To help medical device companies better understand the requirements associated with gaining regulatory approval of their new product introductions, the U.S. Food and Drug Administration has identified the 10 most common deficiencies that result in indications of noncompliance. Siemens PLM Software and Tata Consultancy Services have jointly prepared a guide to examine these deficiencies and outline the steps that companies can take to improve their rate of regulatory compliance.
Establishing regulatory compliance in the medical device industry

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The public health community and its providers are continually improving their ability to deliver new procedures, treatments, diagnostic methods and preventive practices. Breakthrough advances by medical device companies have facilitated both earlier disease detection and better long term healthcare.

However, productivity within the medical device industry has been inhibited by the complexity of today's health and safety regulations — and the cost and time required to comply with their associated regulatory approval processes.

New initiatives must be made available to help medical device companies focus more of their resources on new product development and less on regulatory compliance. With this in mind, the U.S. Food and Drug Administration (FDA) has carefully studied recent trends across multiple audits/inspections and identified the following deficiencies as the 10 most common reasons for issuing nonconformance indications to medical device companies requesting regulatory approval for their new product introductions.

- No corrective action/preventive action (CAPA) system
- Inadequate management controls
- No medical device record (MDR) system
- No written procedures
- Inadequate auditing procedures
- Missing or poorly maintained complaint files
- Inadequate complaint handling procedures
- No device master records (DMRs)
- No device history records (DHRs)
- Inadequate employee training

The following white paper examines most of these deficiencies and outlines steps that medical device companies can take to more effectively comply with the FDA's established regulations.

Management controls and employee training are usually defined and implemented in most companies’ total quality systems. Similarly, DHRs are maintained and managed as part of most companies’ manufacturing execution systems (MES). As a result, this white paper does not discuss these issues or their related initiatives.
The Food and Drug Administration is the regulatory agency for the United States Department of Health and Human Services responsible for regulating food, drugs, medical devices, biologics (vaccines, blood products), animal feed and drugs, cosmetics and radiation-emitting devices. Essentially, the FDA has the authority to prevent any entity from exposing the public to harmful products, substances and processes as detailed in the U.S. Code of Federal Regulations (CFR) administrative law. Two key sections of this code are especially crucial to the medical device industry.

- **21 CFR Part 11 Electronic Records and Electronic Signatures.** Title 21 Part 11 of the Code of Federal Regulations (commonly known as 21 CFR Part 11) "sets forth the criteria under which the agency considers electronic records, electronic signatures and handwritten signatures executed to electronic records to be trustworthy, reliable and generally equivalent to paper records and handwritten signatures executed on paper."

  This regulation covers the implementation of controls, including audits, validation systems and documentation for computer hardware and software systems involved in processing data as part of business operations and the product development process.

- **21 CFR Part 820 Quality System Regulation.** Title 21 of the Code of Federal Regulations (commonly known as FDA 21 CFR Part 820 or the Quality System Regulation, QSR) outlines Current Good Manufacturing Practice (CGMP) requirements that “govern the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation and servicing of all finished devices intended for human use.”

  These requirements are meant to ensure that medical devices are safe and effective. Responsibility for ensuring QSR compliance rests with the manufacturer of the final product.

**Corrective action and preventive action (CAPA) processes**

*Establishing the CAPA process.* Each medical device manufacturer is required to establish and maintain procedures for implementing corrective and preventive actions. All complaints directed to a medical device company must be investigated to determine whether the failure can be confirmed and whether its cause can be determined.

Once the failure is confirmed, the company needs to demonstrate that it has established procedures for implementing corrective and preventive action. In cases where the failure cannot be determined, the company can establish trending or continual monitoring of complaints related to the specific failure as an appropriate corrective and preventive action.

*Inspecting the CAPA process.* FDA audits are conducted at three levels. The first level starts with written procedures that the company has established to indicate who is responsible for determining whether the CAPA process is closely linked to the device’s design controls and/or its production and process controls. This determination can be presented in a variety of formats, including as a quality audit report, quality record, service record, complaint or returned service report. The company also is required to produce evidence of the statistical methodology adopted to detect and prevent recurring quality problems.

The second level of inspection identifies a specific product for which the correction or preventive action was performed. This inspection tracks the implementation of the action in the form of design changes or process changes that will be performed in the manufacturing facility.
The third level of inspection consists of a follow up to the second level of inspection. Its purpose is:

- To verify that adequate corrections and corrective actions have been implemented to fix the identified quality problems
- Or, if the corrections and corrective actions were not implemented (or if they were not implemented effectively), to verify that the deficiencies continue to exist and provide adequate evidence to support a possible regulatory action

**Complaint files and complaint handling procedures**

*Establishing complaint procedures.* Each device manufacturer must establish and maintain procedures for receiving, reviewing and evaluating all complaints (including oral complaints) to determine if the complaint represents an event that needs to be reported to the FDA. Records of these complaints need to be maintained in complaint files with information describing the complaint itself, the complainant, the investigation into the complaint and any corrective action taken.

