Chapter 15

ISO 13485:2016: Medical Devices—Quality Management Systems—Requirements for Regulatory Purposes

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This chapter describes the origin, implementation and use of the quality management system requirements in medical device globally based on a commonly used standard ISO 13485.

15.1 Introduction

A standard is, in essence, an agreed repeatable way of doing something. It is a document, published after collective work from one or more committees, which contains a technical specification or other precise criteria designed to be used consistently as a rule, guideline, or definition. Standards help to make life simpler and to increase the reliability and the effectiveness of many goods and services we use. Standards are created by bringing together the experience and expertise of all interested parties such as the producers, sellers, buyers, users and regulators of a particular material, product, process or service.

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Standards are designed for voluntary use and do not impose any regulations. However, laws and regulations may refer to certain standards and make compliance with them compulsory.

15.2 Background and Origins of ISO 13485:2016

ISO 13485:2016 is a Quality Management System (QMS) for medical devices specifically for regulatory purposes and, whilst based upon the foundation of ISO 9001:2000 (quality management system standard), is a standalone standard.

ISO 13485:2016 is published by various organizations and when it is published by those organizations this is recognized by letters being placed before the ISO 13485:2016. For example, in the Netherlands it is published by Nederlands Normalisatie Instituut (NEN) and this is denoted by the Standard being NEN ISO 13485:2016 and as it is also a European Norm it is published as NEN EN ISO 13485:2016.

Some of the changes that had been introduced with the publication of ISO 9001:2000, including the reduction in the number of required documented procedures and the inclusion of concepts such as customer satisfaction and continual improvement were not in alignment with the regulatory requirements for medical devices.

The standard ISO 13485:2016 Medical devices—Quality Management systems–requirements for regulatory purposes has grown to be the certification standard of choice for medical device manufacturers. All the requirements are specific to organizations that are providing medical devices or services to the medical device industry and this does not depend on the size or type of the organization. To facilitate comparison to the underlying ISO 9001 standard, a comparison table has been provided in one of the annexes of the standard, including some explanatory notes.

The ISO 13485:2016 standard is built on the historic structure for the quality management standards, and did not follow the general restructuring of most quality management system standards. The key objectives in the latest update focused around getting the requirements closer to the state of art expectations in the global regulatory environment. Many elements

from the US Quality System Regulations (QSR) that did not make it into the previous version of the standard have now made it in. Also, key concepts from the global audit model MDSAP (the IMDRF Medical Device Single Audit Program) have been integrated, as well as the changes in the new EU Medical Device Regulations (EU-MDR).

These additional and new elements compared to the previous version of the standard (ISO 13485:2003) include the following:

- Increased focus on compliance with regulatory requirements
- Process controls based on risk management
- Increased requirements for design and development, including considerations of usability, use of standards, verification and validation, design and development transfer and design records
- Increased controls for outsourced processes and suppliers
- Increased requirements for process validation
- Increased requirements for 'feedback', including complaint handling
- Introduction of statistical techniques for data analysis

The main difference between ISO 13485:2003 and ISO 9001:2015 besides its structure is related to customer satisfaction and continuous improvement, elements that are not included in ISO 13485. In ISO 13485 these items are replaced by processes for ensuring continuing effectiveness of the quality system to meet customer and regulatory requirements. Second, it promotes active systems for customer feedback related to if the organizations need to meet customer and regulatory requirements

In addition, the requirements of ISO 13485:2016 include many more requirements for documented procedures, documented requirements and records, supporting its use in meeting regulatory requirements.

A last diverging element is the focus in ISO 9001 on the company risk assessment and strategy, whereas ISO 13485 remains focused on the risks and safety of the medical devices a company produces.

15.3 Quality Management Systems

Quality Management Systems consist of common elements that are expressed as the organizational structure, processes, procedures, work instructions and resources needed to implement quality management (Fig 15.1).

