1 Setting up a Quality Management System

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Introduction

Building a quality management system (QMS) from scratch can be challenging, especially when the appropriate regulatory standards or compliance guidelines are not followed. Management system standards make best practices available to organizations of all sizes, in all sectors. Any organization can implement a system to improve efficiency and effectiveness and manage its way of doing things by:

- ensuring nothing important is omitted
- clearly defining who is responsible
- describing what to do, why, when, how and where
- ensuring people are not just "doing their own thing"
- ensuring the organization goes about its business in an orderly way[1]

Quality management is the set of coordinated activities to direct and control an organization with regard to quality.[2] Quality management systems are central to the medical device regulatory process in many countries to ensure safe products entering the market perform as intended. Streamlining and automating design documentation and quality processes to align with major industry regulations and standards are key criteria for setting up a quality management system. In this chapter, the focus is on ISO 9001 and ISO 13485,[3,4] and subsequently, US FDA's *Quality System Regulation (QSR)*[5] contained in 21 CFR 820. ISO 13485:2016 *Medical Devices—Quality Management Systems—Requirements for Regulatory Purposes* is a QMS standard based on ISO 9001 *Quality Management Systems Requirements*. The ISO 9000 series, originally published in 1987, was based on the British Standards Institution's (BSI) BS 5750 series of standards.[6] ISO 9001 covers both product quality assurance (providing confidence that quality requirements will be fulfilled) and enhanced customer satisfaction. Key differences between ISO 9001 and ISO 13485 are shown in **Table 1-1**.[7] Similarities between ISO 9001 and ISO 13485 are shown in **Table 1-2.** The standard can be applied to all products and services. ISO 9001 is based on the eight quality management principles:

1. process approach
2. system approach to management
3. continual improvement
4. factual approach to decision making
5. mutually beneficial supplier relationship
6. customer focus
7. leadership
8. involvement of people[8]

Table 1-1. Key Differences Between ISO 9001 and ISO 13485

ISO 9001	ISO 13485
6 documents	27 documents
Aims for customer satisfaction through continuous improvement	Does not include customer satisfaction and continuous improvement as objectives
Covers all products	Different requirements for different types of products
Basis for voluntary certification	Basis for regulatory certification

Table 1-2. Similarities Between ISO 9001 and ISO 13485

Clause in ISO 9001:2015	Clause in ISO 13485:2016
1 Scope	1 Scope
4 Context of the organization	4 Quality Management System
4.1 Understanding the Organization and its Context	4.1 General Requirements
4.2 Understanding the Needs and Expectations of Interested Parties	4.1 General Requirements
4.3 Determining the Scope of the Quality Management System	4.1 General Requirements 4.2.2 Quality Manual
4.4 Quality Management System and its Processes	4.1 General Requirements
5 Leadership	5 Management Responsibility
5.1 Leadership and Commitment	5.1 Management Commitment
5.1.1 General	5.1 Management Commitment
5.1.2 Customer Focus	5.2 Customer Focus
5.2 Policy	5.3 Quality Policy
5.2.1 Establishing the Quality Policy	5.3 Quality Policy
5.2.2 Communicating the Quality Policy	5.3 Quality Policy
5.3 Organizational Roles, Responsibilities and Authorities	5.4.2 Quality Management System Planning 5.5.1 Responsibility and Authority 5.5.2 Management Representative
6 Planning	5.4.2 Quality Management System Planning
6.1 Actions to Address Risks and Opportunities	5.4.2 Quality Management System Planning 8.5.3 Preventive Action
6.2 Quality Objectives and Planning to Achieve Them	5.4.1 Quality Objectives
6.3 Planning of Changes	5.4.2 Quality Management System Planning
7 Support	6 Resource Management
7.1 Resources	6 Resource Management
7.1.1 General	6.1 Provision of Resources
7.1.2 People	6.2 Human Resources
7.1.3 Infrastructure	6.3 Infrastructure
7.1.4 Environment for the Operation of Processes	6.4.1 Work Environment
7.1.5 Monitoring and Measuring Resources	7.6 Control of Monitoring and Measuring Equipment
7.1.5.1 General	7.6 Control of Monitoring and Measuring Equipment
7.1.5.2 Measurement Traceability	7.6 Control of Monitoring and Measuring Equipment
7.1.6 Organizational Knowledge	6.2 Human Resources
7.2 Competence	6.2 Human Resources
7.3 Awareness	6.2 Human Resources
7.4 Communication	5.5.3 Internal Communication
7.5 Documented Information	4.2 Documentation Requirements

Table 1-2. Similarities Between ISO 9001 and ISO 13485 (cont.)

Clause in ISO 9001:2015	Clause in ISO 13485:2016
7.5.1 General	4.2.1 General
7.5.2 Creating and Updating	4.2.4 Control of Documents 4.2.5 Control of Records
7.5.3 Control of Documented Information	4.2.3 Medical Device File 4.2.4 Control of Documents 4.2.5 Control of Records 7.3.10 Design and Development Files
8 Operation	7 Product Realization
8.1 Operational Planning and Control	7.1 Planning of Product Realization
8.2 Requirements for Products and Services	7.2 Customer-Related Processes
8.2.1 Customer Communication	7.2.3 Communication
8.2.2 Determining the Requirements for Products and Services	7.2.1 Determination of Requirements Related to Product

The ISO 9001 family of standards, including ISO 13485, promotes the process approach, which uses resources and is managed to transform inputs into outputs (**Figure 1-1**). The process approach applies a system of processes and the processes' identification and interaction and their management. The process approach emphasizes the following:

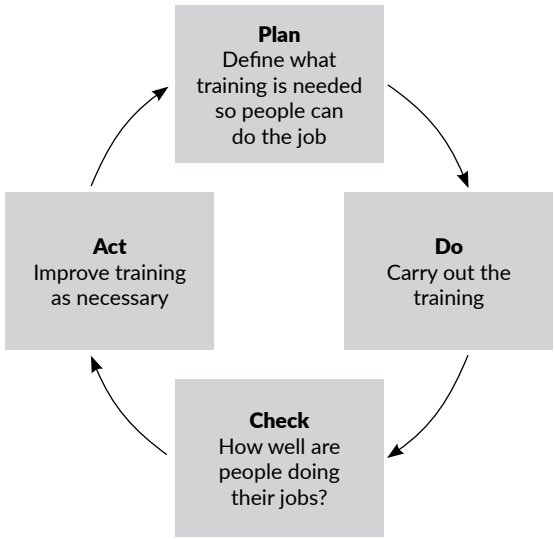
- understanding and meeting requirements
- looking at processes in terms of added value
- obtaining process performance results
- continual process improvement

Plan-Do-Check-Act (PDCA)[9] (**Figure 1-2**) applies to all processes. Each ISO 9001 main clause starts with a 'planning' activity, has a 'doing' activity, has a 'checking' activity (measurement may be implied) and has an 'acting' activity (improvement may be applied).

EN ISO 13485:2016 is the latest harmonized European publication used by organizations wishing to implement a QMS in conformance with the EU *Medical Devices Directive* (93/42/EEC, *MDD*), *Active Implantable Medical Devices Directive* (90/385/EEC, *AIMDD*) and *In Vitro Diagnostics Directive* (98/79/EC, *IVDD*).[10-12] The standard is applicable to manufacturers placing medical devices on the EU market. For the rest of the world, ISO 13485:2003 remains the applicable standard. The two versions have the same requirements. The 2016 version includes annexes detailing the ISO 13485 sections, where the notified body focuses on the directives' additional requirements for CE marking. The standard is used to assess medical devices' and related services' ability to meet customer and regulatory requirements. It is not intended to imply uniformity in the QMS structure or documentation. The standard is complementary to product and technical requirements. Some requirements in the standard apply to specific products, such as implantable or sterile devices. ISO 13485 is a standalone standard based on ISO 9001, containing all of the ISO 9001 clauses except, primarily, those concerning continuous improvement and customer satisfaction. ISO/TR 14969[13] gives guidance on implementing ISO 13485. ISO 13485 is not intended to include requirements specific to other

Figure 1-1. Basic Process Model

Figure 1-2. PDCA Cycle in Resource Management



management systems (e.g., environmental or health and safety), but it allows an integrated approach with those standards (e.g., ISO 14001).[14] ISO 13485 specifies requirements for organizations that:

- design, develop, produce, install or service medical devices
- design, develop or provide related services[15]

ISO 13485 certification is available to organizations producing products regulated as medical devices in at least one country in the world (ISO 13485 certificates should not be issued to pharmaceutical or cosmetic product manufacturers). For example, human tissue, although not medical devices in the EU, are covered under Japanese MHLW Ministerial Ordinance 169[16] and could be covered by an ISO 13485 QMS. Examples of related services that can be certified to ISO 13485 include contract sterilizers and packers, manufacturers of significant medical device components (e.g., machining implants) and warehouses.[17]

Exclusions and non-applications to ISO 13485 should be listed and justified in the organization's quality manual. Exclusions are limited to design and development controls (Clause 7.3). Regulations may be considered a justification for exclusion, e.g., 93/42/EEC, Annex V). Parts of Clause 7 may not be applicable due to the medical device's nature (e.g., a non-sterile, non-implantable, non-active device).

