Industry Brief

MasterControl™

Automating Document Control Processes to Comply With FDA and ISO Requirements

How Medical Device Manufacturers Simplify Compliance by Automating Document Control

MasterControl™

The FDA has been implementing TMAP through cutting-edge innovation, updated systems, and an interoperable, secure infrastructure to support the rapidly increasing regulatory review workload and improve our overall digital and technological capabilities as an organisation. - Amy Abernethy, former Principal Deputy Commissioner and Acting Chief Information Officer, FDA.[1]

As a regulated product manufacturer, you have likely heard that oft recited phrase "if it isn't documented, it didn't happen." This motto, shared among life sciences companies, means an efficient document control system is at the core of quality management. Documents and records are evidence that your company follows the good manufacturing and document management practices required for compliance.

Standard operating procedures (SOPs), specifications, calibration instructions, procedures, packaging and storage instructions, test plans, and validation process reports are just a few of the documents you create and use during your medical device's development life cycle. When your device is on the market, you add in design history files, change orders, complaints, and corrective action/preventive action (CAPA) reports.

Careful handling of the large amounts of documentation required for regulated products is critical for achieving compliance. Furthermore, document control guidelines enforced by the U.S. Food and Drug Administration (FDA) and the standards set by the International Organization for Standardization (ISO) continue to evolve. This means your document control system should be agile and scalable to keep up with the changing regulatory landscape.

This industry brief details the FDA guidelines and ISO standards that apply to document control, and it illustrates how digitising document control processes is essential for ensuring ongoing compliance and future relevance.

Regulatory Bodies Driving Modernisation

Traditional approaches to regulatory compliance commonly include checking boxes and resolving nonconformances as they occur — but not always identifying root causes. Modernised technologies are edging this strategy toward extinction. The FDA and ISO organisations as well as other global regulators have been proactive with initiatives to encourage modernisation to keep up with the rapidly advancing life sciences industry.

Technology Modernisation Action Plan (TMAP)/Data Modernisation Action Plan (DMAP)

The innovations currently moving through the regulatory pathways are made possible through advanced technologies enabling connectivity, interoperability, and the use of more data. In 2019, the FDA introduced its Technology Modernisation Action Plan (TMAP). The programme is designed to bring the

agency up to speed with the latest technology and scientific advancements as well as to introduce new methods for product oversight.

A central part of the FDA's TMAP blueprint is making better use of data. Data is more abundant, more focus-area specific, and has a wide range of uses in life sciences. This type of progress led the agency to develop the Data Modernisation Action Plan (DMAP). At a high level, the DMAP will enable the FDA to enhance its data practices and allow efficient interconnectivity and collaboration across its growing, diverse workforce.[2]

ISO 14971:2019

As technology advances, the FDA must keep pace with the increasing complexity of rapidly developing technology and continue to modernise and evaluate our programs and processes, ensuring they continue to be efficient, consistent, and scientifically rigorous. - Jeffrey Shuren, Director of the FDA's Centre for Devices and Radiological Health (CDRH).[3]

The ISO 14971 standard specifies the principles and processes for risk management of medical devices. This includes:

- Identifying hazards.
- Estimating and evaluating the associated risks.
- Controlling risks.
- Monitoring the effectiveness of the controls.

ISO updated the standard in 2019 with more focus on the documentation requirements in risk assessments. Companies must fully document the medical device's appropriate use and associated risks. This includes the reasonably foreseeable misuse errors (including abnormal use) and its correct use.[4]

European Union Medical Device Regulation/ In-vitro Diagnostics Regulation

One aspect of the European Union's Medical Device Regulation (MDR) that medical device companies can count on is an obligation to have more things in writing. For example, compliance requirements include establishing and documenting a risk management plan for each device.

Another document added to the lineup is a summary of safety and clinical performance (SSCP). This is an annual report that manufacturers must provide throughout the device's life cycle in order to remain compliant to sell products in the EU. The document needs to include:[5]

- Information about the device's safety and performance, including the clinical benefits and the success rate of achieving the intended outcomes.
- Information clarifying the residual risks and side effects with implantable devices used by the patient.
- A summary of the clinical evaluation results of all the available clinical data related to the device.

It's important to understand that efficient internal processes are essential to remain relevant in the future life sciences ecosystem. Data from a KPMG survey of life sciences companies revealed:[6]

- 55% have or plan to implement a digital data strategy.
- 45% have already implemented technologies to increase internal efficiency.
- 44% have completed or are in the process of implementing automation.
- 64% already apply cloud structures in their IT environments.