*If no investigation was made,* the complaint file must explain the reason why no investigation was performed, and the name of the individual responsible for deciding not to investigate. If the complaint involves failure (or possible failure) of the device, its labeling or its packaging, then these specifications must be reviewed, evaluated and investigated.

*Inspecting complaints.* Complaints are the starting point of every inspection, where the parties who are responsible for conducting the inspection determine whether the manufacturer has received complaints of possible (or potentially) defective devices. The medical device company is required to maintain complaint files with information indicating the date when the complaint was received, name/address/phone number of the complainant, nature and details of the complaint, and any device identification and control numbers.

The company is required to maintain records of the investigation to determine whether the device failed to meet specifications or whether the device was being used for treatment or diagnosis, and the relationship (if any) of the device to the reported incident or adverse event. The investigation records need to include the name of the device, dates and results of the investigation, any corrective action taken and any reply to the complainant.

**Device master record**

*Establishing DMRs.* Each manufacturer is required to ensure that each DMR is prepared and approved for each type of device the company makes. DMRs need to include the following information:

- Device specifications
- Product process specifications
- Quality assurance procedures and specifications
- Packaging and labeling specifications
- Installation, maintenance and servicing procedures and methods

The intent of this requirement is to determine whether the device design and/or its process changes are— or may be— contributing to defective devices.
Inspecting DMRs. DMRs are inspected during level 2 after a determination has been made to audit the device's design controls as a result of a compliant or CAPA process. Traceability is required from the originally designed DMR for that device and the changes that resulted in the DMR as the result of the CAPA. DMRs for the device under inspection are validated for completeness to make sure they contain the following information:

- Device specifications, which include appropriate drawings, compositions, formulations, component specifications and software specifications
- Production process specifications, which include appropriate equipment specifications, production methods, production procedures and production environment specifications
- Quality assurance procedures and specifications, which include acceptance criteria and the quality assurance equipment to be used
- Packaging and labeling specifications, which include methods and processes used
- Installation, maintenance and servicing procedures and methods

Managing the medical device lifecycle end-to-end

Siemens' Teamcenter® software provides an integrated cross-discipline solution for end-to-end management of the medical device industry's product lifecycle. The Teamcenter solution takes a holistic approach to product lifecycle and regulatory compliance management by enabling medical device companies to capture a take-to-market program's product and marketing requirements – and then tracing these requirements to ideas, concepts, design prototypes, parts, product definitions, bills of materials, process models and after-market service definitions.

The resulting body of knowledge is made available to every lifecycle participant and every mission-critical application that drives the medical device lifecycle. This comprehensive approach to product and process management enables medical device companies to proactively address strategic issues that influence a product's marketplace success, constrain its lifecycle costs, and treat regulatory compliance as a systematically manageable product requirement.

Teamcenter leverages a high level systems engineering approach with tight change management controls to make certain that all design, manufacturing and test processes have been qualified and deemed suitable for use – as well as that all operational methodologies have been validated to ensure that they can – and actually have – performed their declared functions.

Teamcenter assures the completeness and quality of all submitted products by ensuring correctness at every step in the product lifecycle – thereby accelerating time to device approval by requiring fewer iterations. Built on an industry-leading distributed and modular service-oriented architecture (SOA), Teamcenter's medical device solution is able to unify all of the disparate sources of product, process and compliance information in an enterprise, including its PDF, XML, J2EE-compliant web applications and back-end data sources.
Dynamic multi-CAD integration

Teamcenter provides multi-CAD support for companies that want to use the full capabilities of the end-to-end medical device solution. This enables product developers from different organizations to work with their authoring tool-of-choice while ensuring that their designs are seamlessly integrated into unified product definitions.

In addition, Teamcenter enables medical device companies to automatically capture a product’s design history into a product-focused context rather than the document-centric or CAD-centric context that other IT systems support. Companies use Teamcenter to establish templates with approval processes and workflows that reflect industry-best practices.

Companies also use Teamcenter to incorporate Adobe’s rich document-rights management features into the end-to-end medical device solution. Product development teams leverage the integration to render both Microsoft Office documents and CAD designs into PDFs at the end of an approval cycle. In addition, teams can apply digital signatures to appropriate PDFs using encryption techniques that prevent documents from being falsified both inside and outside of their Teamcenter-controlled environment.
Leveraging rich document management under Teamcenter

Improving FDA regulatory compliance

Teamcenter’s medical device solution is especially valuable for companies that want to improve the way they comply with FDA regulations. With this objective in mind, companies use Teamcenter to make compliance management a natural and systematic part of their product development environment.