ISO 13485 is structured as follows (Clauses 4 through 8 are the auditable requirements and are shown in more detail):

0. Introduction
1. Scope
2. Normative References
3. Terms and Definitions
4. Quality Management System
4.1 General Requirements
4.2 Documentation Requirements
4.21 General documentation specified by national or regional regulations: each type or model of medical device requires a file containing product specification and QMS requirements. These shall define the complete manufacturing process.
4.22 Quality Manual
4.23 Medical Device File
4.24 Control of Documents
4.25 Control of Records
5. Management Responsibility
5.1 Management Commitment
5.2 Customer Focus
5.3 Quality Policy
5.4 Planning
5.4.1 Quality Objectives
5.4.2 Quality Management System Planning
5.5 Responsibility, Authority and Communication
5.5.1 Responsibility and Authority
5.5.2 Management Representative
5.5.3 Internal Communication
5.6 Management Review
5.6.1 Management Review General
5.6.2 Management Review Input
5.6.3 Management Review Output
6. Resource Management

6.1 Provision of Resources
6.2 Human Resources
6.3 Infrastructure
6.4 Work Environment and Contamination Control
6.4.1 Work Environment
6.4.2 Contamination Control
7. Product Realization
7.1 Planning of Product Realization
7.2 Customer-Related Processes
7.2.1 Determination of Customer Requirements
7.2.2 Review of Requirements Relating to the Product
7.2.3 Customer Communications
7.3 Design and Development
7.3.1 General
7.3.2 Design and Development Planning
7.3.3 Design and Development Inputs
7.3.4 Design and Development Outputs
7.3.5 Design and Development Review
7.3.6 Design and Development Verification
7.3.7 Design and Development Validation
7.3.8 Design and Development Transfer
7.3.9 Control of Design and Development Changes
7.3.10 Design and Development Files
7.4 Purchasing
7.4.1 Purchasing Process
7.4.2 Purchasing Information
7.4.3 Verification of Purchased Product
7.5 Production and Service Provision
7.5.1 Control of production and Service Provision
7.5.2 Cleanliness of Product
7.5.3 Installation Activities
7.5.4 Servicing Activities
7.5.5 Particular Requirements for Sterile Medical Devices
7.5.6 Validation of Processes for Production and Service Provision
7.5.7 Particular Requirements for Validation of Process for Sterilization and Sterile Barrier Systems
7.5.8 Identification and Traceability
7.5.9 Customer Property
7.5.10 Preservation of Product
7.6 Control of Monitoring and Measuring Devices
8. Measurement, Analysis and Improvement
8.1 General
8.2 Monitoring and Measurement
8.2.1 Feedback
8.2.2 Complaint Handling
8.2.3 Reporting To Regulatory Authorities
8.2.4 Internal Audit
8.2.5 Monitoring and Measurement of Processes
8.2.6 Monitoring and Measurement of Product
8.3 Control of Nonconforming Product
8.3.1 General
8.3.2 Actions in Response to Nonconforming Product Detected Before Delivery
8.3.3 Actions in Response to Nonconforming Product Detected After Delivery
8.3.4 Rework
8.4 Analysis of Data
8.5 Improvement
8.5.1 General
8.5.2 Corrective Action
8.5.3 Preventive Action

ISO 13485:2016

ISO 13485:2016 was published on 26 February 2016. A comparison of ISO 13485:2003 and ISO 13485:2016 is shown in **Table 1-3**. ISO 13485:2016 makes it easier to model internal audits on the Medical Device Single Audit Program (MDSAP) approach, and in particular, introduces its new scoring system for nonconformances.

The new grading system attempts to apply a more objective standard to determining the risk associated with a given issue, eliminating the concepts of "major" or "minor" nonconformance. In short, the system assigns a numerical risk score for each quality system problem (nonconformance) identified in an internal audit). Nonconformances related to areas of the QMS that have an indirect impact on safety and performance (e.g., documentation, management responsibility, resource management) would receive a lower score than those

Table 1-3. Comparison of ISO 13485:2003 and ISO 13485:2016

ISO 13485:2003	ISO 13485:2016
4 Quality Management System	4 Quality Management System
4.1 General Requirements	4.1 General Requirements
4.2 Documentation Requirements	4.2 Documentation Requirements
4.2.1 General	4.2.1 General
4.2.2 Quality Manual	4.2.2 Quality Manual
***	4.2.3 Medical Device File
4.2.3 Control of Documents	4.2.4 Control of Documents
4.2.4 Control of Records	4.2.5 Control of Records
5 Management Responsibility	5 Management Responsibility
5.1 Management Commitment	5.1 Management Commitment
5.2 Customer Focus	5.2 Customer Focus
5.3 Quality Policy	5.3 Quality Policy
5.4 Planning	5.4 Planning
5.4.1 Quality Objectives	5.4.1 Quality Objectives
5.4.2 Quality Management System Planning	5.4.2 Quality Management System Planning
5.5 Responsibility, Authority and Communication	5.5 Responsibility, Authority and Communication
5.5.1 Responsibility and Authority	5.5.1 Responsibility and Authority
5.5.2 Management Representative	5.5.2 Management Representative
5.5.3 Internal Communication	5.5.3 Internal Communication
5.6 Management Review	5.6 Management Review
5.6.1 General	5.6.1 General
5.6.2 Review Input	5.6.2 Review Input
5.6.3 Review Output	5.6.3 Review Output
6 Resource Management	6 Resource Management
6.1 Provision of Resources	6.1 Provision of Resources
6.2 Human Resources	6.2 Human Resources
6.2.1 General	***
6.2.2 Competence, Awareness, and Training	***
6.3 Infrastructure	6.3 Infrastructure
6.4 Work Environment	6.4 Work Environment and Contamination Control
***	6.4.1 Work Environment
***	6.4.2 Contamination Control
7 Product Realization	7 Product Realization
7.1 Planning of Product Realization	7.1 Planning of Product Realization
7.2 Customer-Related Processes	7.2 Customer-Related Processes
7.2.1 Determination of Requirements Related to the Product	7.2.1 Determination of Requirements Related to the Product
7.2.2 Review of Requirements Related to Product	7.2.2 Review of Requirements Related to Product
7.2.3 Customer Communication	7.2.3 Communication
7.3 Design and Development	7.3 Design and Development

Table 1-3. Comparison of ISO 13485:2003 and ISO 13485:2016 (cont.)

ISO 13485:2003	ISO 13485:2016
***	7.3.1 General
7.3.1 Design and Development Planning	7.3.2 Design and Development Planning
7.3.2 Design and Development Inputs	7.3.3 Design and Development Inputs
7.3.3 Design and Development Outputs	7.3.4 Design and Development Outputs
7.3.4 Design and Development Review	7.3.5 Design and Development Review
7.3.5 Design and Development Verification	7.3.6 Design and Development Verification
7.3.6 Design and Development Validation	7.3.7 Design and Development Validation
***	7.3.8 Control of Design and Development Transfer
7.3.7 Control of Design and Development Changes	7.3.9 Control of Design and Development Changes
***	7.3.10 Design and Development Files
7.4 Purchasing	7.4 Purchasing
7.4.1 Purchasing Process	7.4.1 Purchasing Process
7.4.2 Purchasing Information	7.4.2 Purchasing Information
7.4.3 Verification of Purchased Product	7.4.3 Verification of Purchased Product
7.5 Production and Service Provision	7.5 Production and Service Provision
7.5.1 Control of Production and Service Provision	7.5.1 Control of Production and Service Provision
7.5.1.1 General Requirements	***
7.5.1.2 Control of Production and Service Provisions - Specific Requirements	***
7.5.1.2.1 Cleanliness of Product and Contamination control	7.5.2 Cleanliness of Product
7.5.1.2.2 Installation Activities	7.5.3 Installation Activities
7.5.1.2.3 Servicing Activities	7.5.4 Servicing Activities
7.5.1.3 Particular Requirements for Sterile Devices	7.5.5 Particular Requirements for Sterile Devices
7.5.2 Validation of processes for production and service provision	7.5.6 Validation of processes for production and service provision
7.5.2.1 General Requirements	***
7.5.2.2 Particular requirements for sterile medical devices	7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems
7.5.3 Identification and Traceability	***
7.5.3.1 Identification	7.5.8 Identification
7.5.3.2 Traceability	7.5.9 Traceability
7.5.3.2.1 General	7.5.9.1 General
7.5.3.2.2 Particular requirements for active implantable devices and implantable devices	7.5.9.2 Particular Requirements for Implantable Devices
7.5.3.3 Status Identification	***
7.5.4 Customer Property	7.5.10 Customer Property
7.5.5 Preservation of Product	7.5.11 Preservation of Product
7.6 Control of Monitoring and Measuring Equipment	7.6 Control of monitoring and Measuring Equipment
8 Measurement, Analysis and Improvement	8 Measurement, Analysis and Improvement
8.1 General	8.1 General

Table 1-3. Comparison of ISO 13485:2003 and ISO 13485:2016 (cont.)

ISO 13485:2003	ISO 13485:2016
8.2 Monitoring and Measurement	8.2 Monitoring and Measurement
8.2.1 Feedback	8.2.1 Feedback
***	8.2.2 Complaint Handling
***	8.2.3 Reporting to Regulatory Authorities
8.2.2 Internal Audit	8.2.4 Internal Audit
8.2.3 Monitoring and Measurement of Processes	8.2.5 Monitoring and Measurement of Processes
8.2.4 Monitoring and Measurement of Product	8.2.6 Monitoring and Measurement of Product
8.2.4.1 General requirements	***
8.2.4.2 Particular requirement for active implantable devices and implantable devices	***
8.3 Control of Nonconforming Product	8.3 Control of Nonconforming Product
***	8.3.1 General
***	8.3.2 Actions in response to nonconforming product detected before delivery
***	8.3.3 Actions in response to nonconforming product detected after delivery
***	8.3.4 Rework
8.4 Analysis of Data	8.4 Analysis of Data
8.5 Improvement	8.5 Improvement
8.5.1 General	8.5.1 General
8.5.2 Corrective Action	8.5.2 Corrective Action
8.5.3 Preventive Action	8.5.3 Preventive Action

found in areas with a direct impact and therefore greater risk (e.g., contamination control, design inputs and outputs, validation, equipment installation and servicing). Additional points would be given for repeat observations.

The standard has many additions, some new requirements, some expansions and clarifications, and provides increased clarity on the interrelationships among clauses and requirements. There is an increased focus on meeting regulatory requirements, and the definitions have expanded. Sub-clause numbering has been changed to facilitate alignment with the MDSAP. Since the MDSAP is built on multiple regulations from the five participating countries, a manufacturer who complies with the MDSAP automatically complies with the regulations for the five participating countries.

National regulatory authorities, including FDA, will have to consider how these ISO 13485 revisions may affect their national regulatory schemes. Significant changes to each auditable clause are summarized below.

QMS

Clause 4 now includes requirements for a risk-based approach when developing QMS processes and documenting organization roles, with regulatory implications for those in the supply chain, such as manufacturers, authorized representatives, importers or distributors. There also are new requirements for keeping records to demonstrate compliance with regulatory requirements and for monitoring and controlling outsourced processes commensurate with risk. Special requirements for control over outsourced processes are provided in

Clause 4. Those controls should be proportionate to the risk related to the process and should include written quality agreements.

A significant addition is a requirement to validate QMS computer software (in addition to software used in the product) prior to initial use and following any changes; this includes software used in production, design and development, testing, inventory control, labeling, distribution, calibration, maintenance, Corrective and Preventive Action (CAPA), data management and complaints handling. Clause 4 includes the requirement to develop a device file that demonstrates conformity with ISO 13485 and regulatory requirements.

Clause 4 now includes a detailed list of the technical documentation that could be used to meet regulatory requirements, including product description, classification, preclinical testing, clinical evaluation, user information (e.g., labels and IFU), standards applied and risk management documentation.

