OpenText

SEPTEMBER 2013

Comply or Perish:

Maintaining 21 CFR Part 11 Compliance

The biggest challenges of Life Sciences companies today are maintaining a robust product pipeline and reducing time to market while complying with an increasing and evolving multitude of Federal and international regulations. In this paper, we discuss the particular requirements of rule 21 CFR Part 11 and describe how OpenText Regulated Documents, built on OpenText Content Server - the leading collaborative knowledge management software from OpenText, enables Life Sciences companies to comply with 21 CFR Part 11.

OPENTEXT

Table of Contents

Introduction

All companies that develop new products are interested in reducing the time that it takes to get their products to market. For Life Sciences companies, the challenge of reducing time-to-market for new products is even greater than for other industries due to the strict regulatory environment in which they must operate.

Historically, Life Sciences companies have managed and tracked documents in paper format. The methods and practices for ensuring that the paper records included in submissions or maintained for possible inspection were authentic and unaltered were well established and well understood. Substituting electronic documents and signatures for paper required new procedures to insure authenticity, integrity and confidentiality.

The FDA requirements for certifying that electronic records and electronic signatures are trustworthy, reliable, and essentially equivalent to paper records and handwritten signatures are described in 21 CFR Part 11.

21 CFR Part 11 contains two major sections that contain requirements for:

- **Electronic Records**—defined as "any combination of text, graphics, data, audio, pictorial, or other information in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system."1 (The rules apply to any records covered by FDA regulations that exist in an electronic form, including records that are required to be maintained whether they are submitted to the FDA or not.)
- **Electronic Signatures**—defined as "a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature."2

The determination of whether to use an electronic signature is up to an individual organization.

Clarifications:

- **Federal Register/Vol. 62, No 54/Rules & Regulations/Part 11, Section 11.3 (6) Electronic Record 21 CFR Part 11** applies to those records and signatures required by an FDA predicate rule, as well as to signatures that are not required, but that appear in required records.
- **Even though 21 CFR Part 11** applies to all FDA program areas, it does not mandate electronic record keeping. Rather, it describes the technical and procedural requirements that must be met if a submitting entity chooses to maintain records electronically and use electronic signatures.

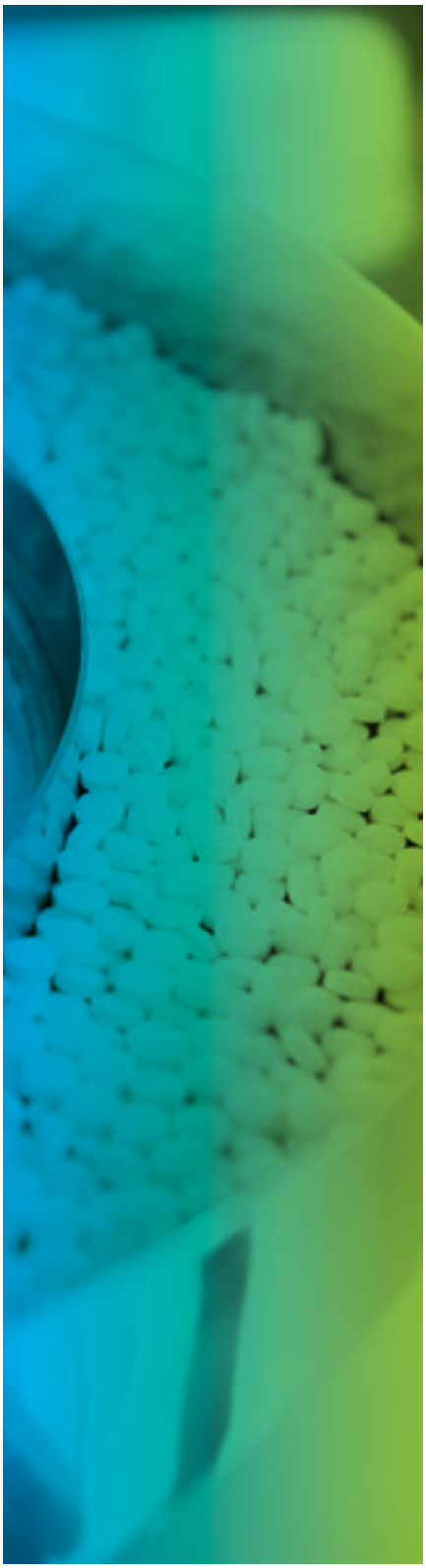
Enterprise Information Management Overview

OpenText is the leader in Enterprise Information Management (EIM). EIM enables organizations to grow the business, lower costs of operations, and reduce information governance and security related risks. OpenText focuses on the key drivers of business success to improve business insight, strengthen business impact, accelerate process velocity, address information governance and provide security.