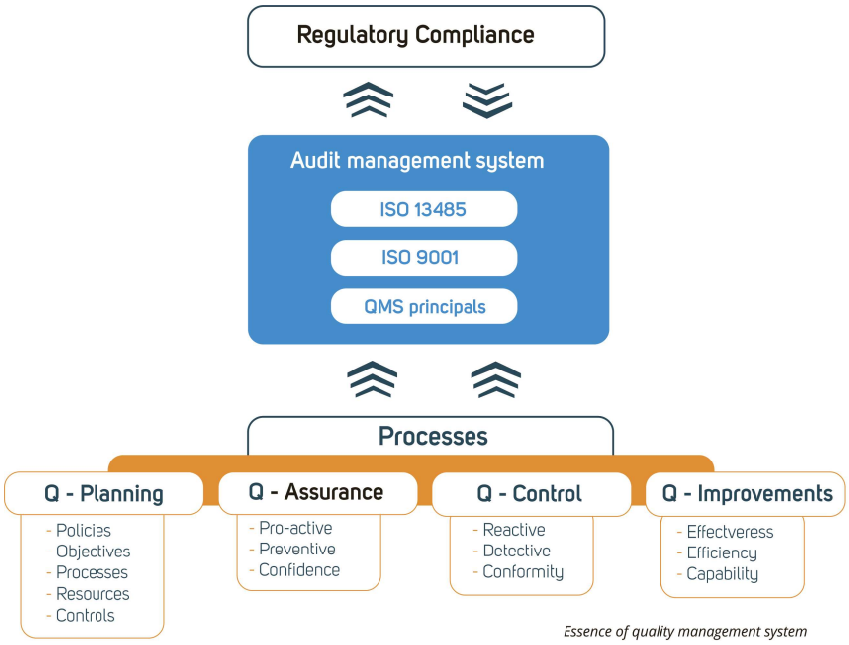

Figure 15.1 Quality management system essence.

Shared elements of organizational structure, authorities and responsibilities, methods and processes, data management, resources, training, maintenance, customer satisfaction/requirements, product quality and continuous improvement are based on the principles of quality management:

(i) Customer and regulatory focus: By understanding current and future customer needs, organizations can meet their requirements whilst ensuring that all known applicable regulations are applied.

(ii) Leadership on purpose and direction: Leaders, by establishing unity of purpose and direction of the organization,

should create and maintain the internal environment in which people can become fully involved in achieving the organizations objectives.

(iii) **Involvement of people at all levels**: People are the essence of an organization and their full involvement enables best performance in the organization.

(iv) **Process approach to resources and activities**: This principle commonly this leads to the PDCA approach of Plan–Do–Check–Act.

(v) **Systems approach to management**: Core in the system's smooth running is identifying, understanding and managing inter-related processes of a system as it contributes to the organizations effectiveness and efficiency in achieving its objectives and reducing overall process risks.

(vi) **Factual approach to decision making**: Decisions based on analysis of data and information are typically more effective. Monitoring and measuring will allow an organization to understand its ability to supply a safe and effective product and service.

(vii) **Mutually beneficial supplier relationships**: An organization is responsible for ensuring control of its outsourced processes, and with increasing regulatory pressure, supply chain management truly becomes one of the keys to success.

(viii) **Improvement as an ongoing objective**: Long withheld in medical device industry, legislation is now changing to stimulate product improvement in a continuous effort.

15.4 ISO 9000 and ISO 13485 Quality Management System Family of Standards

ISO 13485:2016 is commonly seen as part of the 9000 series of standards, despite it being a standalone standard. That means that effective implementation can best be achieved by combining the requirement of ISO 13485 with content, views and guidance of a series of adjacent standards, representing further detail and in some cases national variations:

(i) ISO 9000:2005 describes the fundamentals & vocabulary.

