing methods of acquiring, transferring, and storing data.
- There can be diverse processes depending on the products/programs and organizations involved.
- There is no standard method for authenticating discrete data sets, which hinders confident data reuse.
- Information must be converted and reformatted for exchange between entities within the process.
- Conversion between diverse media introduces data redundancy, data synchronization issues between media, and potential data errors.
- Paper-based information must be transferred to a digital format by scanning or manually entering individual pieces of data such as protocol titles, investigator information, or product information.
- Documents must often be printed when signatures are required. Paper forms must then be tracked and maintained concurrently with electronic data.

User profiles and what they need

In order to satisfy the life sciences industry's diverse requirements, a solution for the drug development process should provide certain capabilities for specific user roles:

- **Information providers**—Information must be easily captured from multiple sources and media. The information should be validated and certified at the source.
- **Information consumers**—The documents created should be stored in such a way as to make consumption dependable, consistent, and easily accessible. The documents must support the functionality required by the consumer's organization.
- **Information maintainers**—The technologies used must be reliable and fulfill the providers' and consumers' requirements, as well as the requirements of any relevant regulatory agencies. Additionally, metadata for access, context, and maintenance should be available and searchable.

To help ensure data integrity and consistency, Adobe LiveCycle Forms:

- Provides a consistent look and feel between paper and digital versions of PDF documents
- Supports the use of life sciences' industry-specific XML data standards such as those defined by CDISC and HL7
- Provides increased data integrity by merging structured data storage and validation with precise document presentation in a single container
- Enables automatic form prefilling and data extraction by back-office systems
- Supports field-level help, embedded data validation, and business logic to help ensure data accuracy
- Enables accessibility for people with disabilities (compliance with Section 508 guidelines)
- Provides long-term form availability through backward compatibility and the ability to "flatten" documents in support of archival standards such as PDF/A

Streamlining the drug development process

In the demanding life sciences industry, any competitive advantage that removes the encumbrances of antiquated paper-based processes while reducing operating costs and turnaround times is a win-win scenario for sponsors and consumers. Adobe LiveCycle enterprise solutions provide a number of industrial-strength products to automate the acquisition, manipulation, distribution, and protection of information integral to the drug development process.

Following are a few of the benefits provided by Adobe LiveCycle enterprise solutions:

Support for industry standards

A number of organizations in the drug development lifecycle exchange various types of information. Adobe LiveCycle Forms software enables users to streamline the process by supporting industry data standards such as those proposed by the Health Level 7 (HL7) and the Clinical Data Interchange Standards Consortium (CDISC). By combining industry data standards and Adobe Portable Document Format (PDF), organizations within the life sciences industry can easily and confidently exchange information without transformation or conversion.

Reduced data entry costs

The same data bound to the industry-standard XML data within LiveCycle Forms is used for both data processing and form presentation, which helps ensure data synchronization throughout the drug development process. When initially populating a form, LiveCycle Forms can automatically prefill the data from back-office applications such as a clinical investigator database. For a form like the FDA Form 1571, which is typically completed manually, LiveCycle Forms can provide field-level help as well as execute embedded field validation and business logic during data entry.

With Adobe LiveCycle Reader® Extensions software, form creators can enable their target audiences to complete forms with free Adobe Reader software, which is available on most computing platforms. The PDF form is entirely self-contained, including the form's view, the business logic, and the XML structure for data storage, so it can be completed offline while maintaining data validation and integrity. By using PDF, organizations can be assured that the form will maintain a consistent look and feel regardless of the environment and media used for presentation. Documents will be preserved long-term, thanks to Adobe Acrobat® software's support for the PDF/A archiving standard as well as its backward compatibility with previous versions of the PDF specification. The power and flexibility of LiveCycle Forms can significantly improve data processing quality while decreasing the cost of data entry.

Reduced paper handling costs

Adobe LiveCycle enterprise solutions help reduce printing and copying costs by leveraging electronic document distribution and digital signatures. Electronic document transfer also simplifies data exchange and eliminates the costs of faxing, mailing, and courier services. Additional cost savings can be achieved by replacing the requirement for paper filing, storage space, and document retrieval. In the event that a hard copy is needed, an intelligent PDF form can be printed with the assurance that the paper and digital versions will maintain a consistent look and feel.

Better managed business processes

Adobe LiveCycle Workflow software automates document-based business processes, handling virtually all facets including data access, exchange, and integration. Leveraging frequently implemented functionality in predefined Quick Process Action Components (QPACs), designers can visually implement their organization's workflows using a drag-and-drop interface. Developers can modify or create their own QPACs, enabling unlimited customization of their workflows and packaging of business rules. Since the QPACs are hot-swappable, users can change the workflow dynamically without server downtime. Business activity monitoring (BAM) enables the user to evaluate current workflows for potential optimization. This is particularly important in a dynamic market like the drug development industry where partners and products change frequently.