Document Control CGMP

As regulatory agencies continue to elevate their documentation requirements, speed and efficiency with document control processes are imperative for achieving and maintaining compliance. FDA regulations and ISO standards for current good manufacturing practices (CGMP) mandate that all companies manufacturing regulated products have some type of a document control system.

In its simplest form, document control refers to procedures for collaboration, distribution, approval, and change of all documentation associated with regulated products throughout their life cycle.

FDA Document Control Requirements

The document control section of the FDA's 21 CFR 820.40 cites that document control refers to procedures for approval, distribution, and change of documentation. Manufacturers must establish and maintain document control procedures that adhere to the following guidelines:

- Designate staff to review and approve documents.
- Document changes must go through a review and approval process.
- Ensure all approved documents include the date and approver's signature.
- Documents must be available at all locations they are designated for.
- Promptly remove obsolete documents to prevent unintended use.
- Maintain records of changes to documents, including a description of changes, approval date, and approvers' signatures.

ISO Documentation Standards

The ISO 9001:2015 standard includes guidelines for how to control your documents and records through a comprehensive document management system. These controls include:

- Unique identification for all documents.
- Version control.
- Identification of revisions.

According to the ISO 9001:2015 standard, each organisation determines its approach to documentation management. The standard also addresses document control processes companies should have in place, including procedures for:

- Updating documents such as instructional materials.
- Archiving documents and completed records to provide historical evidence of compliance.
- Ensuring that all documentation includes adequate identifying information that facilitates easy search and retrieval.
- Ensuring that subject matter experts regularly review and approve documents.

Risk management is not a quality-only responsibility, it needs to be integrated into all areas of the company.
- Kim Jackson, Senior Product Manager overseeing risk and quality event solutions, MasterControl.

- Governing control, maintenance, distribution, storage, retention, security, and disposition of all documents.

The standard also addresses the concept of including risk-based thinking as it directly influences the complexity of the documentation. The greater the risk of uncertainty surrounding the product, the more stringent the requirements are for the documentation and the actions the organisation must take to mitigate the risk.[7]

Why It's Important to Exceed Compliance Expectations

Building regulated products requires a significant amount of documentation. Documents that are outdated or have errors can cause problems that lead to noncompliance with regulatory guidelines and ISO standards. Therefore, document control is the responsibility of all employees who create or use documents. Each staff member needs to understand the purpose of document control and how to follow your company's document control procedures.

Document control processes that meet the basic "checklist" requirements for compliance can still be prone to errors, posing more obstacles to your production and time-to-market timelines. There are too many moving parts in document control to rely on manual processes and paper documents.

Given the frequent revisions, approvals, search and retrieval tasks, archiving previous versions, and redrafting lost documents, issues can easily occur. Many problems go unnoticed until later in the production process. Common documentation-related observations cited in Form 483s and warning letters include:

- Document errors, including missing dates or missing numbering schemes.
- Uncontrolled documents in circulation.
- Document changes without approvals, explanations, or records.
- Lack of access to critical documents.
- Missing documents.

Companies doing business in regulated environments are endeavoring to eliminate documentation errors and inadequacies by implementing automated document control processes.

Document Control Solution

There has been a shift from checking that manufacturing operations are being completed correctly to a much greater scrutiny of documentation in areas such as risk assessment, change control, and deviation.[8]
- Deloitte Centre for Health Solutions

A digital document control solution automates this critical aspect of your product development and quality management. It's more efficient and helps ensure compliance to documentation-related regulations and standards. An effective document control solution should have the following capabilities:

- Collaborative workspace.
- Efficient document management.
- Revision control.
- Secure architecture
- Part of an integrated platform.

Collaborative Workspace

Not long into 2020, the traditional workplace scenario began to unravel as the social distancing mandates became the norm. Because document control is not confined to a single department or role, organisations using paper-based or hybrid documents and document control systems soon discovered the limitations of those systems and processes.

Arranging for all stakeholders to be present for document reviews is logistically challenging due to conflicting schedules and a geographically dispersed workforce. The next option is interacting through email, which can be slow, cumbersome, and unsecure. In addition, people approving a document may not have been involved in its creation, which increases the likelihood of conflicting edits that need to be reconciled.