Product development teams use Teamcenter to create, modify and route compliance-related documents through process-driven workflows that ultimately result in FDA-approved documents that are dynamically converted into a secure format (such as a PDF file).

Product teams use rules-driven product documents to ensure design control that applies to device packaging and labeling, as well as production and process controls that interface with existing MES, application (software) control and training management systems.

In addition, product teams use Teamcenter to create DMRs to ensure that a device’s designs meets established regulatory requirements and that the risks of noncompliance have been captured, understood, analyzed and controlled during the product development cycle.

Beyond this, teams use Teamcenter to maintain complaints (originating from both external and internal sources) in a single information system that provides workflow-capabilities for creating, managing, tracking and reporting on CAPA processes.

Teamcenter-managed design history file (DHF)
Teamcenter capabilities for CAPA inspection. Teamcenter provides robust capabilities for managing CAPA processes, including the ability to:

- Record complaints and trigger a CAPA workflow for each device
- Associate and maintain necessary documents (including quality audit reports, quality records and service records) as investigative reference to the CAPA workflow
- Maintain necessary statistical documentation associated with CAPA processes
- Group multiple CAPAs when multiple failures converge to a single cause
- Trigger a design change (engineering change requests) or deviation/changes in the manufacturing processes if warranted by the CAPA
- Generate offline reports to plot the trend of the CAPAs with associated causes (in instances when failure cannot be converged to one particular cause)

Managing complaints using Teamcenter’s CAPA process management capability

Design issues report generated by Teamcenter
**Teamcenter capabilities for complaint inspection.** Teamcenter provides several key capabilities to help medical device companies manage complaints, including the ability to:

- Record complaints through a web interface, including retaining information about receiving the complaint, the complainant, the device's lot/serial numbers and a description of the complaint
- Launch an investigation of the complaint to start a CAPA process
- Link the complaint to the product definition of the specific device, part or component part
- Create an audit trail through the CAPA process

**Teamcenter capabilities for DMR inspection.** Teamcenter enables medical device companies to maintain and manage DMRs by providing the ability to:

- Create the DMR automatically during product design
- View and validate the DMR, as well as link/configure its documents to a specific device
- Revise the DMR and its documents independently with automatic obsolescence
- Retrieve the DMR and its documents based on effectivity
- Create DMR templates to pre-configure DMR content and configuration
Integrating the design-through-manufacturing process

Word class medical device manufacturers consistently bring compliant products to market ahead of the competition. They distinguish themselves by meeting these objectives while delivering the right features at the right price for an increasingly diverse global marketplace. To accomplish these objectives, medical device manufacturers face a variety of challenges, including the need to:

- Connect all of the different teams involved in today's design-through-manufacturing process
- Find and re-use proven manufacturing methods
- Locate correct and accurate product information
If manufacturers fail to meet these challenges, they often face higher planning and manufacturing costs, longer product introduction cycles and declining levels of product and process quality. Teamcenter’s medical device solution addresses these challenges by providing a single, shared source of design and manufacturing information that companies can use to streamline the design-through-manufacturing process, enable process participants to easily retrieve the right data and facilitate the re-use of proven manufacturing methods.

Companies can use Teamcenter’s manufacturing process management capabilities to leverage this single, traceable, secure source of manufacturing data to support a complete medical device lifecycle that extends from concept ideation through actual production. This single source of manufacturing data includes product, process, resource and plant information that enables manufacturing to directly influence product innovation and significantly improve a company’s time-to-market, quality and regulatory compliance performance.

Marking up an exploded view of a manufacturing assembly
Regulatory compliance needs to become an integral part of the medical device lifecycle. Unless medical device companies approach compliance from this kind of holistic perspective, they will continue to spend too much valuable time and resources trying to mitigate the risk of FDA noncompliance.

Teamcenter’s medical device solution enables companies to maintain and manage their product and process knowledge in a globally accessible product lifecycle management (PLM) system. This system’s ability to capture audit trails, maintain electronic signatures and facilitate instant information retrieval is closely attuned to the need for effective compliance management.

Teamcenter’s comprehensive approach to product and manufacturing management enables medical device companies to design, collaborate and track their design devices and manufacturing information in a single system that allows their product developers to do what they do best – innovate to meet the needs of today’s global healthcare community.

Just as importantly, Teamcenter provides medical device companies with full and complete set of capabilities that will enable them to address all 10 of the issues raised by the FDA as today’s primary causes of regulatory noncompliance.
About Siemens PLM Software

Siemens PLM Software, a division of Siemens Automation and Drives (A&D), is a leading global provider of product lifecycle management (PLM) software and services with 4.3 million licensed seats and 47,000 customers worldwide. Headquartered in Plano, Texas, Siemens PLM Software’s open enterprise solutions enable a world where organizations and their partners collaborate through Global Innovation Networks to deliver world-class products and services. For more information on Siemens PLM Software products and services, visit www.siemens.com/plm.