Management Responsibility

Clause 5 requires top management to communicate the importance of meeting customer and regulatory requirements within the organization (previously, this was explicitly the management representative's remit). There also is a new requirement to document authorities and responsibilities. Action item identification and implementation to meet quality objectives are required, along with documentation of progress and any revisions. The management representative's responsibility to liaise with external parties now includes regulatory authorities. Management review frequency and rationale also should be documented, including a documented procedure for management review. The list of inputs for management review includes complaint handling, reporting to regulators, process monitoring and product monitoring. An additional management review output is needed to respond to new or revised regulatory requirements.

Resource Management

Clause 6 now specifies organization personnel working at all levels in product quality, process fulfilment, regulatory requirements and QMS compliance shall be competent on the basis of education, training, skills and experience. Staff competence should be maintained, and training effectiveness verification must be commensurate with the risk of the work for which the training is provided, requiring a documented process.

If maintenance activities can affect product safety or performance, documented procedures must exist for that equipment. Additionally, if the work environment can affect product safety or performance, the organization must document the requirements and have procedures in place for monitoring and measuring the work environment, e.g., an organization must document the requirements for contamination and cleanliness for sterile medical devices.

Product Realization

Clause 7.1 requires a risk management process to be established, with specific criteria for product and product acceptance: verification, validation, revalidation, monitoring, measurement, inspection, test activities, handling storage and traceability. Clause 7.2 requires the organization to determine user training needs and to develop provisions for protecting confidential health information. A new clause contains requirements on communicating with regulatory authorities.

In addition, the updated standard contains more details on design planning, with an emphasis on decision points and provides further details on transfer activities (to ensure design outputs have been verified before transfer to production occurs). Further details are provided on verification and validation (V&V) requirements. V&V activities require a specific plan, with details on methodology, sample sizes and acceptance criteria. The standard also contains a new clause on design transfer, specifying planning activities for suppliers, personnel, materials and equipment.

Clause 7.3 requires organizations to maintain a file that shows the design and development process has been properly followed, including documenting the following:

- the methods used to ensure traceability of design outputs to design inputs

- the resources needed for design and development, including personnel competence
- design inputs that include usability requirements and standards
- how design inputs are verified and validated, including statistical techniques and rationales for sample sizes
- design transfer and design change procedures

Clause 7.4 contains specific requirements on approving (including planning and evaluating) and monitoring suppliers and maintaining records; a risk-based approach is required (including the extent of purchased product verification).

Clause 7.5 has a number of new requirements and clarifications for implementing defined labeling and packaging operations. Organizations must analyze service records and document the statistical basis for process validation, including sample size.

Processes that cannot be verified should be validated. Specific requirements for packaging validation and planning and documentation are also included. A Unique Device Identifier (UDI) system is specified if required by relevant regulatory requirements. The standard also contains specific requirements for device packaging and product preservation during distribution.

Clause 7.6 includes addressing feedback for both production and post-production information.

Measurement, Analysis and Improvement

Clause 8 has a feedback process requirement for risk management and statistical analysis, tools and techniques to determine the need for feedback data to be escalated into CAPA. Clause 8.2 includes procedures to document complaints, including both production and post-production information. This clause also contains further details on minimum complaint handling requirements. For example, in the EU, organizations currently are required to perform trend analysis of complaints, and some complaints may trigger a report to the EU. Another new requirement is for internal audits to explicitly answer whether the QMS conforms to regulatory standards.

Under section 8.3, organizations are responsible for documenting requirements for non-conformities. Sections 8.4 and 8.5 stipulate that data analysis include valid statistical techniques and inputs from audits and service reports.

There is a new requirement for equipment and personnel to be identified and recorded for product monitoring. The standard contains more detailed nonconforming product requirements, depending on whether the nonconformity was detected before or after delivery, and considerations for escalating to CAPA. Corrective actions should be commensurate with the risk and taken without undue delay. Process and product data should be reviewed to identify inputs to the CAPA process. Analysis should be an input to management review.

In summary, the revisions to the standard address the following:

- regulatory requirements emphasized throughout the standard at all levels of the organization and product lifecycle
- risk management used throughout the standard, with actions and decisions commensurate with risk
- planning activities required for more processes
- additional design verification, validation and transfer requirements
- more-detailed requirements on outsourced processes and supplier control
- feedback analyzed statistically to determine escalation to CAPA
- additional nonconforming product requirements and CAPA escalation considerations
- specific design and development file contents and technical documentation

The documentation level required for an ISO 13485 QMS is higher than that for a typical ISO 9001 QMS, due to the risk of products an ISO 13485 system covers (medical devices) and the traceability requirements for issues after products have been placed on the market.

Mandatory procedures and documents for an ISO 13481-compliant system are shown in **Figure 1-3.**

An ISO 13485-certified QMS can support regulatory compliance in a number of jurisdictions, as shown in **Table 1-4**. The data to support regulatory submission depend on properly trained and qualified personnel performing tests, standard operating procedures, properly calibrated test equipment, documentation and configuration control of test articles, design controls, etc.—all QMS elements. This is an ongoing process with links between the QMS and postmarketing surveillance (PMS). From an ISO perspective, PMS is one of the key QMS activities listed in Clause 8 linking to CAPA, complaint handling and adverse event/vigilance reporting, etc. At some point, changes driven by CAPA may require a new regulatory submission.

Figure 1-3. Mandatory Procedures and Documents for ISO 13485:2003

4.2	4.2.1 Quality manual, quality policy and quality objectives 4.2.3 Control of documents 4.2.4 Control of records
6	6.2.2 Competence, awareness and training* 6.3 Infrastructure 6.4 Work environment
7.1	Planning of product realisation
7.3	Design and development
7.4	Purchasing
7.5.1	7.5.1.1 Production and service provision-Control of production and service provision 7.5.1.2.1 Cleanliness of product and contamination control 7.5.1.2.2 Installation activities 7.5.1.2.3 Servicing activities
7.5.2	7.5.2.1 Validation of processes for production and service provision** 7.5.2.2 Particular requirements for sterile medical devices
7.5.3	Identification and traceability
7.5.5	Preservation of product
7.6	Control of monitoring and measuring devices
8.1	General***
8.2	8.2.1 Feedback 8.2.2 Internal audit 8.2.4 Monitoring and measurement of product
8.3	Control of nonconforming product
8.4	Analysis of data
8.5	8.5.1 General (advisory notices and adverse events) 8.5.2 Corrective action 8.5.3 Preventive action

*National or regional regulations might require the organization to establish documented procedures for identifying training needs.
**The organization shall establish documented procedures for validating computer software applications (and changes to such software and/or its application) for production and service provision affecting the product's ability to conform to specified requirements. Such software applications shall be validated prior to initial use.
***National or regional regulations might require documented procedures for implementation and control of the application of statistical techniques.

Table 1-4. Applicability of ISO 13485 in Various Global Jurisdictions

Australia	Requires an audited quality system. ISO 13485 meets those requirements.
Canada	Requires an ISO 13485 registered system for CMDCAS certification for Class II or higher devices. Allows permissible exclusions depending on class of device.
EU	A QMS is required for CE marking that must accompany any medical device sold in the EU. A registered ISO 13485 system is recognized as proof of a QMS for CE marking when the certificate is issued by a Notified Body.
Japan	Requires establishment of a QMS that conforms to MO No. 169, which is similar to ISO 13485. ISO 13485 is an option but not a requirement.
Taiwan	The GMP requirements for Taiwan are based on ISO 13485.
US	Medical device companies are required to establish a QMS that conforms to FDA Quality System Regulations. ISO 13485 is an option but not a requirement (and does not connote full conformity with the QSR).

Regulatory requirements for the region where products are being sold would be part of an organization's ongoing ISO 13485 certification assessment.

Compliance to ISO 13485 is assessed by a certification body, and CE marking, where required, is assessed by a notified body (NB). These entities are regulated differently: NBs by competent authorities and QMS certification by an accreditation body, e.g., United Kingdom Accreditation Service (UKAS) and the Standards Council of Canada (SCC). The scope of the QMS certificate and CE certificate are dependent on the organization's activities and must be demonstrated by the organization before they can be included in the certificate's scope.

Process Approach

The organization shall:

- identify the processes needed for the quality management system and their application throughout the organization
- determine the sequence and interaction of these processes
- determine criteria and methods needed to ensure that both the operation and control of these processes are effective

To implement an ISO 13485 QMS (or any kind of QMS, voluntary or mandatory), the following steps may be followed (discussed in more detail below and shown in **Figure 1-4**):

1. gain top management commitment
2. appoint implementation team
3. promote awareness
4. perform gap analysis
5. develop an implementation plan
6. approve the implementation plan
7. implement the plan
8. operate and assess the system
9. continually improve the system
10. certification and registration

Gain Top Management Commitment

Top management must provide a commitment to develop, implement and maintain an effective QMS. Management is responsible for ensuring customer requirements are determined and met. Management also is responsible for creating the organization's quality policy and ensuring it is appropriate, effective, complete, communicated and maintained. In addition to the policy, management should set measurable quality objectives consistent with the policy. Management also should ensure adequate resources are available during planning to meet requirements and the company's objectives, including changes to the QMS. Top management should establish the responsibilities, authorities and relationships within the organization.

- Top management should appoint a management representative to manage the QMS, report on performance, promote QMS awareness within the organization and interact with regulatory bodies.
- Management should establish internal communication procedures, including those about QMS effectiveness and changes. It also should review the QMS at planned intervals (management review) to determine whether the QMS is effective and fit for its purpose.
- The management review has required inputs and outputs that must be documented (e.g., new regulatory requirements, resource needs and internal audits).

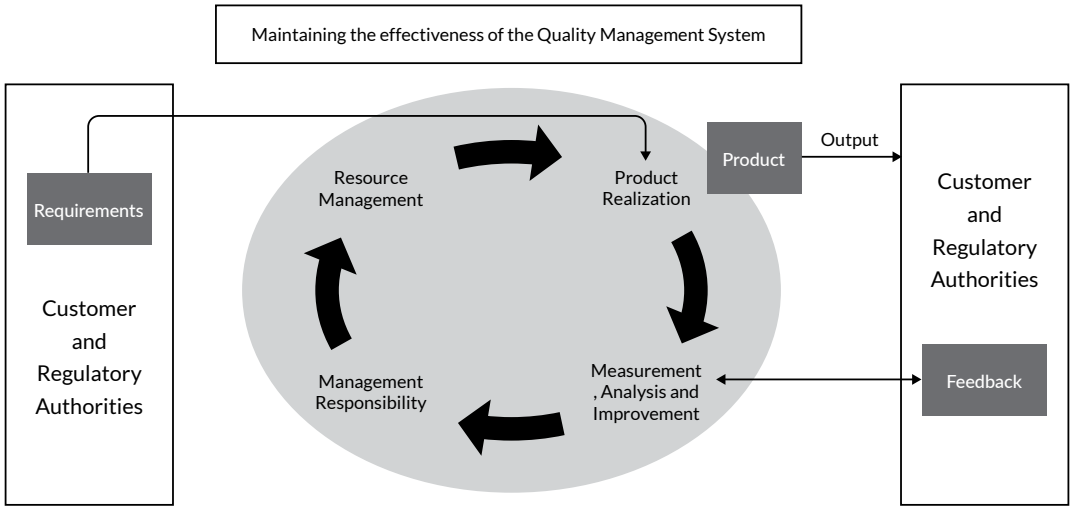
Before implementing the QMS, management must answer the following questions:
Why ISO 13485?