OpenText Enterprise Content Management (ECM), an EIM offering, helps you manage information through its lifecycle, improve business productivity, mitigate risk, and control costs of growing volumes of content.

OpenText ECM software unites records management, archiving, search and eDiscovery to minimize organizational risk and cost, and maximize business insight and efficiency.

From information capture, to classification, management, storage, distribution, archiving, and disposition, ECM software manages the flow of information across the organization. Fast and seamless access from multiple environments—web, desktop, mobile, within business processes and applications—improves user productivity and organizational efficiency.



Enterprise Content Management Software Products

CONTENT MANAGEMENT	Manage and archive corporate content in a consistent and compliant manner with fully integrated records, metadata, archiving, and storage management services.
ARCHIVING	Meet compliance requirements, reduce storage and eDiscovery risks and costs, and maintain seamless access to content for business users.
RECORDS MANAGEMENT	Control risks and costs by managing the retention and disposition of content according to internal policies and external regulations.
EMAIL MANAGEMENT	Reduce costs and mitigate the risks of compliance and litigation concerning email content.
DATA AND CONTENT INTEGRATION	Intelligently consolidate and transform data and content throughout the entire information ecosystem to increase the business impact of your information and unify information channels across application boundaries.
LEGAL CONTENT MANAGEMENT (EDOCS)	Support business practices, proactive compliance and information governance needs throughout the matter lifecycle from client intake through to final disposition.
LEARNING MANAGEMENT	Successfully manage the learning process, reduce training costs and improve user satisfaction through support of independent learning styles.
CONTENT-CENTRIC APPLICATIONS	Provide the right task and resource support in your enterprise value chain while leveraging your secure ECM repository and other foundational infrastructure investments.

OpenText Solutions for Pharmaceutical & Life Sciences

Achieving compliant management of all electronic records and documents

Pharmaceutical and Life Sciences companies operate in a highly regulated environment with long product lifecycles. The operations are both data and document-intensive. Pharmaceutical product development can take up to 15 years and over $2 billion for a product to reach the market. Recent demands for increased public accountability against a trend of fewer new products and expiring patents are threatening traditional profitability and revenue growth. Life sciences departments must share key information with team members and make the best decisions possible based on all relevant information, while complying with government regulations including the US's 21 CFR Part 11 and conforming to industry standards such as GxP.

OpenText solutions for the Pharmaceutical and Life Sciences industries support critical processes where compliant management of all paper and electronic records and documents is essential. We recognize that these processes range from informal research collaborations to formal procedures like Standard Operating Procedure (SOP) review and approval, and that these processes may be limited to single departments, span your enterprise or even include alliance partners, contractors and consultants. Users can access a variety of interfaces ranging from email clients, Web browsers, as well as office and specialty applications, allowing them to work in the environment that is most natural to them.

OpenText solutions for Pharmaceutical and Life Sciences are based on a framework providing the right task and resource support for the processes in the industry's value chain.

Complying with 21 CFR Part 11

For Life Sciences companies that have chosen to maintain records and make submissions electronically, the challenge is to comply with 21 CFR Part 11 by ensuring that:

- The software products that they use function in a way that enables them to comply with the many requirements of 21 CFR Part 11
- They develop and follow SOPs that describe how to use software functionality in a way that is compliant with 21 CFR Part 11

The requirements of 21 CFR Part 11 for Life Sciences companies can be summarized as follows:

- Ensure the authenticity, integrity, and confidentiality of electronic records
- Generate accurate and complete copies of records for the FDA to inspect and review
- Ensure the security and easy retrieval of electronic records
- Ensure that only authorized individuals can access, manipulate, and electronically sign records
- Maintain a log of all changes made to electronic records throughout their lifecycle
- Record and store electronic signatures with the electronic records to which they have been applied