The ability for stakeholders to collaborate simultaneously on documents in real time moves documents through review and approval cycles faster, allowing companies to keep pace with tight production timelines.

We went from weeks and months to review and approve a document to days. As a quality manager, to get that time back is a significant improvement.
- Haven McCall, Vice President of Quality and Regulatory Affairs, Megadyne[9]

MasterControl provides a virtual collaboration workspace, which eliminates the need for in-person meetings:

- Store all documents in a secure, centralised repository. Authorised users can simultaneously access and mark up documents.
- Team members can access documents anytime and from anywhere without having to wait to receive the document.
- Designate alternate reviewers to step in for employees who are out of the office.

Document Management

Effective document management is critical for maintaining compliance. However, the processes are often fragmented and prone to errors, requiring more time and effort than necessary. Document management issues that companies contend with include:

- **More documentation required** – Regulators are requiring more detailed and comprehensive documentation to provide evidence of compliance.
- **Multiple formats** – Documentation is in the form of Microsoft Word® documents, spreadsheets, emails, etc. and maintained across disparate systems and business units.
- **Document retention** – Regulated companies must retain and manage product documentation, including all revisions, throughout the product's life cycle. Storing paper documents requires provisions to protect them from environmental hazards as well as to maintain their security and data integrity.
- **Document retrieval** – Per regulatory requirements, all documents must be readily available for review during, and sometimes before, an inspection. Paper-based or hybrid document management systems are disconnected and cumbersome. Companies need to scan paper documents to file them electronically and make them accessible to auditors prior to the site visit.

MasterControl boosts efficiency and ensures compliance by eliminating labor-intensive tasks such as physical routing of documents for approval, distribution, storage, and archiving.

- **Effective organisation** – Organise documents by setting up rules to automatically group them based on the document's metadata.
- **Submission templates** – Use templates that align with regulatory document type and format requirements.
- **Universal formats** – Accommodate documents in multiple formats such as Word documents and spreadsheets.
- **Time-stamped audit trail** – Automatically track all documents and records, including past versions, metadata, and approval history from the time they are created until the present.
- **Audit-ready documentation** – Store all documentation in a centralised repository. Easily search for and retrieve any document using configurable document naming and storage methods. Also, give auditors limited access to MasterControl, so they can review select documents before and during an inspection.

> Our [510(k)] submission was smooth because we had all the documents in MasterControl. All I had to do was make an e-copy to send to the reviewer, and then to the FDA. It was a fairly simple process for me to negotiate.
> - Balaji Sudabattula, Vice President of Quality and Regulatory Affairs, BraveHeart.[10]

Revision Control

Completing production tasks based on incorrect or outdated procedures, drawings, or specifications is the source of many errors and product deviations. Therefore, regulated companies are required to perform regular document reviews to ensure the documented processes match the actual processes.

Document revision control is complex and labor-intensive. It's important to involve the right stakeholders from all relevant business units. For example, a change that makes sense to engineering, regulatory, and quality may not be possible without significant changes to the production process. However, involving too many people

will slow the review time. Some challenges companies face with revision control include:

- Lengthy review and approval processes – When document approvers are out of the office, documents can sit for days before getting approved and routed to the next stakeholder.
- Obsolete and uncontrolled documents in circulation – Having older document revisions in circulation is often the result of not retrieving all previous versions after an update. Also, there might be photocopies of outdated versions that the document control staff is unaware of.
- Inability to track document approval routes – With disparate groups of stakeholders reviewing documents, it's difficult to keep track of the location and approval status of documents.

MasterControl enables you to efficiently control all document versions.

- No uncontrolled copies in circulation – Restrict editing rights on documents, and automatically archive old versions of a document when it's updated. Set up timebombs on downloaded PDF documents to ensure they will be in circulation only until the date and time specified.
- View change history – See the context around all the changes. Automatically track and record every change, including the person who made it, when it was made, and the reason for the change.
- Preconfigurable document routing, approval, and escalations – Routes for document collaboration or approval are preconfigurable for use at any time. You can also make adjustments at any time in the route. Assign one or multiple users to each step in a route, allowing you to use a combination of serial and parallel routing. In the event a reviewer is unavailable, the route automatically escalates to a designated alternate.
- Real-time, repeatable email notifications – Customisable email notifications alert reviewers to take action on their specific tasks. Managers are notified when tasks are completed, so they can proactively monitor collaboration, change management, approval, and training cycles.