- What is the business need?
- What are the expected benefits?
- How much employee time is necessary?
- What is the operational impact?
- What is the estimated cost?
- Is certification to ISO 13485 required and/or desired?

At this stage, management is making a commitment to proceed with planning, and the plan itself is subject to approval or revisions before a final implementation process decision occurs. Management must commit resources to the implementation effort, which could include the following:
assigning a manager as a project lead
developing a high-level implementation plan
ensuring adequate project resources
approving ISO 13485 and related training requirements
classifying implementation as a high-priority project
communicating the decision and plan

To gain commitment and support, the organization's top management must understand the implications of their decisions and the need for continued personal involvement. One way to demonstrate commitment is to assign a key management member, perhaps the management representative, to lead the project. Management should be given an initial estimate of the people, time and costs

Figure 1-4. Implementing an ISO 13485:2016 QMS



(resources) expected for the project, and a more accurate estimate provided after the plan is developed (before final approval). Resources should be assigned to implement the QMS and maintain its effectiveness and ability to meet customer and regulatory requirements. Personnel performing work affecting product quality must be competent and have the relevant education, training, skills and experience for the jobs they are performing, and this information should be recorded and maintained. The infrastructure (e.g., IT systems, manufacturing equipment) needed to operate the QMS and ensure product conformity also must be determined. Environmental requirements (e.g., cleanliness and contamination controls) to achieve product conformity also must be outlined.

Appoint Implementation Team

Most organizations will require more than one person to fulfil the implementation initiative successfully. Implementation team members should be trained to ensure they understand the standard's requirements. The project lead typically will be the management representative (who is often the company's quality manager) and should have sufficient organizational influence. Duties may include:

- developing and managing the implementation plan
- ensuring all needed processes are established
- promoting awareness of customer and regulatory requirements
- monitoring QMS performance
- identifying any needs for improvement
- reporting on performance to top management
- communicating with external parties (e.g., suppliers, customers, regulatory bodies) about the QMS

Team members, particularly the project lead, should review and familiarize themselves with guidance documents from global standards organizations and regulatory agencies, including International Medical Device Regulators Forum (IMDRF), International Accreditation Forum (IAF), US Food and Drug Administration (FDA), EU *Medical Devices Directives* (MEDDEVs), guidance on ISO 13485 (ISO/TR 14969) and related standards, such as ISO 19011 (principles of auditing).

Promote Awareness

To promote awareness within the organization, the implementation team should inform employees of the intent to implement the standard, including its benefits, to staff, the organization and customers. Top management ensures communication throughout the organization by:

- announcing implementation plans
- describing benefits to the company
- explaining benefits to the employees
- developing a communications plan
- making progress visible
- conducting an ISO 13485 overview
- encouraging wide participation

It would be a mistake for the implementation team to proceed in near secrecy to avoid interfering with current business activities. Employees should be informed of the plan, why it is happening, how it will impact them, who is involved and scheduled key activities. If employees are kept in the dark about the project, they will be less supportive when their help is needed to implement required practices. Another mistake would be to announce the project and not communicate the status. Employees should be kept informed of progress and how they might be needed. Keeping the project visible, with plans for regular project updates, will ensure management support and encourage everyone to keep to the schedule. Ongoing personnel training is key to the success of any QMS.

Perform Gap Analysis

During this stage, the current system should be reviewed and compared with the standard's requirements, and any gaps should be identified. Gap analysis should be a cross-functional activity. Every organization will have a management system in place at some level. The current system should be understood before defining the new system. Existing quality systems may not be documented

and defined to the degree required by the standard. Processes, responsibilities and resources should be identified, and risks and opportunities considered. Every organization will have existing policies, procedures and processes already compatible with the standard's requirements. Others may require amendment, and some may be redundant. When reviewing the current system, the following should be addressed:

- define processes to meet objectives
- identify process owners
- establish process inputs and outputs
- identify resources to meet objectives
- define methods for process measures
- include processes to maintain effectiveness

Gap analysis outputs may include:

- an inventory of current documents and records
- current quality objectives
- current monitoring and measurement methods
- gaps in ISO 13485 requirements
- missing documents, records and practices
- implementation plan deliverables and activities

QMS implementation assists in providing controls to mitigate risks, which should be among the main drivers for introducing a QMS; as a result, risks and opportunities should be reviewed when performing the gap analysis (see ISO 14971 for guidance on risk management throughout product realization). It is good business practice to determine the day-to-day risks and decide what controls are required to reduce them to the financially appropriate extent.

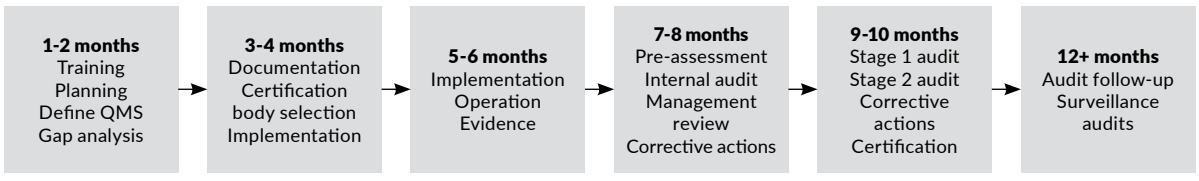
Develop an Implementation Plan

Once the gap analysis determines what has to be achieved, an implementation plan can be developed. In developing the plan, key activities, responsibilities, costs, schedules and resources should be estimated and refined. The following activities should be considered when developing the plan:

- establish system scope and objectives
- assign roles and responsibilities
- determine training needs
- identify development areas from gap analysis
- define and schedule activities
- develop system implementation project plan
- establish budget and approve plan
- review progress, update plan and communicate status
- manage project using practices in standard

The plan may change over time due to unforeseen events, so it should be designed for easy maintenance. At minimum, the plan should list key activities, estimated start and finish dates and responsibilities. Any assumptions and dependencies should be listed to confirm the plan's foundation. The responsibilities identify activity ownership. An overall plan owner must be established to manage the plan's day-to-day aspects. Top management will review and approve the plan. The plan owner will inform management of actual results compared to the plan. Another important consideration is the maintenance of the current system's integrity while planning and implementing the modified system (Clause 5.4.2 of ISO 13485). The following paragraphs and **Figure 1-5** demonstrate a sample schedule, which

Figure 1-5. Sample Schedule for QMS Implementation



can be shortened or lengthened depending on the organization's size, existing gaps and system status.

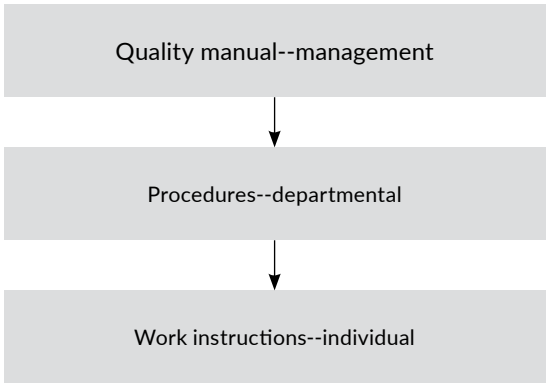
The first one to two months typically are spent organizing, training, planning and performing the gap analysis. The next few months are allocated to corrective actions for any nonconforming practices, preparing the necessary documents and selecting the certification body (certification body selection considerations may include costs, scope of activities, resources and timelines).

After five to six months, it is time to implement the system and make it operational. Records should be kept as evidence of conformity, and conformity must be documented in writing. The next few months are used for pre-assessment to take any corrective actions and undergo the certification audit. After the certification audit, the implementation team responds to any findings, and the QMS is certified and listed in public registries of certified systems. After being certified, the organization prepares for its first surveillance audit by the certification body. Internal audits are conducted to verify closure of identified issues and examine selected system parts defined in the company's internal audit program.

When developing the implementation plan, costs to be considered include certification body (onsite audits and offsite reviews), training (external and in-house), consulting and other internal resource costs. The budget should be agreed with top management.

When identifying resources, committed people should be selected for the implementation team. The workload should be shared across the organization to reduce the impact on other business activities and raise awareness. Management should support resourcing and understand team members' time demands to minimize any changes to the team at a later date that could cause delays and impact the project. Responsibilities and authorities should be clearly defined. The organization already may have job descriptions that define roles, responsibilities, education, experience, training and skill requirements; these may need to be developed, revised or created as part of the implementation process. All of the standard's elements should have a process owner within the organization (**Figure 1-6**).

Figure 1-6. QMS Documentation Defining Responsibilities



If a formal certification audit does not exist, special audits are conducted. These audits should only be used when necessary and should focus on specific elements of the manufacturer's QMS. Special audits may include audits conducted:

- in response to an application for the extension to the scope of an existing certification
- to determine whether the extension can be granted
- as short-notice audits conducted to investigate potentially significant complaints
- if specific information provides reasons to suspect serious non-conformities of the devices

Special audits should be conducted in accordance with the applicable requirements of ISO/IEC 17021-1:2015 Clause 9.6.4 as well as any additional requirements of the MDSAP-recognized auditing organization and/or the MDSAP participating regulatory authorities.[18,19]

Implementation Plan Approval

Top management will decide whether to proceed with the implementation plan or send it back to the project team for revisions. Before requesting approval, the plan should cover:

- assumptions and dependencies
- intermediate milestones

- start and completion dates
- activities and deliverables
- responsibilities and authorities
- resources and estimated costs
- tracking and reporting methods
- expected benefits and returns

The implementation plan should be clearly defined and formally agreed by top management. The plan may need revisions before finally gaining approval.