- Ensure that record processing steps are performed in the proper order
- Ensure that persons who develop maintain, or use the electronic record/electronic signing system are properly trained
- Ensure that individuals are accountable for actions initiated under their electronic signatures
- Maintain control over system documentation
- Establish and maintain SOPs regarding all of the above and other requirements

The OpenText Solution

OpenText Regulated Documents offering helps Life Sciences companies manage electronic records and signatures in compliance with 21 CFR Part 11 in the following ways:

- Through the capabilities of its OpenText Content Server, OpenText Electronic Signatures and other software products, which enable compliance with 21 CFR Part 11 requirements
- Through consulting services that help Life Sciences companies develop the policies, procedures, and best practices to ensure that OpenText software products are used in a 21 CFR Part 11- compliant manner

Regulated Documents enables Life Sciences companies to address not only their need for software that can be used in a Part 11-compliant way, but also to manage the SOPs that describe the procedures and best practices that must be followed to ensure 21 CFR Part 11 compliance. Electronic Signatures is a module specifically designed to address the access control and electronic signature requirements of 21 CFR Part 11.

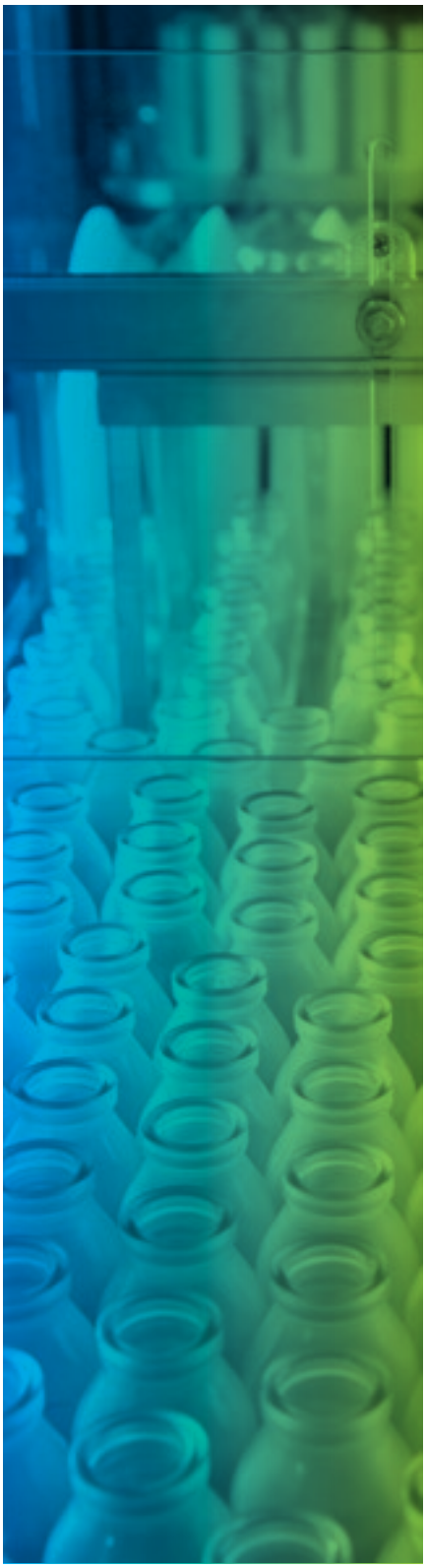
OpenText Content Server

Serving as the foundation of Regulated Documents, Content Server is a highly scalable, collaborative knowledge management application that allows organizations to store and manage a wide range of digital objects—from simple and compound documents, data records, molecular models, image and video files, to search queries and URLs—and provides controlled user access to these objects. All of the electronic records maintained by Life Sciences companies can be stored and managed in Content Server.