Secure Architecture

Effective collaboration is essential for document control. However, when documents are scattered across different areas such as employees' laptops or mobile devices, spreadsheets, or printed documents, stakeholder interaction is haphazard and inconsistent. This might compel people to find creative ways to transfer and access documents.

- Emailing documents – Email is not secure. As soon as a user clicks Send, the email and all attached files are stored in the user's Sent Items folder, which puts the content at risk if the user or recipient's email account is breached. In lengthy email threads involving several people, someone might inadvertently

forward a message containing confidential files to an unintended recipient.

- Transmitting data files from mobile devices – When data files bounce around to various devices and endpoints, all control over the content is lost, and it is difficult to ensure that proprietary data is only accessible to authorised stakeholders.
- Sharing files using online collaboration tools and Wi-Fi connections – Employees can usually connect through a virtual private network (VPN) to remotely access the company's network. However, in the event of connectivity issues, a user might temporarily use an available, but unsecure, Wi-Fi connection to transmit files.
- Portable storage devices – Sometimes document files are too large to send through email. A workaround would be to download the file on a flash drive and then load the information to a laptop or mobile device. This approach also makes it difficult to track a document's revision and review status. Furthermore, if the storage device gets lost or stolen, the company's intellectual property can easily fall into the wrong hands.

MasterControl's cloud infrastructure has multiple security levels, which includes advanced system security and the highest level of data encryption. We also support multifactor authentication and authorisation functionality from third-party organisations. With a centralised database and documentation repository, there is no need to ever operate or transmit documents outside of the architecture. MasterControl's security credentials include:

- HIPAA compliance – Entails extensive data protection and system security measures, so customers can securely store protected health information (PHI) in MasterControl.
- ISO 27001:2013 certified – Focuses on the implementation, maintenance, and continuous improvement of an information security management system (ISMS).
- ISO 27017 certified – Focuses on information security controls specific to cloud computing.

Multiple teams of skilled cybersecurity experts implement and maintain all security measures.

Integrated With Other Quality Processes

The pandemic significantly altered the way businesses and employees function. For example, it's difficult to maintain continuity across all quality processes when employees are required to work remotely and remain at a social distance. This poses a variety of challenges, including:

- Fragmented change control – Change control is closely tied to FDA and ISO compliance. A change in one area will affect others. If other quality areas, such as training, corrective action/preventive action (CAPA), supplier management, audits, etc. are not integrated, the organisation will likely

experience miscommunication and quality-related delays.

- **Documentation changes not communicated** – Changes to documentation often require updating employee training. If updates are not communicated to the relevant stakeholders, the staff could be performing tasks based on outdated information.
- **Disparate systems and databases** – Business units commonly use department-specific tools and databases to perform tasks and store documents, making it difficult to effectively collaborate.

MasterControl's digital quality management system (QMS) software integrates all quality processes within a single architecture. This enables your organisation to more easily remain in sync and stay current with evolving regulations and standards.

- **Quality excellence:** Transform quality management with the most complete, connected, and intelligent QMS. Digitise and automate all quality tasks to ensure compliance throughout the product's life cycle.
- **Compliant document management and storage:** Store and manage documents in accordance with FDA regulations and ISO 9001:2015 standards. This includes documents produced by external companies.
- **Connectivity:** Eliminate silos by harmonising technology systems. Improve real-time communication, collaboration, and data sharing across all business units — streamlining the productivity of systems you already own.

Emerge as an Industry Leader

True document control is imperative for regulated companies, but it's difficult to achieve without a digital system. MasterControl's QMS solutions give you a competitive advantage. Combining our proven digitised processes and automation gives you the tools to establish a culture of quality and efficiency throughout your organisation, enabling you to easily achieve your time-to-market objectives.

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About MasterControl

MasterControl Inc. is a leading provider of cloud-based quality and compliance software for life sciences and other regulated industries. Our mission is the same as that of our customers – to bring life-changing products to more people sooner. The MasterControl Platform helps organisations digitise, automate and connect quality and compliance processes across the regulated product development life cycle. Over 1,000 companies worldwide rely on MasterControl solutions to achieve new levels of operational excellence across product development, clinical trials, regulatory affairs, quality management, supply chain, manufacturing and postmarket surveillance. For more information, visit www.mastercontrol.com.

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