(ii) ISO 9001:2015 provides the basic QMS requirements.
(iii) ISO 9004:2018 provides guidelines for performance improvement beyond general QMS requirements.
(iv) ISO 19011:2018 provides guidelines for quality and/or environmental management systems auditing, including internal audits.
(v) ISO/TR14969:2004 provides guidelines for application of ISO 13485:2003, the older version of the medical device QMS standard; but still contains some useful concepts.

In addition, there is a standard used to supervise third party assessment bodies that audit against, e.g. ISO 13485:2003:

(i) ISO/IEC 17021-1:2015 provides requirements for bodies providing audit and certification of management systems.

15.5 Global Regulatory Footprint of ISO 13485:2016

With the increasing use of ISO 13485 by regulatory authorities worldwide the use of the standard by manufacturers and other organizations is increasing. ISO 13485:2016 supports the regulatory compliance in several countries including the European Union for CE marking, Australia, Canada and Taiwan. Japanese Ministerial Ordinance (MO) No. 169 is similar to ISO 13485:2003. In Europe, it is a harmonized standard for the three medical devices directives and for the new EU MDR and EU IVDR regulations, which means that adhering to it for the quality management systems aspects identified in these directives there is a presumption of conformity, details of which are specified in the so-called annexes Z found at the back of the European versions of the standards. Current annexes are still for directives; annexes for regulations are being drafted.

For the USA ISO 13485:2016 is optional and may typically be the basis for the QMS that is used by many manufacturers, but it is not a distinct requirement. It can also be used for low risk devices manufacturers that are exempt from QSR's 21 CFR 820. The US FDA has been cooperating closely with the development of ISO 13485:2016, in the attempt to further align ISO 13485

and US QSR (Quality System Regulations) requirements. Some of the concepts from ISO 134854:2016 form also the basis of the IMDRF MDSAP program on Medical Device Single Audits.

With the growing interest in regulatory regimes in Asia and other parts of the world, many more regulatory requirements are added to the equation. ISO 13485:2016 certification is a great tool to harmonize the various QMS requirements from all these existing and developing legislations, as it is very easy for national regulators to add some country specific requirements to the general framework provided in the global standard.

15.6 Implementing an ISO 13485:2016 Quality Management System

There are various reasons why an organization implements a certified ISO 13485 quality management system and this primarily includes meeting regulatory requirements when registering medical devices worldwide. In addition, it might help improve customer confidence and increase the organization's competitive edge. As such it makes good business sense and forms an excellent basis for an efficient and effective business to be certified against ISO 13485.

A well-implemented ISO 13485-based QMS supports regulatory compliance and improves customer confidence. It improves the consistency and stability of the processes used by the organization. It can reduce waste and defects, improve employee motivation and participation and is a basis for monitoring, managing or potentially improving the performance of suppliers.

15.7 Process Approach

A process is a set of interrelated or interacting activities that uses resources to transform inputs into outputs. The process approach systematically identifies and manages the linkage, combination, and interaction of a system of processes within an organization, as depicted in Fig. 15.2 linking the various parts of ISO 13485 in a generic process flow. The QMS documentation will reflect the actual process flows of the particular organization.

The process approach considers the importance in understanding and meeting requirements by looking at processes in terms of the value that they can add, in measuring the performance of processes, determining if that process is effective and using the objective measurement of processes to improve that process.

The process model of Plan–Do–Check–Act (PDCA cycle) is used in the ISO 13485 standard to link the clauses of the standard. It is used to show how the requirements of customers and regulatory authorities can be met (Fig 15.3).