Content Server is ideal for managing unstructured electronic records in regulated industries, such as the pharmaceutical sector. The key features of Content Server for 21 CFR Part 11 compliance are:

- Secure repository for storing and distributing electronic records with full version control
- Web-based interface for team collaboration that is easy to access and deploy
- Security features such as password authentication and eight levels of permissions on document objects
- Ability to store custom metadata (such as signature information) with electronic records
- Ability to track the complete version and event history of electronic records, as well as to audit and report on all actions
- Workflow for automating and ensuring the integrity of electronic record review, approval, and signing processes

Content Server provides the ability to perform lifecycle management of all electronic content including Microsoft® Office files, XML files, emails, PDFs, CADs, multi-media, UTF-8 content, etc. This content is stored in the ECM repository, tracked, retained for its lifecycle and disposed of once the end of life is reached for that content. The electronic content can have metadata (data elements) associated with the content providing information about the content. For instance, is the content a Microsoft Word document or an email or an HR record, or an official record of the corporation, or an SOP document? Each of these items has a different lifespan and can be involved in very different business processes during their lifecycles. The access permissions on each of these items vary significantly as well. The ability to classify electronic content, control its access, manage it with defined processes (workflows), retain it for the appropriate length of time and then dispose of it in a legally defensible manner is a cornerstone of the content lifecycle management (CLM) solution. But CLM is not just about controlling and managing business content and the repositories where it resides. It is about understanding the relationship between people, processes and content in a corporation. It is also about documenting how content flows within and across departments, what systems it touches and what processes with which it is associated.



Content can be created from a variety of sources. All forms of data content can be managed as users typically work via their desktops in user-friendly applications such as Microsoft Office or Outlook or Lotus Notes. By logging into the ECM Suite through their preferred browser (Internet Explorer, Firefox, Safari), users can download, upload and edit content within the repository, with all content controlled by access permissions.

As content is received by the ECM repository, it is indexed, associated with any default metadata (categories) and stored in a repository location as specified by the user. Access permissions are also set according to the administrator-configured parameters and the location chosen. It is then exposed to a rich search engine that can perform searches against both the content data and the contents of the metadata using simple and complex full-text and Boolean search strings. The domain of the search can be limited to just a portion of the repository or it can span the entire repository. Through the use of federated searches, the search can be expanded to include file systems and other repositories. A search query can return exact matches or similar matches including “sounds like” search criteria. The results of both the search and the search template can be stored, as desired by the user. Additional searches refining the search template are also available. As with all content stored in the repository, access permissions control what content is returned as a result of a search. If a user does not have permission to see that specific content exists, it will not be shown in the search results. Content is also exposed to a powerful business process engine (workflows) that allow organizations to route documents through the various stages in the documents lifecycle. Approval, review, edits and comments are all possible steps along the workflow process.

As changes occur to content (new versions, edits, deletions) all actions are logged in an audit trail so accountability of all content is maintained across the repository. The system administrator can review this audit log as desired.

When an additional version of the same content are stored in the repository, a newer version is added and becomes the default version when the content is search, opened for viewing or opened for editing. However, previous versions, back to a configured maximum number of versions, are still available for comparisons or as a backup to be reverted if necessary. While content is stored in folders in the repository, users can create shortcuts from their personal repository workspaces to their favorite content or folders for faster access.

When content is added to the ECM repository, notifications can be sent out automatically as desired by users. For instance, a user can choose to be notified by email whenever a new item or version is added to a specific folder. They can choose to receive such a notification immediately, hourly or daily. As workflows process corporate data, users are always notified via an assignment list, and can also be notified via email, when a workflow step requires their participation. This notification can be a review, approval, electronic signature or just informing them that a specific action is needed. A deadline can be imposed and when the user exceeds that deadline, escalations can occur as well. The administrator can review the system-wide list of assignments and tasks and outstanding items are clearly flagged for review. The administrator can re-assign any task if, for instance, a user is out on holiday or otherwise unavailable.

It is also possible for individual users to manage proxy users for approvals while they will be unavailable. Users can easily choose any other user within the system to receive workflow notifications while they are unavailable, such as being out of the office on vacation.

Content can be added to the repository through both local and remote user action, bulk loading utilities or connectors that draw content from other repositories. Content can be kept on file storage or moved to the OpenText Archive Server which performs single-instance archiving, compression and encryption as desired. Storage via the Archive Server can be on disk or worm or optical media or magnetic tape. Content stored within the Archive Server is managed and accessed like all other repository content.