Plan Implementation

Implementation is where the work to meet the standard's requirements takes place. It is not unusual for the management system to be implemented in stages. The approved plan should be carried out, and training should be provided as needed. The implementation team should be given the resources and support needed to complete assigned activities successfully. Progress should be monitored frequently (not just at the points defined in the plan), and encouragement and assistance should be offered. Tracking data should be collected to report to top management. Some activities will be dependent on earlier activities. If delays are anticipated, the impact on later activities should be considered to minimize problems. Documentation is important at this stage, so policies can be created, procedures developed and records kept.

Training on ISO 13485 should be conducted early in the project to aid in planning. Managers and other employees should be included, as appropriate, to ensure staff are aware of the standard, the importance and relevance to their jobs and how the standard is applicable to the organization's products and services. Expertise should be developed to assist and guide implementation activities. The training budget should cover needed courses and travel, and records should be maintained as evidence. Further training will be needed as the QMS is implemented and procedures and policies are developed.

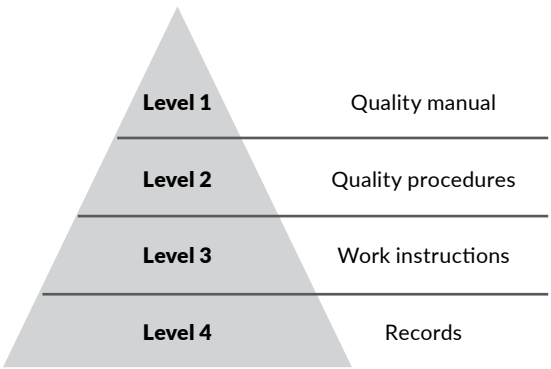
The QMS should be documented, including:

- quality policy and objectives
- quality manual and documented procedures
- necessary planning operation and control documents
- required records, including regulatory

Documents and records required by the QMS should be controlled and maintained. A typical QMS document hierarchy is shown in **Figure 1-7**. The quality manual describes the QMS in accordance with the company's policies and objectives. Procedures define interrelated processes and activities (who, what, why, when and where). Work instructions and other documents needed to plan, operate and control processes are the detailed work documents (how). Records are the evidence of results achieved and activities performed.

The draft quality policy should now be formalized to ensure it is communicated and understood within the organization and reviewed for continuing suitability. Objectives also should be formalized along with measures. The quality manual should include the QMS scope, details and justification for any exclusion or non-applications, documented procedures (or references to them), description of interaction between QMS processes and an outline of the QMS documentation structure. Each organization must choose the manual's format, which will depend on the organization's size, culture and complexity. A small organization may find it appropriate to include a description of the entire QMS within a single manual, including all the documented

Figure 1-7. Typical QMS Document Hierarchy



procedures required by the standard. Large, multi-national organizations may need several manuals at the global, national or regional levels, and a more complex hierarchy of documentation. When implementing the plan, the following should be considered in relation to the documentation:

- What is the value?
- What is required?
- What is needed to support the QMS?
- How extensive should it be?
- What is the format?
  - procedures
  - flow charts
  - work instructions
  - forms
  - electronic
  - hard copy

ISO 13485 has 50 references to required records, generated by executing a process and providing evidence of conformity. Examples of records are completed forms, audit reports, meeting minutes and test data.

The project team should report to top management on the project's overall status from the plan owner, and progress should be reported by process owners (so the project does not appear to only be a quality department initiative). The project tracking data can be used to share a high-level summary of completed activities, show progress, maintain interest and keep the project visible. Involving management ensures the project remains a priority and demonstrates management's ownership and commitment to the system.

During implementation, the certification body typically is contacted if certification is sought. Three to six months of records and metrics usually are required for the certification body to assess and certify the QMS. A few months of lead-time should be factored into the schedule before the certification process is initiated.

Operate and Assess the System

Once the system is operational, it should be assessed continually by monitoring and measurement, documentation, internal audits and management reviews to evaluate whether the QMS is working as intended and is achieving defined goals and objectives. Processes can be implemented as they become ready for release, as long as users are trained and ready to operate their parts of the system. Not all processes need to be implemented concurrently, only those with certain interdependencies. It is important to control documents and records as required by ISO 13485 and internal procedures. Records pre-dating QMS implementation will not be considered by auditors except to check record retention times. Typically, at least three months of evidence of the management system's operation will be required for the certification body to assess conformity before the initial audit.

It is important to determine what to measure, how to measure, who will be responsible and the frequency of measurements to be performed before the implementation project team can begin monitoring and measuring activities. Suitable monitoring methods should be applied. Where applicable, process measurements then can be used as evidence of the processes' ability to achieve planned results. Top management can use the implementation project team to begin its QMS reviews. The tracking meetings probably will not qualify as management reviews, as they may not meet all of the requirements of the relevant regulation clause (Clause 5.6), but they will be good practice in setting agendas, identifying issues, taking actions and recording minutes. Regular review meetings can be the precursor to management review meetings and system reviews. Meetings with core team members should be held frequently to review progress. The review meetings should be short and feedback schedules agreed with top management. Progress and achievements should be communicated to top management. Monitoring and measurements should be performed as soon as processes are in place, with processes reviewed and updated as needed during implementation.

Internal audits also are used to monitor and measure the system. The internal audit program should conform to planned arrangements (implemented and maintained effectively) and meet ISO 13485, organizational, customer and regulatory requirements. Ideally,

the majority of the QMS should be implemented before internal audits are initiated.

The word 'audit' may have negative connotations in some organizations because it often is associated with financial audits. However, audits (a team might be more receptive to the term "inspections") can have great benefits to an organization, its product, services and employees, and this ideally should have been communicated in the earlier promotion of implementation project awareness. Audits help an organization investigate any quality problems and verify solutions are implemented effectively. Management needs factual information to make informed decisions. Audits provide impartial, objective results for management action. Periodic audits keep the quality awareness level high and foster improved internal communication.

Internal audits are expected to examine all areas and shifts, some areas more often, based on previous results (a risk-based approach) and show audit scope (coverage) as part of the schedule. Internal audits should be conducted by properly qualified staff members who are independent from the areas being audited (i.e., not auditing their own work) and impartial. Many auditor training and certification programs are available and recommended for personnel responsible for this task. Programs provided by recognized quality standards organizations (e.g., the American Society for Quality's (ASQ) Certified Quality Auditor (CQA) proficiency qualification) should be considered. Other organizations also train and certify auditors to specific ISO regulations.

Internal audits must follow a documented auditing procedure (Clause 8.2.2). The organization must follow its documented corrective action procedure to resolve any findings in audit reports. A follow-up audit verifies actions taken and reports the results (see ISO 19011 for guidance).[20] Management reviews should be conducted to ensure continuing QMS suitability, adequacy and effectiveness. New or revised regulatory requirements should be included in the review. Opportunities for improvement to maintain QMS effectiveness and QMS changes, including policy and objectives, should be assessed in the management review. Such meetings can be used to review implementation process activities and make immediate improvements. Review outputs should include resource needs and product improvements related to customer requirements. Review records must be controlled and maintained. The reviews analyze several metrics, including audit results, customer feedback and process performance and product conformity.

Based on the system review, improvements or corrections may be proposed. This may result in taking appropriate corrective or preventive action, improving products or processes and determining resource needs or changes. These improvements should be implemented, communicated and fed back into the next planning stage. Improvements should follow a documented procedure for corrective action and the results recorded (Clause 8.5.2). In addition to initiating the corrective action process, quickly identifying any findings in one area potentially can help remaining areas avoid a similar problem (and reduce the number of reported nonconformities).

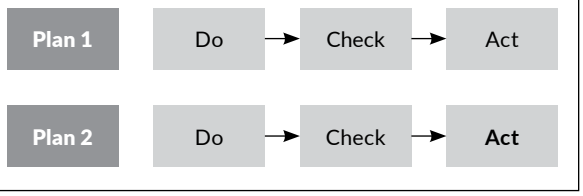
Continuous System Improvement

Organizations must recognize the management system will need continuous improvement to keep meeting quality expectations. ISO 13485 requires organizations to improve their quality management systems continuously; these are audited by the certification body as part of ISO 13485 certification. The system can be improved in a number of ways, including:

- QMS auditing
- monitoring processes, products and services
- collecting customer feedback
- monitoring customer complaints, nonconformances, other inputs to CAPA
- monitoring supplier performance
- reviewing required competencies
- reviewing training needs
- reviewing training effectiveness
- maintaining QMS effectiveness

The Plan-Do-Check-Act (PDCA) cycle is an iterative process that is refined continuously as the QMS

Figure 1-8. Iterative PDCA Cycle



evolves **(Figure 1-8)**.The regulatory professional's role in establishing and maintaining a QMS will depend on how the organization is structured. In some organizations, QMS compliance is under regulatory, but many manufacturers leave the responsibility with the quality function. Responsibilities should be organized to ensure there are no conflicts of interest. In some organizations, quality assurance reports to operations or manufacturing, with a separate regulatory function reporting elsewhere. Within ISO 13485, Clause 5.5 relates to independence, and Clause 8.2.4 discusses planned arrangements to ensure those releasing product are authorized to do so, but there is no reference to quality being a separate function. A close working relationship between the regulatory professional and the QMS group is always required to understand and "interpret" the QMS regulatory requirements.

Certification and Registration

The first step an organization seeking certification should consider is planning for the external audits, performing the pre-assessment and undergoing Stage 1 and 2 (initial) audits (the certification body audit process is described in further detail below). Formal certification is achieved only through external (third-party) assessment; certified bodies are accredited to conduct such QMS audits. Several factors can influence the choice of a certification body, such as cost, timelines and the scope of the certification body's activities. Qualified auditors will be assigned to evaluate the total QMS. They will provide a plan and a written report. Benefits and barriers to certification are listed in **Table 1-5**.

The Stage 1 audit usually is a one-day, on-site audit of the partial system: QMS documentation, management review and internal audits. It also is intended to determine readiness for the Stage 2 audit (typically one to two months later, but ideally no more than

Table 1-5. Benefits and Barriers to Certification

Benefits	Barriers
Expanded access to world markets	Difficulty identifying and creating new processes for the system
Ability to bid for contracts	Developing the necessary documented procedures and instructions
Use as a market differentiator	Lack of visible and demonstrated management commitment and support
Display of the certification mark	Personnel not following the prescribed procedures per their training
Independent audits by professionals	Resistance by some employees to change (e.g., providing process measurements)
	Conflicting interpretations within the organization and by the certification body

Table 1-6. Certification Body QMS Assessment Objectives, Scope and Criteria

Objectives	Scope	Criteria
Conformity of QMS with criteria	Physical locations	Normative QMS documents (e.g., ISO 13485)
Ability to meet applicable requirements	Organizational units	
Effectiveness to meet objectives	Activities	Defined processes and documentation in QMS
Areas for improvement	Processes	

six months). Internal audits are good practice for the external audits to ensure everyone onsite is ready, has a chance to explain their personal involvement, emphasize the business value of audits, give advice on interview behavior and arrange logistical audit support. The Stage 2 assessment is a multi-day, on-site audit of the full system scope to evaluate QMS implementation and effectiveness and to examine evidence of conformity to requirements. The certification body will audit links between requirements, policies, objectives, responsibilities, competence, procedures and performance.