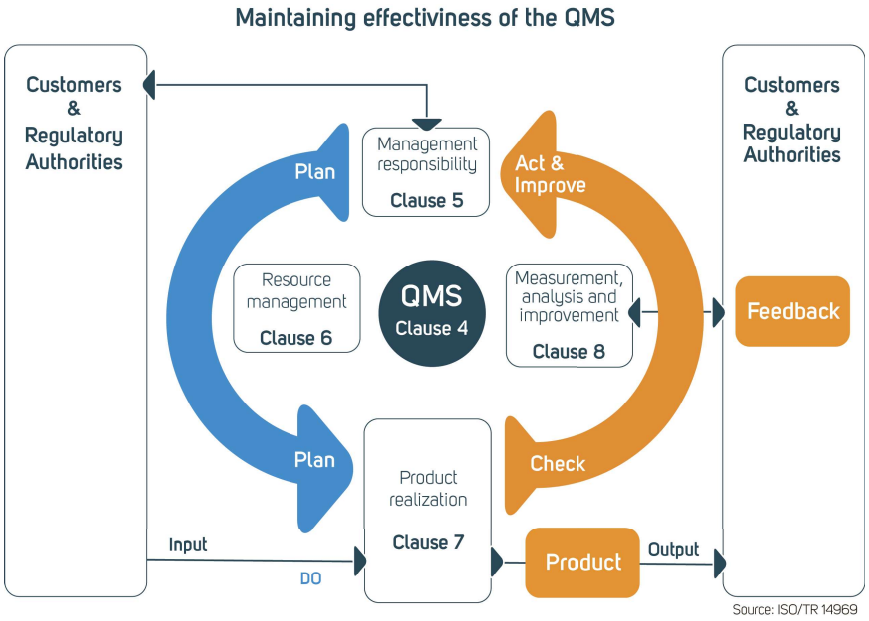

Figure 15.2 Process interactions.

15.8 Planning the Implementation

The implementation process begins with the assumption that the decision to implement has already been taken. Best practice traces back the origin of the decision to implement and the underlying causes or views, such as supply chain requirement, regulatory requirement, or desire to improve performance, reduce waste, etc.

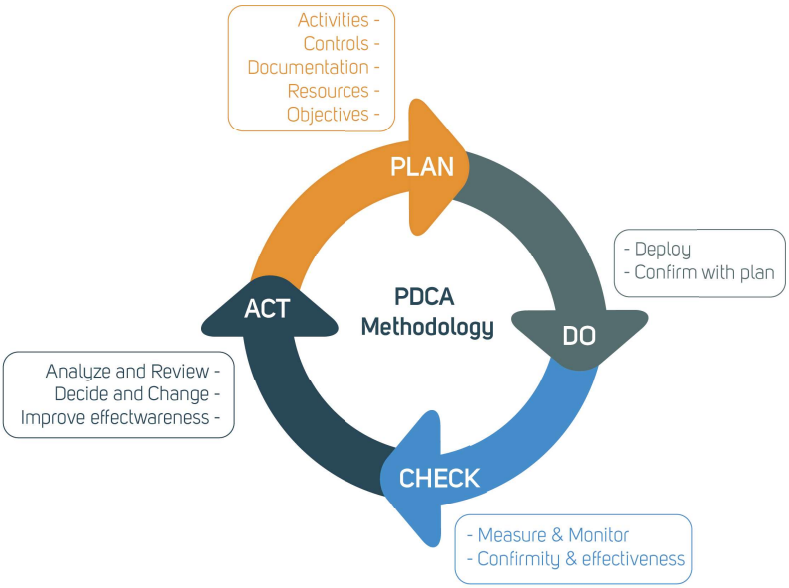

Figure 15.3 NPDCA for your processes.

Some initial general steps for a successful implementation effort would include knowing how to interpret the ISO 13485:2016 requirements for your system, ensuring team members are knowledgeable on the current system, arranging management commitment, and developing a comprehensive project plan which includes monitoring steps. Where needed training should be provided to staff to enhance their knowledge and to boost their commitment which is crucial to the successful implementation and continuing compliance to the requirements of the standard.

Key elements would include promoting awareness, performing a critical gap analysis, and following effective implementation of course getting ready for continually improving the system, where regulatory requirements allow.

The ultimate assessment and verification of the first implementation is in a round of internal audits followed by a management review concluding the effectiveness of the QMS.