Adobe LiveCycle Workflow:

- Automates information capture and processing using workflow components that incorporate validation checkpoints
- Enables the dynamic implementation of user-specific business rules packages
- Reduces complicated, hybrid processes requiring redundant, paper-based, and digital information, as well as “wet” signatures
- Automates data access, exchange, and integration into business processes through automatic document generation, auto-filling forms, and immediate document delivery
- Automates downstream process branching and exception handling
- Provides the ability for further optimization through business activity monitoring (BAM)

Securing the drug development data

The data assets used in the life sciences industry contain personal information about patients, competitive product information from sponsors, and regulatory and marketing strategies. As the life sciences industry becomes more diversified and distributed, it becomes more important to enable partners to protect this information throughout the drug development lifecycle. Also, consumers of the information must be able to authenticate the information’s origin and integrity using digital signatures whenever possible to preserve the fully electronic process and to comply with regulatory mandates such as CFR Part 11 and support industry standards such as Signatures and Authentication for Everyone (SAFE).

Security methods include:

Passwords: At the simplest level, a document can be protected by limiting access to particular functions using a document password. Adobe PDF documents support a password for opening a document and potentially another password for specific functions such as printing, form-filling, and data extraction. This solution requires users to share or distribute a password.

Encryption: A document can also be protected by encrypting the contents using public key infrastructure (PKI). Encrypting the document with a key makes the document illegible to anyone who does not decrypt it with a compatible key. Adobe Acrobat, Reader, and LiveCycle software include robust PKI and document rights-management support. Adobe has also teamed with security partners to provide a full range of security capabilities.

Digital signatures: Digital signatures provide a unique “stamp” of a document’s current state and signify that the signer approves and trusts the document’s contents. Digital signatures can have different levels of trust depending on how the signature is created. A trusted third-party signature allows a user receiving a digitally signed document to verify the credentials of the signing party in a certificate repository. Digital signatures can be used both by the generator of a document and by the transaction participants to approve and authenticate a document.

To provide greater security for all types of drug development documents, Adobe LiveCycle enterprise software:

- Establishes flexible, document-based security policies for different individuals or organizations to provide information confidentiality
- Certifies and digitally signs documents of all types to help ensure authenticity and integrity, and to promote information reuse
- Leverages industry-standard public key infrastructure (PKI)
- Maintains a document audit trail that details the actions taken, who initiated the actions, and when the actions occurred, helping to support compliance with CFR Part 11
- Supports all document types required for a business process (such as Microsoft Office or CAD files)
- Captures customer signatures digitally, keeping information electronic

Protecting documents with security policies

Adobe LiveCycle Policy Server™ software provides control of drug development documents throughout the process by enabling security policies that travel with the document. This type of persistent security policy specifies who can access, modify, or extract information from specific documents. As a document moves through the process, a security policy controls access to confidential information, such as limiting access to study subject data. Security must also be flexible, so LiveCycle Policy Server allows individuals to update security policies even after the document has been distributed. This allows the flexible transfer of documents to other organizations with confidence in the document’s security regardless of where it resides.

Data integrity

Certifying a document using a digital signature allows a consumer of the document to determine if changes have been made since certification, and what those changes were.

Accountability

By capturing the document state at each signing, Adobe LiveCycle enterprise solutions enable a document manager to review an authenticated audit trail of who performed certain actions and when the actions were performed.

Validating and certifying information at the source

When a document is created, the information contained in it must be validated and certified to enable confident reuse by information consumers downstream in the process. Adobe Acrobat, Reader, and Adobe LiveCycle Document Security software allow specific users or groups to digitally sign a document throughout the document's lifespan. Supporting industry-standard security and encryption regulations such as those governed by the Secure Identity Services Accreditation Corporation (SISAC) simplifies access to and authentication of protected data by industry partners. For example, an investigator providing site specifications can digitally sign an FDA Form 1572. Now, regardless of who originally requested the information, authorized individuals within the workflow can authenticate and reuse the information with confidence.

Providing a detailed audit trail

In the life span of a clinical trial, numerous decisions are made based on time-sensitive information provided by other individuals or groups. A sponsor may require an investigator to provide sensitive information about his or her financial holdings. Certification using digital signatures ensures that the current information is "locked down" at the time of signing, but what if something requires an adjustment? Because each digital signature takes a snapshot of the entire document state at the time of signing, changes made after the signing are stored on top of the previous data. This method of layering document changes provides a detailed audit trail of all the changes made to a document. It also enables a user to view the document state at any point in its history to determine when specific changes were made and who made them. By combining digital signatures with policy management, implementers can even create documents that both authenticate time-sensitive information and automatically make it expire on a given date and time.

Conclusion

Adobe LiveCycle enterprise solutions leverage existing infrastructure investments by utilizing valuable information from back-office applications and providing context-specific documents more securely. By maximizing process automation, immediate data validation, and partner authentication in a consistent and customizable document-based workflow that integrates life sciences industry standards, Adobe LiveCycle enterprise solutions provide a faster, more secure, and more cost-effective way to implement efficiencies in the drug development lifecycle.

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