The next steps for organizations seeking certification, following the Stage 1 and 2 audits, are to take corrective action if any nonconformities arise, receive the certificate and then maintain and improve the system. The corrective action plan submitted to the certification body should address root cause(s) of all nonconformities, and the organization must await approval of corrective action(s) from the certification body. The audit team only recommends certification (or not) but does not grant the certificate. The certificate is provided after the certification body's headquarters reviews the team's audit report and makes the final decision. After the final decision, it is time to notify customers, suppliers and other interested parties of successful certification. Some implementation team members may deserve special recognition for their efforts. The certification body guidelines should be followed on the use of the certification mark to publicize ISO 13485 certification.

Receiving the certificate is not the end of the quality process; it is an important and valuable milestone. The system must be maintained and improved continually. The company has embarked on an ongoing process of optimizing the business outcomes across the organization.

ISO 13485 Audits by a Certification Body

Just like the organizations they certify; certification bodies have their own management systems. These systems are assessed and accredited by the accreditation body in the country in which the body is based (e.g., UKAS and SCC), who are members of the International Accreditation Forum (www.iaf.nu). The general requirements for bodies certifying management systems are given in ISO/IEC 17021:2011 *Conformity Assessment—Requirements for Bodies Providing Audit and Certification of Management Systems*. This section focuses on ISO 17021 Clause 9, which applies to audit process requirements.

The standard states the audit program should include a two-stage initial audit, surveillance audits in the first and second years and a recertification audit in the third year prior to certificate expiration (**Figure 1-9**).

The three-year cycle begins with a certification or recertification decision. A plan must be established and documented for each audit identified in the program along with objectives, scope and criteria (**Table 1-6**).

The audit plan, which is communicated to the client in advance, includes at minimum the audit's objectives, scope and criteria as well as the audit's dates, duration and the audit team's roles and responsibilities. Audit team selection will be based on the auditor's competence to achieve the audit's objectives, certification requirements (e.g., the applicable medical device regulatory background), language requirements and impartiality. The audit team also may be supplemented by technical experts, translators and interpreters.

Figure 1-9. ISO 17021 QMS Certification Cycle

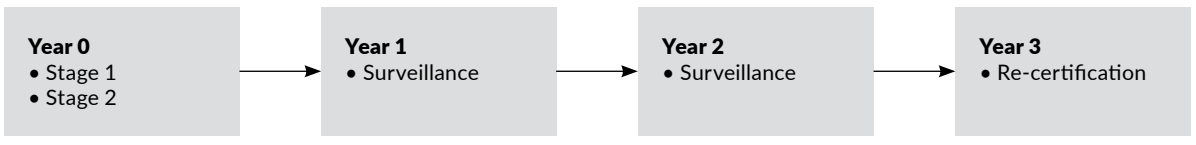


Table 1-7. Audit Duration for Medical Device ISO 13485 Audits Based on Staff Numbers

Effective Number of Personnel	Audit Duration Stage 1 + 2 (days)	Effective Number of Personnel	Audit Duration Stage 1 + 2 (days)
1–5	3	626–875	15
6–10	4	876–1,175	16
11–15	4.5	1,176–1,550	17
16–25	5	1,551–2,025	18
26–45	6	2,026–2,675	19
46–65	7	2,676–3,450	20
66–85	8	3,451–4,350	21
86–125	10	4,351–6,800	22
126–175	11	5,451–6,800	23
176–275	12	6,801–8,500	24
276–425	13	8,501–10,700	25
426–625	14	>10,700	Follow progression above

Source: IAF MD9:2011

Table 1-8. Factors That May Increase or Reduce Audit Durations

Increase	Decrease
Large range of devices	Reduced product range
Device complexity	Reduced design processes
Cannot demonstrate supplied processes' and parts' conformity	Reduced production processes
Poor regulatory compliance	

Source: IAF MD9

The audit's duration is based on the following guidance: IAF Mandatory Document for the Application of ISO/IEC 17021 in Medical Device Quality Management Systems (ISO 13485)—IAF MD 9:2011. This document suggests the number of audit days based on the organization's size (number of personnel) and provides a number of factors that may be used to increase or reduce the number of audit days (**Tables 1-7 and 1-8**). The duration includes offsite planning and reporting activities.

ISO/IEC 17021 allows sampling of multi-site organizations; however, IAF MD 9:2011 does not allow sampling of sites performing design and development and manufacturing. Once the auditors are onsite, the audit starts with a formal opening meeting, where the audit's objectives, criteria and scope are confirmed. Communication during the audit is through the audit team leader to the main site contact (typically the management representative). Observers can be present as part of the audit team, but their presence should be communicated and agreed prior to the audit. The manufacturer needs to provide guides for the audit team; the number should be based on the audit agenda and the number of auditors required to meet the audit plan objectives. The auditors will employ a number of methods to collect and verify information, including observing processes, interviews and reading documentation. The audit team will identify and record audit

findings during the course of the audit (typically by handwritten notes) and produce a formal report at the end of the audit or shortly thereafter.

Before the closing meeting, the auditors will require some time to prepare their conclusions, to determine whether the audit's objectives have been accomplished and whether to recommend certification (initial audit), continued certification (surveillance audit) or re-certification (re-assessment audit). During the meeting, an audit summary will be provided, including any findings (observations and nonconformities) and agreed actions. A corrective action plan will be required for any identified nonconformities to be corrected within the certification body's defined time period. The corrective action plan should contain a number of elements, including traceability to the original nonconformity, the correction and containment to address the nonconformity initially, the nonconformity root cause analysis and investigation, the corrective action to be implemented, preventive action (if applicable), responsibilities, timelines and how the corrective action's effectiveness will be verified.

Additional audits may be required outside the surveillance cycle (e.g., to close a major nonconformity, verify critical or significant suppliers or perform a scope extension for new products or processes). Once the audits have been performed and corrective action plans accepted, the certification body reviews the auditors' recommendation independently before making the final certification decision. The certification body also reviews the contract with its client to ensure that when the initial application is received by the certification body, the required assessments can be delivered in terms of resources and competence. The initial audit comprises Stage 1 and 2 audits, as described above. Stage 1 is an on-site documentation check to ensure the company has the basic and mandatory element in its QMS and to confirm readiness for Stage 2. The Stage 2 audit then will be performed (typically one to six months later to ensure there is adequate design and production documentation and the management review, CAPA and internal audit processes have generated auditable documented evidence). The Stage 2 audit covers applicable parts of the standard. The recertification audit again covers applicable parts of the standard, with the objective of recommending recertification (typically about three months before the end of the three-year certificate life). In surveillance audits, not all standard clauses typically will be audited, as the audit's duration will be shorter than the initial and recertification audits.

FDA has conducted unannounced inspections for a number of years. A relatively new development is notified bodies performing unannounced audits under the EU *Medical Devices Directive* (*MDD*) (always a provision in the *MDD* but a requirement under the new EU *Medical Devices Regulation*).[21,22] These are in addition to scheduled audits and focus on assessing ongoing production of CE-marked devices and linking devices in production to technical documentation and specifications. Taking this into consideration, companies need to have in place one or more Standard Operating Procedures (SOPs) defining their structures, considerations and roles in handling audits, whether anticipated or unannounced. These SOPs should include responsibilities for handling the audits, accessing and tracking documentation and communication within the organization regarding audit initiation and continuation.

Quality System Regulation (QSR), 21 CFR Part 820 (US FDA)

The QSR defines quality system requirements that must be fulfilled to place medical devices on the US market. This section does not detail the requirements but provides an overview of some key aspects to be considered when setting up a QMS to meet QSR requirements. Setting up a QMS that meets QSR requirements is the same as for an ISO 13485 QMS, but consideration must be given to ensuring QSR requirements are included.

The QSR was developed to ensure medical devices used in the US are safe and effective, which is the regulation's prime goal. The regulation has evolved over the years.

- In 1906, the *Pure Food & Drug Act* was enacted following poisoning related to drugs.[23]

- In 1911, adulterating foods or drugs was made illegal.
- In 1938, the *Federal Food, Drug, and Cosmetic Act* was enacted, making it illegal to sell unsafe drugs.[24]
- The law was amended in 1962 to include drug effectiveness, following the Thalidomide scandal in Europe.
- In 1963, the first drug Good Manufacturing Practices (GMPs) were adopted.[25]
- The *Medical Device Amendments* began in 1976 and were published in 1978.[26]
- The *Safe Medical Devices Act* was enacted in 1990.[27]
- In 1996, the *Quality System Regulation* was published, incorporating most ISO principles, becoming effective in June 1997. The design control requirements took effect in June 1998, replacing the 1978 GMP requirements and based on ISO 13485:1996. These changes focused on ensuring safe and effective drugs and medical devices to ensure they caused no harm.

The QSR requires all manufacturers to develop and follow procedures and fill in the details that are appropriate to a given device according to the current state-of-the-art manufacturing for that specific device.

While the QSR provides the framework for manufacturers, the manufacturer is responsible for determining how it will meet the requirements. This enables both large and small organizations to meet the requirements and covers the broad and diverse range of medical devices, technologies and manufacturing processes.

Among other factors, the QMS should be developed to accommodate the risk of devices of any complexity, taking into account relevant manufacturing processes and organizational complexity and size. The QSR outlines basic elements for inclusion. Additional details may be required as device complexity and potential risk increase.

Subsystems of a Quality System

As in ISO 13485, QSR requirements can be segmented around subsystems.

Management

An organization's management needs to demonstrate its understanding, support and leadership for implementing and maintaining a QMS that complies with QSR requirements. This should be demonstrated by a QSR assessment.

The organization's quality policy outlines its aims and how they are fulfilled regarding regulatory requirements as defined by management. It is important to include FDA quality system requirements as part of the policy.

The organizational structure has to be defined. The independence of those responsible for product quality (the quality unit) and product release to customers must be defined clearly; they must be autonomous from influence by those in the organization not responsible for product quality. Typically, product quality responsibility within an organization is a different reporting line from that of those responsible for product research and development, manufacturing, sales and/or marketing.