How OpenText Regulated Documents Addresses 21 CFR Part 11

Regulated Documents addresses each of the various requirements of 21 CFR Part 11 either by:

- Functionality contained in the core Content Server product
- Functionality contained in Regulated Documents bundle which includes:
  - Electronic Signatures (eSign)
  - XML Workflow Extensions
  - XML Workflow Interchange
  - Controlled Viewing & Printing
- Other means such as functionality contained in other OpenText products

The table below summarizes how Regulated Documents addresses each of the requirements of 21CFR Part 11, by indicating whether the requirement is satisfied by the core Content Server product, by the Regulated Documents module, or by some other software or service from OpenText.

21 CFR PART 11 SECTION	ADDRESSED?	ADDRESSED BY
REQUIREMENTS FOR CLOSED SYSTEMS		
11.10 (a) – Validation	■	Policies and procedures
11.10 (b) – Inspection	■	OpenText Content Server
11.10 (c) – Protection	■	OpenText Content Server Records Management module
11.10 (d) – Security	■	OpenText Content Server, OpenText Electronic Signatures, and OpenText Directory Services (OTDS), Controlled Viewing and Printing
11.10 (e) – Audit	■	OpenText Content Server, Controlled Viewing and Printing
11.10 (f) – Operational	■	OpenText Content Server
11.10 (g) – Authority	■	OpenText Content Server and OpenText Electronic Signatures
11.10 (h) – Device	■	OpenText Content Server and OpenText Electronic Signatures
11.10 (i) – Personnel	■	OpenText on-site audit
11.10 (j) – Policies	■	Policies and procedures
11.10 (k) – Documentation	■	Policies and procedures
REQUIREMENTS FOR OPEN SYSTEMS		
11.30 – Authenticity	■	OpenText Directory Services module (OTDS)
11.30 – Integrity	■	OpenText Content Server
11.30 – Confidentiality	■	Secure Sockets, Firewalls
11.30 – Digital Signature	■	Available through 3rd party module
REQUIREMENTS FOR SIGNATURE MANIFESTATIONS		
11.50 (a) – Signing	■	OpenText Electronic Signatures
11.50 (b) – Display/Print	■	OpenText Electronic Signatures
11.70 – Linking	■	OpenText Electronic Signatures
REQUIREMENTS FOR ELECTRONIC SIGNATURES		
11.100 (a) -Uniqueness	■	Policies and procedures
11.100 (b) -Verification	■	Policies and procedures
11.100 (c) -Certification	■	OpenText Electronic Signatures
11.200 (a) (1) (i) -Signature	■	OpenText Content Server
11.200 (a) (1) (ii) -Signing	■	OpenText Content Server and OpenText Electronic Signatures
11.200 (a) (2) and (3) – Identity	■	OpenText Content Server andOpenText Electronic SIgnatures
11.200 (b) – Biometrics	Not applicable	
11.300 (a) -Uniqueness	■	OpenText Content Server
11.300 (b) -Passwords	■	OpenText Content Server
11.300 (c) -Lost codes	■	OpenText Content Server
11.300 (d) -Attempts	■	OpenText Electronic Signatures
11.300 (e) -Devices	Not applicable	

Summary

Coordinating and streamlining the efforts of research and development, production, distribution and marketing, while achieving regulatory compliance, are challenges that face Life Sciences organizations today. The opportunity to cut costs and reduce dependency on paper processes is of enormous benefit. 21 CFR Part 11 is a key regulation to which Life Sciences companies must conform if they want to take advantage of electronic records and electronic signatures.

The regulations in 21 CFR Part 11 seek to reduce fraud by ensuring that electronic signatures and records are as reliable as their traditional paper versions. Content Server is a solution that allows companies to closely adhere to these regulations.

Life Sciences organizations can rely on Content Server to perform the following functions in a manner that is compliant with the requirements in 21 CFR Part 11:

- Store and access documents for review
- Deliver information about clinical trials
- Track regulatory applications
- Manage records
- Communicate and assign tasks
- Monitor research and development
- Control workflows and processes
- Store and manage changes to SOPs