With 2016 as basis, it might be considered to claim also continued compliance to ISO 13485:2003 version for those countries where that version (and EN ISO 13485:2012 for Europe) is still used by the legislators as semi-legislative requirement.

15.9 Scope, Exclusions and Non-Applicability

ISO 13485 can be applied to any organization who wishes to demonstrate the ability to provide medical devices and/or related services that meet customer and regulatory requirements ISO 13485. ISO 13485 can be applied irrespective of type or size. Providing it is permitted in the regulatory requirements that apply to the organization that is implementing ISO 13485 exclusions are permitted. Organizations can exclude design and development controls, Clause 7.3 but the justification for the exclusions must be clearly documented in the organizations quality system and must be an appropriate exclusion for any regulatory system being followed. Other clauses can be excluded if they are not applicable, e.g. sterilization if the manufacturer does not produce sterile medical devices.

In the 2016 version, the scope is expanded to include broader supporting stakeholders such as consultancy firms, authorized representatives, etc.

15.10 Document Control

To be efficient and effective an organization must manage how to ensure that those working within that organization carry out process in a consistent way. This includes both large and small organizations. In large organizations, this means that tasks are completed in the same systematic way. Large organizations or those with complicated processes will benefit significantly with the adoption and implementation of an appropriate quality management system.

Section 4.2 of ISO 13485 describes the requirements for documents and records that are used to support the quality management system, which very often is divided into four tiers with their own types of documentation (Fig. 15.4).

15.11 Record Completion and Control

Quality records are an important part of any quality management system and especially in ISO 13485 as they are the evidence that

activities that are required as part of the quality management system have been completed. Requirements for records are referenced in at least 50 places within the standard but many organizations will have the need for records for other aspects of the Quality Management system due to the nature of the business. To meet regulatory compliance demands, the number of records needed is continuously increasing.

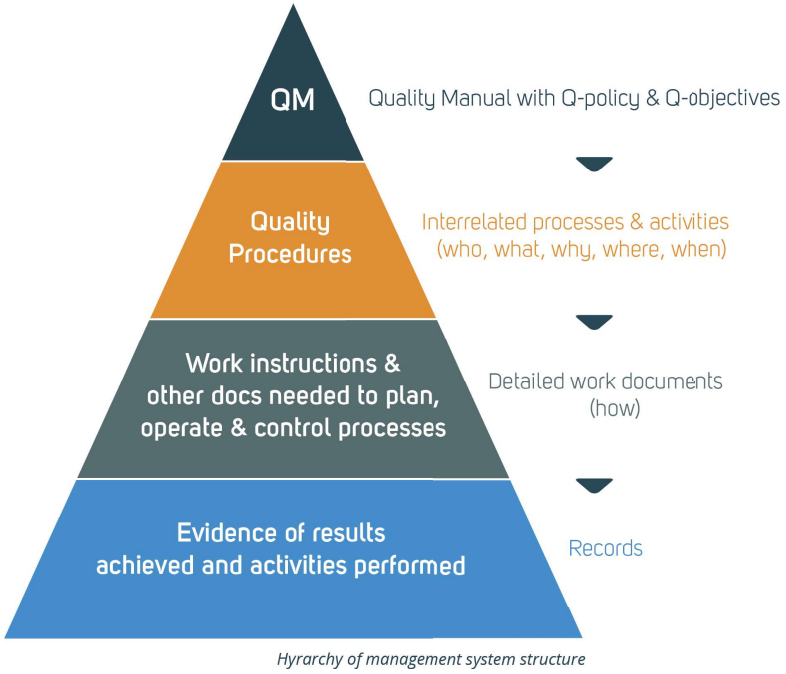

Figure 15.4 Typical four-tier quality management system setup.

15.12 Management Responsibility

The emphasis in Clause 5 is on the role top management has within the quality management system in ensuring that the system is maintained and remains effective, and that customer and regulatory requirements are met by the organization.

Top management has to ensure that the organizations quality policy is defined and that this is linked to the quality objectives in