Management review is the opportunity for executive management to confirm the quality system remains effective. Clearly defined inputs, usually in the form of metrics for each subsystem, should assess how the system is functioning while ensuring the metrics demonstrate products remain safe and effective. It is important to follow through on any actions (e.g., via the CAPA system) resulting from the management review. The intervals at which management review occurs must be defined and scheduled on a regular basis. The review must take place annually, at a minimum; however, reviews typically are quarterly. Annual reviews are not sufficient to ensure quality system effectiveness.

The management representative's role is key within the organization. Executive management appoints the management representative and documents it in writing. The QSR defines the management representative's responsibilities in ensuring the QMS is established and maintained effectively and requires the representative to report on QMS performance to executive management. This is done primarily through regular management review meetings.

Quality audits are key elements of any QMS. They are the means by which an organization can assess QMS 'health' and look to areas needing changes. It is important to have an annual audit program covering all QSR aspects. The program is not static; changes may be implemented to address problem areas. An audit also may be classified as internal or external, depending on the interrelationships among participants. Internal audits are performed by employees of your organization. External audits are performed by an outside agent. Auditors must be independent of the areas they are auditing. Further, as noted above, auditors must be trained appropriately (e.g., ASQ CQA).

Internal (and external) audits can be difficult for small organizations where "independence" often is not defined clearly, especially for auditing QMS quality and regulatory aspects. Typically, small companies engage external consulting auditors to fulfill both internal and external audit functions. Any issues (nonconformities) identified by internal audits should result in corrective actions. There should be clear input from internal audit results to management review, and equally clear actions and justification for those tasks.

The QSR also includes personnel requirements. There should be sufficient resources for the organization's activities, and the personnel should be educated or trained appropriately for their roles. Organizations must have job descriptions for each position, which must be linked to individual training plans. The QSR has specific requirements for training personnel to recognize defects that could occur in relation to the product. This should be an element of personnel training, and the link between the potential defects and training to those issues should be documented. This includes personnel performing verification and validation activities.

Document and Record Control

When setting up a QMS to meet QSR requirements, once management has determined the system's scope, the document and record control support processes should be established.

This should include document review and approval authority and how documents are made available to all personnel who use them. Changes to documents also must be controlled and approved, at minimum, by the same function or personnel approving the original document. The procedure for record control needs to include how they are completed to become permanent records, their retention period in relation to the device's life, and how to prevent their destruction. The record control system must recognize the various types of records listed in the QSR.

CAPA

The CAPA system is an important QMS element that the organization must establish and maintain to meet 21 CFR 820 requirements. Organizations usually have one CAPA system for action with one procedure. Organizations can implement very complex systems, usually based on databases to manage CAPA, but for smaller organizations, a simpler approach may be possible. It is important the system inputs come from all parts of the quality system, not just those related to product, which often is the focus. The CAPA processes have defined wide-ranging inputs to cover all QMS parts. Nonconformity or other potential quality problem causes that are system inputs must be investigated and identified in a timely manner. CAPA processes to prevent recurrence must be planned. It is necessary to ensure any actions taken will not have an unanticipated impact on the finished medical device. CAPA should be linked clearly to management review. An overview of the issues that are inputs to CAPA, ensuring they have been implemented effectively, provides management a real indication of the health of the QMS for which it is responsible.

Nonconforming product needs to be identified and controlled to prevent its unintended use or delivery. The process controls and responsibilities for nonconforming product must be defined in a documented procedure. This should include nonconforming product identification, segregation and disposition. The product must be segregated in a timely manner to ensure it cannot be used, for

example, either by having the product under lock and key or using a stock control system to ensure no one can take the material and use it as a medical device or component thereof. If an organization reworks nonconforming material, the rework must demonstrate the medical device still meets the product's defined specifications. Elements that need to be included in the control process for nonconforming product should be defined. These should include how the product is identified and controlled, so it is not used inadvertently. Personnel responsible for deciding on the disposition of nonconforming product must be identified and documented. If the nonconformity is detected during finished medical device testing, the disposition decision probably would be made by more senior personnel, so the quality and regulatory impact can be considered by those with the widest knowledge of the organization.

A formally designated complaint unit should be responsible for the specific requirements relating to complaint files. All complaints have to be documented, including those received verbally by telephone or received by other members of the organization who normally would not receive complaints. There is a defined timescale for assessing all complaints to determine whether they are medical events under the requirements of 21 CFR Part 803 (Medical Device Reporting).[28] The period from receipt of a complaint to its review must be within the timescale. If a service report is a medical event, this would be included in the reporting system the manufacturer must have in place. In the system, the manufacturer has to ensure service report review to determine whether they are medical events. 21 CFR Part 806's requirements relating to corrections and removals also must be included in organization procedures.[29] In addition, the organization must ensure the procedure can be implemented at any time, even on a public holiday. Medical device tracking needs to be built into the quality system, and 21 CFR Part 821 states the manufacturer or importer is responsible for devices that fall under the regulation.[30] This will be covered in an FDA assessment. The organization must ensure it can locate the device in a timely manner, so the customer can be contacted in the event the device is subject to a correction or removal. There should be procedures in place for any statistical techniques used in the QMS, manifested in at least quarterly analysis of quality trending by the quality assurance function.

Design Control

Design and development include all aspects of bringing the medical device to the customer. This ranges from determining the design inputs and ensuring they are in line with the user and regulatory requirements through product availability and customer service. It also includes managing design changes. QSR requirements identify various ways to approach this:

- planning
- inputs
- outputs
- review
- verification
- validation
- transfer
- design changes
- design history file (DHF)

Design control procedures are required, including some specified in the QSR. Each device must have a DHF. This may include all the documents relating to the device's development and should include any change(s) made once the device has been placed on the market and throughout its lifecycle. There should be clear traceability, linking inputs to outputs that demonstrate the input has been achieved. This usually is managed using a trace matrix. These matrices often use databases to ensure clear linkage of the requirements, especially for a complex device. The DHF also will include evidence of the design reviews that took place during the device's development, and key decisions made. The design review must include an independent review by someone not involved in the device's development but with sufficient knowledge to assess the device's safety and effectiveness and ensure the design is appropriate for its intended use. This often occurs at two levels: assessing

the device development process and ensuring user and product requirements are met, and, at a management level, assessing the decisions made allowing the device to move from one design control phase to the next. The reviews should consider whether the device is on track to be safe and effective. Often linked to the reviews, the device risk analysis will be revisited to ensure risks remain as expected for the development stage, and no unresolvable new risks have been introduced.

Figure 1-10 demonstrates these linkages. The inputs are the user requirements, which also include regulatory requirements, with the device as part of the output.

Production and Process Control

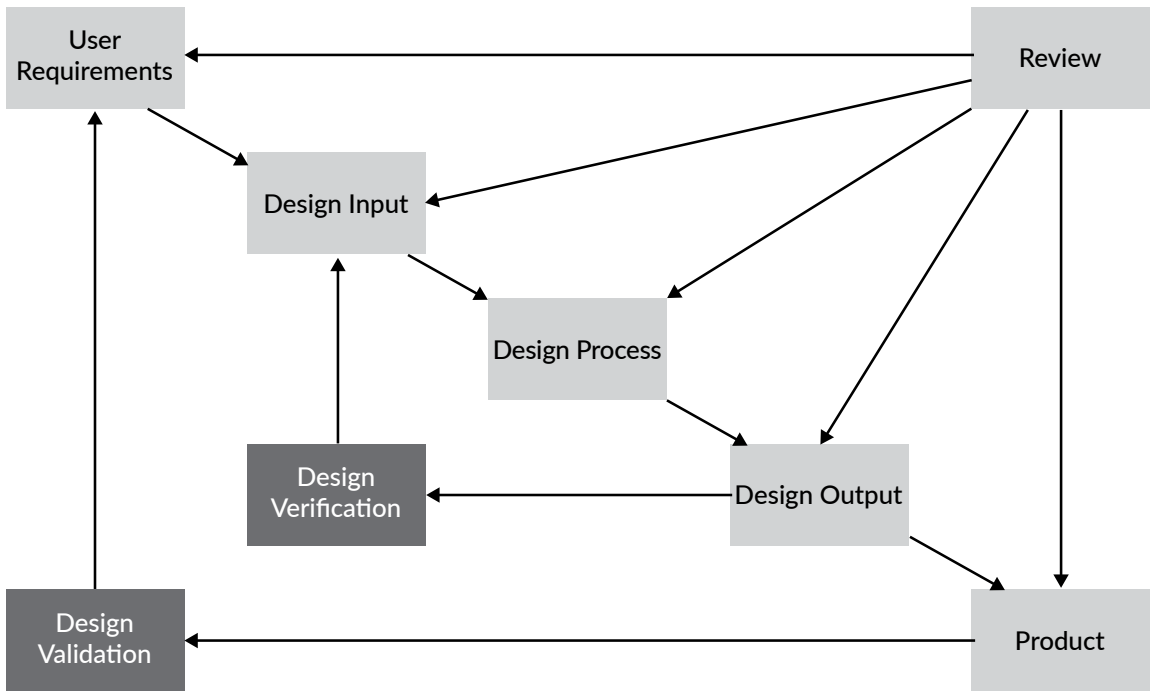
Production and process control, equipment and facility control, and material control cover how the device is manufactured or supplied in a controlled way and all the processes bringing the device to the customer. These include purchasing materials and services, production and manufacturing and device delivery, the facility and calibration and maintenance of equipment used in these processes.

Purchasing

Requirements for purchasing materials or services include identifying, evaluating and managing suppliers.

Supplier management is part of the purchasing process and includes selecting, evaluating, and monitoring (re-evaluating) suppliers. The amount of control required for suppliers depends on the risk and nature of the product or service being supplied, e.g., control over the supply of a catalogue item like a simple chemical will be very different from a critical medical device component. New products or services or a product or service change would need to be considered during the design and development process or change

Figure 1-10. Design Process



control process. The Global Harmonization Task Force (GHTF) guidance, GHTF/SG3/N17:2008 *Quality Management Systems—Medical Devices—Guidance on the Control of Products and Services Obtained from Suppliers*, describes the process of establishing controls for products and services obtained from suppliers and includes a process flow detailing more information related to the six phases of working with suppliers throughout a medical device's lifecycle.[31]

Traceability and Identification

Traceability and identification are linked: identifying the materials and equipment used to provide a product or service makes traceability possible. Identification comprises the product lot number or material status. The QSR documents procedures for identification throughout product realization, from the organization's receipt of materials through finished device delivery and customer use. The QSR requires an organization to have a documented traceability procedure. Often, organizations have a combined traceability and identification procedure. Where traceability is required, the organization must have a record of the item's identification. The traceability record will need to be maintained for the device's lifetime, and normally the organization's manufacturing system maintains batch records that provide lot identification as required in the DHR.

FDA now requires finished, high-risk medical devices to have unique identification numbers (UDIs).

The facility must be appropriate to maintain the device's quality. When a manufacturing facility is being established, considerations should include:

- how the facility is constructed
- how the equipment is installed
- proper equipment maintenance
- facility cleanliness
- how the product will flow through the facility to ensure segregation
- facility, utilities, equipment and cleaning qualification
- work environment influences on product quality—how the work environment is established, the process equipment used and the personnel working within that environment, relating the work environment to the product, the impact the environment can have on the product and the impact of the health of the employees on the medical device
- equipment and facility calibration and maintenance

Process validation[32] means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications:

- Where the results of a process cannot be fully verified by subsequent inspection and testing, the process shall be validated with a high degree of assurance and approved according to established procedures. The validation activities and results, including the date and signature of the individual(s) approving the validation and, where appropriate, the major equipment validated, shall be documented.
- Each manufacturer shall establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met.[33]

Verification confirms by examination and objective evidence the specified requirements have been fulfilled. Process validation demonstrates processes' ability to meet the planned results. A validation protocol or plan has to be established and must be approved before starting validation. This protocol or plan must include defined criteria the process must meet for successful validation, including:

- approval of equipment and personnel qualification
- use of specific methods and procedures
- records requirements
- revalidation

A validation master plan is useful in defining the validation approach for a site or product range as well as individual processes. For complex or large systems, a plan can be used to define what processes require validation and what validations will be performed

(installation qualification (IQ), operational qualification (OQ), process qualification (PQ) or software). A validation master plan often will include details of the organization's approach to validation, setting out the types of facilities and equipment and the approach to process and test method validation. The validation master plan will define how a process is to be validated or verified, and spreadsheets can be used to prioritize the processes and/or equipment requiring revalidation or requalification.

Acceptance activities include incoming, in-process, and final activities and acceptance status. A system is required to accept purchased materials and services and define the type of inspection, testing or checking used to ensure they meet the organization's needs. Labeling must be inspected by designated individuals before release to storage. The component manufacturing process must ensure the requirements are met. Usually, there also are defined requirements for final acceptance activities. Throughout all these stages, the materials' or device's status must be clear to ensure only devices meeting requirements are supplied to customers. During handling, storage, distribution, and installation, traceability and identification processes must be maintained, and the product must be stored and handled so its quality, e.g., temperature and sterility, is not affected. All processes, from research to dispatch and label storage, must be designed to prevent mix-ups.

The QSR includes specific requirements for labeling and packaging control. Processes must be in place to ensure labeling integrity (labels and package inserts) is maintained and all labeling can be accounted for fully. Examples of the labels used for each batch must be kept in the DHR. Device packaging must be appropriate to maintain the device's quality during processing and distribution.

QSR vs. ISO 13485

QSR and ISO 13485 requirements are fundamentally the same, so a QMS can fulfill the requirements of both FDA and ISO 13485. ISO 13485 supports implementing QMS systems fulfilling regulatory requirements in many countries, and the QSR establishes US regulatory requirements. The differences include areas where FDA includes prescriptive requirements for records, documents and labeling. The QSR is a mandatory regulatory framework in the US ensuring a medical device is safe and effective. This differs from ISO 13485, which is a voluntary standard supporting regulatory requirements in a number of regions, including the EU and Canada.

Differences between the QSR and ISO 13485 include:

- definitions of corrective and preventive action
- defined complaint file requirements
- requirements for specific types of records, including device master record, device history record, quality system record
- requirement for an approved supplier list
- training to handle potential product defects
- enhanced requirements for controlling nonconforming product to prevent inadvertent use
- design transfer requirements
- risk management is mentioned only in the QSR preamble; risk management is expected to be used as it is in an ISO 13485 QMS
- purchasing controls specify consultants as well as other suppliers

FDA does not have access to internal audit reports and management review records, although it can access any CAPA actions resulting from internal audits and management reviews. Manufacturers must show evidence internal audits and management reviews have taken place by providing the internal audit schedule and a statement saying the audits have been completed; for management review, evidence can be in the form of a management review schedule, a list of attendees and the agendas showing the items discussed. Notified bodies for CE marking have access to internal audits and management review minutes, which differs from FDA practice. With the proposed changes to ISO 13485 published in 2015, the two QMS system requirements are expected to be more aligned than those in the current published standard.

Vendor Quality Systems

Management of suppliers and their materials or services can affect product quality and services the organization provides to its customers. Without good supplier management of appropriate materials or services, an organization will not be able to deliver its products or services. Supplier management and purchasing controls are emerging topics of interest, and inadequate supplies can result in unintended consequences, some very serious. The manufacturer has the ultimate responsibility and cannot delegate it. Supplier management is of increasing importance, and a systems approach to supplier quality can help reduce unintended consequences. Manufacturers should remember suppliers are an extension of the company's business. Within the medical device industry, subcontractors frequently supply critical components or complete products. In recent years, issues have resulted that point to the need for greater control over subcontractors; counterfeit electronic components and contaminated heparin have been high-profile examples of supplier issues impacting medical device safety. Regulatory expectations for purchasing controls and acceptance have increased due to these issues. GHTF published *GHTF/SG3/N17:2008 Quality Management Systems—Medical Devices—Guidance on the Control of Products and Services Obtained from Suppliers*, which provides a good basis for any supplier and material or service purchasing control system.

How to Audit Suppliers

The manufacturer should assess potential suppliers' ability to meet selection criteria, which could include various methods, such as a questionnaire or an audit. It is not possible for any organization to audit all its suppliers, so this is where risk management should be applied, where the evaluation's depth and the methods used are related directly to the product or service's risk.

How the Process Differs from Internal and Third-Party Audits

An audit is a systematic, independent and documented process for obtaining evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled. This definition is taken from ISO 19011: 2011 Clause 3.1. ISO's *Guidelines for Auditing Quality Management Systems* is a helpful framework for an organization setting up an internal audit program or conducting supplier audits. It also includes information on third-party audits when an organization is audited by a certification body.[34]

Strategic Considerations and Customizing a QMS

All companies differ in size, maturity, culture, products and many other factors. Important QMS considerations for any organization include the following:

- Engage in discussions with the certification body as early as possible to ensure the certification body has the right competency and resources to deliver audits and reviews, and there are no significant issues with QMS plans.
- Ensure the QMS, regulatory projects and design and development activities are resourced adequately and have top management's commitment.
- Personnel involved in the QMS should have relevant, documented background and training. Any gaps can be addressed in training plans.
- The QMS should be the responsibility of not only the quality department but also should have the involvement, understanding and commitment of staff from virtually every part of the business, who have been appropriately trained on the QMS: quality, regulatory, research and development, engineering, production, sales, marketing, HR, top management and administration.
- There are many documentation and record requirements due to medical devices' high-risk nature. Record retention based on device lifetime also is an important consideration.
- What are the environment and infrastructure considerations to ensure product conforms to requirements and how are these documented?
- Exclusions or non-applications should be documented in the quality manual. Just because a

process is outsourced does not mean it can be excluded or not applied in the QMS; it may need to be covered in supplier agreements and audits.

- The company's assignment of responsibilities should be clearly documented, e.g., through an organizational chart and job descriptions.
- The internal audit program should allow all processes to be covered in a reasonable time period. This can be adapted based on the organization's size and particular processes' risk and importance in the QMS.
- Management review frequency and format, like the internal audit program, will depend on the organization's size and maturity. A monthly meeting onsite may be appropriate for a small organization; for a larger organization, each site may dial into a meeting chaired by the corporate site.
- A reasonable amount of objective documented evidence must be in place before the initial audit. Ideally, a batch or lot of medical devices will have undergone the entire production process and be documented (this can be prototype product).
- Common mistakes and areas of nonconformities under ISO 13485:2016 include:
  - not fulfilling the internal audit schedule or setting an unrealistic internal audit plan (8.2.4); the schedule can be adjusted over time if this is documented with a reasonable rationale
  - not following up on CAPAs in timely manner (8.5); extending CAPAs for various reasons may be acceptable, but repeatedly missing CAPA deadlines indicates the CAPA process is not effective, and the process may need to be amended and addressed
  - not following up on previous audit nonconformities (8.3); again, this indicates an ineffective CAPA process, and the certification body likely will upgrade the nonconformance to a major nonconformance, requiring immediate attention
  - not reporting adverse events (8.3) is an often-cited major nonconformance due to the manufacturer's failure to fulfill its regulatory obligations
  - document/record retention time not based on device lifetime (4.2) when clinical data indicate device lifetime is longer than that defined
  - incomplete training records (6.2); no personnel training records verifying individuals are trained and competent for their defined roles and responsibilities
  - training effectiveness not verified (6.2) or documented
  - CAPA or internal audit findings not verified (8.2, 8.5) or documented
  - change process does not contain provisions for informing regulatory authorities or notified body of significant changes (7.5)
  - changes implemented but not verified and validated (7.5)
  - no documented environmental control or condition requirements (6.4)
  - product regulatory requirements not considered (7.2), including product-specific standards and requirements
  - inadequately defined team roles and responsibilities (7.3)
  - no design and development plan (7.3)
  - undocumented or poorly defined design inputs and outputs (7.3)
  - product placed on market or progressed to design transfer stage before verification and validation completed (7.3)
  - process risks not considered in addition to design and clinical risks (7.1)
  - no evidence of new or revised regulatory requirements considered in management review (5.6)
  - inadequate supplier control in terms of audits, contracts, monitoring and evaluation (7.4)
  - limited or no process and product monitoring (8.2)
  - instruments calibrated, but with reference materials not calibrated themselves (7.6)
  - inadequate segregation or marking of nonconforming product (8.3)
  - quality manual does not list and justify non-applicable or excluded clauses (4.2)

- quality objectives not measurable or inconsistent with quality policy (5.4)
- document changes and approvals or reviews not clear in revised documents (4.2)
- internal auditors not independent from areas being audited (8.2)
- customer property requirements not fulfilled even though the organization retains customer property, such as intellectual property, patient records, designs and drawings onsite (7.5)

Conclusion

Overall, setting up a robust quality management system requires following compliant processes per ISO standards/regulations, adhering to continuous improvement principles, engaging appropriate stakeholders and oversight from senior management. Organizations that plan and execute strategies per the approach described above have been successful in implementing a QMS.

Note: This chapter is from Harde A. Setting up a Quality Management System. In Takes PA and Nozawa S, eds. Global Medical Device Regulatory Strategy, 2nd ed. Rockville, MD: Regulatory Affairs Professionals Society; 2020:59-92.

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